

International Painful Bladder Foundation

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

IPBF E-Newsletter, Issue 24, January 2011

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

THE INTERNATIONAL PAINFUL BLADDER FOUNDATION WOULD LIKE TO WISH YOU A HAPPY AND HEALTHY NEW YEAR 2011!

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

- **Essic Website Video Section Further Expanded**
- **The Bladder Pain/Interstitial Cystitis Symptom Score (BPIC-SS)**
- **A Further Anti-NGF Pain Drug Clinical Trial Halted**
- **Upcoming Meetings**
- **Setting Up IC Support Groups or Websites**
- **Books and Websites Review**
- **Research Highlights**
- **Donations and Sponsoring**

ESSIC WEBSITE VIDEO SECTION FURTHER EXPANDED

The new video section on the ESSIC website has been further expanded. Go to <http://www.essic.eu/videomenu.html> where you will also find instructions for use. The section is still under construction and has the purpose of providing clinical information on a wide variety of patients of all different ages with different presentations. However, you will find that it already has a large number of videos available for viewing, including in most instances information on the patient history, and a selection of photos.

THE BLADDER PAIN/INTERSTITIAL CYSTITIS SYMPTOM SCORE (BPIC-SS)

A preview copy of the Pfizer Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS) can be seen on the ESSIC website: [Click here for a preview copy](#). This symptom score is intended as a short screening tool which might aid identification of IC/BPS patients for inclusion in trials. A paper has been submitted for publication and when this takes place, a page will be created on the Patient Reported Outcomes in Lower Urinary Tract Symptoms (LUTS) and Sexual Health (PROLUTS) website: <http://www.prolutssh.com/index.html>. It will then be possible to request copies, scoring manual and translations free of charge. We will keep you updated.

A FURTHER ANTI-NGF PAIN DRUG CLINICAL TRIAL HALTED

It was recently announced that the US Food and Drug Administration (FDA) has suspended clinical trials of Johnson & Johnson's new experimental anti-nerve growth factor pain medication fulranumab - which formed part of their neuroscience programme - due to concerns that this class of drugs known as nerve growth factor inhibitors may increase the risk of damage to joints and be associated with a rapidly progressive osteoarthritis condition that can lead to the need for total joint replacement. This medication is in Phase II testing. As we mentioned in the last IPBF e-Newsletter, research into tanezumab – likewise a nerve growth factor inhibitor drug - was also suspended by Pfizer, as the result of a request by the FDA.

This in turn led AstraZeneca to halt research into a similar product, medi-578. These drugs are all designed to block NGF. We can now expect to see the drug companies re-evaluating this class of drug to see if it is likely to be feasible to continue with research.

UPCOMING MEETINGS:

- EUROPEAN ASSOCIATION OF UROLOGY (EAU), 18-22 March, Vienna

On Sunday 20 March, ESU Course 13 Chronic Pelvic Pain Syndromes (CPPS) with special focus on Chronic Prostatitis (CP) and Painful Bladder Syndrome/Interstitial Cystitis (PBS/IC) will be chaired by Professor JJ Wyndaele from Antwerp. On Monday, 21 March: Poster Session 81 – Interstitial Cystitis.

- SOCIETY FOR URODYNAMICS AND FEMALE UROLOGY (SUFU)

2011 Winter Meeting, March 1 – 5, 2011, Arizona Biltmore, Phoenix, Arizona

On 2 March, there is a presentation on: RAND IC Epidemiology Study Update by Sandra Berry and also a session with a panel of experts on MAPP moderated by Deborah Erickson. On 3 March there is a General Session with many presentations on IC/PBS and urogenital pain, ending with a question and answer session.

- INTERNATIONAL CONFERENCE ON ACCELERATING THE DEVELOPMENT OF ENHANCED PAIN TREATMENTS, 25-26 March 2011 Bermuda

This conference has a session that sounds interesting devoted to phenotyping chronic pain patients on Saturday 26 March.

