

# International Painful Bladder Foundation

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

## IPBF e-Newsletter and Research Update

Issue 31, November 2012

*An IPBF update for patient support groups, healthcare professionals and friends around the world in the field of interstitial cystitis (bladder pain syndrome, painful bladder syndrome, hypersensitive bladder syndrome, chronic pelvic pain) and associated disorders.*

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

- **Meeting Reviews**
  - Review of the Annual Scientific Meeting of the International Continence Society, October 2012 Beijing, China
  - World Congress on Pain, Milan, Italy, 27-31 August, 2012 with PUGO Symposium on Taking Care of the Patient with Chronic Pelvic Pain, Sunday 26 August.
  - 1<sup>st</sup> Sensory Bladder Meeting webcasts now online
- **Upcoming Meetings**
  - Bladder Pain Syndrome/Interstitial Cystitis: A New Insight into a Puzzle, Rome, 17 November 2012
  - Urogenital Pain Meeting, Royal Society of Medicine, London, Friday 18 January 2013
  - Joint 3rd International Consultation on Interstitial Cystitis Japan (ICICJ) and the Essic Annual Meeting 21-23 March 2013
  - 1<sup>st</sup> World Congress on Abdominal & Pelvic Pain, 30 May-1 June 2013, Amsterdam, The Netherlands
  - International Neuromodulation Society (INS) 11<sup>th</sup> World Congress, Berlin, Germany, 8-13 June 2013
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## MEETING REVIEWS

### REVIEW OF THE 42ND ANNUAL SCIENTIFIC MEETING OF THE INTERNATIONAL CONTINENCE SOCIETY (ICS), 15-19 OCTOBER 2012, BEIJING, CHINA.

This was the first time that the ICS annual scientific meeting has been held in China and it was an amazing cultural and scientific experience at the Chinese National Convention Centre in Beijing. While Chinese doctors publish regularly in scientific journals, we don't usually have the chance to hear about their everyday clinical experience and this meeting presented the perfect opportunity. This year's meeting, chaired by Professor Limin Liao from Beijing and hosted jointly by the Chinese Urological Association, Chinese Continence Society and Chinese Medical Association, had much to offer in the field of chronic pelvic pain, IC/painful bladder and related topics: no fewer than two IC workshops, for the first time for years a dedicated scientific session with oral presentations on IC/painful bladder, associated disorders and IC-like symptoms in ketamine abuse, many posters on IC and related topics, a superb state-of-the-art lecture on Chronic Pelvic Pain and its Sexual Implications by Professor Kristene Whitmore from Philadelphia with an in-depth look at every aspect of chronic pelvic pain, and a fascinating lecture on Chinese acupuncture and how this ancient Chinese therapy has been adapted to meet the needs of the modern world by Chinese acupuncture expert Professor

Ji-Sheng Han from Beijing. Furthermore, with its population of 1.3 billion, China potentially has a huge number of patients with IC and consequently is of great interest to the IC world. Online you will find a detailed review of presentations and posters. **Read more....**

**REVIEW OF THE 14<sup>TH</sup> WORLD CONGRESS ON PAIN, MILAN CONVENTION CENTRE, MILAN, ITALY, 27-31 AUGUST, 2012 WITH PUGO SYMPOSIUM ON TAKING CARE OF THE PATIENT WITH CHRONIC PELVIC PAIN, SUNDAY 26 AUGUST.**

The World Congress on Pain (WCP), organised every two years by the International Association for the Study of Pain (IASP), is devoted to pain research and treatment. The 2012 congress in Milan was attended by over 7500 delegates from 110 different countries, with all stakeholders represented at this international, multidisciplinary and multicultural congress. The IASP leads the way worldwide in promoting research, education and training in the field of pain. It brings together scientists, clinicians, healthcare providers and policy-makers to stimulate and support the study of pain and to translate that knowledge into improved pain relief worldwide. Each year, the IASP chooses a specific topic as a theme. In the coming year, the theme will be visceral pain and therefore of particular interest to IC/PBS patients.

On the Sunday prior to the start of the congress, satellite symposiums were organised by the IASP special interest groups or SIGs, including the symposium on "Taking Care of the Patient with Chronic Pelvic Pain", organised by the Pain of UroGenital Origin (PUGO) special interest group. Many patients suffer from chronic pelvic pain – including bladder pain, vulvodynia, irritable bowel syndrome, endometriosis etc – and many different disciplines are involved in caring for these patients. This satellite symposium underlined the fact that a multidisciplinary approach is needed. **Read more...**

**1<sup>ST</sup> SENSORY BLADDER MEETING (HELD 22 JUNE 2012 ANNECY) WEBCASTS NOW ONLINE**

Videos of all presentations at the 1st Sensory Bladder Meeting held in June in Annecy are now available online at: <http://www.sifud-pp.org/congres/sensory-bladder-meeting/2012/index.phtml>  
Professor Amarenco informs us that the 2<sup>nd</sup> sensory Bladder Meeting will be held in June 2014

**UPCOMING MEETINGS: DATES FOR YOUR DIARY**

**BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS A NEW INSIGHT INTO A PUZZLE, ROME, 17 NOVEMBER 2012.**

Invited leading world experts who deal with Interstitial Cystitis / BPS will meet in Rome for a global conference, organized by **ESSIC**, the *International Society for the Study of Bladder Pain Syndrome* ([www.essic.org](http://www.essic.org)), to compare views and insights into nomenclature, definitions, research and therapies. On November 17 an open symposium is scheduled for doctors and specialists at which these world experts will present an overview of this disease in terms of diagnosis and therapy. The participation fee is € 100.00 and entitles acquisition of ECM. The programme starts at 8.30 am and ends at 18.00 and includes coffee break and lunch.

Link to the programme flyer: [http://www.painful-bladder.org/pdf/2012\\_11\\_Rome.pdf](http://www.painful-bladder.org/pdf/2012_11_Rome.pdf)

**UROGENITAL PAIN MEETING, ROYAL SOCIETY OF MEDICINE, LONDON, Friday 18 January 2013**

A meeting on Urogenital Pain will be held on Friday 18 January 2013 at the Royal Society of Medicine, 1 Wimpole Street, LONDON, W1G 0AE, United Kingdom. The aim is to provide an overview of urogenital pain and how to manage this complex group of patients.

Objectives of this meeting are as follows:

1. To provide information about the science and aetiology behind UGP.
2. To define the epidemiology of UGP in the UK.
3. To discuss the clinical picture, including investigations and specialised imaging in UGP.
4. To discuss management strategies and options in UGP.
5. To discuss long term care and strategies in managing the patient with UGP.

Who should attend: Consultant, GPs, SpR, SHO and nurses, physiotherapists, psychologists and patient liaison groups. Further information may be obtained from:

[www.rsm.ac.uk/academ/pnd01.php](http://www.rsm.ac.uk/academ/pnd01.php)

#### **JOINT 3rd INTERNATIONAL CONSULTATION ON INTERSTITIAL CYSTITIS JAPAN (ICICJ) AND THE ESSIC ANNUAL MEETING 21-23 MARCH 2013**

The Comfortable Urology Network (CUN) of Japan, the International Society for the Study of BPS (ESSIC) and the Society of Interstitial Cystitis of Japan (SICJ) have pleasure in announcing a joint meeting of the 3rd International Consultation on Interstitial Cystitis Japan (ICICJ) and the ESSIC annual meeting 2013 to be held in Kyoto, Japan 21-23 March, 2013 to mark the 10th Anniversary of the first ICICJ. The theme of this meeting will be: **PHENOTYPING BLADDER PAIN BASED ON PATHOPHYSIOLOGY** and will form an important step in a multi-stage international approach to phenotyping the disease based on the pathophysiology and a redefinition of interstitial cystitis/bladder pain syndrome/hypersensitive bladder syndrome (IC/BPS/HBS) suitable for clinical and scientific use worldwide. The meeting website for this unique international event is now open and has full details of abstract submission, registration, schedule and contact address:

[http://www.hainyo-net.org/study/icicj/index\\_e.html](http://www.hainyo-net.org/study/icicj/index_e.html)

For pdf version of the meeting flyer, [click here](#).

#### **1<sup>ST</sup> WORLD CONGRESS ON ABDOMINAL & PELVIC PAIN, 30 MAY-1 JUNE 2013, AMSTERDAM, THE NETHERLANDS**

The 1st World Congress on Abdominal and Pelvic Pain is a new initiative in the world of visceral pain. It is being set up by three organizations active in the field of pelvic pain. Pain of UroGenital Origin (PUGO), the International Pelvic Pain Society (IPPS) and ConvergencesPP (ConPP) have joined forces to organize this unique meeting. In the early stages, it became increasingly evident that because pelvic pain is in its nature a type of visceral pain, it was essential to include abdominal pain in the scientific programme and in the theme of the meeting. The meeting will be held 30 May-1 June 2013, which is right in the middle of the Global Year Against Visceral Pain launched in October 2012 by the International Association for the Study of Pain. Apart from disseminating high quality information, the organisers hope and trust that this initiative will contribute to raising further awareness and increasing knowledge about this debilitating condition. Further information: [www.pelvicpain-meeting.com](http://www.pelvicpain-meeting.com).

