

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 46, October 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:

- Review of ESSIC 2017
- Review of ICS 2017
- Review of Societal Impact of Pain (SIP) Symposium
- Pain Research Forum in partnership with IASP
- eUrogen – Urogenital diseases
- Publications
- Calendar of Upcoming Events
- Research Update
- Donations & Sponsoring

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

The 2017 annual meeting of ESSIC (International Society for the Study of BPS) held at the Hungarian Academy of Sciences in Budapest and chaired by Dr Sándor Lovász attracted over a hundred IC/BPS experts from around the world. However, it was not only a meeting of medical experts in the field, but also an opportunity for IC/BPS patient advocates from as far afield as Israel and India to meet and exchange experiences as well as learn about the latest developments and provide input on the patient point of view. This highlighted the need for all of us - the first generation of IC patient advocates - to find better ways of passing on our knowledge and know-how to the younger, upcoming generation, and perhaps most important of all to give them encouragement and support in their challenging and often daunting and overwhelming task.

A particularly welcome aspect of this year's meeting was the increased time allowed for discussion and questions after each session, thereby facilitating greater interaction and participation by attendees, including patient representatives.

In general terms, every presentation and every discussion session highlighted just how complex this bladder disease (or diseases) is and how relatively little we know. It is in fact a question of "the more we learn, the less we know"! Multi-centre studies are needed since there is a lack of reliable data in many areas.

[Click here](#) to read more... or go to IPBF website www.painful-bladder.org

REVIEW OF THE INTERNATIONAL CONTINENCE SOCIETY ANNUAL SCIENTIFIC MEETING 12-15 SEPTEMBER 2017, FLORENCE, ITALY.

The 47th annual scientific meeting of the International Continence Society (ICS) was held at Fortezza da Basso in the ancient and beautiful Italian city of Florence. It was good to see that the 2,766 delegates included a number of patient representatives. For all of us in the IC/BPS and chronic pelvic pain/hypersensitivity special interest group, the ICS annual meeting has become increasingly important not only as an invaluable source of information about new developments and insights, but also as a discussion forum. This year there were workshops, presentations and round table discussions in the field of chronic pelvic pain and IC/BPS.

- IPBF chair completes term on ICS Standardisation Steering Committee as patient representative in Florence

The ICS meeting in Florence was a special moment for IPBF chair Jane Meijlink since she retired after completion of her term (9 years) on the ICS Standardisation Steering Committee as patient representative. Jane was presented with a certificate of appreciation by Dr Bernie Haylen, chair of the ICS Standardisation Steering Committee. Jane said she was very grateful to the ICS for giving her this unique opportunity to learn so much about standardisation. This has helped a great deal in her work for the patient movement. She would like to encourage other patient representatives to get involved. Inaccurate names, definitions and diagnostic criteria can cause multiple problems for patients, including non-reimbursement of treatment. The IC/BPS patient world has experienced this first-hand. With increasing use of electronic systems and coding, it is now vital that patient representatives understand what standardisation is all about, realize why it is important to know how it works and that they should be fully involved in developments and changes. It is likewise important for societies, government bodies and national/international agencies involved in guidelines, criteria, standardised terminology, reimbursement and the scientific evaluation, supervision and safety monitoring of medicines to ensure that patient experts are consulted and involved to ensure that the diseases and disorders they are describing are truly the diseases and disorders as suffered by the “real” patients and not simply based on hypotheses or wishful thinking.

[Click here](#) to read more... or go to IPBF website www.painful-bladder.org

“STRUCTURED CO-OPERATION TO TACKLE THE SOCIETAL IMPACT OF PAIN”, 8-9 JUNE 2017, VALLETTA, MALTA

The 7th Societal Impact of Pain (SIP) Symposium was held in Malta, 7-9 June, 2017 and was attended by some 300 participants from more than 200 organisations, including healthcare professionals, pain advocacy groups, researchers and specialists in the field of pain as well as insurers, budget holders and European politicians. A substantial number of patient representatives from the IC/BPS world attended this symposium and held a separate meeting prior to the start. Working groups developed individual suggestions regarding the following issues:

1. Establish an EU platform on the societal impact of pain
2. Develop instruments to assess the societal impact of pain
3. Initiate policies addressing the impact of pain on employment
4. Prioritise pain within education for health care professionals, patients and the general public
5. Increase investment in research on the Societal Impact of Pain.

Martin Seychell, Deputy Director General in the Health and Food Safety's Directorate, announced in his speech at SIP 2017 that the European Commission is following SIP's lead and has launched the EU Health Policy Platform to build a bridge between health systems and policy makers. The societal impact of pain is also included in the platform. A further achievement of the SIP initiative is that the European Health Ministers have agreed that it is time to evaluate access to treatment for patients with chronic pain. [Click here](#) for further information and press release.

For further information about SIP: <https://www.sip-platform.eu>

TIME FOR A NEW CAMPAIGN FOR PUBLIC TOILETS

During the SIP meeting in Malta, the IPBF had an info table and took the opportunity to draw attention to the urgent need for more public toilets. This need recently received attention in the Dutch media when a woman was ultimately fined €90 (fine was initially € 140) in Amsterdam for urinating in public in sheer desperation. It turned out that the whole centre of Amsterdam has no more than 3 public toilets for women as opposed to some 35 for men! The judge ruled that she would have to pay up since women could perfectly well climb on top of a men's street urinal to urinate! The judge therefore did not feel it was necessary to have an equal number of toilets for men and women. The judge also added that the woman should have thought about going to the toilet before going out! The case once again underlines how difficult it is for any woman, particularly after closing time, and even more difficult for those with a bladder disorder. Time for a new campaign!

THE PAIN RESEARCH FORUM (PRF), THE PARENT ORGANIZATION OF RELIEF, HAS ANNOUNCED A MAJOR PARTNERSHIP WITH THE NON-PROFIT INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN (IASP)

The PRF will now fully merge with IASP and immediately benefit from IASP's established infrastructure, expertise and long-term commitment to advancing pain research. Read [more here](#). RELIEF pain research news: <http://relief.news/>

eUROGEN – UROGENITAL DISEASES

eUROGEN is one of the 24 European Reference Networks (ERN) approved and funded by the European Union (EU). ERNs are an exciting new form of cooperation at European level between healthcare providers with specialised expertise with the aim of improving care for patients with rare diseases or complex conditions. eUROGEN aims to improve diagnosis, create more equitable access to high-quality treatment and care for patients with rare urogenital diseases and complex conditions needing highly specialised surgery. See more: <http://eurogen-ern.eu/>

eUROGEN will work in partnership with the EAU in developing new clinical guideline for rare urogenital diseases and complex conditions. An overview of the existing guidelines and where there are gaps is currently being undertaken by eUROGEN and the EAU and, together with the input from patient organisations, new guidelines will be developed. Interstitial cystitis has not been forgotten and has been included in **Workstream 2: Functional urogenital conditions requiring highly specialised surgery**. See: <http://eurogen-ern.eu/patient-information/info-per-condition/>

PUBLICATIONS:

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 now available. For further information: <http://www.springer.com/gp/book/9783319484624>

PAIN 101: LOOKING TO THE BRAIN TO UNDERSTAND FIBROMYALGIA AND OTHER CHRONIC PAIN CONDITIONS

<http://relief.news/pain-101-looking-to-the-brain-to-understand-fibromyalgia-and-other-chronic-pain-conditions/>

Interesting article for those interested in chronic pain conditions.

CALENDAR OF UPCOMING EVENTS

INTERNATIONAL CONFERENCE ON MEDICAL CANNABIS AND CANNABINOIDS

22-24 November 2017

Corinthia Hotel Prague, Kongresová 1, Prague 4, 140 69, Czech Republic

<http://medical-cannabis-conference.com/2017/>

THE SECOND ANNUAL MEETING OF THE SOCIETY FOR PELVIC RESEARCH 2017

December 2-3, 2017 - Reno, NV, USA

<https://www.pelvicresearch.com/spr-2017-meeting.html>

2ND INTERNATIONAL CONGRESS ON THE MULTIDISCIPLINARY MANAGEMENT OF PELVIC FLOOR DISEASES

14-15 December 2017, Pisa, Galilei Hotel, Italy.

<https://www.pfdcongress.org/>

SUFU

SOCIETY OF URODYNAMICS, FEMALE PELVIC MEDICINE AND UROGENITAL RECONSTRUCTION

International Painful Bladder Foundation

2018 WINTER MEETING

February 27 - March 3, 2018, Hilton Austin, Austin, Texas, USA

<https://sufuorg.com/meetings.aspx>

EUROPEAN ASSOCIATION OF UROLOGY (EAU)2018

16-20 March 2018, Copenhagen, Denmark

<http://eau18.uroweb.org/>

JOINT MEETING OF THE 4th INTERNATIONAL CONSULTATION ON INTERSTITIAL CYSTITIS, JAPAN (ICICJ) AND THE ESSIC ANNUAL MEETING 2018,

16-17 April, 2018, Kyoto International Conference Center, Japan.

www.icicj.jp/en/meeting/2018/.

**INTERNATIONAL ALLIANCE OF PATIENTS' ORGANIZATIONS (IAPO)
8TH GLOBAL PATIENTS CONGRESS**

23 - 26 May 2018, Miami, USA.

<https://www.iapo.org.uk/>

AMERICAN UROLOGICAL ASSOCIATION (AUA) 2018

18-22 May 2018, San Francisco, CA, USA

www.aa2018.org

INTERNATION UROGYNECOLOGICAL ASSOCIATION (IUGA)

26-30 June 2018, Vienna, Austria

<https://iugameeting.org/>

INTERNATIONAL CONTINENCE SOCIETY ANNUAL SCIENTIFIC MEETING 2018

28-31 August 2018, Philadelphia, USA

www.ics.org/2018

IASP 17th WORLD CONGRESS ON PAIN

12-16 September 2018, Boston, USA

<https://www.iaspworldcongressonpain.org/>

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.