- EURORDIS ANNUAL MEMBERSHIP MEETING 2011, 13/14 May, Amsterdam

The Annual EURORDIS Membership Meeting 2011 will take place on 13 and 14 May, 2011 in Amsterdam, the Netherlands with the General Assembly being held on 13 May. The purpose and objectives of the Annual Membership Meeting are to provide networking opportunities to patients and patient organisations, capacity building in the form of interactive workshops and empowerment to patients and patient organisations as a direct result of the capacity-building sessions. EURORDIS is a non-governmental patient-driven alliance of patient organisations representing more than 434 rare diseases patient organisations in over 43 countries. Venue: Hotel Casa 400 - Eerste Ringdijkstraat 4 - 1097 BC Amsterdam For more information: Anja Helm, Manager of Relations with Patient Organisations, + (33) 1 56 53 52 17 anja.helm@eurordis.org

- INTERNATIONAL PELVIC PAIN SOCIETY (IPPS) ANNUAL SCIENTIFIC MEETING 25-29 May 2011, Istanbul

The aim of the International Pelvic Pain Society (IPPS) is to serve as an educational resource for health care professionals, to optimize diagnosis and treatment of patients suffering from chronic pelvic pain, to collate research in chronic pelvic pain and to inform men and women, to serve as a resource of education for treatment options and professional health care members. In 2011, its annual scientific meeting will be held in Istanbul. According to the preliminary scientific programme for 2011 ([click here](#)), Session IV will include a session on interstitial cystitis, neurobiology & treatments, irritable bowel syndrome, neurobiology & treatments and pudendal and other pelvic floor neuralgias, Session V will cover vulvodinia and vestibulitis, Session VI to IX will deal with endometriosis.

- ESSIC ANNUAL MEETING, June 2011

ESSIC will be holding its 2011 Annual Meeting in Moscow, Russia, preliminary date 2-4 June 2011. Scientific sessions will be open to all registered delegates. Educational courses will be given following the annual meeting. Further information will be published on the [ESSIC website](#) as soon as it is available.

- INTERNATIONAL SYMPOSIUM ON SJÖGREN'S SYNDROME (ISSS) 28 September - 1 October 2011, Athen, Greece

A date for the diaries of those of you with an interest in research on Sjögren's syndrome. We will let you know when further information is available.

- ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY (EULAR)

25-28 May 2011, London, UK

EULAR provides a forum of the highest standard for scientific (both clinical and basic), educational and social exchange between professionals involved in rheumatology, liaising with patient organisations, in order to achieve progress in the clinical care of patients with rheumatic diseases.

Congress venue: ExCeL London, One Western Gateway, Royal Victoria Dock, London E16 1XL, United Kingdom.

BRIEF CALENDAR OVERVIEW OF SELECTED UPCOMING MEETINGS IN 2011

March

- SOCIETY FOR URODYNAMICS AND FEMALE UROLOGY (SUFU), Winter Meeting, March 1 – 5, Phoenix, Arizona
- EUROPEAN ASSOCIATION OF UROLOGY (EAU), 18-22 March, Vienna
- INTERNATIONAL CONFERENCE ON ACCELERATING THE DEVELOPMENT OF ENHANCED PAIN TREATMENTS, 25-26 March 2011 Bermuda

May

- AMERICAN UROLOGICAL ASSOCIATION (AUA) ANNUAL MEETING, 14-19 May, Washington DC, USA
- EURORDIS ANNUAL MEMBERSHIP MEETING, 13 and 14 May, Amsterdam, the Netherlands
- INTERNATIONAL CONFERENCE FOR RARE DISEASES AND ORPHAN DRUGS (ICORD), 21-23 May, Tokyo, Japan
- ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY (EULAR), 25-28 May 2011, London, UK
- INTERNATIONAL PELVIC PAIN SOCIETY (IPPS), 26-29 MAY, 2011, Istanbul, Turkey

June

- ESSIC ANNUAL MEETING, Moscow, Russia, preliminary date 2-4 June 2011.

August

- INTERNATIONAL CONTINENCE SOCIETY (ICS) ANNUAL SCIENTIFIC MEETING, 29 August-2 September, Glasgow, Scotland

September

- INTERNATIONAL SYMPOSIUM ON SJÖGREN'S SYNDROME (ISSS), 28 SEPTEMBER - 1 OCTOBER 2011, ATHENS, GREECE

October

- SOCIETE INTERNATIONALE D'UROLOGIE (SIU) annual congress, ICC Berlin 16-20 October

