

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 41, December 2015

An IPBF update 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:

- Patient Organization News: anniversaries
- Global Pain Management Survey
- Meeting Reviews:
 - ESSIC Annual Meeting 2015
 - ICS Annual Scientific Meeting 2015
 - Grünenthal European Pain Day
- Calendar of Upcoming Events
- Publications
- New Professional Society: Society for Pelvic Research
- UN World Toilet Day reveals lack of sanitary facilities worldwide and risks to women and girls
- Research Highlights, including TAU IC/BPS Supplements Parts I and II
- Donations & Sponsoring

**SEASON'S GREETINGS AND BEST WISHES FOR A
HAPPY, HEALTHY, PEACEFUL AND SUCCESSFUL 2016!**

PATIENT ORGANIZATION NEWS

ANNIVERSARIES

AICI 20th anniversary

The Associazione Italiana Cistite Interstiziale (AICI) (Italian Interstitial Cystitis Association) is celebrating its 20th anniversary this year. Many congratulations to AICI, and especially to Loredana Nasta, for the support group's hard work over two decades during which they have greatly raised awareness at all levels in Italy.

New Zealand Painful Bladder Support Group 20th anniversary

New Zealand is also celebrating the 20th anniversary of its support group and now has a new website at www.nzpbsg.org. In their newsletter, support group chair Dot Milne writes that they started with just three people around a dining table. That rings a bell with many of us! Many congratulations to the support group and especially to Dot Milne who has kept it going from strength to strength.

IPBF 10th anniversary

The IPBF was set up 10 years ago. Among its many other activities, the IPBF promotes the interests of IC/BPS patients worldwide through patient advocacy and presentations, and endeavours to ensure that the viewpoints

and interests of patients and patient organizations are taken into account at medical, scientific and political levels.

GLOBAL PAIN MANAGEMENT SURVEY: GLOBAL PERCEPTIONS AND ATTITUDES ABOUT CHRONIC PAIN AND PAIN MANAGEMENT.

The International Pain Management Network (IPMN) – in which the IPBF also plays a role - is a group devoted to advancing awareness, understanding, and management of pain care throughout the world. To improve pain care globally, the IPMN must understand the problems you face as well as attitudes about pain where you live. It needs your help.

The IPMN has developed a survey to gain a better understanding how pain is assessed, treated and viewed by others worldwide. The survey will take about ten minutes to complete. Thank you for your help. Please click here to begin the survey:

https://www.surveymonkey.com/r/IPM_Network_Survey

MEETING REVIEWS

REVIEW OF THE ESSIC (INTERNATIONAL SOCIETY FOR THE STUDY OF BPS) ANNUAL MEETING, ROME, ITALY, 17-19 SEPTEMBER 2015

The 2015 annual meeting of ESSIC (International Society for the Study of BPS, founded 2004) was held in Rome, Italy, 17-19 September, at the Gemelli Hospital Catholic University of Rome where over 200 delegates received a warm welcome from Professor Mauro Cervigni who organized and chaired this year's meeting, Professor Jean-Jacques Wyndaele, president of ESSIC, Professor Giovanni Scambia, head of gynaecology at Gemelli Hospital and via Skype from Professor Adrian Wagg, General Secretary of the International Continence Society (ICS). This was a unique opportunity to meet people involved in all aspects of IC/BPS and its comorbidities, to hear about the latest research and insights from top speakers from around the world. It was good to see so many younger healthcare professionals attending. With many experts now around retirement age, it is important to encourage younger doctors to continue the crusade. Patients were not forgotten either, with a patient speaker session forming part of the programme, and a number of patient representatives, particularly from Italy, in the audience. Simultaneous translation was provided for Italian delegates and vice versa where necessary. The meeting was divided into themed sessions and each session was followed by a question and answer session. Particularly interesting at this meeting was a new device from Hungary, presented by Dr Sandor Lovasz as an option to replace catheters for instillations and also a study for a promising new drug. Session topics covered assessment, diagnosis and treatment and also a patient organisation session. [Click here](#) for detailed review on the IPBF website.

45TH INTERNATIONAL CONTINENCE SOCIETY (ICS) ANNUAL SCIENTIFIC MEETING, 6-9 OCTOBER, 2015, MONTREAL, CANADA

In recent years, the International Continence Society (ICS) has increasingly developed a special interest in pelvic dysfunction and pelvic pain, including interstitial cystitis/bladder pain syndrome (IC/BPS) and hypersensitive bladder (HSB) in addition to the field of incontinence. This has made the ICS annual scientific meeting an important date in the conference calendar for those with a focus on IC/BPS. This year's meeting in Montreal was no exception with podium sessions on research, a selection of workshops in the field of pelvic pain and dysfunction, bladder sensation, pudendal neuralgia, a round table discussion on urgency (which rather regrettably focused on overactive bladder urgency only, with painful urgency as in IC/BPS largely forgotten), an update on IC/BPS, vestibulodynia and pelvic pain syndromes in the Pan-Arab Continence Society (PACS) session (stressing multimodal treatment and a multidisciplinary team), while a large part of the final morning was devoted to understanding pelvic pain and – a first for the ICS – a round table discussion and presentations around the topic of bladder pain syndrome/interstitial cystitis: pain and phenotypes. [Read more.](#)

GRÜNENTHAL EUROPEAN PAIN DAY, 2 NOVEMBER 2015, KASTEEL BLOEMENDAAL, VAALS, NETHERLANDS

The pharma company Grünenthal organized a unique European Pain Day for its employees on 2 November, with presentations in several areas of pain (Duchenne, IC/BPS, Vulvodynia), given in each case by an interacting team of a health professional and a patient, including also a presentation on the role of patient associations as advocates and in clinical development. The idea was to hear about, discuss and reflect on different disorders/indications for which there are limited or no treatments. There was a very lively discussion between the presenters and the audience. IC/BPS was represented by Professor J-J Wyndaele from Antwerp and IPBF chair Jane Meijlink from the Netherlands, who talked about the problems of diagnosis and treatment, the difficulties faced by IC/BPS patients in their daily life, the lack of adequate treatments and the need for new approaches to treatment that will truly improve the patient's quality of life. This meeting was a very successful initiative, on the one hand giving us as patients an insight into the many aspects and problems of drug development and on the other giving the Grünenthal delegates a deeper insight into the disorders and their impact on the patient.

CALENDAR OF UPCOMING EVENTS

LUTFORUM SUMMARY MEETING

22-23 January 2016, Van der Valk Hotel Brussels Airport, Brussels, Belgium.

This meeting will discuss the latest clinically relevant data in functional urology presented at the EAU, AUA and ICS annual meetings with the international LUTforum faculty. Further information: www.lutforumsummarymeeting.com

ADVANCES IN PAIN MEDICINE WINTER SYMPOSIUM, TIGNES LE LAC, FRENCH ALPS, 17-22 JANUARY 2016

A six-day programme of lectures, discussions and workshops with an international faculty. Further information: <http://www.winterpainsymposium.com> or ciaranwazir@gmail.com

EUROPEAN ASSOCIATION OF UROLOGY (EAU)

11-15 March 2016, Munich, Germany.

<http://eaumunich2016.uroweb.org>

INTERNATIONAL ALLIANCE OF PATIENTS' ASSOCIATIONS (IAPO)

7th Global Patients Congress, 9-11 April 2016, Selsdon Park Hotel, South London UK.

The 7th Global Patients Congress will bring together around 200 patient advocates from across the world. Organizations of all sizes will share best practice, gain insight into pressing healthcare issues and meet with others passionate about patient-centred healthcare. Delegates representing dozens of causes will unite to strengthen the global patient voice and improve the lives of patients worldwide. They will:

- Meet others in the healthcare field
- Create national and regional networks
- Share expertise and speak out on behalf of the patients
- Learn from leading healthcare experts
- Discuss the changing healthcare climate

The over-arching theme for the upcoming Congress is 'For Patients' Organizations, By Patients' Organizations'. Sessions will focus on how to extend the reach, raise the effectiveness and maximize the impact of patients' organizations at the local, national and global level. The Congress will provide practical advice and real case studies for delegates to learn and improve their own work. Patients' organizations will also learn about using human rights based approaches to advocate for change in healthcare services and systems. Patients' representatives will meet academics and researchers, policy-makers, industry representatives, healthcare professionals and other influential figures in the healthcare world. Further information: <https://www.iapo.org.uk/7th-congress>

AMERICAN UROLOGICAL ASSOCIATION (AUA)

7-10 May 2016, San Diego, California, USA. <https://www.auanet.org>

INTERNATIONAL CONTINENCE SOCIETY (ICS) ANNUAL SCIENTIFIC MEETING + 6TH INTERNATIONAL CONSULTATION ON INCONTINENCE (ICI)

13-16 September 2016, in Tokyo, Japan.

The ICS annual scientific forum is increasingly becoming an important platform for chronic pelvic pain and IC/BPS. The 2016 meeting will be combined with the 6th International Consultation on Incontinence with presentations on many different conditions, including IC/BPS.

CONVERGENCES PP 2016

International meeting on chronic pelvic and abdominal pain, 15-17 September 2016, Palais des Congres, Aix en Provence, France.

16TH WORLD CONGRESS ON PAIN

The IASP World Congress on Pain, 26–30 September, 2016, Yokohama, Japan

<http://www.iasp-pain.org/Yokohama?navItemNumber=593>

ESSIC ANNUAL MEETING 2016

The ESSIC (International Society for the Study of IC/BPS) will hold its 2016 Annual Meeting in New Delhi, India, 17-19 Nov 2016. www.essic.eu.