BRAIN SIGNATURE AND FUNCTIONAL IMPACT OF CENTRALIZED PAIN: A MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN (MAPP) NETWORK STUDY

Kutch J, Ichesco E Hampson, Johnson P, Labus J, Farmer M, Martucci K, Ness T, Deutsch G, Apkarian AV, Mackey SC, Klumpp DJ, Schaeffer AJ Rodriguez LV, Kreder KJ, Buchwald D, Andriole GL, Lai H, Mullins C, Kusek JW, Landis JR, Mayer EA, Clemens JQ, Clauw DJ, Harris RE, for the MAPP Research Network. Pain. 2017 Oct;158(10):1979-1991. PMID: 28692006

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

Chronic pain is often measured with a severity score that overlooks its spatial distribution across the body. This widespread pain is believed to be a marker of centralization, a central nervous system process that decouples pain perception from nociceptive input. Here, Kutch and colleagues investigated whether centralization is manifested at the level of the brain using data from 1079 participants in the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network (MAPP) study. Participants with a clinical diagnosis of urological chronic pelvic pain syndrome (UCPPS) were compared to pain-free controls and patients with fibromyalgia, the prototypical centralized pain disorder. Participants completed questionnaires capturing pain severity, function, and a body map of pain. A subset underwent functional and structural magnetic resonance imaging. Patients with UCPPS reported pain ranging from localized (pelvic) to widespread (throughout the body). Patients with widespread UCPPS displayed increased brain grey matter volume and functional connectivity involving sensorimotor and insular cortices. These changes translated across disease diagnoses as identical outcomes were present in patients with fibromyalgia but not pain-free controls. Widespread pain was also associated with reduced physical and mental function independent of pain severity. Brain pathology in patients with centralized pain is related to pain distribution throughout the body. These patients may benefit from interventions targeting the central nervous system.

THE ROLE OF C-FIBERS IN THE DEVELOPMENT OF CHRONIC PSYCHOLOGICAL STRESS INDUCED ENHANCED BLADDER SENSATIONS AND NOCICEPTIVE RESPONSES: A MULTIDISCIPLINARY APPROACH TO THE STUDY OF UROLOGIC CHRONIC PELVIC PAIN SYNDROME (MAPP) RESEARCH NETWORK STUDY.

Gao Y, Zhang R, Chang HH, Rodríguez LV. NeuroUrol Urodyn. 2017 Aug 9. doi: 10.1002/nau.23374. [Epub ahead of print] PMID: 28792095

The purpose of this MAPP Research Network Study was to evaluate C fiber-mediated changes in bladder sensation and nociception in an animal model of stress induced bladder hyperalgesia and urinary frequency. Female Wistar-Kyoto (WKY) rats were exposed to a chronic (10 days) water avoidance stress (WAS) and compared to controls. Rats were evaluated by cystometrogram (CMG) and visceromotor reflex (VMR) to bladder infusion with room temperature (RT) or cold saline. Cold saline activates afferent C-fibers via cold bladder receptors. To further evaluate bladder hyperalgesia, CMG and VMR were also obtained during RT isometric bladder distention (RT-iBD) at variable pressures. During RT infusion, WAS rats had significant decreases in pressure threshold (PT) and in the ratio of VMR threshold/maximum intravesical pressure (IVPmax), and a significant increase in VMR duration. Cold infusion also induced significant decreases in PT and in the ratio of VMR threshold/IVPmax in WAS rats. During RT-iBD, rats exposed to WAS showed a significant decrease in VMR latency and a significant increase in VMR area under the curve (AUC) compared to controls. The authors concluded that chronic WAS induced bladder hypersensitivity manifested by earlier voiding with earlier VMR appearance. Chronic stress also enhanced bladder nociceptive responses. WAS leads to increase responses to ice cold water infusion, implying a role of sensitized C-fibers and mechanoreceptors in WAS-induced bladder dysfunction and hypersensitivity.

ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR TREATMENT DECREASES BLADDER PAIN IN CYCLOPHOSPHAMIDE CYSTITIS: A MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN (MAPP) RESEARCH NETWORK ANIMAL MODEL STUDY.

Lai HH, Shen B, Vijairania P, Zhang X, Vogt SK, Gereau RW 4th. *BJU Int.* 2017 Jun 5. doi: 10.1111/bju.13924. [Epub ahead of print] PMID: 28581681

The purpose of this study was to investigate whether treatment with anti-vascular endothelial growth factor (VEGF)-neutralizing antibodies can reduce pain and voiding dysfunction in the cyclophosphamide (CYP) cystitis model of bladder pain in mice. Adult female mice received anti-VEGF-neutralizing antibodies or saline (control) pre-treatment, followed by CYP (150 mg/kg i.p.) to induce acute cystitis. Pelvic nociceptive responses were assessed by applying von Frey filaments to the pelvic area. Spontaneous micturition was assessed using the void spot assay. Systemic anti-VEGF-neutralizing antibody treatment significantly reduced the pelvic nociceptive response to CYP cystitis compared with control (saline). In the anti-VEGF pre-treatment group, there was a significant increase in pelvic hypersensitivity, measured by the area under the curve (AUC) using von Frey filaments at 5 h post-CYP administration; however, by 48 h and 96 h post-CYP administration, pelvic hypersensitivity had reduced by 54% and 47%, respectively, compared with the 5 h post-CYP administration time point, and were no longer significantly different from baseline. There was no difference in urinary frequency and mean voided volume between the two pre-treatment groups. It was concluded that systemic blockade of VEGF signalling with anti-VEGF-neutralizing antibodies was effective in reducing pelvic/bladder pain in the CYP cystitis model of bladder pain. The authors are of the opinion that their data support the further investigation of the use of anti-VEGF antibodies to manage bladder pain or visceral pain.

CLINICAL AND PSYCHOSOCIAL PREDICTORS OF UROLOGIC CHRONIC PELVIC PAIN SYMPTOM CHANGE OVER ONE YEAR: A PROSPECTIVE STUDY FROM THE MAPP RESEARCH NETWORK.

Naliboff BD, Stephens AJ, Lai HH, Griffith JW, Clemens JQ, Lutgendorf S, Rodriguez LV, Newcomb C, Sutcliffe S, Guo W, Kusek JW, Landis JR; *MAPP Research Network.* *J Urol.* 2017 May 18. pii: S0022-5347(17)71368-7. doi: 10.1016/j.juro.2017.05.065. [Epub ahead of print] PMID: 28528930

The purpose of this study was to examine baseline clinical and psychosocial characteristics that predict 12-month symptom change in men and women with urologic chronic pelvic pain syndromes (UCPPS). 221 female and 176 male UCPPS patients were recruited from 6 academic medical centres in the United States and evaluated at baseline with a comprehensive battery of symptom, psychosocial, and illness-impact measures. Based on biweekly symptom reports, a functional clustering procedure classified participant's outcome as worse, stable, or improved on pain and urinary symptom severity. Cumulative logistic modelling was used to examine individual predictors associated with symptom change as well as multiple predictor combinations and interactions. About 60% of participants had stable symptoms with smaller numbers (13% to 22%) showing clear symptom worsening or improvement. For both pain and urinary outcomes, the extent of widespread pain, amount of non-urological symptoms and poorer overall health were predictive of worsening outcomes. Anxiety, depression and general mental health were not significant predictors of outcomes, but pain catastrophizing and self-reported stress were associated with pain outcome. Prediction models did not differ between men and women and for the most part were independent of symptom duration and age. These results demonstrate for the first time in a large multisite prospective study that presence of widespread pain, non-urological symptoms and poorer general health are risk factors for poorer pain and urinary outcomes in both men and women. The results point to the importance of broad based assessment in UCPPS and future studies of mechanisms that underlie these findings.

CHARACTERIZATION OF WHOLE BODY PAIN IN UROLOGICAL 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.* *Urol.* 2017 Sep;198(3):622-631. doi: 10.1016/j.juro.2017.03.132. Epub 2017 Mar 31. PMID: 28373134

Lai and colleagues characterized the location and spatial distribution of whole body pain in patients with urological chronic pelvic pain syndrome using a body map. They also compared the severity of urinary symptoms, pelvic pain, nonpelvic pain and psychosocial health among patients with different pain patterns. A total of 233 women and 191 men with urological chronic pelvic pain syndrome enrolled in a multicenter, 1-year observational study completed a battery of baseline measures, including a body map describing the location of pain during the last week. Participants were categorized with pelvic pain if they reported pain in the abdomen and pelvis only. Participants who reported pain beyond the pelvis were further divided into 2 subgroups based

on the number of broader body regions affected by pain, including an intermediate group with 1 or 2 additional regions outside the pelvis and a widespread pain group with 3 to 7 additional regions. Of the 424 enrolled patients 25% reported pelvic pain only and 75% reported pain beyond the pelvis, of whom 38% reported widespread pain. Participants with a greater number of pain locations had greater nonpelvic pain severity, sleep disturbance, depression, anxiety, psychological stress and negative affect scores, and worse quality of life. No difference in pelvic pain and urinary symptom severity was observed according to increasing pain distribution. Three-quarters of the men and women with urological chronic pelvic pain syndrome reported pain outside the pelvis. Widespread pain was associated with greater severity of nonpelvic pain symptoms, poorer psychosocial health and worse quality of life but not with worse pelvic pain or urinary symptoms.

EFFECTS OF WATER AVOIDANCE STRESS ON PERIPHERAL AND CENTRAL RESPONSES DURING BLADDER FILLING IN THE RAT: A MULTIDISCIPLINARY APPROACH TO THE STUDY OF UROLOGIC CHRONIC PELVIC PAIN SYNDROME (MAPP) RESEARCH NETWORK STUDY.

Wang Z, Chang HH, Gao Y, Zhang R, Guo Y, Holschneider DP, Rodriguez LV. *PLoS One.* 2017 Sep 8;12(9):e0182976. doi: 10.1371/journal.pone.0182976. eCollection 2017. PMID: 28886046

According to this MAPP team, stress plays a role in the exacerbation and possibly the development of functional lower urinary tract disorders. Chronic water avoidance stress (WAS) in rodents is a model with high construct and face validity to bladder hypersensitive syndromes, such as interstitial cystitis/bladder pain syndrome (IC/BPS), characterized by urinary frequency and bladder hyperalgesia and heightened stress responsiveness. Given the overlap of the brain circuits involved in stress, anxiety, and micturition, Wang and colleagues evaluated the effects chronic stress has on bladder function, as well as its effects on regional brain activation during bladder filling. They are of the opinion that their findings show a visceral hypersensitivity during bladder filling in WAS animals, as well as increased engagement of portions of the micturition circuit responsive to urgency, viscerosensory perception and its relay to motor regions coordinating imminent bladder contraction. Results are consistent with recent findings in patients with interstitial cystitis, suggesting that WAS may serve as an animal model to elucidate the mechanisms leading to viscerosensitive brain phenotypes in humans with IC/BPS.