SETTING UP IC SUPPORT GROUPS OR WEBSITES

If you are thinking about setting up a support group for IC patients, don't forget that the IPBF has guidelines on setting up a support group on its website (click [here](#) to access or see menu). In recent years, doctors and nurses have sometimes taken the lead by setting up or helping to set up a website with patient information. These are sometimes combination bladder websites for e.g. IC, urinary incontinence and/or overactive bladder and sometimes for IC alone. This can help to set the ball rolling in countries where there is no patient support group at all and sometimes little or no tradition of patient associations. The keyword however is: begin small. Don't be too ambitious at the start and don't try to re-invent the wheel: make a start by translating existing, basic English information into your own language, with adaptations to the local situation. The IPBF has a range of leaflets and brochures with information that you can use. The translations should always be checked by a medical professional for medical accuracy and correct medical terminology. A patient website in your own language invariably has a further spin-off in raising awareness among medical professionals in the country concerned. If you would like to survey the existing market of support groups before starting, take a look at the list on the IPBF website: http://www.painful-bladder.org/globalgroups_etc.html. This should give you some ideas.

BOOKS AND WEBSITES REVIEW

GUIDE TO PAIN MANAGEMENT IN LOW-RESOURCE SETTINGS

Editors: Andreas Kopf, MD, and Nilesh B. Patel, PhD

A free pain guide online from the International Association for the Study of Pain (IASP). This Guide to Pain Management in Low-Resource Settings is intended to support health care providers in low-resource settings (developing countries, poor communities etc). The chapters were written by a multidisciplinary and multinational team of authors. Practitioners in settings with limited resources will benefit from easy-to-read information about simple and cost-effective approaches that can provide maximum effects in managing pain in their patients. The IASP has made this book freely available for educational purposes. It can be downloaded on its website. Practitioners in settings with limited resources will benefit from easy-to-read information about simpler and cost-effective approaches with maximum effects in managing pain in their patients.

More information: www.iasp-pain.org/lowresourceguide

FIBROMYALGIA

A Practical Clinical Guide

D.A. Marcus, A. Deodhar

Published by Springer, 2010

ISBN: 978-1-4419-1608-2

Fibromyalgia is still often poorly understood and often goes undiagnosed and consequently untreated. This book is designed to provide clinicians with up-to-date information on the pathogenesis of fibromyalgia, clinical evaluation and guidelines for effective treatment. While Part II discusses common co-morbidities and fibromyalgia, with information on headache, chronic fatigue syndrome, irritable bowel syndrome, sleep disturbance, depression & anxiety and obesity and metabolic syndrome, there is unfortunately no mention of interstitial cystitis/painful bladder syndrome or any other urological problems being associated with fibromyalgia in this edition. Nevertheless, despite its limitations where the bladder is concerned, this is a useful reference book on Fibromyalgia which is easy to read. Although intended for clinicians, many patients will find it useful. Link to further information on the publisher's website: <http://www.springer.com/978-1-4419-1608-2>

UROTODAY WEBSITE (www.urotoday.com)

You will need to log in or sign up (for free) to access this text.

[Beyond the Abstract - Long-term results of intravesical hyaluronan therapy in bladder pain syndrome/interstitial cystitis](#), by Dr. Paul F. Engelhardt, FEBU, et al.

This useful beyond-the-abstract update on hyaluronan (Cystistat®) by Dr Engelhardt and colleagues is based on the study reviewed in our November 2010 e-Newsletter: [Long-Term Results of Intravesical Hyaluronan Therapy in Bladder Pain Syndrome /Interstitial Cystitis](#). Engelhardt PF, Morakis N, Daha LK, Esterbauer B, Riedl CR. *Int Urogynecol J Pelvic Floor Dysfunct.* 2010 Oct 12. [Epub ahead of print]. PMID: 2093864. This study from Austria looked at the long-term outcome of intravesical hyaluronan for the treatment of bladder pain syndrome/interstitial cystitis. The authors concluded from their findings that in addition to demonstrating a high rate of acute symptom remission, intravesical hyaluronan also shows long-term efficacy in a considerable number of BPS/IC patients. The UroToday review provides useful additional information.

UROTODAY: UPDATE ON ITS CAUTI CENTER (CATHETER ASSOCIATED URINARY TRACT INFECTIONS)

Even more has been added to the UroToday CAUTI Center. You will find a treasure trove of information here on every aspect of catheter associated urinary tract infections, including prevention and management, lecture series, protocols and case reports.