#### **INTERNATIONAL NEUROMODULATION SOCIETY (INS) 11<sup>TH</sup> WORLD CONGRESS, BERLIN, GERMANY, 8-13 JUNE 2013**

The INS 11th World Congress will be held in Berlin on 8-13 June 2013. The INS informs us that it will feature a session on treating painful bladder symptoms and dysfunction with neuromodulation/neurostimulation on Tuesday, 11 June, in the afternoon. More information will soon be available at: <http://www.neuromodulation.com/ins-congress>.

**Reminder to conference organisers - Registration fees are often too high for voluntary patient advocates**

*There are a number of upcoming meetings in the field of chronic pelvic/bladder pain which are of interest to both patients and healthcare professionals. A recurrent problem for patient advocates is the unaffordability of registration fees for many of these conferences. We would like to put in a plea to all conference organisers for fee waivers or very low registration fees for voluntary patient representatives from non-profit organisations.*

**BOOKS, VIDEOS, WEBSITES...**

**IPBF WEBSITE updates:**

The International Painful Bladder Foundation has recently updated its large brochure (54 pages) on Interstitial Cystitis/Painful Bladder: Diagnosis & Treatment. A quick link to this can be found in the top right-hand corner of the home page or **click here** to access directly.

For Dutch speakers, Dr Joop P. van de Merwe is working hard on the translation of his English-language book on Sjögren's syndrome into Dutch. Many more chapters in Dutch have now been added, **click here for more information**.

**DIAGNOSIS AND TREATMENT FOR URINARY INCONTINENCE (in Chinese)**

Published 2012 by People's Military Press

ISBN: 978-7-5091-6139-5

Hardback, 509 pp

Chapters 47 and 48: Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome (Chapter 48 by Jane Meijlink in both Chinese and English)

**PAIN COMORBIDITIES**

Edited by M.A. Giamberardino, S.T. Jensen

Published by IASP Press, pp 507

ISBN 978-0-931092

An in-depth analysis of complex clinical situations involving multiple concurrent diseases, this book reviews the clinical presentation and management of interactions among medical conditions, including myofascial pain, headache, fibromyalgia, visceral pain, hypertension, diabetes, osteoarthritis, low back pain, obesity, depression, and anxiety. For online information, **click here**.

**NVA NEWS**

The National Vulvodynia Association (NVA) publishes NVA News several times a year. It is packed with the latest information on research, diagnosis and treatment. The Fall 2012 issue has an excellent article on Treating GVD with Multilevel Nerve Blocks, Results of an NVA-funded Study. For further information about the NVA, **click here**.

**INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN (IASP) PUBLISHES UPDATED CLASSIFICATION OF CHRONIC PAIN ONLINE (www.iasp-pain.org)**

An updated, free version of what was formerly published in book form, *Classification of Chronic Pain*, is now exclusively available in downloadable PDFs on the IASP website. This popular publication provides researchers and clinicians dealing with pain an approved vocabulary, definitions, and codes for their field. Originally published in 1986 and updated in 1994, the book includes pain definitions (taxonomy) which were revised in 2011 and two areas – one section on Complex Regional Pain Syndromes (CRPS) and six sections on abdominal, pelvic, and urogenital pain – which were revised in 2012.

In order to find the section on chronic pelvic pain syndromes, go to:

[http://www.iasp-pain.org/AM/Template.cfm?Section=Classification\\_of\\_Chronic\\_Pain&Template=/CM/ContentDisplay.cfm&ContentID=16280](http://www.iasp-pain.org/AM/Template.cfm?Section=Classification_of_Chronic_Pain&Template=/CM/ContentDisplay.cfm&ContentID=16280)

And then look for: [GROUP XXIII: CHRONIC PELVIC PAIN SYNDROMES](#)

### **IASP GLOBAL YEAR ON VISCERAL PAIN**

The IASP has launched its 2012-2013 Global Year against Visceral Pain campaign. This year, the IASP initiative will focus global attention on pain that originates in or near the internal organs of the body. Visceral pain is the most frequent form of pain, felt by most people at one time or another, the number one reason for patients to seek medical attention, and yet it is insufficiently treated as it is considered just a symptom of an underlying disease: if we treat the disease the pain will go away - an approach that ignores that many forms of visceral pain are diseases in their own right and require focused and specific therapies. **Click here for further information.**

### **RESEARCH HIGHLIGHTS**

#### **A REVIEW OF SELECTED RECENT SCIENTIFIC LITERATURE ON INTERSTITIAL CYSTITIS 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 syndrome, chronic pelvic pain (syndrome) or combinations of these. When reviewing the article, we generally use the terminology used by the authors.

#### **PROGNOSTIC FACTORS FOR RECENT-ONSET INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.**

Warren JW, Clauw DJ, Langenberg P. *BJU Int.* 2012 Aug 9. doi: 10.1111/j.1464-410X.2012.11422.x. [Epub ahead of print]. PMID: 22882525

As diagnosed at present, interstitial cystitis/painful bladder syndrome (IC/PBS) is primarily identified in adult women. Although a chronic disease, its natural history has not been well studied. In a prospective study of 304 incident female IC/PBS cases followed for a median of 33 months after onset, women with baseline chronic fatigue syndrome had a worse prognosis for IC/PBS. Mild IC/PBS at baseline was the only variable that was directly associated with a good prognosis. The purpose of this study from the University of Michigan was to identify baseline variables that predict the prognosis of interstitial cystitis/painful bladder syndrome (IC/PBS) in women seeking medical care for recent onset of this syndrome. In a prospective study of women with incident IC/PBS ( $\leq 12$  months of symptoms), Warren and colleagues contacted patients at intervals and asked standardized questions about IC/PBS symptoms in the previous week. Logistic regression analyses assessed baseline variables as predictors of mild versus more severe IC/PBS at the last follow-up. Median length of follow-up was 33 months after onset of IC/PBS; 304 (97%) patients had at least one follow-up assessment. Mild IC/PBS at baseline was the only variable that was directly associated with a mild IC/PBS endpoint. Conversely, a history of chronic fatigue syndrome (CFS) was inversely associated with a mild endpoint of IC/PBS (i.e. individuals with CFS had a worse prognosis for their IC/PBS symptoms). The authors concluded that at a median of nearly 3 years after onset, baseline mild IC/PBS was directly associated with a milder disease severity. Baseline co-morbid CFS was associated

with more severe disease. Whether CFS was uniquely associated or represented several co-morbid non-bladder syndromes (NBSs) could not be determined.

#### **IS THERE A HIGH INCIDENCE OF HYSTERECTOMY AND OTHER NONBLADDER SURGERIES BEFORE AND AFTER ONSET OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME?**

Warren JW, Howard FM, Morozov VV. *Am J Obstet Gynecol.* 2012 Oct 15. pii: S0002-9378(12)01080-0. doi: 10.1016/j.ajog.2012.10.008. [Epub ahead of print] PMID: 23092763

The objective of this study was to compare with controls the incidence of nonbladder pelvic surgeries in the months before and after the onset of interstitial cystitis/bladder pain syndrome (IC/BPS). The design of the study used an existing database from a retrospective case-control study of 312 incident IC/BPS cases and matched controls plus a longitudinal study of the cases that examined lifetime approximated annual incidence of surgeries with that in the months before and after the onset of IC/BPS. In cases, in the month before the onset of IC/BPS, the approximated annual incidence of nonbladder pelvic surgeries was 15 times higher and of hysterectomy 25 times higher than the incidences of previous years and similarly higher than controls. This rate declined to preindex levels over the first 2 years of IC/BPS. The authors conclude that there may be a very high incidence of nonbladder surgeries just before IC/BPS onset that decreases to historical levels over the first years of the syndrome.

#### **HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND FREQUENTLY ASSOCIATED COMORBIDITIES.**

Suskind AM, Berry SH, Suttorp MJ, Elliott MN, Hays RD, Ewing BA, Clemens JQ. *Qual Life Res.* 2012 Oct 7. [Epub ahead of print] PMID: 23054497

The purpose of this study was to estimate the association of chronic non-urolologic conditions [i.e., fibromyalgia (FM), chronic fatigue syndrome (CFS), and irritable bowel syndrome (IBS)] with health-related quality of life (HRQOL) in patients with interstitial cystitis/bladder pain syndrome (IC/BPS). A total of 276 women with established diagnoses of IC/BPS completed a telephone interview which included demographics, self-reported medical conditions, the SF-36 health survey, and the interstitial cystitis symptom index (ICSI). Multivariate linear regression analysis was used to identify correlates of SF-36 physical and mental component summary scores. It was concluded that in patients with IC/BPS, the presence of FM, CFS, and IBS has a significant association with HRQOL, equivalent in impact to the bladder symptoms themselves. These results emphasize the importance of a multidisciplinary approach to treating patients with IC/BPS and other conditions.