IC/BPS/HSB BASIC SCIENCE, DIAGNOSIS AND TREATMENT

DIAGNOSTIC VALUE OF URINARY CXCL10 AS A BIOMARKER FOR PREDICTING HUNNER TYPE INTERSTITIAL CYSTITIS.

Niimi A, Igawa Y, Aizawa N, Honma T, Nomiya A, Akiyama Y, Kamei J, Fujimura T, Fukuhara H, Homma Y. *NeuroUrol Urodyn.* 2017 Oct 19. doi: 10.1002/nau.23431. [Epub ahead of print] PMID: 29048741

Niimi and colleagues investigated the feasibility of chemokines and cytokines potentially elevated in the bladder tissue of Hunner type interstitial cystitis(HIC) as urinary markers for distinguishing HIC from non-Hunner type interstitial cystitis (NHIC). Urine specimens were collected from 41 HIC patients, 25 NHIC patients, and 31 healthy volunteers (control). The supernatants of urine specimens were subjected to ELISA kits for measurements of 10 cytokines and chemokines, whose gene expression was known to be elevated in HIC bladder tissue. Urinary levels normalized by urinary creatinine (Cr) concentration were compared among three groups. Efficiency in differentiating IC and IC subtypes was explored by ROC analysis. The correlation of marker levels with symptom severity, assessed by O'Leary-Sant's symptom index (OSSI) and problem index (OSPI), was examined. The urinary levels of CXCL10 and NGF were significantly higher in HIC than NHIC. CXCL10 and NGF differentiated HIC against NHIC with AUC of 0.78 and 0.68, respectively. Combination of CXCL10 and NGF levels yielded an AUS of 0.81. The CXCL10 cut-off of 53.2 pg/mg Cr had sensitivity of 46.1%, specificity of 93.7%, positive predictive value of 97.7%, and negative predictive value of 60.0%. The urinary level of other cytokines showed no significant difference between HIC and NHIC. Significant correlation with symptoms was detected for CXCL10 alone. The results suggested that increased urinary level of CXCL10 combined with or without high NGF level could be a promising supplementary biomarker for differentiating HIC from NHIC with modest sensitivity and high specificity.

DEVELOPMENT OF NOVEL AND NON-INVASIVE DIAGNOSTIC MARKERS FOR LOWER URINARY TRACT SYMPTOMS USING UROTHELIAL CELLS IN VOIDED URINE.

Shimura H, Mitsui T, Tsuchiya S, Miyamoto T, Ihara T, Kira S, Nakagomi H, Sawada N, Imai Y, Mochizuki T, Takeda M. *Neurourol Urodyn*. 2017 Oct 17. doi: 10.1002/nau.23436. [Epub ahead of print] PMID: 29044760

Shimura and colleagues evaluated the association between lower urinary tract symptoms (LUTS) and the expression of connexin (Cx) and transient receptor potential (TRP) channel on urothelial cells non-invasively collected from voided urine in humans. A total of 55 patients (36 males and 19 females, median age: 71 years old), who were followed up at University of Yamanashi Hospital, were enrolled in the present study. Urothelial cells were collected from voided urine of patients, and the mRNA expression of each subtype of Cxs and TRP channels was measured using quantitative real-time reverse transcription polymerase chain reaction. They then analyzed the correlation between the expression of Cxs and TRP channels and symptom scores in International Prostate Symptom Score and Overactive Bladder Symptom Score, in addition to Interstitial Cystitis Symptom Index (ICSI) from only interstitial cystitis (IC) patients. The expressions of Cxs and TRP channels on urothelial cells in voided urine could be related to LUTS. Further analysis of urothelial cells in voided urine has the potential to reveal the mechanism of the LUTS and develop new markers with non-invasive methods.

[INTRA-TRIGONAL ONABOTULINUM TOXIN A IMPROVES BLADDER SYMPTOMS AND QUALITY OF LIFE IN BLADDER PAIN SYNDROME /INTERSTITIAL CYSTITIS PATIENTS - A PILOT, SINGLE CENTRE, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.](#)

Pinto R, Costa D, Morgado A, Pereira P, Charrua A, Silva J, Cruz F. *J Urol*. 2017 Oct 12. pii: S0022-5347(17)77723-3. doi: 10.1016/j.juro.2017.10.018. [Epub ahead of print] PMID: 29031769

Pinto and colleagues compared the efficacy and safety of trigonal injections of onabotulinumtoxinA and saline in Bladder Pain Syndrome/Interstitial Cystitis patients. OnabotulinumtoxinA 100U caused significant and clinically relevant improvements in bladder pain and quality of life in Bladder Pain Syndrome/Interstitial Cystitis patients refractory to common therapy and was well tolerated.

[BLADDER PAIN IN AN LL-37 INTERSTITIAL CYSTITIS AND PAINFUL BLADDER SYNDROME MODEL.](#)

Jia W, Schults AJ, Jensen MM, Ye X, Alt JA, Prestwich GD, Oottamasathien S. *Am J Clin Exp Urol*. 2017 Sep 1;5(2):10-17. eCollection 2017. PMID: 29034266

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The objective of this study was to evaluate the pain response in an LL-37 induced murine model for interstitial cystitis/painful bladder syndrome (IC/PBS). The authors particularly sought to characterize the dose dependence, time-course, and relationship of LL-37 induced bladder inflammation and pain. Interestingly, pain responses did not attenuate across time but increased significantly after 5 and 7 days. Comparison with MPO data suggested that pain responses could be independent of inflammation. They demonstrated within their LL-37 induced IC/PBS model that pain occurs in a dose-dependent fashion, pain responses persist beyond the initial point of insult, and their dose response and time course experiments demonstrated that pain was independent of inflammation.

[SIGNIFICANT LINKAGE EVIDENCE FOR INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME ON CHROMOSOME 3.](#)

Allen-Brady K, Rowe K, Cessna M, Lenherr S, Norton P. *J Urol*. 2017 Jul 19. pii: S0022-5347(17)77178-9. doi: 10.1016/j.juro.2017.07.068. [Epub ahead of print] PMID: 28734863

Interstitial cystitis/painful bladder syndrome (IC/PBS) is a chronic pelvic pain condition with unknown etiology. The authors hypothesized that related IC/PBS cases were more likely to have a genetic etiology. The purpose of this study was to perform a genetic linkage analysis. IC/PBS cases were identified using diagnostic codes linked to a population-based genealogy resource (Utah Population Database) and electronic medical records. While the etiology of IC/PBS is unknown, this study provides evidence that a genetic variant(s) on chromosome 3, and possibly chromosomes 1, 4, 9, and 14, contribute to IC/PBS predisposition. Sequence analysis of affected cases in identified pedigrees may provide insight into genes contributing to IC/PBS.

[EXPRESSION PROFILE OF UROTHELIAL TRANSCRIPTION FACTORS IN BLADDER BIOPSIES WITH INTERSTITIAL CYSTITIS.](#)

Kaga K, Inoue KI, Kaga M, Ichikawa T, Yamanishi T. *Int J Urol*. 2017 Aug;24(8):632-638. doi: 10.1111/iju.13391. Epub 2017 Jun 18. PMID: 28626955

The aim of this study by Kaga and colleagues from Japan was to characterize interstitial cystitis pathology based on the expression profile of urothelial tissue-specific master transcription factors. Bladder carcinoma cell lines derived from the urothelial stem cells (epithelial or mesenchymal) were used to identify candidate urothelial master transcription factors. Gene expression was measured with quantitative reverse transcription polymerase chain reaction. The authors concluded that urothelial master transcription factors could serve as novel diagnostic markers and potentially explain the molecular pathology of interstitial cystitis.

INTERSTITIAL CYSTITIS INTRAVESICAL THERAPY.

Ha T, Xu JH. Transl Androl Urol. 2017 Jul;6(Suppl 2):S171-S179. doi: 10.21037/tau.2017.06.18. PMID: 28791236

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

Interstitial cystitis (IC) is a progressive bladder disorder that presents with symptoms of bladder urgency, frequency and pain. The aetiology of the disease remains uncertain, but it is postulated that there is an initial infective insult which damages the glycosaminoglycan (GAG) layer of the bladder urothelium. This defect allows an influx of ions, particularly potassium, which initiates an inflammatory reaction in the bladder wall, which incites the symptoms described above. Treatment initially involves behavioural and oral medication, with second line being intravesical instillation therapy. Treatment strategies focus on restoring lower urinary tract epithelial function, inhibiting neural activation, controlling allergies and relieving symptoms. This review from Australia discusses current intravesical therapy, as well as what lies on the horizon for intravesical therapy in IC.

FLOATING HYDROGEL WITH SELF-GENERATING MICRO-BUBBLES FOR INTRAVESICAL INSTILLATION.

Lin T, Zhao X, Zhang Y, Lian H, Zhuang J, Zhang Q, Chen W, Wang W, Liu G, Guo S, Wu J, Hu Y, Guo H. Materials (Basel). 2016 Dec 12;9(12). pii: E1005. doi: 10.3390/ma9121005. PMID: 28774123

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Intravesical instillation is the main therapy for bladder cancer and interstitial cystitis. However, most drug solutions are eliminated from bladder after the first voiding of urine. To solve this problem, Lin and colleagues from China proposed a floating hydrogel with self-generating micro-bubbles as a new delivery system.

A SYSTEMATIC REVIEW OF THE LITERATURE ON CYSTODISTENSION IN BLADDER PAIN SYNDROME.

Olson LE, Dyer JE, Haq A, Ockrim J, Greenwell TJ. Int Urogynecol J. 2017 May 26. doi: 10.1007/s00192-017-3355-y. [Epub ahead of print] PMID: 28550461

There is significant variability in technique for cystodistension and an international discrepancy in the role in its treatment of bladder pain syndrome (BPS). In this review study from the UK, the authors evaluate the evidence base for the use of cystodistension for BPS with particular reference to patient-related outcomes. A review of the literature was performed using the search terms cystodistension and hydrodistension of the bladder using the PubMed database on 6 October 2016. The authors concluded that cystodistension is increasingly popular, despite a weak evidence base by current standards. The quality of available evidence falls below the level that would be expected of a new intervention. This review highlights the need for cystodistension to be further investigated with randomised control trials.