US FOOD & DRUG ADMINISTRATION NEW WEBSITE: FDA BASICS FOR INDUSTRY

While this new website is intended for industry, it will nevertheless undoubtedly have some interesting information for everyone else who wishes to know more about FDA regulation. This forms part of a broader effort by the FDA to rebrand itself as a more transparent, accessible agency.

<http://www.fda.gov/ForIndustry/FDABasicsforIndustry/default.htm>

RESEARCH HIGHLIGHTS

A REVIEW OF SELECTED RECENT SCIENTIFIC LITERATURE

A continually updated selection of new scientific literature can be found on our website: <http://www.painful-bladder.org/pubmed.html>. 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.

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.

SEXUALITY AND REPRODUCTIVE RISK FACTORS FOR INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME IN WOMEN.

Warren JW, Clauw DJ, Wessellmann U, Langenberg PW, Howard FM, Morozov V. Urology. 2011 Jan 6. [Epub ahead of print]. PMID: 21215994

The purpose of this study was to determine whether interstitial cystitis/painful bladder syndrome (IC/PBS) in women is associated with antecedent sexual and reproductive characteristics. On the basis of their results, the authors concluded that three antecedents to IC/PBS were prominent. Female hormone use was consistent with a pharmacologic effect or as a marker of its indications. A history of fewer pregnancies among premenopausal, but not postmenopausal, women with IC/PBS was consistent with pregnancy postponing the occurrence of IC/PBS, a marker for decisions to avoid pregnancy, or a result of recruitment bias. Nonbladder syndromes, especially the total number experienced by the participant, had the strongest correlation with IC/PBS. The authors are of the opinion that this finding suggests that knowledge of the pathogenesis of these nonbladder syndromes, many of which are functional somatic syndromes, might reveal that of IC/PBS.

PREVALENCE AND CORRELATES OF SEXUAL DYSFUNCTION AMONG WOMEN WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.

Bogart LM, Suttrop MJ, Elliott MN, Clemens JQ, Berry SH. Urology. 2011 Jan 5. [Epub ahead of print]. PMID: 21215432

The purpose of this study was to examine the prevalence and correlates of general and bladder pain syndrome/interstitial cystitis (BPS/IC)-specific sexual dysfunction among women in the RAND Interstitial Cystitis Epidemiology study using a probability sample survey of U.S. households. Sexual dysfunction can contribute to a reduced quality of life for women with bladder pain syndrome/interstitial cystitis (BPS/IC). 146 231 households were telephoned to identify women who reported bladder symptoms or a BPS/IC diagnosis. Those who reported either of these subsequently underwent a second-stage screening using the RAND Interstitial Cystitis Epidemiology study high-specificity symptom criteria. Of those with a current sexual partner (75%), 88% reported ≥ 1 general sexual dysfunction symptom and 90% reported ≥ 1 BPS/IC-specific sexual dysfunction symptom in the past 4 weeks. In the multivariate models, BPS/IC-specific sexual dysfunction was significantly associated with more severe BPS/IC symptoms, younger age, worse depression symptoms, and worse perceived general health. Multivariate correlates of general sexual dysfunction included non-Latino race/ethnicity, being married, and having depression symptoms. The results of this USA study indicate that women with BPS/IC symptoms experience very high levels of sexual dysfunction. Furthermore, sexual dysfunction co-varies with symptoms.

INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME: WHAT DO PATIENTS MEAN BY "PERCEIVED" BLADDER PAIN?

Warren JW, Diggs C, Horne L, Greenberg P. Urology. 2010 Dec 10. [Epub ahead of print]. PMID: 21146863

This is another "hands-on" study from the Maryland team where they go back to the patients and ask them to describe what they feel in their own words. Bearing in mind that the perception of the bladder as being the source of pain in forms part of many new definitions of IC/PBS, the object of this study was to report on the reasons patients with interstitial cystitis/painful bladder syndrome give for the perception that the bladder is the source of their pain. This was a follow-up in the US national study reported previously in *Events Preceding Interstitial Cystitis*. At 18 months after the baseline interview, the patients were asked an open-ended question about their reasons for perceiving the bladder to be the source of their pain. No predominant reason was found that patients with IC/PBS gave for suspecting the bladder to be the source of pain. The common reasons included pain location, changes with the urinary cycle, and an association with other urinary symptoms. The authors suggest that these features of IC/PBS should be queried in order to clarify the relationship of IC/PBS to other chronic pain syndromes, which often are comorbidities.