PUBLICATIONS

New: CAMPBELL-WALSH UROLOGY, 11th EDITION

Edited by Alan J. Wein, Louis R. Kavoussi, Alan W. Partin, Craig A. Peters.

ISBN: 978-1-4557-7567-5, Elsevier, 2016

Volume I, Part 2, Chapter 14: Bladder Pain Syndrome (Interstitial Cystitis) and Related Disorders, p 334-370.

Includes new guidelines on IC/BPS.

IASP PAIN: CLINICAL UPDATES

“Neurostimulation for Neuropathic Pain: Outcomes and New Paradigms”

September 2015 (Volume 23, Issue 5). Srinivasa N. Raja, MD and Mark Wallace, MD

Download in English: [Pain Clinical Update Volume 23 No 5 September 2015](#)

NEW PROFESSIONAL SOCIETY

SOCIETY FOR PELVIC RESEARCH

<http://www.pelvicresearch.com/>

A Scientific Society founded by and for career basic and translational scientists interested in normal function and benign disease states of the pelvic viscera and pelvic floor. Affiliate membership is also open to patient advocates. President: Matthew O. Fraser, Ph.D. info@pelvicresearch.com

UNITED NATIONS WORLD TOILET DAY REVEALS LACK OF SANITARY FACILITIES WORLDWIDE AND RISKS TO WOMEN AND GIRLS

While many of the IC/BPS patients in the developed world are concerned about finding toilets in public places, they at least have the “luxury” of a toilet in their own home. In many countries, this is sadly not the case for our fellow-patients. Thursday 19 November was World Toilet Day when the United Nations highlighted that 2.4 billion people still don't have access to sanitary facilities, increasing the risk of disease. Because women and girls are often attacked on their way to defecate, “we have a moral imperative to end open defecation and a duty to ensure women and girls are not at risk of assault and rape simply because they lack a sanitation facility,” said Ban Ki-moon, UN secretary-general. Launching its World Toilet Day campaign, which aims to break the taboo around toilets and basic hygiene, the UN said poor sanitation increases the risk of illness and malnutrition, especially for children, and called for women and girls in particular to be offered safe, clean

facilities. In a 2010 report "Risking rape to reach a toilet", Amnesty International found that: "The shortage of toilets (including latrines) and places to wash in the slums exacerbates women's insecurity and heightens the risk of gender-based violence. "Many women have suffered rape and other forms of violence as a result of attempting to walk to a toilet or latrine some distance from their home," the report said. Many nations in the world are failing to give sanitation the political prioritization and financing required. Everyone has a right to a safe, private place to relieve themselves, and to live healthy lives without the threat of illness from poor sanitation and hygiene.

RESEARCH HIGHLIGHTS

A REVIEW OF SELECTED RECENT SCIENTIFIC LITERATURE ON INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME 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 and Hunner Disease and Classic IC are synonymous. When reviewing the article, we generally use the terminology used by the authors.

TRANSLATIONAL ANDROLOGY AND UROLOGY (TAU) SUPPLEMENTS FOCUSED ON INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: PART I AND PART II (Open Access)

It is always greatly appreciated when an IC/BPS supplement is produced with open access. This allows not only all healthcare professionals to have easy access to the full text, but also provides patients and their organizations with the opportunity to update their knowledge. In the case of the TAU supplement, it is a double pleasure with Part I published in October and Part II in December. The many articles provide a picture of IC/BPS around the world and include contributions by many familiar faces, including patient advocates, from the IC/BPS world. Part I includes an article by IPBF chair Jane Meijlink on the need for patient participation in terminology and definitions.

Many thanks are due to Translational Andrology and Urology (TAU) and to professors Grannum Sant and Ricardo Saban for giving us this unique access to a state-of-the-art compendium of the global approaches to insights into and diagnosis and treatment of IC/BPS. Also many thanks to all the authors who gave their time and effort to make this a memorable international supplement.

PART I: TRANSLATIONAL ANDROLOGY AND UROLOGY VOL 4, NO 5 (OCTOBER 2015),

<http://www.amepc.org/tau/issue/view/362>. This link takes you to an overview of the articles with open access to HTML or pdf.

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[A survey on clinical practice of interstitial cystitis in Japan](#)

Yukio Yamada, Akira Nomiya, Aya Niimi, Yasuhiko Igawa, Takaaki Ito, Hikaru Tomoe, Mineo Takeji, Tomohiro Ueda, Yukio Homma

[The Interstitial Cystitis Association of America: lessons learned over the past 30 years](#)

Vicki Ratner

[Patient-centred standardization in interstitial cystitis/bladder pain syndrome—a PLEA](#)

Jane M. Meijlink

[Interstitial cystitis/painful bladder syndrome: the influence of modern diagnostic criteria on epidemiology and on Internet search activity by the public](#)

Niall F. Davis, Sanjith Gnanappiragasam, John A. Thornhill

[Clinical presentation and treatment of bladder pain syndrome/interstitial cystitis \(BPS/IC\) in India](#)

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[Novel research approaches for interstitial cystitis/bladder pain syndrome: thinking beyond the bladder](#)

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[Sympathetic nervous system and chronic bladder pain: a new tune for an old song](#)

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[Treatment of painful bladder syndrome/interstitial cystitis with botulinum toxin A: why isn't it effective in all patients?](#)

Neil S. Lamarre, Dale E. Bjorling

[Angiogenic factors, bladder neuroplasticity and interstitial cystitis—new pathobiological insights](#)

Ricardo Saban

[Increased bladder permeability in interstitial cystitis/painful bladder syndrome](#)

Robert E. Hurst, Beverley Greenwood-Van Meerveld, Amy B. Wisniewski, Samuel VanGordon, Hsueh Kung Lin, Bradley P. Kropp, Rheal A. Towner

[Intravesical liposome drug delivery and IC/BPS](#)

Joseph J. Janicki, Michele A. Gruber, Michael B. Chancellor

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[Mast cell activation syndrome](#)

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PART II: TRANSLATIONAL ANDROLOGY AND UROLOGY VOL 4, NO 6 (DECEMBER 2015)

<http://www.amepc.org/tau/issue/current>. This link takes you to an overview of the articles with open access to HTML or pdf.

Contents in HTML

If you click on the titles below, you will go directly to the HTML version.

[Focused issue on interstitial cystitis/bladder pain syndrome \(IC/BPS\) 2015: Part 2](#)

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[Test-retest reliability and discriminant validity for the Brazilian version of “The Interstitial Cystitis Symptom Index and Problem Index” and “Pelvic Pain and Urgency/Frequency \(PUF\) Patient Symptom Scale” instruments](#)

Marcella Lima Victal, Carlos Arturo Levi D’Ancona, Roberto Gomes Junqueira, Daniel Carlos da Silva, Henrique Ceretta Oliveira, Maria Helena Baena de Moraes Lopes

[In what type of interstitial cystitis/bladder pain syndrome is DMSO intravesical instillation therapy effective?](#)

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[A multidisciplinary approach to the evaluation and management of interstitial cystitis/bladder pain syndrome: an ideal model of care](#)

Priyanka Gupta, Natalie Gaines, Larry T. Sirls, Kenneth M. Peters

[Interstitial cystitis/painful bladder syndrome: diagnostic evaluation and therapeutic response in a private urogynecology unit](#)

Oscar Flores-Carreras, Maria Isabel González-Ruiz, Claudia J. Martínez-Espinoza, Fabiola Monroy-Rodríguez, Rocio M. Zaragoza-Torres

[Role of cystoscopy and hydrodistention in the diagnosis of interstitial cystitis/bladder pain syndrome](#)

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Jennifer Yonaitis Fariello, Robert M. Moldwin

[The Chinese approach to complementary and alternative medicine treatment for interstitial cystitis/bladder pain syndrome](#)

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Megan Danielle Atchley, Nima M. Shah, Kristene E. Whitmore

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[Current guidelines in the management of interstitial cystitis](#)

Marc Colaco, Robert Evans

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

[UNIQUE MICROSTRUCTURAL CHANGES IN THE BRAIN ASSOCIATED WITH UROLOGICAL CHRONIC PELVIC PAIN SYNDROME \(UCPPS\) REVEALED BY DIFFUSION TENSOR MRI, SUPER-RESOLUTION TRACK DENSITY IMAGING, AND STATISTICAL PARAMETER MAPPING: A MAPP NETWORK NEUROIMAGING STUDY.](#)

*Woodworth D, Mayer E, Leu K, Ashe-McNalley C, Naliboff BD, Labus JS, Tillisch K, Kutch JJ, Farmer MA, Apkarian AV, Johnson KA, Mackey SC, Ness TJ, Landis JR, Deutsch G, Harris RE, Clauw DJ, Mullins C, Ellingson BM; [MAPP Research Network](#). *PLoS One*. 2015 Oct 13;10(10):e0140250. doi: 10.1371/journal.pone.0140250. eCollection 2015. PMID: 26460744*

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

Studies have suggested chronic pain syndromes are associated with neural reorganization in specific regions associated with perception, processing, and integration of pain. Urological chronic pelvic pain syndrome (UCPPS) represents a collection of pain syndromes characterized by pelvic pain, namely Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPSP) and Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS), that are both poorly understood in their pathophysiology, and treated ineffectively. Woodworth and colleagues hypothesized patients with UCPPS may have microstructural differences in the brain compared with healthy control subjects (HCs), as well as patients with irritable bowel syndrome (IBS), a common gastrointestinal pain disorder. Results showed significant differences in specific anatomical regions in UCPPS patients when compared with IBS patients, consistent with microstructural alterations specific to UCPPS. While IBS patients showed clear sex related differences in fractional anisotropy (FA), mean diffusivity (MD), generalized anisotropy (GA), and track density consistent with previous reports, few such differences were observed in UCPPS patients. Heat maps illustrating the correlation between specific regions of interest and various pain and urinary symptom scores showed clustering of significant associations along the cortico-basal ganglia-thalamic-cortical loop associated with pain integration, modulation, and perception. Together, results suggest patients with UCPPS have extensive microstructural differences within the brain, many specific to syndrome UCPPS versus IBS, that appear to be localized to regions associated with perception and integration of sensory information and pain modulation, and seem to be a consequence of longstanding pain.