EFFICACY, SIDE EFFECTS, AND MONITORING OF ORAL CYCLOSPORINE IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Crescenze IM, Tucky B, Li J, Moore C, Shoskes D. Urology. 2017 May 18. pii: S0090-4295(17)30509-5. doi: 10.1016/j.urology.2017.05.016. [Epub ahead of print] PMID: 28528859

The purpose of this study was to evaluate the efficacy of oral Cyclosporine A (CyA) in treatment of refractory interstitial cystitis/bladder pain syndrome (IC/BPS) and assess safety using drug level and renal function monitoring. Patients with IC/BPS who failed at least 2 prior treatments were enrolled in an open-label study of oral CyA. Medication was started at 3 mg/kg divided twice daily for 3 months. Dose was adjusted based on side effects and drug level measured 2 hours after the morning dose (C2). Primary end point was marked or moderate improvement of global response assessment (GRA) or >50% improvement on the Interstitial Cystitis Symptom Index (ICSI) or Interstitial Cystitis Problem Index (ICPI) at 3 months. The authors concluded that per AUA guidelines Cyclosporine A can be effective in a proportion of patients with refractory IC/BPS. Patients with HL are more likely to benefit. Monitoring of C2 rather than trough levels, can lead to dose reduction thereby minimizing toxicity.

DISULFIDE HIGH MOBILITY GROUP BOX-1 CAUSES BLADDER PAIN THROUGH BLADDER TOLL-LIKE RECEPTOR 4.

Ma F, Kouzoukas DE, Meyer-Siegler KL, Westlund KN, Hunt DE, Vera PL. BMC Physiol. 2017 May 25;17(1):6. doi: 10.1186/s12899-017-0032-9. PMID: 28545586

Bladder pain is a prominent symptom in several urological conditions (e.g. infection, painful bladder syndrome/interstitial cystitis, cancer). Understanding the mechanism of bladder pain is important, particularly when the pain is not accompanied by bladder pathology. Stimulation of protease activated receptor 4 (PAR4) in the urothelium results in bladder pain through release of urothelial high mobility group box-1 (HMGB1). HMGB1 has two functionally active redox states (disulfide and all-thiol) and it is not known which form elicits bladder pain. Therefore, Ma and colleagues from the USA investigated whether intravesical administration of specific HMGB1 redox forms caused abdominal mechanical hypersensitivity, micturition changes, and bladder inflammation in female C57BL/6 mice 24 hours post-administration. The authors concluded that the disulfide form of HMGB1 mediates bladder pain directly (not secondary to inflammation or injury) through activation of TLR4 receptors in the bladder. Thus, TLR4 receptors are a specific local target for bladder pain.

SENSORY MAPPING OF PELVIC DERMATOMES IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Sanses T, McCabe P, Zhong L, Taylor A, Chelimsky G, Mahajan S, Buffington T, Hijaz A, Ialacci S, Janata J, Chelimsky T. Neurourol Urodyn. 2017 Jun 19. doi: 10.1002/nau.23330. [Epub ahead of print] PMID: 28628232

The aim of this study by Sanses and colleagues from the USA was to describe a sensory map of pelvic dermatomes in women with Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS). They hypothesized that if IC/BPS involves changes in central processing, then women with IC/BPS will exhibit sensory abnormalities in neurologic pelvic dermatomes. Women with IC/BPS and healthy controls underwent neurologic examination that included evaluation of sharp pain sensitivity and vibration in dermatomes T12, L1, L2, S1-5. Peripheral nervous system sensitivity to pressure, vibration, and pinprick were scored using numeric rating scales (NRS). Bilateral comparisons were made with Wilcoxon signed-rank test and comparisons between groups were made by the Mann-Whitney U-test. Total of 74 women with IC/BPS and 36 healthy counterparts were included. IC/BPS and control groups had similar age, respectively. Women with IC/BPS reported hyperalgesia (elevated bilateral NRS pain intensity) in all pelvic dermatomes compared to healthy controls. S4-S5 region had the highest pain intensity in all participants. All IC/BPS participants exhibited vibration sensation hypoesthesia, at least unilaterally, in all of the pelvic dermatomes except L1 compared to healthy controls. This detailed map of neurologic pelvic dermatomes in women with IC/BPS found hyperalgesia in all pelvic dermatomes, and some evidence of vibration sensation hypoesthesia, compared to healthy controls. These findings support the hypothesis that IC/BPS may involve changes in central signal processing biased towards nociception.

SURGICAL TECHNIQUE FOR REMOVAL OF TINED LEAD FOR INTERSTIM.

Okhunov Z, Farhan B, Ahmed A, Pulford C, Ghoniem G. Can J Urol. 2017 Aug;24(4):8918-8920. PMID: 28832311

Okhunov and colleagues aimed to introduce their technique describing the removal of a chronic implanted tined-lead in patients with a sacral neuromodulator implant. They performed a retrospective review of patients who had chronic sacral neuromodulator (InterStim) implanted by a single surgeon from 2001 through 2015. This simple surgical technique was developed and successfully performed to remove the leads. Primary reasons for removal were elective due to poor symptoms control and failure to maintain response or lead migration. Primary indications for sacral nerve stimulation were overactive bladder in 16 (64%), mixed incontinence in 6 (24%), urinary retention in 2 (8%), and interstitial cystitis 3 (12%). Mean implant duration was 24.2 (0.5-90) months. The existing tined lead was removed and replaced in 11 (44%) patients while the remaining 14 (56%) underwent complete removal of the unit without subsequent replacement. Successful lead removal without complications was achieved in 24 (96%) patients. The authors concluded that this minimally invasive technique is a simple, safe, and effective method of removing chronic implanted tined leads en bloc.

EFFICACY OF BOTULINUM TOXIN A FOR THE TREATMENT OF BLADDER PAIN SYNDROME: A SYSTEMATIC REVIEW.

[Article in English, Spanish]

Ochoa Vargas DC, García Perdómo HA. *Actas Urol Esp.* 2017 Jul 4. pii: S0210-4806(17)30068-2. doi: 10.1016/j.acuro.2017.02.005. [Epub ahead of print] PMID: 28687365

The purpose of this review was to determine the efficacy and safety of BTX-A, compared with other interventions for the treatment of BPS to improve quality of life. The authors concluded that there is not enough evidence to conclude the efficacy of BTX-A for the treatment of interstitial cystitis to improve quality of life.

IS CLINICAL PRACTICE ALIGNED WITH THE LATEST SCIENTIFIC EVIDENCE ON GAG THERAPY?

Janssen DAW. *Urologia.* 2017 Aug 17;0. doi: 10.5301/uj.5000259. [Epub ahead of print] PMID: 28862729

The role of glycosaminoglycans (GAGs) as key components of the protective bladder barrier is well accepted. Replenishment of the GAG layer could restore the normal protective barrier function of the damaged bladder urothelium and re-establish normal permeability. A number of bladder diseases, including interstitial cystitis/bladder pain syndrome, recurrent urinary tract infections, radiation cystitis, and other forms of cystitis may benefit from GAG therapy.

USE OF BOTULINUM TOXIN FOR VOIDING DYSFUNCTION.

Eldred-Evans D, Dasgupta P. *Transl Androl Urol.* 2017 Apr;6(2):234-251. doi: 10.21037/tau.2016.12.05. PMID: 28540231

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The use of botulinum toxin A (BoNT-A) has expanded across a range of lower urinary tract conditions. This review from London provides an overview of the current indications for BoNT-A in the lower urinary tract and critically evaluates the published evidence within each area. The classic application of BoNT-A has been in the management of refractory neurogenic detrusor overactivity (NDO) and overactive bladder (OAB). At present, the results for painful bladder syndrome (PBS) are promising and BoNT-A injections are recommended as a fourth line option in recent international guidelines, although larger randomized study with longer follow-up are required to confirm the initial findings. Finally, the results for the treatment of BPH have been variable and recent high quality randomized controlled trials (RCTs) have suggested no benefit over placebo so at present it cannot be recommended for routine clinical practice. Future advances of BoNT-A include liposome encapsulated formulations which are being developed as an alternative to intravesical injections.

TOLL-LIKE RECEPTOR 7 IS OVEREXPRESSED IN THE BLADDER OF HUNNER-TYPE INTERSTITIAL CYSTITIS, AND ITS ACTIVATION IN THE MOUSE BLADDER CAN INDUCE CYSTITIS AND BLADDER PAIN.

Ichihara K, Aizawa N, Akiyama Y, Kamei J, Masumori N, Andersson KE, Homma Y, Igawa Y. *Pain.* 2017 Aug;158(8):1538-1545. doi: 10.1097/j.pain.0000000000000947. PMID: 28595240

Toll-like receptor 7 (TLR7) is associated with the pathophysiology of systemic lupus erythematosus and Sjögren syndrome, well-known diseases accompanying interstitial cystitis (IC). The authors from Japan and Denmark studied TLR7 expression in the bladder of patients with Hunner-type IC (HIC) and its functional roles in bladder inflammation and nociception using mice. Bladder biopsy specimens were obtained from patients with HIC. Specimens from the noncancerous portion of the bladder of patients with bladder cancer served as controls. Toll-like receptor 7 was up-regulated in the bladder mucosa of patients with HIC, and activation of TLR7 in the mouse bladder induced cystitis with sensory hyperactivity of the bladder. Blocking the TLR7 pathway may be an innovative treatment target of HIC.

THE THERAPEUTIC APPROACH TO DIFFERENT FORMS OF CYSTITIS: IMPACT ON PUBLIC HEALTH.

Droupy S. *Urologia.* 2017 Aug 17;0. doi: 10.5301/uj.5000262. [Epub ahead of print] PMID: 28862726

Interstitial cystitis/bladder pain syndrome, recurrent urinary tract infections and other forms of cystitis significantly impact the quality of life of patients with chronic bladder disorders and impose a considerable economic burden on health systems. Effective management is essential to provide symptom relief and to reduce the negative impact of chronic bladder disorders. Identifying the appropriate pharmacological or non-pharmacological approach is essential, and there is a growing evidence base for the use of intravesical hyaluronic acid and chondroitin sulfate in several bladder conditions, including recurrent urinary tract infections.

INHIBITION OF MICRORNA-214 PROMOTES EPITHELIAL-MESENCHYMAL TRANSITION PROCESS AND INDUCES INTERSTITIAL CYSTITIS IN POSTMENOPAUSAL WOMEN BY UPREGULATING MFN2.

Lv JW, Wen W, Jiang C, Fu QB, Gu YJ, Lv TT, Li ZD, Xue W. *Exp Mol Med.* 2017 Jul 21;49(7):e357. doi: 10.1038/emm.2017.98. PMID: 28729638

This study from China aims to investigate the roles that microRNA-214 (miR-214) plays in the epithelial mesenchymal transition (EMT) process and the development of interstitial cystitis (IC) in postmenopausal women by targeting Mitofusin 2 (Mfn2). IC bladder tissues and adjacent normal bladder tissues were collected from postmenopausal women. The authors report that their findings indicate that the inhibition of miR-214 promotes the EMT process and contributes to bladder wall fibrosis by up-regulating Mfn2, thus leading to the occurrence of IC in postmenopausal women.