#### **COMORBIDITIES OF INTERSTITIAL CYSTITIS**

Chelimsky G, Heller E, Buffington CA, Rackley R, Zhang D, Chelimsky T. *Front Neurosci.* 2012;6:114. Epub 2012 Aug 10. PMID: 22907988

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

There is currently greatly increasing interest in comorbidities (associated disorders). This USA study aimed to estimate the proportion of patients with interstitial cystitis/painful bladder syndrome (IC/BPS) with systemic dysfunction associated co-morbidities such as irritable bowel syndrome (IBS) and fibromyalgia (FM). Two groups of subjects with IC/BPS were included: (1) physician diagnosed patients with IC/BPS and (2) subjects meeting NIDDK IC/PBS criteria based on a questionnaire (ODYSA see note below). These groups were compared to healthy controls matched for age and socio-economic status. NIDDK criteria required: pain with bladder filling that improves with emptying, urinary urgency due to discomfort or pain, polyuria >11 times/24 h, and nocturia >2 times/night. The ODYSA questionnaire evaluates symptoms pertaining to a range of disorders including chronic fatigue, orthostatic intolerance, syncope, IBS, dyspepsia, cyclic vomiting syndrome, headaches and migraines, sleep, Raynaud's syndrome, and chronic aches and pains. IC/BPS was diagnosed in 26 subjects, 58 had symptoms of IC/BPS by NIDDK criteria and 48 were healthy controls. Co-morbid

complaints in the IC/BPS groups included gastrointestinal symptoms suggestive of IBS and dyspepsia, sleep abnormalities with delayed onset of sleep, feeling poorly refreshed in the morning, waking up before needed, snoring, severe chronic fatigue and chronic generalized pain, migraines, and syncope. The authors report that patients with IC/BPS had co-morbid central and autonomic nervous system disorders. They note that their findings mirror those of others in regard to IBS, symptoms suggestive of FM, chronic pain, and migraine. High rates of syncope and functional dyspepsia found in the IC/BPS groups merit further study to determine if IC/BPS is part of a diffuse disorder of central, autonomic, and sensory processing affecting multiple organs outside the bladder. This study demonstrates widespread co-morbidities in patients with interstitial cystitis, both physician and questionnaire diagnosed, with very similar findings in the two groups. Known co-morbid disorders were confirmed, including migraine headache, IBS, and widespread pain. New co-morbidities emerged, including dyspepsia-like symptoms and orthostatic intolerance. The multiple involvement of organ systems far from the bladder supports the theory that IC/BPS is not a primary bladder disorder, but rather that the bladder is one more organ system involved in a systemic, possibly neurologic disorder.

*Note: The Ohio Dysautonomia (ODYSA) questionnaire evaluates for 12 autonomic diagnoses: complex regional pain syndrome, chronic fatigue syndrome, cyclic vomiting syndrome, fibromyalgia, functional abdominal pain, functional dyspepsia, interstitial cystitis, irritable bowel syndrome, migraine, orthostatic intolerance, Raynaud's syndrome and reflex syncope.*

*Orthostatic intolerance (OI) is the development of a set of characteristic symptoms while standing or sitting upright. It has been associated with chronic fatigue syndrome (CFS) in both adults and children. Symptoms of OI can include lightheadedness, dizziness, nausea, fatigue, tremors, breathing or swallowing difficulties, headache, visual disturbances, sweating and pallor*

#### **A CASE-CONTROL STUDY ON THE ASSOCIATION BETWEEN RHEUMATOID ARTHRITIS AND BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.**

*Keller JJ, Liu SP, Lin HC. *Neurourol Urodyn*. 2012 Nov 5. doi: 10.1002/nau.22348. [Epub ahead of print]. PMID: 23129416*

While bladder pain syndrome/interstitial cystitis (BPS/IC) has been suggested by a number of studies to have an autoimmune character, no population-based study to date has been conducted investigating its association with rheumatoid arthritis (RA). This study from Taiwan aimed to examine the association between IC/BPS and having previously been diagnosed with RA. Keller et al conducted this study by using administrative claims data sourced from the Taiwan National Health Insurance Database. Their study included 9,269 cases with BPS/IC and 46,345 randomly selected controls. Conditional logistic regression was performed to calculate the odds ratio (OR) for the association between previously diagnosed RA and IC/BPS. RA was found among 202 (2.2%) cases and 504 (1.12%) controls. Conditional logistic regression analysis suggested that when compared with controls, the odds ratio for prior RA among cases was 1.66 after adjusting for diabetes, hypertension, coronary heart disease, obesity, hyperlipidemia, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraine, sicca syndrome, allergy, endometriosis, asthma, overactive bladder, tobacco use disorder, and alcohol abuse. Additionally, BPS/IC was consistently and significantly associated with a previous diagnosis of RA regardless of prescription drug use. It was concluded that there is indeed an association between RA and BPS/IC after adjusting for socio-demographic characteristics and medical co-morbidities.

#### **COMORBIDITIES OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: A POPULATION-BASED STUDY.**

*Keller JJ, Chen YK, Lin HC. *BJU Int*. 2012 Sep 28. doi: 10.1111/j.1464-410X.2012.11539.x. [Epub ahead of print] PMID: 23020942*

The purpose of this study from Taiwan was to explore the comorbid medical conditions of patients with bladder pain syndrome/interstitial cystitis (BPS/IC) in Taiwan using a cross-sectional study design and a population-based administrative database. With the exception of metastatic cancer, the subjects with BPS/IC had a significantly higher prevalence of all the medical comorbidities analysed than subjects without BPS/IC. With the exception of metastatic cancer, separate conditional logistic regression analyses suggested that subjects with BPS/IC were consistently more likely than subjects without BPS/IC to have any of the medical comorbidities investigated in this study. When compared with subjects without BPS/IC, subjects with BPS/IC had particularly higher odds of comorbid neurological diseases, rheumatological diseases and mental illnesses. The authors concluded that their results indicated that subjects with BPS/IC had an increased prevalence of multiple comorbidities.

#### **FULGURATION FOR HUNNER ULCERS: LONG-TERM CLINICAL OUTCOMES.**

*Hillelsohn JH, Rais-Bahrami S, Friedlander JI, Okhunov Z, Kashan M, Rosen L, Moldwin RM. J Urol. 2012 Oct 18. pii: S0022-5347(12)04450-3. doi: 10.1016/j.juro.2012.08.013. [Epub ahead of print]. PMID: 23083651*

Cystoscopic fulguration of Hunner ulcers in patients with interstitial cystitis/bladder pain syndrome is a recommended therapy because it has the potential to rapidly ameliorate symptoms. Hillelsohn and colleagues reviewed their experience with Hunner ulcer fulguration. They retrospectively reviewed the records of patients with interstitial cystitis/bladder pain syndrome treated with Hunner ulcer fulguration who were seen at their pelvic pain referral center between 1993 and 2011. Patient demographics, clinical characteristics, intraoperative findings and long-term clinical outcomes were assessed. The Kaplan-Meier product limit method was used to evaluate time to the first repeat procedure. Potential risk factors associated with repeat procedures were examined using the log rank test. A total of 106 procedures were performed in 59 patients. The mean history of illness before first fulguration was 5 years and overall median followup was 44.8 months (IQR 52.2), as calculated from the time of the first fulguration. There were no significant associations between time to the first repeat procedure and any demographic criteria analyzed, patient reported interstitial cystitis/bladder pain syndrome associated conditions or the number of Hunner ulcers fulgurated at the initial session. A total of 27 patients (45.8%) required repeat fulguration. Time to event analysis demonstrated that 12 months after the initial fulguration 13.1% of patients required repeat treatment. This rate increased to 57.2% at 48 months, when it plateaued. The authors concluded that fulguration of Hunner ulcers can be an effective treatment for patients with interstitial cystitis/bladder pain syndrome and focal Hunner ulcers involving less than 25% of the bladder who have symptoms refractory to other therapies. However, a significant subset requires repeat treatment and some patients may even go on to require cystectomy.