[ASSESSMENT OF THE LOWER URINARY TRACT MICROBIOTA DURING SYMPTOM FLARE IN WOMEN WITH UROLOGIC CHRONIC PELVIC PAIN SYNDROME: A MAPP NETWORK STUDY.](#)

Nickel JC, Stephens A, Landis JR, Mullins C, van Bokhoven A, Lucia MS, Ehrlich GD; MAPP Research Network. *J Urol.* 2015 Sep 26. pii: S0022-5347(15)04883-1. doi: 10.1016/j.juro.2015.09.075. [Epub ahead of print]. PMID: 26410734

Nickel and colleagues compared culture independent assessment of microbiota of the lower urinary tract in standard culture negative female patients with urological chronic pelvic pain syndrome who reported symptom flare vs those who did not report a flare. Initial stream (VB1) and midstream (VB2) urine specimens (233 patients with urological chronic pelvic pain syndrome) were analyzed with Ibis T-5000 Universal Biosensor system technology for comprehensive identification of microorganism species. Differences between flare and nonflare groups for presence or number of different species within a higher level group (richness) were examined by permutational multivariate analysis of variance and logistic regression. Among women with urological chronic pelvic pain syndrome the prevalence of fungi (*Candida* and *Saccharomyces* sp.) was significantly greater in those who reported a flare compared to those who did not.

[PAIN AND URINARY SYMPTOMS SHOULD NOT BE COMBINED INTO ONE SCORE: PSYCHOMETRIC FINDINGS FROM THE MULTI-DISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN \(MAPP\) RESEARCH NETWORK.](#)

Griffith JW, Stephens-Shields AJ, Hou X, Naliboff B, Pontari M, Edwards TC, Williams DA, Clemens JQ, Afari N, Tu F, Lloyd R, Patrick DL, Mullins C, Kusek JW, Sutcliffe S, Hong BA, Lai HH, Krieger JN, Bradley CS, Kim J, Landis JR. *J Urol.* 2015 Nov 13. pii: S0022-5347(15)05226-X. doi: 10.1016/j.juro.2015.11.012. [Epub ahead of print]. PMID: 26585679

The purpose of this MAPP Research Network study was to create symptom indices – in other words scores derived from questionnaires - to accurately and efficiently measure symptoms of interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome, collectively referred to as urologic chronic pelvic pain syndromes (UCPPS). Griffith and colleagues created these indices empirically, by investigating the structure of symptoms using exploratory factor analysis. As part of the Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network, 424 participants completed questionnaires including the Genitourinary Pain Index (GUPI), the Interstitial Cystitis Symptom Index (ICSI), and the Interstitial Cystitis Problem Index (ICPI). Individual items from questionnaires about bladder and pain symptoms were evaluated by principal components and exploratory factor analysis to identify indices with fewer questions to comprehensively quantify symptom severity. Additional analyses included correlating symptom indices with symptoms of depression, a known comorbidity of patients with pelvic pain. Exploratory factor analyses suggested that two factors, pain severity and urinary severity, provided the best psychometric description of

items contained in the GUPI, the ICSI, and the ICPI. These factors were used to create two symptom indices for pain and urinary symptoms. Pain, but not urinary symptoms, was associated with symptoms of depression in a multiple regression analysis, suggesting that these symptoms may impact patients with UCCPS differently; for pain severity, B (SE) = 0.24 (0.04), 95% CI of B = 0.16-0.32, β = 0.32, $p < .001$. Their results suggest that pain and urinary symptoms should be assessed separately, rather than combined into one total score. Total scores that combine the separate factors of pain and urinary symptoms into one score may be limited for clinical and research purposes.

IC/BPS/HSB BASIC SCIENCE, DIAGNOSIS AND TREATMENT

ALTERATION OF UROTHELIAL INFLAMMATION, APOPTOSIS, AND JUNCTION PROTEIN IN PATIENTS WITH VARIOUS BLADDER CONDITIONS AND STORAGE BLADDER SYMPTOMS SUGGEST COMMON PATHWAY INVOLVED IN UNDERLYING PATHOPHYSIOLOGY.

Liu HT, Jiang YH, Kuo HC. *Low Urin Tract Symptoms*. 2015 May;7(2):102-7. doi: 10.1111/luts.12062. Epub 2014 May 12. PMID: 26663690

Lower urinary tract symptoms (LUTS) are common in various bladder disorders. This study from Hualien, Taiwan investigated urothelial dysfunction and chronic inflammation in the urothelium in different types of lower urinary tract dysfunction (LUTD), which causes bladder storage symptoms. Bladder tissues were obtained from patients with LUTD including 17 with interstitial cystitis/bladder pain syndrome (IC/BPS), 15 with bladder outlet obstruction (BOO), 12 with spinal cord injury (SCI), 12 with recurrent urinary tract infection (UTI), 13 with ketamine related cystitis (KC) and 10 controls. The bladder specimens were investigated using immunofluorescence (IF) staining of the urothelial junction protein E-cadherin and the TUNEL assay for urothelial apoptosis. Mast cell activation was also measured by IF using tryptase for mucosal inflammation. Statistical analysis was performed using the Kruskal-Wallis and Wilcoxon rank-sum test and P-values less than 0.05 were considered significant. Highly significant increases of mast cell infiltration were observed in patients with KC, IC/BPS, recurrent UTI, SCI, and BOO compared with controls. Statistically significant increases of apoptotic cells were observed in patients with KC, IC/BPS, SCI, recurrent UTI, and BOO compared with controls. Significantly decreased expression of E-cadherin in patients with IC/BPS, KC, and recurrent UTI was found compared to controls and patients with SCI or BOO. The authors concluded that increased urothelial inflammation and urothelial cell apoptosis seem to share common pathophysiologies of various LUTDs that cause similar bladder symptoms.

NOVEL TARGETED BLADDER DRUG-DELIVERY SYSTEMS: A REVIEW.

Zacchè MM, Srikrishna S, Cardozo L. *Res Rep Urol*. 2015 Nov 23;7:169-178. PMID: 26649286

The objective of pharmaceuticals is the development of drugs with increased efficacy and reduced side effects. Prolonged exposure of the diseased tissue to the drug is of crucial importance. Drug-delivery systems (DDSs) have been introduced to control rate, time, and place of release. Drugs can easily reach the bladder through a catheter, while systemically administered agents may undergo extensive metabolism. Continuous urine filling and subsequent washout hinder intravesical drug delivery (IDD). Moreover, the low permeability of the urothelium, also described as the bladder permeability barrier, poses a major challenge in the development of the IDD. DDSs increase bioavailability of drugs, therefore improving therapeutic effect and patient compliance. This review by Zacchè and colleagues from the Department of Urogynaecology, King's College Hospital, London focuses on novel DDSs to treat bladder conditions such as overactive bladder, interstitial cystitis, bladder cancer, and recurrent urinary tract infections. The rationale and strategies for both systemic and local delivery methods are discussed, with emphasis on new formulations of well-known drugs (oxybutynin), nanocarriers, polymeric hydrogels, intravesical devices, encapsulated DDSs, and gene therapy. The authors give an overview of current and future prospects of DDSs for bladder disorders, including nanotechnology and gene therapy.

INCREASED EXPRESSION OF NEUREGULIN 1 AND ERBB2 TYROSINE KINASE IN THE BLADDER OF RATS WITH CYCLOPHOSPHAMIDE-INDUCED INTERSTITIAL CYSTITIS.

Song KH, Youn CS, Lee CL, Yang SW, Chang YS, Jeong SW, Sul CK. *Int Neurourol J*. 2015 Sep;19(3):158-163. Epub 2015 Sep 22. PMID: 26620897

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

The aim of this study from Korea was to evaluate changes in expressions of neuregulin (NRG)1 and erbB2 tyrosine kinase (ErbB2) in bladders of rats with cyclophosphamide (CYP)-induced interstitial cystitis (IC). Twenty-four Sprague-Dawley rats were divided into the IC group (n=16) and the control group (n=8). After inducing IC with intraperitoneal CYP injection, expressions of NRG1 and ErbB2 were analyzed using western blotting and reverse transcriptase-polymerase chain reaction. Song and colleagues report that their study has demonstrated significant changes in mRNA expression and immunoreactivity of NRG1 and ErbB2 receptors in the urinary bladder after CYP-induced IC and that these results suggest that the up-regulated NRG1 may play a role in inducing an overactive bladder and promoting regeneration in the inflammatory bladder with CYP-induced IC.

INTERLEUKIN-33 AND MAST CELLS BRIDGE INNATE AND ADAPTIVE IMMUNITY: FROM THE ALLERGOLOGIST'S PERSPECTIVE.