INTERSTITIAL CYSTITIS INTRAVESICAL THERAPY.

Ha T, Xu JH. *Transl Androl Urol.* 2017 Jul;6(Suppl 2):S171-S179. doi: 10.21037/tau.2017.06.18. PMID: 28791236

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Interstitial cystitis (IC) is a progressive bladder disorder that presents with symptoms of bladder urgency, frequency and pain. The aetiology of the disease remains uncertain, but it is postulated that there is an initial infective insult which damages the glycosaminoglycan (GAG) layer of the bladder urothelium. This defect allows an influx of ions, particularly potassium, which initiates an inflammatory reaction in the bladder wall, which incites the symptoms described above. Treatment initially involves behavioural and oral medication, with second line being intravesical instillation therapy. Treatment strategies focus on restoring lower urinary tract epithelial function, inhibiting neural activation, controlling allergies and relieving symptoms. In this review, current intravesical therapy will be discussed, as well as what lies on the horizon for intravesical therapy in IC.

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

Rawls WF, Cox L, Rovner ES. *Neurourol Urodyn.* 2017 Sep;36(7):1677-1684. doi: 10.1002/nau.23204. Epub 2017 Feb 21. PMID: 28220525

The purpose of this review was to update the current understanding of dimethyl sulfoxide (DMSO) and its role in the treatment of interstitial cystitis (IC). A systematic review was conducted using the PRIMSA checklist to identify published articles involving intravesical DMSO for the treatment of 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 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.

CHILDHOOD BLADDER AND BOWEL DYSFUNCTION PREDICTS IRRITABLE BOWEL SYNDROME PHENOTYPE IN ADULT INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENTS.

Doiron RC, Kogan BA, Tolls V, Irvine-Bird K, Nickel JC. *Can Urol Assoc J.* 2017 Aug;11(8):255-259. doi: 10.5489/cuaj.4251. PMID: 28798827

Many clinicians have suggested that a history of bladder and bowel dysfunction (BBD) in childhood predisposes to the development of interstitial cystitis/bladder pain syndrome (IC/BPS) or irritable bowel syndrome (IBS) in adulthood. Doiron and colleagues hypothesized that BBD symptoms in childhood would predict the IBS-associated phenotype in adult IC/BPS patients. 190 consecutive female patients with a diagnosis of IC/BPS were administered a modified form of a clinical BBD questionnaire (BBDQ) to capture childhood BBD-like symptoms, as well as Interstitial Cystitis Symptoms Index (ICSI), Interstitial Cystitis Problem Index (ICPI), Pelvic Pain and Urgency/Frequency (PUF) questionnaires and UPOINT categorization. Patients were stratified to IBS-positive or IBS-negative according to clinical assessment of IBS-like symptoms. The 127 patients (67%) identified with IBS-like symptoms recalled significantly higher BBDQ scores than the 63 patients (33%) who were IBS-negative. The IBS-positive patients also reported a higher number of UPOINT domains than their non-IBS counterparts, while their PUF total scores were significantly higher. IBS-positive patients more often recalled that in childhood they did not have a daily bowel movement (BM) and had "to push for a BM". In childhood, they "urinated only once

or twice per day" and recalled "painful urination" more than those without IBS ($p=0.03$). There were no significant differences between the groups in answers to the other five questions of the BBDQ. According to the authors, their symptom recollection survey was able to predict the IBS phenotype of IC/BPS based on a childhood BBDQ. Further prospective studies are needed to further evaluate these novel findings.

IMPROVED EFFICACY AND IN VIVO CELLULAR PROPERTIES OF HUMAN EMBRYONIC STEM CELL DERIVATIVE IN A PRECLINICAL MODEL OF BLADDER PAIN SYNDROME.

Kim A, Yu HY, Lim J, Ryu CM, Kim YH, Heo J, Han JY, Lee S, Bae YS, Kim JY, Bae DJ, Kim SY, Noh BJ, Hong KS, Han JY, Lee SW, Song M, Chung HM, Kim JK, Shin DM, Choo MS. *Sci Rep.* 2017 Aug 21;7(1):8872. doi: 10.1038/s41598-017-09330-x. PMID: 28827631

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Interstitial cystitis/bladder pain syndrome (IC/BPS) is an intractable disease characterized by severe pelvic pain and urinary frequency. Mesenchymal stem cell (MSC) therapy is a promising approach to treat incurable IC/BPS. Here, Kim and colleagues show greater therapeutic efficacy of human embryonic stem cell (hESC)-derived multipotent stem cells (M-MSCs) than adult bone-marrow (BM)-derived counterparts for treating IC/BPS and also monitor long-term safety and in vivo properties of transplanted M-MSCs in living animals. This study provides the first evidence for improved therapeutic efficacy, long-term safety, and in vivo distribution and cellular properties of hESC derivatives in preclinical models of IC/BPS.

EVALUATION OF THE INCIDENCE AND RISK FACTORS ASSOCIATED WITH PERSISTENT FREQUENCY IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND THE EFFICACY OF ANTIMUSCARINIC TREATMENT.

Kim A, Hoe KO, Shin JH, Choo MS. *Investig Clin Urol.* 2017 Sep;58(5):353-358. doi: 10.4111/icu.2017.58.5.353. Epub 2017 Aug 3. PMID: 28868507

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The purpose of this study was to investigate the incidence and risk factors associated with persistent urinary frequency, and to evaluate the efficacy of antimuscarinic treatment. Interstitial cystitis/bladder pain syndrome (IC/BPS) patients complaining of persistent urinary frequency despite improved pain were evaluated. About half of the patients with IC/BPS showed persistent frequency, with poor voiding function identified as a risk factor; antimuscarinic treatment was not effective in these patients.

KENALOG INJECTION INTO HUNNER'S LESIONS AS A TREATMENT FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Rittenberg L, Morrissey D, El-Khawand D, Whitmore K. *Curr Urol.* 2017 Aug;10(3):154-156. doi: 10.1159/000447171. Epub 2017 Jul 30. PMID: 28878600

This study aimed to evaluate the effectiveness of kenalog injection into Hunner's lesions. All patients had cystoscopy and bladder hydrodistention with corticosteroid injection into Hunner's lesions over a 2.5-year period. Data include patient characteristics and pre- and post-operative validated questionnaires. Spearman Correlation and Wilcoxon *t*-tests were used for analysis. One hundred patients were reviewed retrospectively. There was a 1.1 point decrease in pain at 12 weeks post-operation. Urinary frequency decreased from a mean of 11.7 to 9.1 daily episodes, and nocturia from a mean of 3 to 1.6 nightly episodes. It was concluded that the use of a corticosteroid may be beneficial to symptom control and improvement in the quality of life of interstitial cystitis/painful bladder syndrome patients. Patients had improved frequency and nocturia 12 weeks post injection.

IMMUNOTHERAPY OPTIONS FOR PAINFUL BLADDER SYNDROME: WHAT'S THE POTENTIAL?

Mykoniatis I, Katafigiotis I, Sfoungaristos S, Yutkin V. *Expert Opin Biol Ther.* 2017 Sep 5:1-10. doi: 10.1080/14712598.2017.1375094. [Epub ahead of print] PMID: 28874100

Painful bladder syndrome/interstitial cystitis (PBS/IC) is an enigmatic disease characterized by lack of evidence-based knowledge and an ongoing scientific debate regarding its definition, pathogenesis, diagnostic and treatment algorithm. An autoimmune theory for PBS/IC etiology has suggested immunotherapy as a potential treatment choice. In this review, the authors report existing and future immunotherapeutic options, potentially valuable to the management of PBS/IC while evidence for the immunological aspect of PBS/IC pathogenesis are also presented. Relevant data reported in human clinical studies but also in experimental studies using animal

PBS/IC models have been reviewed. Promising data has emerged lately regarding use of immunotherapy drugs for PBS/IC treatment. Specifically, human monoclonal antibodies inhibiting nerve growth factor and tumor necrosis factor- α have shown high efficacy in pain control for PBS/IC. Also, many other agents modulating immunopathways linked to PBS symptom etiology and leading to positive treatment effects have been reported lately mainly in experimental animal studies. Immunotherapy could potentially improve disease-related and patient-reported outcome; nevertheless, lack of consensus regarding PBS/IC diagnostic criteria, leading to high heterogeneity of patients enrolled in PBS/IC treatment studies, and low number of well-designed randomized clinical trials are limitations which must be addressed in the future.

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

Oh-Oka H. Urology. 2017 Aug;106:50-54. doi: 10.1016/j.urology.2017.02.053. Epub 2017 Apr 20. 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 (IC)/bladder pain syndrome (BPS) in stable condition who were followed up in the author's hospital. In cooperation with the nutrition control team, they created a basic IC/BPS diet menu for 1 month. Data regarding daily food intake and food-related symptoms were collected by conducting a detailed interview of each patient, and 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 noninvasiveness, without alterations to the other treatments.

[PSYCHOSOCIAL CO-MORBIDITIES IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME \(IC/BPS\): A SYSTEMATIC REVIEW.](#)

McKernan LC, Walsh CG, Reynolds WS, Crofford LJ, Dmochowski RR, Williams DA. Neurourol Urodyn. 2017 Oct 9. doi: 10.1002/nau.23421. [Epub ahead of print] PMID: 28990698

Psychosocial factors amplify symptoms of Interstitial Cystitis (IC/BPS). While psychosocial self-management is efficacious in other pain conditions, its impact on an IC/BPS population has rarely been studied. The objective of this review was to learn the prevalence and impact of psychosocial factors on IC/BPS, assess baseline psychosocial characteristics, and offer recommendations for assessment and treatment. It was concluded that the psychological impact of IC/BPS is pervasive and severe. Existing evidence of treatment is lacking and suggests self-management intervention may be helpful.

[COMPARISON OF 5 DIFFERENT RAT MODELS TO ESTABLISH A STANDARD ANIMAL MODEL FOR RESEARCH INTO INTERSTITIAL CYSTITIS.](#)

Song PH, Chun SY, Chung JW, Kim YY, Lee HJ, Lee JN, Ha YS, Yoo ES, Kwon TG, Kim J, Kim DH, Kim BS. Int Neurourol J. 2017 Sep;21(3):163-170. doi: 10.5213/inj.1734898.449. Epub 2017 Sep 12. PMID: 28954463.