#### **POLYMORPHISM IN THE SCN9A VOLTAGE-GATED SODIUM CHANNEL GENE ASSOCIATED WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.**

*Reeder JE, Byler TK, Foster DC, Landas SK, Okafor H, Stearns G, Wood RW, Zhang Y, Mayer RD. Urology. 2012 Oct 24. pii: S0090-4295(12)00978-8. doi: 10.1016/j.urology.2012.07.072. [Epub ahead of print]. PMID: 23102778*

The purpose of this study was to determine whether an association exists between interstitial cystitis/bladder pain syndrome (IC/BPS) and a nonsynonymous single nucleotide polymorphism in the SCN9A voltage-gated sodium channel gene previously associated with other chronic pain syndromes. Germline deoxyribonucleic acid was sampled from archived bladder biopsy specimens from patients with a documented diagnosis of IC/BPS. Deoxyribonucleic acid from hysterectomy specimens was obtained as a control population. The genotype of single nucleotide polymorphism rs6746030 was determined by deoxyribonucleic acid sequencing after polymerase chain reaction amplification. Contingency analysis of genotypes was performed using Pearson's chi-square test and



Fisher's exact test. Polymerase chain reaction product was obtained from 26 of 31 control specimens and from 53 of 57 IC/BPS biopsy specimens. Of the 26 control subjects, 3 (11.5%) were genotype AG and 23 were GG. In contrast, AA or AG genotypes were present in 21 of 53 (39.6%) patients with IC/BPS, a statistically significant difference compared with the controls (Pearson's chi-square,  $P = .036$ ). Similarly, the A allele was at a greater frequency in the IC/BPS group using Fisher's exact test ( $P = .009$ ). According to the authors, these data strongly suggest that pain perception in at least a subset of patients with IC/BPS is influenced by this polymorphism in the SCN9A voltage-gated sodium channel.

#### **DISABILITY IN WOMEN SUFFERING FROM INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.**

*Katz L, Tripp DA, Nickel JC, Mayer R, Reimann M, van Ophoven A. BJU Int. 2012 May 11. doi: 10.1111/j.1464-410X.2012.11238.x. [Epub ahead of print] PMID: 22578191*

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a disease that is associated with significant disability in the areas of self-care, sexual functioning, occupation, family and home responsibilities, and social functions. Compared to age- and cohort-matched controls, patients with IC/BPS reported poorer mental and physical quality of life (QoL), as well as greater pain, depression, anxiety, catastrophizing, sexual dysfunction and less social support. In particular, catastrophizing and depression are suggested to be important for understanding the factors promoting a poorer QoL in IC/BPS. The findings of this multi-centre study suggest that psychosocial factors are significant in mediating the relationship between impairments and patient disability, with negative affect (i.e. depression, anxiety) and pain catastrophizing acting as significant mediators. These findings argue that catastrophizing and negative affect may be the mechanisms by which pain and symptoms elevate reports of patient disability. Understanding how pain and pain-associated symptoms may become disabling through cognitive mechanisms represents an importance advance for IC/BPS management. Clinical interventions in women suffering from IC/BPS should target catastrophizing and mood for reduction using cognitive behavioural strategies aiming to decrease pain-related disability. The purpose of this study was to examine a biopsychosocial framework of patient disability in patients suffering from interstitial cystitis/bladder pain syndrome (IC/BPS) and to evaluate the impact of psychosocial factors on the relationship between pain and disability within women with IC/BPS. Questionnaires completed by 196 women with IC/BPS provided data for the present study. The measurement model showed good fit to the data. Negative affect and catastrophizing were significant in explaining the relationship between impairments and functional disability, whereas social support did not. It was concluded that disability in patients suffering from IC/BPS is partially explained by the impact of negative affect and catastrophizing. As a result of the refractory nature of IC/BPS, patient management within a biopsychosocial framework represents an essential area of investigation. Decreases in negative affect and catastrophizing will probably lead to improvements in pain-related disability.

#### **NEUROTROPHINS AS REGULATORS OF URINARY BLADDER FUNCTION.**

*Ochodnický P, Cruz CD, Yoshimura N, Cruz F. Nat Rev Urol. 2012 Nov;9(11):628-37. doi: 10.1038/nrurol.2012.178. Epub 2012 Oct 9. PMID: 23045265*

In this Review, Ochodnický and colleagues discuss the clinical and experimental evidence that supports a role for neurotrophins in the neural control of bladder function and in the emergence of lower urinary tract symptoms related to overactive bladder (OAB) and bladder pain syndrome/interstitial cystitis. They also consider the potential utility of neurotrophins as urinary biomarkers for improving the accuracy of OAB diagnosis and monitoring therapy efficacy, and review proof-of-principle clinical evidence that confirms nerve growth factor as a potential target in the treatment of bladder disorders. Increased voiding frequency and urgency are among the most prevalent storage lower urinary tract symptoms (LUTS), often diagnosed as part of overactive bladder syndrome (OAB). It has been suggested that these symptoms are caused by excessive sensory

activation of the neural micturition circuit. It seems likely that sensory pathway remodelling is also responsible for pain perception upon bladder filling in patients with bladder pain syndrome (BPS). Neurotrophins-including nerve growth factor (NGF), brain-derived nerve factor (BDNF), neurotrophin-3 (NT-3) and neurotrophin-4 (NT-4)-represent master modulators of neural plasticity, both in peripheral and central nervous systems. Accumulating evidence points towards a role for neurotrophins in the control of neural sensory function during micturition and indicates their involvement in the emergence of OAB-related and BPS-related LUTS. Neurotrophins could potentially be used as urinary biomarkers to improve diagnostic accuracy for OAB and BPS and monitor therapy effectiveness. Proof-of-principle clinical evidence has confirmed that NGF is a potential target for treating human bladder overactivity.

**BLADDER PAIN SYNDROME ASSOCIATED WITH HIGHEST IMPACT ON SEXUAL FUNCTION AMONG WOMEN WITH LOWER URINARY TRACT SYMPTOMS.**

*Sacco E, D'Addessi A, Racioppi M, Pinto F, Totaro A, Bassi P. Int J Gynaecol Obstet. 2012 May;117(2):168-72. Epub 2012 Feb 22. PMID: 22361478*

The purpose of this study from Agostino Gemelli Hospital, Rome, Italy was to investigate the differential impact of lower urinary tract symptoms (LUTS) on female sexual function (FSF). 188 sexually active patients with LUTS, as assessed by self-reported questionnaires, underwent comprehensive urologic and urodynamic examination between January 2008 and December 2010. Patients with urinary incontinence, voiding-phase LUTS, overactive bladder (OAB), and bladder pain syndrome (BPS) were included. FSF was assessed by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire –12 (PISQ-12), and scores were compared between the patients and a group of age-matched women without lower urinary tract symptoms. It was found that the global PISQ-12 mean score was significantly higher among patients with lower urinary tract symptoms than among controls (18.4). Women with BPS reported the highest global PISQ-12 score (46.1), followed by those with urodynamic detrusor overactivity (45.0), clinical urgency (41.4), mixed (37.7) and stress urinary incontinence (28.1), dry OAB (22.2) and voiding-phase LUTS (19.6). Age, urinary incontinence, BPS, and detrusor overactivity were independent predictors of FSF. The authors concluded that BPS was associated with the greatest impairment of FSF among women with lower urinary tract symptoms.

**CONSTRUCT VALIDITY OF AN INSTRUMENT TO MEASURE NEUROPATHIC PAIN IN WOMEN WITH BLADDER PAIN SYNDROME.**

*Arya LA, Harvie HS, Andy UU, Cory L, Propert KJ, Whitmore K. Neurourol Urodyn. 2012 Sep 12. doi: 10.1002/nau.22314. [Epub ahead of print]*

The aim of this study was to determine the construct validity of an instrument to measure neuropathic pain in women with bladder pain syndrome (BPS). The hypothesis of Arya and colleagues was that neuropathic, bladder, and bowel pain represent different constructs in women with BPS. The study was carried out on the basis of secondary planned analysis of a prospective cross-sectional study of 150 women with BPS. The relationship between neuropathic pain, urinary, and bowel symptoms was assessed. The correlation of the total neuropathic pain score with total urinary and bowel symptom scores was low to moderate. The correlation of specific neuropathic pain items with bladder and bowel pain was also low to moderate. Women with BPS report pain in organs such as the bowel and bladder and also somatosensory pain such as burning pain and hypersensitivity to touch in the lower abdomen, urethra, lower back, anus, and vagina.<sup>2,3</sup> Visceral pain is perceived in organs such as the bladder or the bowel and is transmitted via “silent,” unmyelinated C-fibers. Women with neuropathic pain had significantly higher scores for urinary urgency, bladder pain, abdominal pain, diarrhoea, and constipation than women with non-neuropathic pain. The authors concluded that somatosensory neuropathic pain and “visceral” bladder and bowel pain represent separate but related constructs in women with BPS.