Jang TY, Kim YH. *Int Neurourol J.* 2015 Sep;19(3):142-150. Epub 2015 Sep 22. PMID: 26620895

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Interleukin (IL) 33, a member of the IL-1 superfamily, is an "alarmin" protein and is secreted in its active form from damaged cells undergoing necrotic cell death, as noted by Yang and Kim from Korea. Mast cells are one of the main effector cell types in allergic disorders. They secrete a variety of mediators, including T helper 2 cytokines. As mast cells have high-affinity IgE receptors (FcεRI) on their surface, they can capture circulating IgE. IgE-bound mast cells degranulate large amounts of histamine, heparin, and proteases when they encounter antigens. As IL-33 is an important mediator of innate immunity and mast cells play an important role in adaptive immune responses, interactions between the two could link innate and adaptive immunity. IL-33 promotes the adhesion of mast cells to laminin, fibronectin, and vitronectin. IL-33 increases the expression of adhesion molecules, such as intracellular adhesion molecule-1 and vascular cell adhesion molecule-1, in endothelial cells, thus enhancing mast cell adhesion to blood vessel walls. IL-33 stimulates mast cell proliferation by activating the ST2/Myd88 pathway; increases mast cell survival by the activation of survival proteins such as Bcl-XL; and promotes the growth, development, and maturation of mast cell progenitors. IL-33 is also involved in the activation of mature mast cells and production of different proinflammatory cytokines. The interaction of IL-33 and mast cells could have important clinical implications in the field of clinical urology. Epithelial dysfunction and mast cells could play an important role in the pathogenesis of interstitial cystitis. Urinary levels of IL-33 significantly increase in patients with interstitial cystitis. In addition, the number of mast cells significantly increase in the urinary bladders of patients with interstitial cystitis. Therefore, inhibition of mast cell activation and degranulation in response to increase in IL-33 is a potential therapeutic target in the treatment of interstitial cystitis.

INTERLEUKIN-33 AS A POTENTIAL THERAPEUTIC TARGET FOR INTERSTITIAL CYSTITIS: NEW PERSPECTIVES ON MAST CELL REGULATION.

Editorial

Choo MS. *Int Neurourol J.* 2015 Sep;19(3):132. PMID: 26620893

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ADVANCES IN INTRAVESICAL THERAPY FOR URINARY TRACT DISORDERS.

Tyagi P, Kashyap M, Hensley H, Yoshimura N1. *Expert Opin Drug Deliv.* 2015 Oct 19:1-14. [Epub ahead of print]. PMID: 26479968

Intravesical therapy is a valuable option in the clinical management of urinary tract disorders such as interstitial cystitis/ painful bladder syndrome (IC/PBS) and refractory overactive bladder. This review covers the latest advances in this field using polymer and liposomes as delivery platform for drugs, protein and nucleic acids, summarizing the significance of intravesical therapy for lower urinary tract disorders. It discusses the recent advancement of liposomes as a drug delivery platform for botulinum toxin, tacrolimus and small interfering RNA. It also looks at the importance of polymers forming indwelling devices and hydrogels, where all preparations improved efficacy parameters in rodent models. Clinical experience of treating IC/PBS with indwelling devices and liposomes are summarized and preclinical evidence about the downregulation of target gene expression in rodent bladder with liposomes complexed with siRNA is reviewed. Expert opinion: There have been several advances in the field of intravesical therapy for improving clinical outcomes. One of the most

promising research avenues is the repurposing of drugs, given previously by other routes of administration, such as tacrolimus. Intravesical therapy also opens up novel therapeutic targets with improved efficacy and safety for underactive bladder.

AN ASSESSMENT OF CLINICIANS' AND PATIENTS' EXPERIENCES IN THE MANAGEMENT OF BLADDER PAIN SYNDROME.

Tirlapur SA, Khan KS. J Obstet Gynaecol. 2015 Oct 14:1-5. [Epub ahead of print] PMID: 26467216

Current management of bladder pain syndrome (BPS) was evaluated through a prospective electronic questionnaire posted on three patient support groups and sent to all members on the British Society of Urogynaecology (BSUG) database. Methods of diagnosis and treatment were assessed. 133 patients and 69 clinicians participated in the survey. Patients reported their main symptom to be pain when their bladder was full in 80% (n = 107) and the most bothersome symptom was pelvic pain (22%, n = 29). 93% (n = 64) of clinicians made their diagnosis by history and cystoscopy. 78% (n = 54) of clinicians treated patients with amitriptyline and 75% (n = 52) by dietary modification while 77% (n = 102) of patients reported using simple analgesia, 74% (n = 98) dietary modification and 62% (n = 83) low-dose long-term antibiotics. There is wide variation in diagnostic methods and treatments of BPS used by clinicians and experienced by patients with no obvious consensus. National guidance is needed to help standardise care.

TRANSCRIPTOME ANALYSIS OF BLADDER BIOPSY FROM INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENTS.

Walker SJ, Colaco M, Koslov DS, Keys T, Evans RJ, Badlani GH, Andersson KE. Genom Data. 2014 Oct 20;2:366-8. doi: 10.1016/j.gdata.2014.10.009. eCollection 2014. PMID: 26484132

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Interstitial cystitis and bladder pain syndrome (IC/BPS) are terms used to describe a heterogeneous chronic pelvic and bladder pain disorder. Despite its significant prevalence, the disease etiology is not well understood and providing diagnosis and treatment can be challenging. In a study, published recently in the Journal of Urology (Colaco et al., 2014), Walker and colleagues describe the use of microarrays as a tool to characterize IC/BPS and to determine if there are clinical factors that correlate with gene expression. This data-in-brief article describes the methodology for that study, including data analysis, in further detail. Deposited data can be found in the Gene Expression Omnibus (GEO) database: GSE57560.

INJECTION OF DENTAL PULP STEM CELLS PROMOTES HEALING OF DAMAGED BLADDER TISSUE IN A RAT MODEL OF CHEMICALLY INDUCED CYSTITIS.

Hirose Y, Yamamoto T, Misako N, Funahashi Y, Matsukawa Y, Yamaguchi M, Kawabata S, Gotoh M. Cell Transplant. 2015 Sep 21. [Epub ahead of print] PMID: 26395427

Dental pulp stem cells (DPSCs) are reported as one of the sources of mesenchymal stem cells (MSCs). MSCs are used as cell therapy options for various diseases. The present work examined the healing effects of DPSC injection on damaged bladder tissue in a chemically induced cystitis rat model. Cystitis was induced by hydrochloride injection into the bladder of female F344/NSlc rats. On the following day, DPSCs suspended in phosphate-buffered saline (PBS) were injected into the bladder and maintained for 1 h (DPSC injection group), while PBS alone was injected as the standard for comparison (PBS injection group). After two days following injection, considerable submucosal edema, vascular structure destruction, hemorrhage, and inflammatory cell invasion were observed both in the DPSC and PBS injection groups, with no difference in their degree of submucosal edema and hemorrhage. After six days following injection, vascular structure regeneration was observed in both groups; however, unlike the DPSC injection group, the PBS injection group showed traces of submucosal edema and hemorrhage. These results correlated with the tissue concentrations of myeloperoxidase (MPO) and the inflammatory cytokines IL-1 β , IL-6, and TNF- α . Furthermore, the intercontraction interval was prolonged, and the frequency of nociceptive behaviors was reduced in the DPSC injection group compared with the PBS injection group. DPSCs were found on the bladder epithelium until day 3 after injection. In the DPSC conditioned media (CM), the trophic factors FGF-2, VEGF and the C-C and C-X-C families of chemokines were detected. The results of DPSC injection into the cystitis rat model suggested that the injected cells promote the healing of the damaged bladder tissue by exerting various trophic effects while

localizing on the bladder epithelium and that MSC injection is a potential novel therapy for interstitial cystitis/painful bladder syndrome.

INFLUENCE OF POLYUNSATURATED FATTY ACIDS ON UROLOGIC INFLAMMATION.

Tamma SM, Shorter B, Toh KL, Moldwin R, Gordon B. Int Urol Nephrol. 2015 Sep 28. [Epub ahead of print]. PMID: 26411429

Studies demonstrate that polyunsaturated fatty acids, fish oils, and alpha-linoleic acid are beneficial anti-inflammatory agents, which suppress inflammatory mediators and their activity. This review by Tamma and colleagues from the USA focuses on the effects of omega-3 fatty acids (O-3FAs) on three primary urologic organs (bladder, kidney, and prostate) and associated conditions such as urolithiasis, kidney transplantation, interstitial cystitis/bladder pain syndrome, bladder cancer, prostate cancer (CaP), and chronic prostatitis/chronic pelvic pain syndrome. The following themes emerged: the potential influence of O-3FA in suppressing urologic inflammation; the supportive role of O-3FA in therapeutic interventions; pro-inflammatory mechanisms of omega-6 fatty acids (O-6FAs) associated with disease progression; and the importance of the optimal ratio of O-6FAs/O-3FAs. It was concluded that there is a need for further research on the role of PUFAs in suppressing urological inflammation precipitated.

THE CHALLENGES OF INTERSTITIAL CYSTITIS: CURRENT STATUS AND FUTURE PROSPECTS.

Belknap S, Blalock E, Erickson D. Drugs. 2015 Dec;75(18):2057-63. doi: 10.1007/s40265-015-0504-9. PMID: 26603875

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a syndrome of unpleasant bladder sensations and lower urinary tract symptoms. The three main proposed etiologies are bladder urothelial dysfunction, bladder inflammation (possible neurogenic), and neuropathic pain. Despite decades of basic and clinical research, IC/BPS remains difficult to treat. A variety of treatments are used, each aimed towards one etiology. For example, glycosaminoglycans are thought to improve the urothelial permeability barrier, anti-inflammatory agents are used to decrease general inflammation, and mast cell stabilizers and/or antagonists of mast cell products are used in the treatment of neurogenic inflammation. In the (unfortunately frequent) event that a treatment fails, possible reasons are that (1) the clinician is aiming towards the wrong etiology for that patient (i.e., the treatment is off target) or (2) the correct etiology is being targeted, but the treatment is not ameliorating it (i.e., the treatment is sub-therapeutic). This is a crucial distinction, because an off-target treatment should be abandoned, but a sub-therapeutic treatment should be escalated. Currently, our inability to make this crucial distinction is the greatest obstacle to effective treatment. An important future advance would be to identify urine or serum biomarkers specific to each etiologic target. Then, each biomarker could be used to select appropriate patients for each treatment and monitor the treatment's effect on its intended target.