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Song and colleagues from Korea evaluated 5 different rat models using different agents in order to establish a standard animal model for interstitial cystitis (IC) in terms of the functional and pathologic characteristics of the bladder. Five IC models were generated in 8-week-old female Sprague-Dawley rats via transurethral instillation of 0.1M hydrogen chloride (HCl) or 3% acetic acid (AA), intraperitoneal injection of cyclophosphamide (CYP) or lipopolysaccharide (LPS), or subcutaneous injection of uroplakin II (UPK2). Among the 5 different agents, the injection of UPK generated the most effective IC animal model, showing consequent urothelial barrier loss, inflammatory reaction, tissue fibrosis stimulation, and persistent hyperactive bladder.

PATIENT PERSPECTIVE

[BLADDER PAIN: THE PATIENT PERSPECTIVE.](#)

Meijlink JM. Urologia. 2017 Aug 17;0. doi: 10.5301/uj.5000261. [Epub ahead of print] PMID: 28862727

Patients with chronic pain, discomfort and other urinary symptoms related to bladder pain syndrome or urinary tract infections may experience severely diminished quality of life and psychological and social problems, including depression, anxiety, and a sense of helplessness and hopelessness. These patients require empathy, understanding and practical support to allow them to cope with their chronic bladder disorder.

GUIDELINES

[CYSTITIS AND PELVIC PAIN MANAGEMENT: GUIDELINES VERSUS REAL-WORLD PRACTICE.](#)

C Goddard J. Urologia. 2017 Aug 17;0. doi: 10.5301/uj.5000260. [Epub ahead of print] PMID: 28862731

Clinical practice guidelines for the management of bladder pain syndrome/chronic pelvic pain aim to help guide clinicians in diagnosing and treating patients they see on a day-to-day basis in the clinic. However, the approaches suggested by current clinical guidelines may not always align with the practicalities of routine clinical practice, where patient expectations must also be taken into consideration.

[CHANGING CURRENT PRACTICE IN UROLOGY: IMPROVING GUIDELINE DEVELOPMENT AND IMPLEMENTATION THROUGH STAKEHOLDER ENGAGEMENT.](#)

MacLennan SJ, MacLennan S, Bex A, Catto JW, De Santis M, Glaser AW, Ljungberg B, N'Dow J, Plass K, Trapero-Bertran M, Van Poppel H, Wright P, Giles RH. Eur Urol. 2017 Aug;72(2):161-163. doi: 10.1016/j.eururo.2017.02.008. Epub 2017 Feb 22. PMID: 28237788

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According to MacLennan and colleagues, effective stakeholder integration for guideline development should improve outcomes and adherence to clinical practice guidelines. The role of stakeholders in the development of CPGs should be shaped to minimise bias within this process. All panel members are expected to contribute appropriate comments to the discussion. For patient members, discussion needs to be framed in terms of the process of care and how to prioritise clinical questions. Importantly, the patient representative brings another perspective on the design and delivery of care to the discussion, rather than making decisions on which treatment is best. However, in helping to prioritise the outcomes of most importance in deciding whether one treatment is better than another, the patient voice is clearly important. The authors propose a model that addresses all the different agents (patients, carers, charitable organisations, and health care funders, in addition to specialists) involved in health-related decisions. Importantly, our proposed model incorporates key stakeholders as non-tokenistic panel members with clearly defined responsibilities

KETAMINE CYSTITIS

[DELAYED URINARY SYMPTOMS INDUCED BY KETAMINE.](#)

Robles-Martínez M, Abad AC, Pérez-Rodríguez V, Ros-Cucurull E, Esojo A, Roncero C. J Psychoactive Drugs. 2017 Sep 21:1-4. doi: 10.1080/02791072.2017.1371364. [Epub ahead of print] PMID: 28934076

One of the side-effects of ketamine abuse is genito-urinary damage. This report from Spain describes a case of a former ketamine user who presented with urinary symptoms associated with ketamine years after stopping consumption. This was a 26-year-old male with a history of ketamine abuse. He started treatment for alcohol dependence at age 19. He smoked marijuana daily and denied any other drug use. During the follow-up, urinary symptoms were evidenced (dysuria, frequency, urgency, incontinence, nocturia, hematuria, and suprapubic pain). Urinary symptoms started two years ago and worsened over time. The patient was referred to a urologist. A cystoscopy revealed lesions compatible with interstitial cystitis like the ones that appear in some ketamine abusers. Given the medical history, the urologist asked him about ketamine consumption and the patient declared a daily use of 50 milligrams intranasally from age 15 to age 17. Given these findings, not reported previously in the medical literature, future research should follow up patients who at some point in their life made an abusive consumption of ketamine in order to understand the pathogenesis and to be able to intervene before clinical disease manifests itself.

[THE RISK OF UPPER URINARY TRACT INVOLVEMENT IN PATIENTS WITH KETAMINE-ASSOCIATED UROPATHY.](#)

Yee CH, Teoh JY, Lai PT, Leung VY, Chu WC, Lee WM, Tam YH, Ng CF. *Int Neurourol J.* 2017 Jun;21(2):128-132. doi: 10.5213/inj.1732704.352. Epub 2017 Jun 21. PMID: 28673061.

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The aims of this study from Hong Kong were to investigate the prevalence of upper tract involvement in ketamine-associated uropathy, and to determine the predictors of hydronephrosis in patients with a history of ketamine abuse. Ketamine-associated uropathy can involve the upper urinary tract. Patient demographics as well as investigations of UFM, renal function tests, and liver function tests may allow us to identify at-risk patients.

[RISK FACTORS OF LOWER URINARY TRACT SYNDROME AMONG KETAMINE USERS.](#)

Chen IC, Lee MH, Chen WC, Hu TC, Lin HY. *Low Urin Tract Symptoms.* 2017 Jul 13. doi: 10.1111/luts.12178. [Epub ahead of print] PMID: 28707385.

This study from Taiwan investigated the risk factors of ketamine associated-lower urinary tract symptoms (LUTS), such as duration of use, dosage of ketamine, co-occurring substance use of other psychoactive drugs, comorbidities, and depression. This study was a cross-sectional survey. LUTS was assessed with the O'Leary symptom and problem index (OSPI) scores. The authors included the comorbidities of interstitial cystitis/painful bladder syndrome (IC/PBS) as comorbid factors. It was concluded that depression and longer duration of exposure to ketamine are significantly associated with the development of LUTS among ketamine users. Early evaluation and intervention of depression should be considered in patients of ketamine-associated LUTS.

[KETAMINE-INDUCED BLADDER FIBROSIS INVOLVES EPITHELIAL-TO-MESENCHYMAL TRANSITION MEDIATED BY TRANSFORMING GROWTH FACTOR- \$\beta\$ 1.](#)

Wang J, Chen Y, Gu D, Zhang G, Chen J, Zhao J, Wu P. *Am J Physiol Renal Physiol.* 2017 Mar 22;ajprenal.00686.2016. doi: 10.1152/ajprenal.00686.2016. [Epub ahead of print] PMID: 28331066

Bladder wall fibrosis is a major complication of ketamine-induced cystitis (KC), but the underlying pathogenesis is poorly understood. The aim of this study from Guangzhou was to elucidate the mechanism of ketamine-induced fibrosis in association with epithelial-to-mesenchymal transition (EMT) mediated by transforming growth factor- β 1 (TGF- β 1). Withdrawal from ketamine did not lead to recovery of bladder urinary function or decreased fibrosis. Their study shows for the first time that EMT might contribute to bladder fibrosis in KC. TGF- β 1 may have an important role in bladder fibrogenesis via an EMT mechanism.

[SPECIAL K: ONCE THE FUN IS OVER AN EMT ARRIVES FOR THE BLADDER.](#)

Hill WG, Yu W. *Am J Physiol Renal Physiol.* 2017 May 24;ajprenal.00239.2017. doi: 10.1152/ajprenal.00239.2017. [Epub ahead of print] PMID: 28539335

Wang et al. report that in rats exposed to daily ketamine for sixteen weeks, the urothelium begins to undergo phenoconversion to a more mesenchymal state. This epithelial to mesenchymal transition (EMT), has several classic molecular hallmarks and Wang et al. demonstrate convincingly that a number of these including downregulation of E-cadherin, upregulation of mesenchymal markers vimentin and fibroblast specific protein (FSP-1), colocalization of both epithelial and mesenchymal markers in a subset of urothelium-associated cells and upregulation of TGF β expression in urothelium are all present.

URINARY TRACT INFECTIONS

[CAN CRANBERRIES CONTRIBUTE TO REDUCE THE INCIDENCE OF URINARY TRACT INFECTIONS? A SYSTEMATIC REVIEW WITH META-ANALYSIS AND TRIAL SEQUENTIAL ANALYSIS OF CLINICAL TRIALS.](#)

Luís A, Domingues F, Pereira L. *J Urol.* 2017 Sep;198(3):614-621. doi: 10.1016/j.juro.2017.03.078. Epub 2017 Mar 10. PMID: 28288837

This team from Portugal sought to clarify the association between cranberry intake and the prevention of urinary tract infections. This systematic review, which complies with the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) statement, was done as a meta-analysis and trial sequential analysis of clinical trials. The findings clearly showed the potential use of cranberries for the clinical condition of urinary

tract infection. Cranberry products significantly reduced the incidence of urinary tract infections as indicated by the weighted risk ratio. The results of subgroup analysis demonstrated that patients at some risk for urinary tract infections were more susceptible to the effects of cranberry ingestion. The authors concluded that the results of the current study could be used by physicians to recommend cranberry ingestion to decrease the incidence of urinary tract infections, particularly in individuals with recurrent urinary tract infections. This would also reduce the administration of antibiotics, which could be beneficial since antibiotics can lead to the worldwide emergence of antibiotic resistant microorganisms.

PAIN

PAIN AS A DISEASE: AN OVERVIEW.

Raffaelli W, Arnaudo E. J Pain Res. 2017 Aug 21;10:2003-2008. doi: 10.2147/JPR.S138864. eCollection 2017. PMID: 28860855

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The acknowledgment of pain as a pathologic entity in its own right remains debated. Notwithstanding the data showing the burden of pain as a disease, an ultimate recognition of the pathologic nature of this condition is lacking. In this study, the authors analyze the notion of pain as a disease through an historical overview of its several conceptualizations and report the main evidence supporting this notion. They believe that a clear definition of pain as a disease is necessary, especially considering the enormous global burden of this condition. Indeed, the recognition of pain as a definite pathologic state is crucial to raise awareness about this neglected global health problem and to promote the exploration of new specific therapeutic approaches.