**INCREASED RISK OF DEPRESSIVE DISORDER FOLLOWING DIAGNOSIS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.**

*Keller JJ, Liu SP, Lin HC. Neurourol Urodyn. 2012 Sep 21. doi: 10.1002/nau.22316. [Epub ahead of print] PMID: 23001581*

Using a longitudinal follow-up design, this study from Taipei, Taiwan aimed to examine the risk of depressive disorder (DD) among women with BPS/IC compared to the general population during a 1-year period following their diagnosis. This study used data from the Taiwan "Longitudinal Health Insurance Database." A total of 832 patients with BPS/IC were included in the study group and 4,160 matched non-BPS/IC enrollees were included as the comparison group. Each patient was individually tracked for a 1-year period to identify those who subsequently received a diagnosis of DD. Cox proportional hazards regressions (stratified by age group and the index year) were used to estimate the risk of subsequent DD following a diagnosis of BPS/IC. Keller and colleagues found that during the 1-year follow-up the incidence rate of DD was 4.69 per 100 person-years in patients with BPS/IC and 0.94 per 100 person-years in comparison patients. The hazard ratio (HR) of DD during the 1-year follow-up period for patients with BPS/IC was 5.06 that of comparison patients after adjusting for patient monthly income, geographic location, and urbanization level. The adjusted HR for DD associated with BPS/IC was 10.33 for patients aged between 40 and 49. The authors note that their study did have a number of limitations but nevertheless conclude that their study demonstrated that there is an increased risk for being diagnosed with DD during the first year subsequent to being diagnosed with BPS/IC after adjusting for socio-demographic characteristics. They suggest that clinical practitioners dealing with patients suffering from BPS/IC be alert to the increased prevalence of clinically depressive symptoms in this population.

**RISK FACTORS THAT AFFECT THE TREATMENT OF INTERSTITIAL CYSTITIS USING INTRAVESICAL THERAPY WITH A DIMETHYL SULFOXIDE COCKTAIL.**

*Hung MJ, Chen YT, Shen PS, Hsu ST, Chen GD, Ho ES. Int Urogynecol J. 2012 Nov;23(11):1533-9. doi: 10.1007/s00192-012-1699-x. Epub 2012 Mar 17. PMID: 22426874*

Dimethyl sulfoxide (DMSO) bladder instillation is a standard therapy for interstitial cystitis (IC); however, there are varying degrees of success. Hung and colleagues from Taiwan hypothesize that first-line intravesical therapy with a DMSO cocktail will optimize treatment outcome. Ninety women with newly diagnosed IC were enrolled consecutively for the treatment. The IC symptom and problem index was used as an outcome measure. Six (6.7%) patients dropped out of the treatment due to intolerable bladder irritation. Fifty-five (65.5%) of the remaining 84 patients, who completed the treatment, experienced  $\geq 50\%$  symptomatic improvement. After a regression analysis, three clinical variables were found to affect treatment adversely, i.e., the presence of advanced cystoscopic glomerulations, microscopic hematuria, and urodynamic detrusor underactivity, respectively. The authors believe that their results suggest bladder instillation with a DMSO cocktail may well be considered as first-line therapy for IC patients. However, there exists a subgroup of nonresponders who may have severe disease.

**MCP-1-INDUCED HISTAMINE RELEASE FROM MAST CELLS IS ASSOCIATED WITH DEVELOPMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME IN RAT MODELS.**

*Lv J, Huang Y, Zhu S, Yang G, Zhang Y, Leng J, Bo J, Liu D. Mediators Inflamm. 2012;2012:358184. doi: 10.1155/2012/358184. Epub 2012 Sep 19. PMID: 23049171*

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Interstitial cystitis/bladder pain syndrome (IC/BPS) is characterized by overexpression of monocyte chemoattractant protein-1 (MCP-1) in bladder tissues and induction of mast cell (MC) degranulation. This study from Chinawas undertaken to explore the mechanism of action of MCP-1 in the development of IC/BPS. A rat model of IC/BPS was developed by perfusing bladders of nine SPF-grade female Sprague-Dawley rats with protamine sulfate and lipopolysaccharide (PS+LPS). MCP-1

and histamine levels in bladder tissue and urine were detected by immunohistochemistry and ELISA. MC degranulation was measured by immunofluorescence techniques and chemokine (C-C motif) receptor 2 (CCR2) was assayed by flow cytometry. Increased MCP-1 expression in bladder tissue and elevated MCP-1 and histamine levels were observed in the urine of LS+LPS-treated rats. This was accompanied by the expression of CCR2 on MC surfaces, suggesting MCP-1 may induce MC degranulation through CCR2. Exposure to LPS stimulated MCP-1 expression in bladder epithelial cells, and exposure to MCP-1 induced histamine release from MCs. It was concluded that MCP-1 upregulation in IC/BPS is one of possible contributing factors inducing histamine release from MCs. CCR2 is involved in the process of mast cell degranulation in bladder tissues. These changes may contribute to the development of symptoms of IC/BPS.

**INCREASED URINE AND SERUM NERVE GROWTH FACTOR LEVELS IN INTERSTITIAL CYSTITIS SUGGEST CHRONIC INFLAMMATION IS INVOLVED IN THE PATHOGENESIS OF DISEASE.**

*Liu HT, Kuo HC. PLoS One. 2012;7(9):e44687. doi: 10.1371/journal.pone.0044687. Epub 2012 Sep 17. PMID: 23028581*

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Interstitial cystitis/bladder pain syndrome (IC/BPS) is considered a bladder disorder due to localized chronic inflammation. This study from Taiwan investigated the nerve growth factor (NGF) levels in serum and urine in patients with IC/BPS. Thirty patients with IC/BPS and 28 normal subjects without lower urinary tract symptoms were recruited from an outpatient clinic. IC/BPS was diagnosed by frequency, bladder pain, and the presence of glomerulations during cystoscopic hydrodistention. Serum and urine were collected before any treatment was given. Serum NGF and urinary NGF/Cr levels were compared between IC/BPS and the controls. Urinary NGF levels were significantly higher in patients with IC/BPS than in controls. After normalization, the urinary NGF/Cr levels were significantly greater in IC/BPS than controls. Relative to the levels in control subjects, the mean serum NGF levels were higher in patients IC/BPS patients. No significant correlation was found between the serum and urinary NGF levels in IC/BPS patients. However, the clinical characteristics and medical co-morbidities did not show significant difference between IC/BPS patients with a higher and lower serum NGF level. It was concluded that increased urinary NGF levels in IC/BPS patients suggest that chronic inflammation is involved in this bladder disorder. Increased circulating serum NGF levels were noted in over half of patients with IC/BPS, however, the urinary and serum NGF were not inter-correlated and elevated serum NGF did not relate with clinical features.

**STONES: DO URINARY CALCULI INCREASE RISK OF BLADDER PAIN SYNDROME?**

*Warren JW. Nat Rev Urol. 2012 Nov;9(11):607-8. doi: 10.1038/nrurol.2012.184. Epub 2012 Oct 9. PMID: 23045260*

A Taiwanese study has established an association between bladder pain syndrome (BPS) and prior diagnosis of urinary stones. The study authors suggest that stones initiate a process that results in BPS. According to Warren, an alternative hypothesis is that patients with BPS are more likely to undergo imaging, revealing incidental stones.

Two articles discussing the pros and cons of sacral neuromodulation:

**1. SACRAL NEUROMODULATION IS AN EFFECTIVE TREATMENT FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: CON.**

*Evans RJ. J Urol. 2012 Sep 20. pii: S0022-5347(12)04942-7. doi: 10.1016/j.juro.2012.09.073. [Epub ahead of print] PMID: 23000858*

**2. SACRAL NEUROMODULATION IS AN EFFECTIVE TREATMENT FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME:PRO.**

*Peters KM. J Urol. 2012 Sep 20. pii: S0022-5347(12)04941-5. doi: 10.1016/j.juro.2012.09.072. [Epub ahead of print] PMID: 23000855*

#### **DETERMINATION OF URINARY HEXOSAMINES FOR DIAGNOSIS OF BLADDER PAIN SYNDROME**

*Buzzega D, Maccari F, Galeotti F, Volpi N. Int Urogynecol J. 2012 Oct;23(10):1367-72. Epub 2012 Apr 21, PMID: 22527561*

Buzzega and colleagues from Italy note that bladder pain syndrome (BPS) is a chronic disease characterized by urgency, bladder pain, and frequency, and urinary glycosaminoglycans are thought to reflect bladder epithelial deficiency in BPS. Sensitive and specific evaluation of total urinary glycosaminoglycans may be useful for the clinical diagnosis of BPS and its treatment. A procedure for the simultaneous determination of glucosamine and galactosamine produced from urinary glycosaminoglycans was performed in BPS patients and healthy subjects. The total content of urinary hexosamines in BPS patients significantly increased by ~130% with the increase in glucosamine greater than galactosamine. It was found that a significant increase in total hexosamines content and in particular in glucosamine belonging to urinary heparan sulfate was determined in BPS patients compared with controls. The authors propose HS and in particular its low-molecular mass fragments and glucosamine assay as useful markers for a biochemical diagnosis of BPS and for monitoring this syndrome.