THE ROLE OF A LEAKY EPITHELIUM AND POTASSIUM IN THE GENERATION OF BLADDER SYMPTOMS IN INTERSTITIAL CYSTITIS/OVERACTIVE BLADDER, URETHRAL SYNDROME, PROSTATITIS AND GYNAECOLOGICAL CHRONIC PELVIC PAIN.

Parsons CL. BJU Int. 2010 Dec 22. doi: 10.1111/j.1464-410X.2010.09843.x. [Epub ahead of print]. PMID: 21176078

The author notes that the traditional diagnosis of interstitial cystitis (IC) only recognizes the severe form of the disease. He considers that the far more common early and intermittent phases of the disease are not always perceived to be part of IC, but rather are misdiagnosed as urinary tract infection, urethral syndrome, overactive bladder, chronic prostatitis, urethritis, or a type of gynaecologic pelvic pain (such as endometriosis, vulvodynia, or some type of vaginitis). Parsons is of the opinion that all of these patient groups actually suffer from the same bladder disease, and that this disease results from a leaky bladder epithelium and subsequent potassium leakage into the bladder interstitium that generates the symptoms of frequency, urgency, pain or incontinence in any combination. This article reviews the scientific data supporting this concept. The conclusions derived from these data substantially alter the paradigms for urology and gynaecology in the generation of frequency, urgency and pelvic pain. All the above-mentioned syndromes unite into one primary disease process, lower urinary dysfunction epithelium, or LUDE disease, and not the 10 plus syndromes traditionally recognized.

EXPRESSION OF NITRIC OXIDE SYNTHASE AND AQUAPORIN-3 IN CYCLOPHOSPHAMIDE TREATED RAT BLADDER.

Cho KH, Hyun JH, Chang YS, Na YG, Shin JH, Song KH. Int Neurourol J. 2010 Oct;14(3):149-56. Epub 2010 Oct 31. PMID: 21179332

[Free access article. Click on title to access.](#)

The purpose of this rat study from Korea was to evaluate the expression of inducible NOS (iNOS), aquaporin-3 (AQP-3) in cyclophosphamide (CYP) induced rat bladder. The authors are of the opinion that the results suggest that inflammatory change activates NOS and AQP-3 expression in the bladder tissue of rats. This may imply that NOS and AQP-3 have a pathophysiological role in the cyclophosphamide induced interstitial cystitis. Further study on the NOS and AQP-3 in bladder is needed for clinical application.

HIGHER LEVELS OF CELL APOPTOSIS AND ABNORMAL E-CADHERIN EXPRESSION IN THE UROTHELIUM ARE ASSOCIATED WITH INFLAMMATION IN PATIENTS WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.

Shie JH, Kuo HC. BJU Int. 2010 Dec 16. doi: 10.1111/j.1464-410X.2010.09911.x. [Epub ahead of print]. PMID: 21166752

The purpose of this study from Taiwan was to investigate the relationship between chronic bladder inflammation and urothelial dysfunction such as in interstitial cystitis/painful bladder syndrome. 20 women with symptoms characteristic of IC/PBS were enrolled in this study. A control group was formed by 6 patients with stress urinary incontinence without irritative bladder symptoms. The preliminary

results indicated that urothelial dysfunction in IC/PBS, such as higher apoptosis cell number and lower E-cadherin expression, is associated with chronic inflammation of the bladder wall and causes clinical symptoms. A limitation of the study was the small number of bladder specimens from IC/PBS and control patients. In a further study, the authors plan to increase the number of patients and investigate the connection of molecules in inflammation and urothelial apoptosis

KETAMINE-INDUCED VESICOPATHY: A LITERATURE REVIEW.

Middela S, Pearce I. Int J Clin Pract. 2011 Jan;65(1):27-30. doi: 10.1111/j.1742-1241.2010.02502.x. PMID: 21155941

It is of considerable concern that ketamine abuse appears to be on the increase as a recreational drug. It has been reported to cause lower urinary tract symptoms, including IC-like symptoms. In this literature review, the authors found that while the effect on the bladder of ketamine abuse appears to be universally similar, there is as yet no uniform method for reporting the symptoms, diagnosis and management. They note that very little is known regarding the pathogenesis of its effects on the urinary tract. Patients with severe irritative lower urinary tract symptoms, a positive history of ketamine abuse and the absence of any other etiology should be considered to have ketamine-induced vesicopathy. They emphasise that when no cause can be found of the LUTS, particularly in the young, an effort should be made to discover whether there is any possibility that the patient may have been using ketamine recreationally. They suggest that interstitial cystitis-type treatment appears to be the most effective for this ketamine-induced bladder condition. At the present time, the only way of resolving the symptoms is complete cessation of the ketamine abuse.