CHRONIC PELVIC PAIN SYNDROME

PAIN AREAS AND MECHANOSENSITIVITY IN PATIENTS WITH CHRONIC PELVIC PAIN SYNDROME: A CONTROLLED CLINICAL INVESTIGATION.

Quaghebeur J, Wyndaele JJ, De Wachter S. Scand J Urol. 2017 Jul 5:1-6. doi: 10.1080/21681805.2017.1339291. [Epub ahead of print] PMID: 28678646

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A thorough clinical assessment including physical examination is crucial in a diagnostic work-up, including in patients with chronic pelvic pain syndrome (CPPS). This study investigated the prevalence of pain areas and the mechanosensitivity of peripheral nerves in patients with CPPS and compared the findings with a healthy control group. Patients with CPPS showed a variety of pain from different musculoskeletal origins. Neurodynamic testing demonstrated significant mechanosensitivity in at least one nerve of the lumbosacral plexus in 88% of the patients with CPPS, suggesting minor nerve injuries. Pudendal nerve mechanosensitivity was found in 85% of patients, while 42% had multiple nerves involved. Unilateral or bilateral pudendal channel palpatory pain was present in 62% of the CPPS group and not in controls. This study shows musculoskeletal pain and a high prevalence of minor nerve injuries in CPPS patients, indicating the presence of abnormal impulse generation sites that can help in understanding the clinical picture in CPPS patients and guiding their treatment.

DEVELOPMENT OF AUTOIMMUNITY

HORMONAL CONTRACEPTION AND THE DEVELOPMENT OF AUTOIMMUNITY: A REVIEW OF THE LITERATURE.

Williams WV. Linacre Q. 2017 Aug;84(3):275-295. doi: 10.1080/00243639.2017.1360065. Epub 2017 Aug 18. PMID: 28912620

Estrogens and progestins are known to have profound effects on the immune system and may modulate the susceptibility to autoimmune diseases. A comprehensive literature search was carried out using PubMed for any of 153 autoimmune disease terms and the terms contraception, contraceptive, or their chemical components with limits of Humans + Title or Abstract. Over 1,800 titles were returned and scanned, 352 papers retrieved and reviewed in depth and an additional 70 papers retrieved from the bibliographies. Based on this review, substantial evidence exists linking the use of combined oral contraceptives to a lower incidence of hyperthyroidism, an increase in multiple sclerosis, ulcerative colitis, Crohn's disease, Systemic Lupus

Erythematous, and interstitial cystitis. Progesterone only contraceptives are linked to progesterone dermatitis and in one large developing world concurrent cohort study are associated with increases in arthropathies and related disorders, eczema and contact dermatitis, pruritis and related conditions, alopecia, acne, and urticaria. Hormonal contraceptives modulate the immune system and may influence the susceptibility to autoimmune diseases with significant increases in risk for several autoimmune diseases. Hormonal contraceptives (HCs), such as the "pill," Norplant, and vaginal rings, are very potent hormones that have effects on the immune system, which is made up of white blood cells and lymph nodes and normally defends the body against invading bacteria, viruses and parasites. There is good evidence that HC use is associated with an increased risk of several serious autoimmune diseases such as Crohn's disease (which causes inflammation of the bowels), Lupus (which causes inflammation in many organs), and interstitial cystitis (which causes inflammation in the bladder). Several other rarer autoimmune diseases are also linked to HC use. People contemplating the use of HCs should be informed of these risks.

IRRITABLE BOWEL SYNDROME

[IRRITABLE BOWEL SYNDROME DIAGNOSIS AND MANAGEMENT: A SIMPLIFIED ALGORITHM FOR CLINICAL PRACTICE.](#)

Moayyedi P, Mearin F, Azpiroz F, Andresen V, Barbara G, Corsetti M, Emmanuel A, Hungin APS, Leyer P, Stanghellini V, Whorwell P, Zerbib F, Tack J. *United European Gastroenterol J.* 2017 Oct;5(6):773-788. doi: 10.1177/2050640617731968. Epub 2017 Sep 28. PMID: 29026591

Effective management of irritable bowel syndrome (IBS), a common functional gastrointestinal disorder, can be challenging for physicians because of the lack of simple diagnostic tests and the wide variety of treatment approaches available. The objective of this article is to outline a simple algorithm for day-to-day clinical practice to help physicians navigate key stages to reaching a positive IBS diagnosis and guidance on how to prioritise the use of specific management strategies. This algorithm was based on the opinion of an expert panel evaluating current evidence. The key principles forming the foundation of this evidence-supported algorithm are: confidently naming and explaining an IBS diagnosis for the patient, followed by assessment of key patient characteristics likely to influence the choice of therapy, such as predominant symptoms, and exploring the patient agenda and preferences. Consultation should always include education and reassurance with an explanatory model of IBS tailored to the patient. Individualised lifestyle changes, dietary modifications, pharmacological therapies, psychological strategies or a combination of interventions may be used to optimise treatment for each patient. The simple visual tools developed here navigate the key stages to reaching a positive diagnosis of IBS, and provide a stepwise approach to patient-centred management targeted towards the most bothersome symptoms. Establishing a strong patient-physician relationship is central to all stages of the patient journey from diagnosis to effective management.

FIBROMYALGIA

[NEW GUIDELINES FOR THE DIAGNOSIS OF FIBROMYALGIA.](#)

[Article in English, Portuguese]

Heymann RE, Paiva ES, Martinez JE, Helfenstein M Jr, Rezende MC, Provenza JR, Ranzolin A, Assis MR, Feldman DP, Ribeiro LS, Souza EJR. *Rev Bras Reumatol Engl Ed.* 2017 Aug 8. pii: S2255-5021(17)30048-2. doi: 10.1016/j.rbre.2017.07.002. [Epub ahead of print] PMID: 28800969.

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The purpose of this study was to establish guidelines based on scientific evidence for the diagnosis of fibromyalgia. Evidence collection was performed based on 9 questions regarding the diagnosis of fibromyalgia, structured using the Patient, Intervention or Indicator, Comparison and Outcome (P.I.C.O.), with searches in the main, primary databases of scientific information. After defining the potential studies to support the recommendations, they were graded according to evidence and degree of recommendation.

[VISCERAL PAIN AS A TRIGGERING FACTOR FOR FIBROMYALGIA SYMPTOMS IN COMORBID PATIENTS.](#)

Costantini R, Affaitati G, Wesselmann U, Czakanski P, Giamberardino MA. *Pain*. 2017 Jul 3. [Epub ahead of print] PMID: 28683025

Fibromyalgia syndrome (FMS) is a central sensitization syndrome; however, peripheral pain sources potentially exacerbate its symptoms of chronic diffuse musculoskeletal pain and hyperalgesia. This prospective study evaluated visceral pain as a possible triggering factor for FMS pain and hyperalgesia in comorbid patients. Women with (1) FMS + irritable bowel syndrome (IBS); (2) FMS + primary dysmenorrhea (Dys); (3) FMS + Dys secondary to endometriosis (Endo); (4) FMS + colon diverticulosis (Div) were compared with FMS-only women, for fibromyalgia pain (number and intensity of episodes and analgesic consumption) over comparable periods and for somatic hyperalgesia (electrical and pressure pain thresholds) in painful (tender points) and control areas (trapezius, deltoid, quadriceps muscles, and overlying subcutis and skin). In comorbid subgroups, FMS symptoms were also reassessed after treatment of the visceral condition or no treatment. All comorbid groups vs FMS-only had significantly higher FMS pain (number/intensity of episodes and analgesic consumption) and hyperalgesia in deep somatic tissues (subcutis and muscle) at all sites. Visceral pain (number of IBS days, painful menstrual cycles, and abdominal pain episodes from diverticulitis) correlated directly with all parameters of FMS pain and inversely with muscle pain thresholds at all sites. Fibromyalgia syndrome pain and hyperalgesia in all tissues and all sites significantly decreased in patients after visceral comorbidity treatment (dietary for 6 months [IBS], hormonal for 6 months [dysmenorrhea], laser [endometriosis], and surgery [diverticulosis]) vs no change in untreated patients. Visceral pain enhances FMS symptoms, probably augmenting the level of central sensitization typical of the syndrome. Systematic assessment and treatment of visceral pain comorbidities should be a part of FMS management strategy.

AMBROXOL FOR THE TREATMENT OF FIBROMYALGIA: SCIENCE OR FICTION?

Kern KU, Schwickert M. *J Pain Res*. 2017 Aug 16;10:1905-1929. doi: 10.2147/JPR.S139223. eCollection 2017. PMID: 28860846

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Fibromyalgia appears to present in subgroups with regard to biological pain induction, with primarily inflammatory, neuropathic/neurodegenerative, sympathetic, oxidative, nitrosative, or muscular factors and/or central sensitization. Recent research has also discussed glial activation or interrupted dopaminergic neurotransmission, as well as increased skin mast cells and mitochondrial dysfunction. Therapy is difficult, and the treatment options used so far mostly just have the potential to address only one of these aspects. As ambroxol addresses all of them in a single substance and furthermore also reduces visceral hypersensitivity, in fibromyalgia existing as irritable bowel syndrome or chronic bladder pain, it should be systematically investigated for this purpose. Encouraged by first clinical observations of two working groups using topical or oral ambroxol for fibromyalgia treatments, this paper outlines the scientific argument for this approach by looking at each of the aforementioned aspects of this complex disease and summarizes putative modes of action of ambroxol. Nevertheless, at this point the evidence basis for ambroxol is not strong enough for clinical recommendation.

MYOFASCIAL PELVIC PAIN

MYOFASCIAL PELVIC PAIN AND RELATED DISORDERS.

Bonder JH, Chi M, Rispoli L. *Phys Med Rehabil Clin N Am*. 2017 Aug;28(3):501-515. doi: 10.1016/j.pmr.2017.03.005. PMID: 28676361

Myofascial pelvic pain refers to pain in the pelvic floor muscles, the pelvic floor connective tissue, and the surrounding fascia. The cause is often multifactorial and requires treatment that encompasses multiple modalities. This type of pain is often associated with other abdominopelvic disorders, so providers in these specialties need to be aware of these connections. A comprehensive musculoskeletal examination, including evaluation of the pelvic floor muscles, and history are key to diagnosing myofascial pelvic pain. Treatments include physical therapy, muscle relaxers, oral neuromodulators, cognitive-behavioral therapy, and pelvic floor muscle injections.