#### **ALTERATIONS OF MICROBIOTA IN URINE FROM WOMEN WITH INTERSTITIAL CYSTITIS.**

*Siddiqui H, Lagesen K, Nederbragt AJ, Jeansson SL, Jakobsen KS. BMC Microbiol. 2012 Sep 13;12(1):205. [Epub ahead of print]. PMID: 22974186*

The aim of this study was to characterize the microbial community present in the urine from IC female patients by 454 high throughput sequencing of the 16S variable regions V1V2 and V6. The taxonomical composition, richness and diversity of the IC microbiota were determined and compared to the microbial profile of asymptomatic healthy female (HF) urine. The composition and distribution of bacterial sequences differed between the urine microbiota of IC patients and HFs. Reduced sequence richness and diversity were found in IC patient urine, and a significant difference in the community structure of IC urine in relation to HF urine was observed. More than 90% of the IC sequence reads were identified as belonging to the bacterial genus *Lactobacillus*, a marked increase compared to 60% in HF urine. It was concluded that the 16S rDNA sequence data demonstrates a shift in the composition of the bacterial community in IC urine. The reduced microbial diversity and richness is accompanied by a higher abundance of the bacterial genus *Lactobacillus*, compared to HF urine. This study demonstrates that high throughput sequencing analysis of urine microbiota in IC patients is a powerful tool towards a better understanding of this enigmatic disease.

#### **INTERSTITIAL CYSTITIS AND THE OVERLAP WITH OVERACTIVE BLADDER.**

*Elliott CS, Payne CK. Curr Urol Rep. 2012 Oct;13(5):319-26. PMID: 22965225*

The overlap between interstitial cystitis-painful bladder syndrome and overactive bladder can present a diagnostic challenge to the treating practitioner. Both can present with similar patient symptoms. Further compounding this dilemma is the fact that no gold standard test exists to differentiate one from the other. This review highlights their similarities and distinguishing features.

#### **IMMUNOHISTOCHEMICAL EVIDENCE SUGGESTS REPEATED INTRAVESICAL APPLICATION OF BOTULINUM TOXIN A INJECTIONS MAY IMPROVE TREATMENT EFFICACY OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.**

*Shie JH, Liu HT, Wang YS, Kuo HC. BJU Int. 2012 Sep 3. doi: 10.1111/j.1464-410X.2012.11466.x. [Epub ahead of print] PMID: 22943596*

The purpose of this study by Shie and colleagues from Taiwan was to investigate the mechanisms of action of botulinum toxin A (BoNT-A) treatment on interstitial cystitis/bladder pain syndrome (IC/BPS). A total of 23 women with IC/BPS who received single intravesical BoNT-A injection were

studied. Among them, 11 received three repeated injections every 6 months to improve their symptoms. Bladder biopsy was obtained before each BoNT-A injection and the clinical symptoms and urodynamic variables were recorded. Immunohistochemical (IHC) staining for TUNEL and mast cell activity, and western blotting analysis of tryptase, cytokines, Bax and phospho-p38 (p-p38) were carried out. We compared the clinical results and IHC data among baseline, single or repeated BoNT-A treatments. They found that chronic inflammation and apoptotic signalling molecules were significantly reduced after repeated BoNT-A injections in patients with IC/BPS. The IHC improvement was associated with clinical symptom improvement. They suggest that repeated BoNT-A injections are necessary to achieve a greater success rate in the treatment of IC/BPS.

**INTRAVESICAL HYALURONIC ACID FOR INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME: A COMPARATIVE RANDOMIZED ASSESSMENT OF DIFFERENT REGIMENS.**

*Lai MC, Kuo YC, Kuo HC. Int J Urol. 2012 Aug 26. doi: 10.1111/j.1442-2042.2012.03135.x. [Epub ahead of print]. PMID: 22925498*

The purpose of this study from Taiwan by Lai and colleagues was to compare the clinical effectiveness of different regimens of intravesical hyaluronic acid instillation for patients with interstitial cystitis/painful bladder syndrome. A total of 60 patients (age 16-77 years) diagnosed with interstitial cystitis/painful bladder syndrome were enrolled in this prospective, randomized study. A total of 30 patients were assigned to receive four weekly intravesical instillations of 40mg of hyaluronic acid followed by five monthly instillations (hyaluronic acid-9 group). Another 30 patients received 12 intravesical instillations of 40mg hyaluronic acid every 2 weeks (hyaluronic acid-12 group). Symptomatic changes after hyaluronic acid treatments were assessed using Interstitial Cystitis Symptom and Problem Indexes, pain visual analog scale, functional bladder capacity, frequency and nocturia in voiding diary, maximum flow rate, voided volume, postvoid residual volume, and Quality of Life Index at 1, 3 and 6 months. Of the 60 patients, 59 were evaluable at the end of the study. The Interstitial Cystitis Symptom Index, Interstitial Cystitis Problem Index and total score, pain visual analog scale, functional bladder capacity, maximum flow rate, and Quality of Life Index improved significantly after 6 months in both groups. The frequency and voided volume improved significantly only in the hyaluronic acid-12 group. However, patients with moderate and marked improvement were clinically similar in both groups. The measured variables did not differ between the two groups over the course of the study. It was therefore concluded that no significant difference was noted in the therapeutic effect between two hyaluronic acid instillation regimens for treatment of interstitial cystitis/painful bladder syndrome patients. Both groups showed significant improvement in symptom scores and Quality of Life Index.

**MANAGEMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A UROLOGY PERSPECTIVE.**

*Quillin RB, Erickson DR. Urol Clin North Am. 2012 Aug;39(3):389-96. Epub 2012 Jul 3. PMID: 22877722*

Management of interstitial cystitis/bladder pain syndrome (IC/BPS) is individualized for each patient. All patients benefit from education and self-care advice. Patients with Hunner lesions usually respond well to fulguration or triamcinolone injection, which can be repeated when the symptoms and lesions recur. For patients without Hunner lesions, numerous treatment options are available. The tiers of the American Urological Association Guidelines present these options in an orderly progression, balancing the benefits, risks, and burdens. Along with specific IC/BPS treatments, it is also important to have resources for stress reduction, pain management, and treatment of comorbid conditions.

**INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: MANAGEMENT OF THE PAIN DISORDER: A UROGYNECOLOGY PERSPECTIVE.**

*Butrick CW. Urol Clin North Am. 2012 Aug;39(3):377-87. PMID:22877721*

Our understanding of interstitial cystitis/painful bladder syndrome (IC/BPS) has evolved with the advancements in our understanding of visceral pain syndromes. The concept of IC/BPS as a visceral

pain disorder is used as a model to base a targeted approach to the management of patients with IC/BPS. Guidelines for the treatment of both the bladder and nonbladder pain disorders are reviewed.

#### **NERVOUS NETWORK FOR LOWER URINARY TRACT FUNCTION**

*Birder LA. Int J Urol. 2012 Oct 23. doi: 10.1111/j.1442-2042.2012.03210.x. [Epub ahead of print]. PMID: 23088378*

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Traditionally, sensory signalling in the urinary bladder has been largely attributed to direct activation of bladder afferents. There is substantive evidence that sensory systems can be influenced by non-neuronal cells, such as the urothelium, which are able to respond to various types of stimuli that can include physiological, psychological and disease-related factors. The corresponding release of chemical mediators (through activation of a number of receptors/ion channels) can initiate signaling mechanisms between and within urothelial cells, as well as other cell types within the bladder wall including bladder nerves. However, the mechanisms underlying how various cell types in the bladder wall respond to normal filling and emptying, and are challenged by a variety of stressors (physical and chemical) are still not well understood. Alterations or defects in signaling mechanisms are likely to contribute to the pathophysiology of bladder disease with symptoms including urinary urgency, increased voiding frequency and pain. This review discusses some of the components involved in control of lower urinary tract function, with an emphasis on the sensor and transducer roles of the urothelium.

#### **FIBROMYALGIA**

#### **CHARACTERISTICS OF REFERRED MUSCLE PAIN TO THE HEAD FROM ACTIVE TRIGGER POINTS IN WOMEN WITH MYOFASCIAL TEMPOROMANDIBULAR PAIN AND FIBROMYALGIA SYNDROME.**

*Alonso-Blanco C, Fernández-de-Las-Peñas C, de-la-Llave-Rincón AI, Zarco-Moreno P, Galán-Del-Río F, Svensson P. J Headache Pain. 2012 Aug 31. [Epub ahead of print]. PMID: 22935970*

The aim of this study from Madrid, Spain was to compare the differences in the prevalence and the anatomical localization of referred pain areas of active trigger points (TrPs) between women with myofascial temporomandibular disorder (TMD) or fibromyalgia (FMS). Twenty women (age  $46 \pm 8$  years) with TMD and 20 (age  $48 \pm 6$  years) with FMS were recruited from specialized clinic. Bilateral temporalis, masseter, sternocleidomastoid, upper trapezius, and suboccipital muscles were examined for TrPs. TrPs were identified by palpation and considered active when the pain reproduced familiar pain symptoms experienced by the patient. The referred pain areas were drawn on anatomical maps, digitalized and also measured. A new analysis technique based on a center of gravity (COG) method was used to quantitative estimate of the localization of the TrP referred pain areas. Women with FMS exhibited larger areas of usual pain symptoms than women with myofascial TMD. The COG coordinates of the usual pain on the frontal and posterior pain maps were located more superior in TMD than in FMS. The number of active TrPs was significantly higher in TMD than in FMS. Women with TMD exhibited more active TrPs in the temporalis and masseter muscles than FMS. Women with FMS had larger referred pain areas than those with TMD for sternocleidomastoid and suboccipital muscles. Significant differences within COG coordinates of TrP referred pain areas were found in TMD, the referred pain was more pronounced in the orofacial region, whereas the referred pain in FMS was more pronounced in the cervical spine. This study showed that the referred pain elicited from active TrPs shared similar patterns as usual pain symptoms in women with TMD or FMS, but that distinct differences in TrP prevalence and location of the referred pain areas could be observed. Differences in location of referred pain areas may help clinicians to determine the most relevant TrPs for each pain syndrome in spite of overlaps in pain areas.