CURRENT AND EMERGING DRUGS FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME (IC/BPS).

Ogawa T, Ishizuka O, Ueda T, Tyagi P, Chancellor MB, Yoshimura N. Expert Opin Emerg Drugs. 2015 Nov 4:1-16. [Epub ahead of print]. PMID: 26535808

In this review Ogawa and colleagues focus on the current treatments, ongoing clinical trials, and several potential new drugs based on the results of basic and clinical research studies. They discuss the potential etiologies of IC/BPS that include altered barrier lining, afferent and/or central nervous system abnormalities, possible contribution of inflammation or infection and abnormal urothelial signaling. Current therapies of IC/BPS, either systemic or local, are reviewed by critical evaluation of the efficacy and shortcomings of each treatment. Finally, based on proposed etiologies of the disease, potential emerging drugs and treatments are discussed. Expert opinion: Current therapies often fail to control the symptoms of IC/BPS. Several interventions including sustained drug release and retaining techniques, and drugs that act on afferent neural pathways are emerging and may be promising. In addition, phenotyping of IC/BPS patients based on cystoscopic findings (e.g., Hunner vs. non-Hunner lesion) or patients' symptoms would be important for further investigation of IC/BPS etiology and the evaluation of efficacy of new treatments.

A SYSTEMATIC REVIEW AND META-ANALYSIS ON THE EFFICACY OF INTRAVESICAL THERAPY FOR BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.

Barua JM, Arance I, Angulo JC, Riedl CR. *Int Urogynecol J*. 2015 Nov 20. [Epub ahead of print] PMID: 26590137

Bladder pain syndrome/interstitial cystitis (BPS/IC) is a chronic disease characterised by persistent irritating micturition symptoms and pain. The objective was to compare the clinical efficacy of currently available products for intravesical therapy of BPS/IC and to assess their pharmaco-economic impact. A Pubmed/Medline database search was performed for articles on intravesical therapy for BPS/IC. A total of 345 publications were identified, from which 326 were excluded. Statistical evaluation was performed with effect size (ES) assessment of symptom reduction and response rates. The final set of 19 articles on intravesical BPS/IC therapy included 5 prospective controlled trials (CTs), the remaining were classified as uncontrolled clinical studies. The total number of patients included was 801, 228 of whom had been evaluated in a CT. For CTs, the largest ES for symptom reduction as well as response rate was observed for high molecular weight hyaluronic acid (HMW-HA), with similar findings in two uncontrolled studies with HMW-HA. The number needed to treat to achieve a response to intravesical therapy was 2.67 for intravesical pentosan polysulphate and 1.31 for HMW-HA which were superior to all other instillates. HMW-HA was significantly superior in cost effectiveness and cost efficacy to all other instillation regimes. The present meta-analysis combined medical and pharmaco-economic aspects and demonstrated an advantage of HMW-HA over other instillation agents; however, direct comparisons between the different products have not been performed to date in properly designed controlled studies.

THE ROLE OF GLOMERULATIONS IN BLADDER PAIN SYNDROME – A REVIEW

Wennevik GE, Meijlink JM, Hanno P, Nordling J. DOI: <http://dx.doi.org/10.1016/j.juro.2015.06.112> 2015 August 26 [E-pub ahead of print] PMID: 26318984

Glomerulations as a diagnostic marker for bladder pain syndrome/interstitial cystitis (BPS/IC) was first popularized by Messing & Stamey in 1978. Later this was included in the NIDDK criteria for research and consequently used by many urologists as a default diagnostic criterion. Today, the connection between glomerulations and BPS/IC is much debated, as research has found glomerulations in asymptomatic populations. This paper systematically looks at the available research to see if there is valid data to support the use of glomerulations as a marker for BPS/IC. A systematic literature search of the PubMed database in March 2014 using the search term "Cystitis, Interstitial/diagnosis" [MAJR] OR (glomerulations OR glomerulation OR bladder petechiae) was performed and yielded 463 hits, and an Embase search using the search term "glomerulations" yielded 110 references of which 68 were duplicates. Relevant articles were reviewed and included in the study. Bibliographies of reviews, articles and status reports were examined to find studies not included in the search. In total twenty-nine publications were included in this review. There is no consistent relationship between glomerulations and the diagnosis of BPS/IC. In the reviewed studies, the authors found evidence of the grade of glomerulations changing over time. Furthermore, many studies showed no link between the severity of symptoms and the number of glomerulations. There were studies that found glomerulations in healthy asymptomatic populations as well as in symptomatic populations with another primary diagnosis. One study found no glomerulations in an asymptomatic population. The authors found no convincing evidence that glomerulations should be included in diagnosis or phenotyping of BPS/IC. It does not correlate with symptoms and is found in patients without BPS/IC.

A CASE CONTROL STUDY REVEALS THAT POLYOMAVIRURIA IS SIGNIFICANTLY ASSOCIATED WITH INTERSTITIAL CYSTITIS AND VESICAL ULCERATION.

Winter BJ, O'Connell HE, Bowden S, Carey M, Eisen DP. *PLoS One*. 2015 Sep 1;10(9):e0137310. doi: [10.1371/journal.pone.0137310](https://doi.org/10.1371/journal.pone.0137310). eCollection 2015. PMID: 26325074

The purpose of this study from Australia was to investigate whether polyomaviruses contribute to interstitial cystitis pathogenesis. A prospective study was performed with 50 interstitial cystitis cases compared with 50 age-matched, disease-free controls for the frequency of polyomaviruria. Associations between polyomaviruria and disease characteristics were analysed in cases. Polyomavirus in urine and bladder tissue was detected with species (JC virus vs. BK virus) specific, real-time PCR. Case patients were reflective of interstitial cystitis epidemiology with age range from 26-88 years (median 58) and female predominance (41/50 F). There was a significant increase in the frequency of polyomavirus shedding between cases and controls ($p < 0.02$). Polyomavirus shedding, in particular BK viruria, was associated with vesical ulceration, a marker of disease severity, among interstitial cystitis cases after adjustment for age and sex (OR 6.8, 95% CI 1.89-24.4). There was a significant association among cases between the presence of BK viruria and response to intravesical

Clorpactin therapy (OR 4.50, 95% CI 1.17-17.4). The presence of polyomaviruria was found to be associated with the ulcerative form of interstitial cystitis. Clorpactin, which has anti-DNA virus activity, was more likely to improve symptoms in the presence of BK viruria. The data from this pilot study suggest associations between polyomaviruria and interstitial cystitis warranting further investigation.

[BOTULINUM TOXIN TYPE A INJECTION FOR REFRACTORY INTERSTITIAL CYSTITIS: A RANDOMIZED COMPARATIVE STUDY AND PREDICTORS OF TREATMENT RESPONSE](#)

Akiyama Y, Nomiya A, Niimi A, Yamada Y, Fujimura T, Nakagawa T, Fukuhara H, Kume H, Igawa Y, Homma Y. *Int J Urol*. 2015 Sep;22(9):835-41. doi: 10.1111/iju.12833. Epub 2015 Jun 2. PMID: 26041274

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The purpose of this single-center, prospective, open labeled, randomized comparative study from Tokyo was to determine whether botulinum toxin type A can represent an alternative treatment option for patients with interstitial cystitis refractory to conventional therapies. Patients with refractory interstitial cystitis were randomly divided into two groups: immediate injection (group A) or 1-month delayed injection (group B) of botulinum toxin type A after allocation. The rate of treatment response (global response assessment $\geq +1$: slightly improved), and changes in symptom scores and frequency volume chart variables were compared between groups 1 month after allocation. Using subjects of both groups as a single cohort, predictive factors for treatment response at 1 month post-injection and the duration of response were explored. The authors found that botulinum toxin type A injection could be an alternative treatment option for patients with interstitial cystitis refractory to conventional therapies, especially for those who have received repeated hydrodistensions and transurethral fulguration.

[Editorial Comment from Dr Tomoe to Botulinum toxin type A injection for refractory interstitial cystitis: A randomized comparative study and predictors of treatment response](#)

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[Editorial Comment from Dr Manning to Botulinum toxin type A injection for refractory interstitial cystitis: A randomized comparative study and predictors of treatment response](#)

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Letter to editor

[HAVE WE BEEN LED ASTRAY BY THE NGF BIOMARKER DATA?](#)

Gamper M, Moser R, Viereck V. *Neurourol Urodyn*. 2015 Sep 18. doi: 10.1002/nau.22882. [Epub ahead of print]. PMID:26384156

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[UPDATE ON URINARY TRACT MARKERS IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.](#)

Grigorescu B, Powers K, Lazarou G. *Female Pelvic Med Reconstr Surg*. 2015 Nov 13. [Epub ahead of print] PMID: 26571430

Interstitial cystitis (IC)/painful bladder syndrome/bladder pain syndrome (BPS) is a chronic hypersensory condition of unknown etiology. Moreover, the optimal modality for diagnosing IC remains disputed. Several urinary markers have been investigated that may have potential utility in the diagnosis or confirmation of IC/BPS. Thus, inflammatory mediators, proteoglycans, urinary hexosamines, proliferative factors, nitric oxide (NO), BK polyomavirus family, and urothelial proinflammatory gene analysis have been found to correlate with varying degrees with the clinical diagnosis or cystoscopic findings in patients with IC/BPS. The most promising urinary biomarker for IC/BPS is antiproliferative factor, a sialoglycopeptide that has demonstrated inhibitory effects on urothelial cell proliferation and a high sensitivity and specificity for IC/BPS symptoms and clinical findings. In this article, Grigorescu and colleagues review the urinary markers, possible future therapies for IC/BPS, and the clinical relevance and controversies regarding the diagnosis of IC/BPS.