VULVODYNIA/VULVAL PAIN SYNDROME

VULVODYNIA: DIAGNOSIS AND MANAGEMENT.

Stenson AL. Obstet Gynecol Clin North Am. 2017 Sep;44(3):493-508. doi: 10.1016/j.ogc.2017.05.008. PMID: 28778645

Vulvodynia is a common condition that negatively affects sexual health and quality of life for many women. A new classification system has been adopted that divides vulvodynia into subtypes based on pain characteristics. Diagnosis relies on ruling out possible contributing pathologic conditions. A multidisciplinary approach to treatment is likely to achieve the best outcome for all types. Medical therapy with systemic neuromodulators is suggested for generalized vulvodynia. For patients with vestibulodynia, topical therapy may be beneficial. Vestibulectomy has a high success rate and may be a good option if the patient is not responding to treatment.

VULVODYNIA IS NOT CREATED EQUALLY: EMPIRICAL CLASSIFICATION OF WOMEN WITH VULVODYNIA.

Alappattu M, Lamvu G, Feranec J, Witzeman K, Robinson M, Rapkin A. J Pain Res. 2017 Jul 6;10:1601-1609. doi: 10.2147/JPR.S136751. eCollection 2017. PMID: 28740427

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Vulvodynia classification is based on the sensory dimensions of pain and does not include psychological factors associated with the pain experience and treatment outcomes. Previous work has shown that individuals with chronic pain can be classified into subgroups based on pain sensitivity, psychological distress, mood, and symptom severity. The aim of this cross-sectional study from the USA was to identify distinct subgroups of women with vulvodynia enrolled in the National Vulvodynia Registry. The authors hypothesized that women with vulvodynia can be clustered into subgroups based on distress and pain sensitivity. Validation indicated that subgroups differed in terms of clinical pain intensity, sensory aspects of pain, and intercourse pain. Empirical classification indicates that unique subgroups exist in women with vulvodynia. Providers should be aware of the heterogeneity of this condition with respect to pain-related distress and pain sensitivity.

WOMEN'S SUBJECTIVE EXPERIENCES OF LIVING WITH VULVODYNIA: A SYSTEMATIC REVIEW AND META-ETHNOGRAPHY.

Shallcross R, Dickson JM, Nunns D, Mackenzie C, Kiemle G. Arch Sex Behav. 2017 Sep 13. doi: 10.1007/s10508-017-1026-1. [Epub ahead of print] PMID: 28905128

Vulvodynia, the experience of an idiopathic pain in the form of burning, soreness, or throbbing in the vulval area, affects around 4-16% of the population. The current review used systematic search strategies and meta-ethnography as a means of identifying, analyzing, and synthesizing the existing literature pertaining to women's subjective experiences of living with vulvodynia. Four key concepts were identified: (1) Social Constructions: Sex, Women, and Femininity: Women experienced negative consequences of social narratives around womanhood, sexuality, and femininity, including the prioritization of penetrative sex, the belief that it is the role of women to provide sex for men, and media portrayals of sex as easy and natural. (2) Seeking Help: Women experienced the healthcare system as dismissive, sometimes being prescribed treatments that exacerbated the experience of pain. (3) Psychological and Relational Impact of Vulvodynia: Women experienced feeling shame and guilt, which in turn led to the experience of psychological distress, low mood, anxiety, and low self-esteem. Moreover, women reported feeling silenced which in turn affected their heterosexual relationships and their peer relationships by feeling social isolated. (4) A Way Forward: Women found changing narratives, as well as group and individual multidisciplinary approaches, helpful in managing vulvodynia. The findings of the review conclude that interventions at the individual level, as well as interventions aimed at equipping women to challenge social narratives, may be helpful for the psychological well-being of women with vulvodynia.

RHEUMATIC DISEASES

THE ROLE OF GUT MICROBIOTA IN THE PATHOGENESIS OF RHEUMATIC DISEASES.

Zhong D, Wu C, Zeng X, Wang Q. Clin Rheumatol. 2017 Sep 15. doi: 10.1007/s10067-017-3821-4. [Epub ahead of print] Clin Rheumatol. 2017 Sep 15. doi: 10.1007/s10067-017-3821-4. [Epub ahead of print] PMID: 28914372.

Rheumatic diseases refer to many diseases with a loss of immune self-tolerance, leading to a chronic inflammation, degeneration, or metabolic derangement in multiple organs or tissues. The cause of rheumatic diseases remains to be elucidated, though both environmental and genetic factors are required for the development of rheumatic diseases. Over the past decades, emerging studies suggested that alteration of

intestinal microbiota, known as gut dysbiosis, contributed to the occurrence or development of a range of rheumatic diseases, including rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, systemic sclerosis, and Sjogren's syndrome, through profoundly affecting the balance between pro- and anti-inflammatory immune responses. In this article from China, Zhong and colleagues discuss the role of gut microbiota in the pathogenesis of rheumatic diseases based on a large number of experimental and clinical materials, thereby providing a new insight for microbiota-targeted therapies to prevent or cure rheumatic diseases.

[GASTROINTESTINAL SYSTEM INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS.](#)

Li Z, Xu D, Wang Z, Wang Y, Zhang S, Li M, Zeng X. Lupus. 2017 Jan 1:961203317707825. doi: 10.1177/0961203317707825. [Epub ahead of print] PMID: 28523968

Systemic lupus erythematosus (SLE) is a multisystem disorder which can affect the gastrointestinal (GI) system. Although GI symptoms can manifest in 50% of patients with SLE, these have barely been reviewed due to difficulty in identifying different causes. This systematic review study from China aims to clarify clinical characteristics, diagnosis and treatment of the four major SLE-related GI system complications: protein-losing enteropathy (PLE), intestinal pseudo-obstruction (IPO), hepatic involvement and pancreatitis. SLE-related PLE was characterized by edema and hypoalbuminemia, with Technetium 99m labelled human albumin scintigraphy and alpha-1-antitrypsin fecal clearance test commonly used as diagnostic test. The most common site of protein leakage was the small intestine and the least common site was the stomach. More than half of SLE-related IPO patients had ureterohydronephrosis, and sometimes they manifested as interstitial cystitis and hepatobiliary dilatation. Lupus hepatitis and SLE accompanied by autoimmune hepatitis (SLE-AIH overlap) shared similar clinical manifestations but had different autoantibodies and histopathological features, and positive anti-ribosome P antibody highly indicated the diagnosis of lupus hepatitis. Lupus pancreatitis was usually accompanied by high SLE activity with a relatively high mortality rate. Early diagnosis and timely intervention were crucial, and administration of corticosteroids and immunosuppressants was effective for most of the patients.

E-HEALTH

[DR GOOGLE IS HERE TO STAY BUT HEALTH CARE PROFESSIONALS ARE STILL VALUED: AN ANALYSIS OF HEALTH CARE CONSUMERS' INTERNET NAVIGATION SUPPORT PREFERENCES.](#)

Lee K, Hoti K, Hughes JD, Emmerton L. J Med Internet Res. 2017 Jun 14;19(6):e210. doi: 10.2196/jmir.7489. PMID: 28615156

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The Internet offers great opportunities for consumers to be informed about their health. However, concerns have been raised regarding its impact on the traditional health consumer-health professional relationship. This recent survey of 400 Australian adults identified that over half of consumers required some form of navigational support in locating appropriate Web-based health information. The authors propose that support provided by health professionals would be preferred by consumers; this preference is regardless of whether consumers have a need for navigational support. Secondary analysis of the survey dataset is presented here to quantify consumer-reported support preferences and barriers when navigating Web-based health information. Lee and colleagues aimed to quantitatively identify consumers' support preferences for locating Web-based health information and their barriers when navigating Web-based health information. They also aimed to compare such preferences and barriers between consumers identified as needing and not needing support when locating Web-based health information. Of the 400 respondents, the most preferred mode of navigational support was involvement of health professionals; this was reported by participants identified as needing and not needing navigational support. The two most commonly reported barriers when navigating desired Web-based health information were (1) volume of available information and (2) inconsistency of information between sources; these were reported by participants with and without a need for navigational support. While participants identified with a need for navigational support were more likely to report volume and inconsistency of information as barriers, the degrees of association were small to moderate. Despite concerns in the literature that the popularity of the Internet could compromise the health consumer-health professional relationship, the authors' findings suggest the contrary, showing that health professionals were found to be the most commonly preferred mode of navigational support, even among consumers classified as not needing navigational support.

Further research into how health professionals could assist consumers with Web-based health information seeking could strengthen the health consumer-health professional relationship amidst the growing use of "Dr Google."

EFFECTIVENESS OF MINDFULNESS- AND RELAXATION-BASED eHEALTH INTERVENTIONS FOR PATIENTS WITH MEDICAL CONDITIONS: A SYSTEMATIC REVIEW AND SYNTHESIS.

Mikolasek M, Berg J, Witt CM, Barth J. Int J Behav Med. 2017 Jul 27. doi: 10.1007/s12529-017-9679-7. [Epub ahead of print] PMID: 28752414

This systematic review aims to summarize eHealth studies with mindfulness- and relaxation-based interventions for medical conditions and to determine whether eHealth interventions have positive effects on health. A comprehensive search of five databases was conducted for all available studies from 1990 to 2015. Studies were included if the intervention was mainly technology delivered and included a mindfulness- or relaxation-based intervention strategy and if patients with a medical condition were treated. Treatment effects were summarized for different outcomes. A total of 2383 records were identified, of which 17 studies with 1855 patients were included in this systematic review. These studies were conducted in patients with irritable bowel syndrome, chronic fatigue syndrome, cancer, chronic pain, surgery, and hypertension. All but one study were delivered online through a web-based platform; one study delivered the intervention with iPods. The studies indicate that mindfulness- and relaxation-based eHealth interventions can have positive effects on patients' general health and psychological well-being. No effects were found for stress or mindfulness. Only five studies reported economic analyses of eHealth interventions without any clear conclusion. There is some evidence that mindfulness- and relaxation-based eHealth interventions for medical conditions can have positive effects on health outcomes. Therefore, such interventions might be a useful addition to standard medical care. No app studies were retrieved, even though a vast number of smartphone apps exist which aim at increasing users' health. Therefore, more studies investigating those health apps are needed.

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