### **THE ASSOCIATION BETWEEN OVERACTIVE BLADDER AND FIBROMYALGIA SYNDROME: A COMMUNITY SURVEY.**

*Chung JH, Kim SA, Choi BY, Lee HS, Lee SW, Kim YT, Lee TY, Moon HS. Neurourol Urodyn. 2012 Jun 5. doi: 10.1002/nau.22277. [Epub ahead of print]. PMID: 22674758*

Fibromyalgia syndrome (FMS) is the most common disease causing chronic generalized pain, and FMS patients often complain of urinary symptoms such as frequency or urgency. While there have been many studies looking and FMS in associated with painful bladder symptoms, this study from Korea by Chung and colleagues focuses on the association of overactive bladder (OAB) and FMS in adults aged 40 and over. A survey of adults aged 40s and over was conducted in the Guri and Yangpyeong areas of South Korea. The response rate was 74.2% (940/1,266). After excluding subjects with incomplete questionnaires, 920 were included in the final analysis. The association of FMS and OAB was analyzed by univariate and multivariate logistic regression analysis. Individuals with FMS had significantly increased OAB symptoms of after adjustment for gender, age group, and area of residence. The association between FMS and severity of OAB was statistically significant. The authors concluded that OAB is associated with FMS. Moreover FMS increases with severity of OAB.

### **IS CHRONIC FATIGUE SYNDROME THE SAME ILLNESS AS FIBROMYALGIA: EVALUATING THE 'SINGLE SYNDROME' HYPOTHESIS.**

*Abbi B, Natelson BH. QJM. 2012 Aug 26. [Epub ahead of print] PMID: 22927538*

Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are medically unexplained syndromes that can and often do co-occur. For this reason, some have posited that the two are part of the same somatic syndrome-examples of symptom amplification. This hypothesis would suggest that few differences exist between the two syndromes. To evaluate this interpretation, Abbi and Natelson have searched the literature for articles comparing CFS to FM, reviewing only those articles which report differences between the two. This review presents data showing differences across a number of parameters- implying that the underlying pathophysiology in CFS may differ from that of FM. The authors hope that their review encourages other groups to look for additional differences between CFS and FM. By continuing to preserve the unique illness definitions of the two syndromes, clinicians will be able to better identify, understand and provide treatment for these individuals.

### **VULVODYNIA**

#### **RELATIONSHIP BETWEEN VULVODYNIA AND CHRONIC COMORBID PAIN CONDITIONS.**

*Reed BD, Harlow SD, Sen A, Edwards RM, Chen D, Haefner HK. Obstet Gynecol. 2012 Jul;120(1):145-51. PMID: 22914403*

The purpose of this study from the University of Michigan was to estimate the relationship among the presence of vulvodynia, fibromyalgia, interstitial cystitis, and irritable bowel syndrome. Validated questionnaire-based screening tests for the four pain conditions were completed by women with and without vulvodynia who were participating in the Michigan Woman to Woman Health Study, a longitudinal population-based survey in south-eastern Michigan. Weighted population-based estimates of the prevalence and characteristics of participants with these chronic comorbid pain conditions were calculated using regression analyses. Of 1,940 women who completed the survey containing all four screening tests, 1,890 (97.4%) answered all screening questions and were included. The prevalences of the screening-based diagnoses ranged from 7.5% for interstitial cystitis, 8.7% for vulvodynia, 9.4% for irritable bowel syndrome, to 11.8% for fibromyalgia with 27.1% screening positive for multiple conditions. The presence of vulvodynia was associated with the presence of each of the other comorbid pain conditions. Demographic risk factors for each condition varied. Increasing age was not associated with greater numbers of comorbid conditions, and only low socioeconomic status was associated with having multiple comorbid conditions concurrently. It was concluded by the authors that chronic pain conditions are common, and a subgroup of women with



vulvodynia is more likely than those without vulvodynia to have one or more of the three other chronic pain conditions evaluated.

#### STREET KETAMINE AND THE BLADDER

##### **[IMAGING FEATURES OF URINARY DYSFUNCTION ASSOCIATED WITH KETAMINE ABUSE].**

Wu P, Zhao J, Gao LS, Wang Y, Zheng H, Huang ZH, Gu D, Huang J, Zheng SB. *Nan Fang Yi Ke Da Xue Xue Bao.* 2012 Aug;32(8):1143-7. PMID 22931608

[Article in Chinese. [Click here for free full Chinese text](#)]

The purpose of this study in Chinese was to summarize the imaging features of urinary dysfunction associated with ketamine abuse (KAUD) for imaging diagnosis of KAUD. The authors analyzed the imaging findings in 45 patients with KAUD, all having a history of ketamine abuse and presenting with severe lower urinary tract symptoms. The patients underwent imaging examinations with ultrasonography, computed tomography, magnetic resonance imaging or single photon emission computed tomography, and the results were classified and evaluated to identify the common imaging findings. The imaging changes of KAUD were found primarily in the urinary and biliary system. The most common imaging characteristics included thickening of the bladder wall, contracture and decreased functional volume of the bladder, dilation of the ureter and hydronephrosis, stricture of the upper ureter, renal impairment, dilation of the biliary system, and inflammation or swelling of the adjacent organs and lymph nodes. The authors report that KAUD presents with typical imaging changes. Radiologists should be aware of KAUD if the typical imaging features are detected, especially in cases with a history of ketamine abuse.

##### **THE PREVALENCE AND NATURAL HISTORY OF URINARY SYMPTOMS AMONG RECREATIONAL KETAMINE USERS**

Ming Kwomg Yiu, Chi Man Ng, Wai Kit Ma, Kin Chung To, *BJU International* **Volume 110, Issue 6,** pages E164–E165, September 2012 Article first published online: 24 AUG 2012 DOI: 10.1111/j.1464-410X.2012.10742\_3.x

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#### RHEUMATIC PAIN AND IMAGING

##### **ROLE OF FUNCTIONAL BRAIN IMAGING IN UNDERSTANDING RHEUMATIC PAIN.**

Jones AK, Huneke NT, Lloyd DM, Brown CA, Watson A. *Curr Rheumatol Rep.* 2012 Aug 31. [Epub ahead of print]. PMID: 22936576

Rheumatic pain and, in particular, rheumatoid arthritis, osteoarthritis and fibromyalgia, are common and debilitating chronic pain syndromes. Recently, human functional neuroimaging, for example EEG, fMRI, and PET has begun to reveal some of the crucial central nervous system mechanisms underlying these diseases. The purpose of this review from Manchester UK is to summarise current knowledge on the brain mechanisms of rheumatic pain revealed by functional neuroimaging techniques. The evidence suggests that two mechanisms may be largely responsible for the clinical pain associated with these rheumatic diseases: abnormalities in the medial pain system and/or central nervous system sensitisation and inhibition. If we can understand how functioning of the central nociceptive system becomes altered, even in the absence of peripheral nociceptive input, by using functional neuroimaging techniques, in the future we may be able to develop improved, more effective treatments for patients with chronic rheumatic pain.