[EFFECT OF SACRAL NEUROMODULATION ON OUTCOME MEASURES AND URINE CHEMOKINES IN INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME PATIENTS.](#)

Peters KM, Jayabalan N, Bui D, Killinger K, Chancellor M, Tyagi P. Low Urin Tract Symptoms. 2015 May;7(2):77-83. doi: 10.1111/luts.12054. Epub 2014 Mar 17. PMID: 26663686

Sacral neuromodulation (SNM) may improve interstitial cystitis/painful bladder syndrome (IC/BPS) symptoms of urinary frequency, urgency and perhaps even pain, but objective measures of improvement are lacking. Peters and colleagues evaluated the potential for urinary chemokines to serve as measures of treatment response over time to SNM. Women with IC/BPS undergoing SNM consented for this study. Three-day bladder/pain diaries were collected at baseline and validated Interstitial Cystitis Symptom Problem Index (ICSPI) scores and mid-stream urine specimens were collected at baseline and at 24 weeks after successful implant. Collected urine was screened for infection by dipstick and analyzed for chemokines by luminex xMAP analysis. The authors concluded that concomitant decrease in urine levels of chemokines especially MCP-1 was associated with treatment response of SNM. These results support the role of chemokines as downstream effectors of neuromodulation response and could serve as potential non-invasive measures of treatment response.

SACRAL NEUROMODULATION FOR GENITOURINARY PROBLEMS.

Banakhar M, Hassouna M. Prog Neurol Surg. 2015 Sep;29:192-9. doi: 10.1159/000434671. Epub 2015 Sep 4. PMID: 26394134

Sacral neuromodulation (SNM) is a minimally invasive therapeutic option for many voiding dysfunction conditions. It is approved by the US FDA for refractory overactive bladder with and without incontinence and nonobstructive retention. Since SNM has shown a favorable response for these approved indications, other therapeutic applications have been proposed for various conditions such as painful bladder syndrome, chronic pelvic pain and neurological voiding dysfunction in both adult and pediatric age groups. SNM therapy with the most commonly used dedicated SNM device (InterStim) involves insertion of electrode(s) in the third and/or fourth sacral foramen next to the nerve root. The electrode is then connected to a battery-operated pulse generator. All patients need to have a test trial period before definitive device insertion. Here the authors discuss SNM therapy in functional urinary disorders and the technique of device insertion with the potential pitfalls.

TANEZUMAB REDUCES PAIN IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND PATIENTS WITH NON-UROLOGICAL ASSOCIATED SOMATIC SYNDROMES.

Nickel JC, Mills IW, Crook TJ, Jorga A, Smith MD, Atkinson G, Krieger JN. J Urol. 2015 Nov 11. pii: S0022-5347(15)05216-7. doi: 10.1016/j.juro.2015.10.178. [Epub ahead of print] PMID: 26576710

Nickel and colleagues performed pooled analyses from 3 small, clinical trials of tanezumab in patients with urologic chronic pelvic pain, including chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and interstitial cystitis/bladder pain syndrome (IC/BPS), to identify patient subpopulations more likely to benefit from tanezumab treatment. They found that women with IC/BPS and patients with symptoms suggesting concomitant presence of non-urological associated somatic syndromes were more likely to experience significant pain reduction with tanezumab than with placebo therapy. In contrast, no difference was reported in response between tanezumab and placebo therapy for men with CP/CPPS symptoms only.

RECOMMENDATIONS TO THE PRIMARY CARE PRACTITIONERS AND THE PATIENTS FOR MANAGING PELVIC PAIN, ESPECIALLY IN PAINFUL BLADDER SYNDROME FOR EARLY AND BETTER PROGNOSIS.

Chung KJ, Han AN, Kim KH. J Exerc Rehabil. 2015 Oct 30;11(5):251-4. doi: 10.12965/jer.150226. eCollection 2015. PMID: 26535214

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Painful bladder syndrome (PBS) is a common disease presenting with chronic pelvic pain and discomfort with at least one urinary symptom with no identifiable cause. The etiology is still unknown, and the medication has limited effects on pelvic pain or other urinary symptoms. This article presents advanced insight regarding the approach to PBS, particularly pelvic pain for primary care practitioners and patients. Chung and colleagues suggest six tips for medical staff and suspected patients for easy diagnosis and proper treatment of pelvic pain. These six tips cover: Self-awareness of the disease; immediate urine culture test; specifying the location of pain urinary incontinence; frequency, or urgency without functional disorder of an overactive bladder helpful dietary control; complementary, and alternative medicine, and finding an expert. These tips might be helpful in

advancing the schematic approach and in achieving better prognosis of PBS. Further study should be conducted to achieve better treatment for this disease, including development of a definitive test and diagnosis.

COMPLEMENTARY THERAPIES FOR BLADDER PAIN SYNDROME: A SYSTEMATIC REVIEW.

Verghese TS, Riordain RN, Champaneria R, Latthe PM. Int Urogynecol J. 2015 Dec 7. [Epub ahead of print] PMID: 26642800

The purpose of this systematic review was to assess the effectiveness of various complementary therapies available for treatment. This review was conducted in adherence with Preferred Reporting Items for Systematic Reviews. Eligibility consisted of women with bladder pain syndrome, an intervention of alternative/complementary therapies and an outcome of improvement of symptoms. Information regarding study characteristics and primary outcomes was collated. A total of 1,454 citations were identified, 11 studies fulfilled the inclusion criteria (4 randomised control trials [RCTs] and 7 prospective studies). The key interventions studied were acupuncture, relaxation therapy, physical therapy, hydrogen-rich therapy, diet and nitric oxide synthetase. Therapies with the potential for benefit in patients with bladder pain syndrome are dietary management, acupuncture and physical therapy. These findings were obtained from small studies and hence caution is advised. Robustly designed multicentre RCTs on these complementary therapies are needed to guide patients and clinicians.

CORRELATION BETWEEN BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS AND PELVIC INFLAMMATORY DISEASE.

Chung SD, Chang CH, Hung PH, Chung CJ, Muo CH, Huang CY. Medicine (Baltimore). 2015 Nov;94(46):e1878. doi: 10.1097/MD.0000000000001878. PMID: 26579800

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Pelvic inflammatory disease (PID) has been investigated in Western countries and identified to be associated with chronic pelvic pain and inflammation. Bladder pain syndrome/interstitial cystitis (BPS/IC) is a complex syndrome that is significantly more prevalent in women than in men. Chronic pelvic pain is a main symptom of BPS/IC, and chronic inflammation is a major etiology of BPS/IC. This study from Taiwan aimed to investigate the correlation between BPS/IC and PID using a population-based dataset. Chung and colleagues constructed a case-control study from the Taiwan National Health Insurance program. The case cohort comprised 449 patients with BPS/IC, and 1796 randomly selected subjects (about 1:4 matching) were used as controls. A Multivariate logistic regression model was constructed to estimate the association between BPS/IC and PID. Of the 2245 sampled subjects, a significant difference was observed in the prevalence of PID between BPS/IC cases and controls. Multivariate logistic regression analysis revealed that the odds ratio (OR) for PID among cases was 3.69 (95% confidence interval [CI]: 2.89-4.71). Furthermore, the ORs for PID among BPS/IC cases were 4.52, 4.31, 3.00, and 5.35 in the <35, 35-49, 50-64, and >65 years age groups, respectively, after adjusting for geographic region, irritable bowel syndrome, and hypertension. Joint effect was also noted, specifically when patients had both PID and irritable bowel disease with OR of 10.5 (95% CI: 4.88-22.50). This study demonstrated a correlation between PID and BPS/IC. Clinicians treating women with PID should be alert to BPS/IC-related symptoms in the population.

URETHRAL PAIN SYNDROME

[URETHRAL PAIN SYNDROME: FACT OR FICTION - AN UPDATE].

[Article in German]

Dreger NM, Degener S, Roth S, Brandt AS, Lazica DA. Urologe A. 2015 Sep;54(9):1248-1255. PMID: 26337167

Urethral pain syndrome is a symptom complex including dysuria, urinary urgency and frequency, nocturia and persistent or intermittent urethral and/or pelvic pain in the absence of proven infection. These symptoms overlap with several other conditions, such as interstitial cystitis/bladder pain syndrome and overactive bladder. Urethral pain syndrome may occur in men but is more frequent in women. The exact etiology is unknown but infectious and psychogenic factors, urethral spasms, early interstitial cystitis, hypoestrogenism, squamous metaplasia as well as gynecological risk factors are discussed. These aspects should be ruled out or confirmed in the diagnostic approach. Despite the assumption of a multifactorial etiology, pathophysiologically there is a common pathway: dysfunctional epithelium of the urethra becomes leaky which leads to bacterial

and abacterial inflammation and ends in fibrosis due to the chronic impairment. The therapeutic approach should be multimodal using a trial and error concept: general treatment includes analgesia, antibiotics, alpha receptor blockers and muscle relaxants, antimuscarinic therapy, topical vaginal estrogen, psychological support and physical therapy. In cases of nonresponding patients intravesical and/or surgical therapy should be considered. The aim of this review by Dreger and colleagues from Germany is to summarize the preliminary findings on urethral pain syndrome and to elucidate the diagnostic and therapeutic options.

KETAMINE CYSTITIS

POSSIBLE PATHOPHYSIOLOGY OF KETAMINE-RELATED CYSTITIS AND ASSOCIATED TREATMENT STRATEGIES

Jhang JF, Hsu YH, Kuo HC. Int J Urol. 2015 Sep;22(9):816-25. doi: 10.1111/iju.12841. Epub 2015 Jun 18. PMID: 26087832

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Ketamine-related cystitis is characterized by ketamine-induced urinary frequency and bladder pain. It has become a serious problem in recent years. The most typical grossly pathological bladder change with ketamine related cystitis is a contracted bladder and bladder wall thickening. Ulcerative cystitis with an easily bleeding mucosa is a common cystoscopic finding. Microscopically, the urothelium is denuded and is infiltrated by inflammatory cells, such as mast cells and eosinophils. The pathogenesis of ketamine-related cystitis is complicated and involves many different pathways. Past evidence suggests a direct toxic effect, bladder barrier dysfunction, neurogenic inflammation, immunoglobulin-E-mediated inflammation, overexpression of carcinogenic genes, abnormal apoptosis and nitric oxide synthase-mediated inflammation contribute to the pathogenesis of ketamine-related cystitis. The first step to managing ketamine-related cystitis is always asking patients to cease ketamine. Medical treatment might be helpful in patients with early ketamine-related cystitis and abstinence from ketamine. Several case studies showed that the intravesical installation of hyaluronic acid and intravesical injection of botulinum toxin type A were effective for symptom relief in selected patients. For patients with irreversible pathological change, such as contracted bladder, augmentation enterocystoplasty might be the only solution to increase bladder capacity and relieve intractable bladder pain.

EDITORIAL COMMENT TO POSSIBLE PATHOPHYSIOLOGY OF KETAMINE-RELATED CYSTITIS AND ASSOCIATED TREATMENT STRATEGIES

Chi-Fai Ng M.D. Article first published online: 7 JUL 2015. DOI: 10.1111/iju.12873

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CHRONIC (PELVIC) PAIN

PELVIC NEURALGIAS BY NEURO-VASCULAR ENTRAPMENT: ANATOMICAL FINDINGS IN A SERIES OF 97 CONSECUTIVE PATIENTS TREATED BY LAPAROSCOPIC NERVE DECOMPRESSION.

Possover M, Forman A. Pain Physician. 2015 Nov;18(6):E1139-43. PMID:26606029

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Some patients have pelvic, pudendal, or low lumbar pain radiating into the legs that is worse while sitting but differs from pudendal neuralgia. The purpose of this study from Aarhus, Denmark was to present a new clinical entity of neuropathic pelvic pain by pelvic neuro-vascular entrapment and to report on the locations of predilection for pelvic neurovascular entrapment. This was a prospective study in which 97 patients presenting with intractable pelvic neuropathic pain (pudendal pain, gluteal pain, vulvodynia, coccygodynia, and sciatic pain) underwent laparoscopic exploration with decompression of compressed pelvic somatic nerves. The population included 76 (78.3%) women and 21 men. Indication for laparoscopic exploration of pelvic nerves suspected to be involved in pain has been indicated after neuropelvic work up, pelvic neuro-magnetic resonance imaging (MRI) and Doppler-sonography. Pain evolution was recorded over 2 years after the procedure. Three entities were isolated: pudendal neuralgia by compression at the less sciatic notch, sacral radiculopathy at S2-4 by compression at the infracardinal level of the sacral plexus, and sciatica L5-S1/2 by compression at the greater sciatic notch. Pain was worse sitting (98%), during menstrual bleeding in women, and during Valsalva maneuver, but the pain did not wake the patients up at night and was not accompanied by neurologic dysfunctions. A decrease in VAS scores (> 50%) at 2 years' follow-up was observed in 86 patients

(88.6%). It was concluded that neuro-vascular entrapment is a pathophysiologic phenomenon implicated in several pelvic neuropathies. The most common are L5-S1 sciatica, pudendal neuralgia, and sacral radiculopathy. After intraoperative confirmation, laparoscopic exploration of the entire sacral plexus is essential to diagnose conflict. Laparoscopic decompression is a treatment of choice, based on the separation of the offending vessel from the nerves. Those procedures are safe, with a high success rate; the neuropelvic approach is essential in order to obtain good treatment results. The laparoscopic approach gives the possibility of reducing morbidity and improving results by providing wider insight into the operating field with smaller intraoperative injury.

CENTRAL AND PERIPHERAL PAIN GENERATORS IN WOMEN WITH CHRONIC PELVIC PAIN: PATIENT CENTERED ASSESSMENT AND TREATMENT.

Hoffman D. Curr Rheumatol Rev. 2015;11(2):146-66. PMID: 26088216

Women with chronic pelvic pain (CPP) often present without obvious cause on imaging studies, laboratory values or physical exam. Dysfunctional sensory processing in the central nervous system (CNS) may explain pain of unclear origin. Central sensitization (CS), a mechanism of centrally mediated pain, describes this abnormal processing of sensory information. Women with CPP often present with several seemingly unrelated symptoms. This can be explained by co-existing chronic pain syndromes occurring in the same patient. Central sensitization occurs in all of these pain syndromes, also described as dysfunctional pain syndromes, and thus may explain why several often occur in the same patient. Six of the most common pain disorders that co-exist in CPP include endometriosis, painful bladder syndrome/interstitial cystitis, vulvodynia, myofascial pain/ pelvic floor hypertonus, irritable bowel syndrome, and primary dysmenorrhea. Central pain generators, (pain originating from CS) and peripheral pain generators, (pain from local tissue damage), can both occur in each of these six conditions. These pain generators will be described. Chronic pain, specifically dysfunctional sensory processing, is recognized as a systemic disease process like diabetes to be managed as opposed to a local problem to be "fixed" or cured. A multi-disciplinary approach to assessment and treatment with a focus on improving emotional, physical and social functioning instead of focusing strictly on pain reduction is more effective in decreasing disability. This is best achieved by determining the patient's needs and perspective through a patient-centered approach. Algorithms for such an approach to assessment and treatment are outlined.

THE PELVIS AND BEYOND: MUSCULOSKELETAL TENDER POINTS IN WOMEN WITH CHRONIC PELVIC PAIN.

Sanses TV, Chelimsky G, McCabe NP, Zolnoun D, Janata J, Elston R, Buffington CA, Simpson P, Zhang L, Chelimsky T. Clin J Pain. 2015 Oct 21. [Epub ahead of print] PMID: 26491938

The purpose of this study was to determine the feasibility of a detailed pain sensitivity assessment using body wide musculoskeletal tender points (TPs) in women with different types of chronic pelvic pain (CPP) and compare phenotypic differences. Seventy women with CPP and 35 healthy women underwent musculoskeletal evaluation of TPs in the pelvic floor, abdomen, groin, inner thigh, and all 18 fibromyalgia (FM) TPs. Subjects scored elicited pain on a numeric rating scale (NRS). Tender point pain scores were used for intergroup comparison and intragroup correlation. Women with CPP were grouped as having either bladder pain syndrome (BPS, n=24) or myofascial pelvic pain (MPP, n=11) singularly or both concomitantly (BPS+MPP, n=35). Tender point pain scores for all evaluations were higher in women with CPP compared to healthy women (P<0.001). Women with BPS+MPP had elevated TP pain for each evaluation compared to women with BPS alone. Pelvic floor and FM TP scores correlated strongly in the MPP group, moderately in the BPS+MPP group, and weakly in the BPS alone group. While some moderate and strong correlations between different body locations were present in all three groups, only the BPS+MPP group showed moderate to strong correlations between all body TPs. Detailed musculoskeletal evaluation of women with CPP is feasible and well tolerated. Careful phenotyping differentiated BPS, MPP, and BPS+MPP groups. Attending to the differences between these groups clinically may lead to more effective treatment strategies and improved outcomes for patients with CPP.

PELVIC CONGESTION SYNDROME: THE CURRENT STATE OF THE LITERATURE.

Borghi C, Dell'Atti L. Arch Gynecol Obstet. 2015 Sep 24. [Epub ahead of print] PMID: 26404449 PMID: 26404449

Pelvic congestion syndrome is an uncommon poorly understood and frequently misdiagnosed disorder of the pelvic venous circulation, which causes chronic pelvic pain in women in premenopausal age. This condition has typical features, such as pelvic varicosities, pelvic pain worsened by prolonged standing, coitus, menstruation, and pregnancy. The precise etiology of this syndrome remains uncertain, and it is probably multifactorial. Valvular insufficiency, venous obstruction, and hormones all may play a role in the development of congestion of the pelvic veins. Pelvic pain and venous varices are often both present in premenopausal women, but not necessarily causally related. Furthermore, incompetent and dilated pelvic veins are a common finding in asymptomatic women. As such, it is challenging but important to determine which patients have chronic pelvic pain specifically related to pelvic congestion syndrome in order to treat them properly. Once the syndrome has been accurately diagnosed, medical, surgical, or minimally invasive endovascular treatments can improve symptoms in a high percentage of cases. This updated nonsystematic review of the literature from Italy explores the pathophysiology, clinical features, diagnostic investigations, and treatment option of this complex condition that affects young women with considerable implications for their daily social and psychological condition.

BLADDER SYMPTOMS AND URODYNAMIC OBSERVATIONS OF PATIENTS WITH ENDOMETRIOSIS CONFIRMED BY LAPAROSCOPY.