#### IRRITABLE BOWEL SYNDROME

## **RELATIONSHIP BETWEEN OVERACTIVE BLADDER AND IRRITABLE BOWEL SYNDROME: A LARGE-SCALE INTERNET SURVEY IN JAPAN USING THE OVERACTIVE BLADDER SYMPTOM SCORE AND ROME III CRITERIA**

Matsumoto S, Hashizume K, Wada N, Hori J, Tamaki G, Kita M, Iwata T, Kakizaki H. *BJU Int.* 2012 Oct 26. doi: 10.1111/j.1464-410X.2012.11591.x. [Epub ahead of print] PMID: 23106867

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There is known to be an association between overactive bladder (OAB) and irritable bowel syndrome (IBS). The study from Japan investigates the association between OAB and IBS using an internet-based survey in Japan. It is the first to investigate the prevalence and severity of OAB in the general population using the OAB symptom score questionnaire. Questionnaires were sent via the internet to Japanese adults. The overactive bladder symptom score was used for screening OAB, and the Japanese version of the Rome III criteria for the diagnosis of IBS was used for screening this syndrome. The overall prevalence of OAB and IBS was 9.3% and 21.2%, respectively. Among the subjects with OAB, 33.3% had concurrent IBS. The prevalence of OAB among men was 9.7% and among women it was 8.9%, while 18.6% of men and 23.9% of women had IBS. Concurrent IBS was noted in 32.0% of men and 34.8% of women with OAB. Taking into account a high rate of concurrent IBS in patients with OAB, it seems to be important for physicians to assess the defecation habits of patients when diagnosing and treating OAB.

## **DIAGNOSTIC CRITERIA IN IBS: USEFUL OR NOT?**

Mearin F, Lacy BE. *Neurogastroenterol Motil.* 2012 Sep;24(9):791-801. doi: 10.1111/j.1365-2982.2012.01992.x. PMID: 22908861

There are a number of reasons to establish the accurate diagnosis of irritable bowel syndrome (IBS): to relieve patient uncertainty; to avoid adverse effects of unnecessary medications or treatments; to avoid unnecessary diagnostic procedures and surgeries; to conserve limited healthcare resources; and, of course, to initiate the most appropriate treatment. However, making the diagnosis of IBS remains difficult because it is clinically heterogeneous, no biological marker to detect it exists, many other diseases share the same clinical manifestations and it is often difficult for both physicians and patients to accept the uncertainty of a symptom-based diagnosis. Different diagnostic criteria have been developed during the last 4 decades but none have proved to be an ideal method of accurately diagnosing IBS. Just as importantly, physicians are frequently unaware of published guidelines or consciously ignore these diagnostic criteria. Most clinicians still believe IBS is a diagnosis of exclusion and not a positive diagnosis based on history, physical examination, use of published diagnostic criteria such as the Rome III criteria, and the absence of alarm features. In the sections to follow we will address the inherent difficulties of diagnosing IBS, highlight the importance of symptom-based diagnoses to help reign in soaring healthcare costs, and discuss future strategies that may enable a more cost-efficient diagnosis of IBS.

## **FUNCTIONAL SOMATIC SYNDROMES**

### **FUNCTIONAL SOMATIC SYNDROMES: SENSITIVITIES AND SPECIFICITIES OF SELF-REPORTS OF PHYSICIAN DIAGNOSIS.**

Warren JW, Clauw DJ. *Psychosom Med.* 2012 Oct 15. [Epub ahead of print] PMID: 23071343

Warren and Clauw note that functional somatic syndromes have no laboratory or pathologic abnormalities and so are diagnosed by symptom-based case definitions. However, many studies, including recent ones, have used self-reports of physician diagnosis rather than the case definitions. The objective of this study was to determine the sensitivities and specificities of self-report of physician diagnosis for chronic fatigue syndrome (CFS), fibromyalgia (FM), irritable bowel syndrome (IBS), panic disorder, and migraine. Each of 312 female patients with incident interstitial cystitis/bladder pain syndrome and matched population-based controls were queried on self-report

of physician diagnosis and separately on established case definitions for each of these syndromes. Using the symptom-based case definitions as standards, they found that self-report of physician diagnosis did not identify 90% of the controls who had CFS, 77% who had FM, 69% who had IBS, 43% who had panic disorder, and 23% who had migraine. In addition, it missed most individuals with multiple syndromes. Findings in one cohort (controls) were confirmed in another (patients with interstitial cystitis/bladder pain syndrome). It was concluded that self-report of physician diagnosis did not identify most of the three most venerable functional somatic syndromes, IBS, FM, and, especially, CFS; nor did it identify substantial minorities of individuals with panic disorder and migraine. Self-report of physician diagnosis was particularly poor in recognizing persons with multiple syndromes. The insensitivity of this diagnostic test has effects on not only prevalence and incidence estimates but also correlates, comorbidities, and case recruitment. To reveal individuals with these syndromes, singly or together, queries of symptoms, not diagnoses, are necessary.

## PAIN

### **COMPARATIVE EFFECTIVENESS OF TRADITIONAL CHINESE MEDICINE AND PSYCHOSOCIAL CARE IN THE TREATMENT OF TEMPOROMANDIBULAR DISORDERS-ASSOCIATED CHRONIC FACIAL PAIN.**

*Ritenbaugh C, Hammerschlag R, Dworkin SF, Aickin MG, Mist SD, Elder CR, Harris RE. J Pain. 2012 Nov;13(11):1075-89. doi: 10.1016/j.jpain.2012.08.002. Epub 2012 Oct 9. PMID: 23059454*

This dual-site study sought to identify the appropriate role for traditional Chinese medicine (TCM; acupuncture and herbs) in conjunction with a validated psychosocial self-care (SC) intervention for treating chronic temporomandibular disorders (TMD)-associated pain. Participants with Research Diagnostic Criteria for Temporomandibular Disorders-confirmed TMD entered a stepped-care protocol that began with a basic TMD class. At weeks 2 and 10, patients receiving SC whose worst facial pain was above predetermined levels were reallocated by minimization to SC or TCM with experienced practitioners. Characteristic facial pain was the primary outcome. Social activity interference was a secondary outcome. Patients were monitored for safety. TCM provided significantly greater short-term (8-week) relief than SC and greater reduction in interference with social activities. In 2 of 5 treatment trajectory groups, more than two thirds of participants demonstrated clinically meaningful responses ( $\geq 30\%$  improvement) in pain interference over 16 weeks. This study provides evidence that TMD patients referred for TCM in a community-based model will receive safe treatment that is likely to provide some short-term pain relief and improved quality of life. Similar designs may also apply to evaluations of other kinds of chronic pain. This short-term comparative effectiveness study of chronic facial pain suggests that TCM is safe and frequently efficacious alone or subsequent to standard psychosocial interventions. TCM is widely available throughout North America and may provide clinicians and patients with a reasonable addition or alternative to other forms of therapy.

### **FOOD, PAIN, AND DRUGS: DOES IT MATTER WHAT PAIN PATIENTS EAT?**

*Bell RF, Borzan J, Kalso E, Simonnet G. Topical review PAIN. 2012 Oct;153(10):1993-6. doi: 10.1016/j.jpain.2012.05.018. Epub 2012 Jun 16. PMID: 22704855*

Bell and colleagues report that in 2003, the World Health Organization published a report on the global change in diet resulting from industrialization, urbanization, and market globalization, and the impact on the development of chronic disease. The adverse dietary changes are characterized by a high-energy density diet with greater intake of saturated fats and sugars, reduced complex carbohydrates, dietary fibre, and reduced fruit and vegetable intakes. Modern dietary patterns are considered to be risk behaviours, and the World Health Organization identifies nutrition as a “major modifiable determinant of chronic disease.” The authors suggest that adequate nutrition is a basic premise for good health, including pain relief and that the evaluation of diet should be a routine part

of the medical work-up for chronic pain, on a par with other lifestyle factors such as exercise and sleep. They are of the opinion that future research should focus on pain patients' dietary habits, including intake of polyamines, omega-3 and omega-6 PUFAs, vitamin D, and caffeine; and the effects of diet on analgesic treatment. Despite an increasing number of preclinical trials demonstrating a role for nutritional factors in pain, epidemiological and clinical trials are lacking. Well-designed trials are needed to investigate the antihyperalgesic effects of PD diet, Mg<sup>2+</sup>, flavonoids, and antioxidants, and to further explore the potential of nutritional therapy in pain patients.

## VITAMIN D

### **VITAMIN D STATUS: A REVIEW WITH IMPLICATIONS FOR THE PELVIC FLOOR.**

*Parker-Autry CY, Burgio KL, Richter HE. Int Urogynecol J. 2012 Nov;23(11):1517-26. doi: 10.1007/s00192-012-1710-6. Epub 2012 Mar 14. PMID: 22415704*

Vitamin D is a micronutrient vital in calcium homeostasis and musculoskeletal function. Vitamin D insufficiency is a common variant of vitamin D deficiency that shows clinical signs of rickets and osteomalacia. The clinical significance of vitamin D insufficiency is being explored in several medical conditions. However, the most robust work suggests a role in musculoskeletal disease. The pelvic floor is a unique part of the body and the function of which is dependent on interrelationships between muscle, nerve, connective tissue, and bone. Pelvic floor disorders result when these relationships are disrupted. This paper reviews current knowledge regarding vitamin D nutritional status, the importance of vitamin D in muscle function, and how insufficient or deficient vitamin D levels may play a role in the function of the female pelvic floor.

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**[http://www.painful-bladder.org/donations\\_sponsoring.html](http://www.painful-bladder.org/donations_sponsoring.html)**

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