Panel P, Huchon C, Estrade-Huchon S, Le Tohic A, Fritel X, Fauconnier A. Int Urogynecol J. 2015 Sep 28. [Epub ahead of print] PMID: 26415858

Patients with deep infiltrating pelvic endometriosis (DIE) often describe having lower urinary tract symptoms (LUTS). Bladder pain syndrome in women is also often associated with endometriosis. In this study from France, Panel and colleagues aimed to describe the characteristics of LUTS and urodynamic observations in patients with posterior endometriosis versus those with posterior and anterior endometriosis. This was a prospective observational study of 30 patients from two gynecologic surgical settings with experience in DIE surgery. All patients underwent preoperative standardized investigation including detailed evaluation of LUTS and urodynamic studies. During surgery, endometriosis locations were recorded and correlated to symptoms and urodynamic observations. The authors found that endometriosis infiltrating the bladder wall is associated with painful bladder symptoms. Dysfunctional voiding suggests an impairment of the inferior hypogastric plexus by posterior DIE. Clinical preoperative evaluation of bladder function should be systematic; urodynamic tests could be of interest in selected patients with DIE. Endometriosis may be a major cause of bladder pain syndrome.

HORMONAL CONTRACEPTION AND PELVIC FLOOR FUNCTION: A SYSTEMATIC REVIEW.

Champaneria R, D'Andrea RM, Latthe PM. Int Urogynecol J. 2015 Sep 25. [Epub ahead of print] PMID: 26407563.

Hormonal contraceptive use is common practice worldwide. Although the effects of hormone treatments in the pelvic region are well established, there is no clear evidence regarding their effects on incontinence, bladder, bowel, vaginal and sexual symptoms in premenopausal women. Champaneria and colleagues from Birmingham, UK hypothesized that hormonal contraceptives affect pelvic floor function. They therefore performed a comprehensive systematic review of published studies to determine the influence of hormonal contraception on pelvic floor functions. Their results indicate that oral contraceptives may have an effect on pelvic floor function. They could increase the risk of painful bladder and vulvar vestibulitis, but their effect on dyspareunia is inconsistent. However, robustly collected prospective data to establish causal associations are needed.

CHRONIC FATIGUE

THE PREVALENCE OF SEVERE FATIGUE IN RHEUMATIC DISEASES: AN INTERNATIONAL STUDY.

Overman CL, Kool MB, Da Silva JA, Geenen R. Clin Rheumatol. 2015 Aug 15. [Epub ahead of print] PMID: 26272057

Fatigue is a common, disabling, and difficult-to-manage problem in rheumatic diseases. Prevalence estimates of fatigue within rheumatic diseases vary considerably. Data on the prevalence of severe fatigue across multiple rheumatic diseases using a similar instrument is missing. The aim of Overman and colleagues from the

Netherlands was to provide an overview of the prevalence of severe fatigue across a broad range of rheumatic diseases and to examine its association with clinical and demographic variables. Online questionnaires were filled out by an international sample of 6120 patients (88 % female, mean age 47) encompassing 30 different rheumatic diseases. Fatigue was measured with the RAND(SF)-36 Vitality scale. A score of ≤ 35 was taken as representing severe fatigue (90 % sensitivity and 81 % specificity for chronic fatigue syndrome). Severe fatigue was present in 41 to 57 % of patients with a single inflammatory rheumatic disease such as rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, Sjögren's syndrome, psoriatic arthritis, and scleroderma. Severe fatigue was least prevalent in patients with osteoarthritis (35 %) and most prevalent in patients with fibromyalgia (82 %). In logistic regression analysis, severe fatigue was associated with having fibromyalgia, having multiple rheumatic diseases without fibromyalgia, younger age, lower education, and language (French: highest prevalence; Dutch: lowest prevalence). In conclusion, one out of every two patients with a rheumatic disease is severely fatigued. As severe fatigue is detrimental to the patient, the near environment, and society at large, unraveling the underlying mechanisms of fatigue and developing optimal treatment should be top priorities in rheumatologic research and practice.

VULVODYNIA/VULVAL PAIN SYNDROME

DAILY ASSOCIATIONS BETWEEN MALE PARTNER RESPONSES, PAIN DURING INTERCOURSE, AND ANXIETY IN WOMEN WITH VULVODYNIA AND THEIR PARTNERS.

Rosen NO, Bergeron S, Sadikaj G, Delisle I. *J Pain*. 2015 Sep 23. pii: S1526-5900(15)00869-X. doi: 10.1016/j.jpain.2015.09.003. [Epub ahead of print] PMID: 26409115

Vulvodynia is a prevalent vulvovaginal pain condition that disrupts the sexual and psychological health of affected women and their partners. Cross-sectional and daily experience studies suggest that partner responses to this pain influence the psychological and sexual sequelae of affected couples. However, their daily impact on pain and anxiety remain unknown. Using a daily diary method, 69 women diagnosed with vulvodynia and their cohabiting partners reported on male partner responses to women's pain and anxiety symptoms on sexual intercourse days over eight weeks. Women also reported their pain during intercourse. Results indicated that women reported greater pain on days when they perceived higher solicitous and negative male partner responses, and on days when their male partner reported greater solicitous and lower facilitative responses. Women indicated higher anxiety symptoms on days when they perceived more negative male partner responses; men's anxiety symptoms were greater on days when they reported higher negative male partner responses. Targeting partner responses may enhance the quality and efficacy of interventions aimed at reducing pain in women with vulvodynia and couples' psychological distress. This article from Canada examines the daily associations between male partner responses, women's pain during intercourse, and anxiety in couples coping with vulvodynia. Targeting male partner responses may enhance the quality of interventions aimed at reducing women's pain and the psychological distress of couples coping with vulvodynia.

SJOGREN'S SYNDROME

MANAGING SJOGREN'S SYNDROME.

Grossman S, Tagliavini LB. *Home Healthc Now*. 2015 Oct;33(9):487-92. doi: 10.1097/NHH.000000000000295. PMID: 26418108

There are approximately 4 million Americans diagnosed with Sjogren's Syndrome. This article discusses the epidemiology, pathophysiology, diagnostics, and implications for home care clinicians who may encounter patients with this syndrome. Chronic pain is discussed as well as interventions to manage symptoms such as fatigue, dry eyes mouth and skin.

DIAGNOSIS OF SMALL FIBER NEUROPATHY: A COMPARATIVE STUDY OF FIVE NEUROPHYSIOLOGICAL TESTS.

Lefaucheur JP, Wahab A, Planté-Bordeneuve V, Sène D, Ménard-Lefaucheur I, Rouie D, Tebbal D, Salhi H, Créange A, Zouari H, Ng Wing Tin S. *Neurophysiol Clin*. 2015 Nov 17. pii: S0987-7053(15)00158-6. doi: 10.1016/j.neucli.2015.09.012. [Epub ahead of print] PMID: 26596193

The diagnosis of small fiber neuropathy (SFN) is a challenge for clinical neurophysiology. Conventional nerve conduction studies are inappropriate for this purpose and therefore various neurophysiological tests have been

proposed. In this study, Lefaucheur and colleagues compared the diagnostic value of five of these tests in 87 patients with clinically definite (n=33) or possible (n=54) SFN related to amyloid neuropathy secondary to transthyretin gene mutation or monoclonal gammopathy (n=30), primary Sjögren's syndrome (n=20), Fabry's disease (n=2), or unknown cause (n=35). Neurophysiological tests included quantitative sensory testing with determination of warm and cold detection thresholds (WDT, CDT), recording of laser-evoked potentials (LEP) and sympathetic skin responses (SSRs), and measurement of electrochemical skin conductance (ESC) using Sudoscan® device. All tests were performed at the four extremities (hands and feet). All patients with clinically definite SFN and 70% of the patients with possible SFN had at least one abnormal test. The LEP was the most sensitive test (altered in 79% of the patients with at least one abnormal test), followed by ESC (61%), WDT (55%), SSR (41%), and CDT (32%). The combination of LEP, assessing A-delta sensory fibers, WDT, assessing sensory C fibers, and ESC, assessing autonomic C fibers, appears a relevant approach for the diagnosis of SFN. Compared to SSR and CDT, these three tests, LEP, WDT, and ESC, had a significantly better diagnostic sensitivity and their combination further improved diagnostic accuracy.

TEMPOROMANDIBULAR PAIN DISORDER

[A SYSTEMATIC REVIEW OF THE COMORBIDITY BETWEEN TEMPOROMANDIBULAR DISORDERS AND CHRONIC FATIGUE SYNDROME.](#)

Robinson LJ, Durham J, Newton JL. *J Oral Rehabil.* 2015 Nov 9. doi: 10.1111/joor.12367. [Epub ahead of print] PMID: 26549386

The most common cause of chronic oro-facial pain is a group of disorders collectively termed temporomandibular disorders (TMDs). Chronic painful TMD is thought to be a 'central sensitivity syndrome' related to hypersensitivity of the nervous system, but the cause is unknown. A similar understanding is proposed for other unexplained conditions, including chronic fatigue syndrome (CFS). Exploring the comorbidity of the two conditions is a valuable first step in identifying potential common aetiological mechanisms or treatment targets. Robinson and colleagues from Newcastle upon Tyne conducted this systematic literature review. Studies were included if they recruited community or control samples and identified how many reported having both TMD and CFS, or if they recruited a sample of patients with either TMD or CFS and measured the presence of the other condition. The review highlights the limited standard of evidence addressing the comorbidity between oro-facial pain and CFS. There is a valuable signal that the potential overlap in these two conditions could be high. However, studies employing more rigorous methodology including standardised clinical assessments rather than self-report of prior diagnosis are needed.

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