OPTIMAL MANAGEMENT OF CHRONIC CYCLICAL PELVIC PAIN: AN EVIDENCE-BASED AND PRAGMATIC APPROACH.

Won HR, Abbott J. Int J Women Health. 2010 Aug 20;2:263-277. PMID: 21151732

[Open access full text article. Click on title.](#)

This Australian article reviews the literature on management of chronic cyclical pelvic pain (CCPP). This useful review outlines an approach to patients with CCPP through history, physical examination and investigation to identify the cause(s) of the pain and its optimal management.

CHRONIC PERINEAL PAIN: CURRENT PATHOPHYSIOLOGICAL ASPECTS, DIAGNOSTIC APPROACHES AND TREATMENT.

Andromanakos NP, Kouraklis G, Alkiviadis K. Eur J Gastroenterol Hepatol. 2011 Jan;23(1):2-7. PMID: 21079515

Chronic perineal pain is anorectal and perineal pain without underlying organic disease which has been excluded by careful physical examination, radiological and endoscopic investigations. A variety of neuromuscular disorders of the pelvic floor may lead to different conditions such as anorectal incontinence, urinary incontinence and constipation of obstructed defecation, sexual dysfunction and pain syndromes. The most common functional disorders of the pelvic floor muscles, accompanied by perineal pain are: levator ani syndrome, proctalgia fugax, myofascial syndrome and coccygodynia. The diagnosis of these syndromes requires a thorough history, physical examination, selected specialized investigations and exclusion of organic disease with proctalgia. Accurate diagnosis of the syndromes helps to choose an appropriate treatment and to avoid unnecessary and ineffective surgical procedures.

PROSPECTIVE EVALUATION OF COMBINED LOCAL BUPIVACAINE AND STEROID INJECTIONS FOR THE MANAGEMENT OF CHRONIC VAGINAL AND PERINEAL PAIN.

Doumouchtsis SK, Boama V, Gorti M, Tosson S, Fynes MM. Arch Gynecol Obstet. 2010 Nov 16. [Epub ahead of print]. PMID: 21079978

While this article specifically discusses the impact of perineal/vaginal injections for chronic localised vaginal/perineal pain following obstetric trauma or vaginal surgery for prolapse, noting that it may have a serious impact on sexual function and quality of life, the treatment options presented here may be of interest to IC/PBS patients with vaginal and/or perineal pain. In this study, patients underwent local injections with a combination of 0.5% bupivacaine (10 ml), hydrocortisone (100 mg) and hyaluronidase (1,500 IU). Follow-up was undertaken at four-weekly intervals. Further injections were performed as

clinically indicated. It was concluded that in this prospective series of patients, this treatment with bupivacaine, hyaluronidase and hydrocortisone injected locally was well tolerated, safe and significant improvements in pain scores and sexual function were observed.

INTRAVESICAL DIMETHYL SULFOXIDE INHIBITS ACUTE AND CHRONIC BLADDER INFLAMMATION IN TRANSGENIC EXPERIMENTAL AUTOIMMUNE CYSTITIS MODELS.

Kim R, Liu W, Chen X, Kreder KJ, Luo Y. J Biomed Biotechnol. 2011;2011:937061. Epub 2010 Nov 11. PMID: 21113298

[Free access article](#)

New animal models are greatly needed in interstitial cystitis/painful bladder syndrome (IC/PBS) research. The authors recently developed a novel transgenic cystitis model (URO-OVA mice) that mimics certain key aspects of IC/PBS pathophysiology. This paper aimed to determine whether URO-OVA cystitis model was responsive to intravesical dimethyl sulfoxide (DMSO) and if so identify the mechanisms of DMSO action. URO-OVA mice developed acute cystitis upon adoptive transfer of OVA-specific OT-I splenocytes. Compared to PBS-treated bladders, the bladders treated with 50% DMSO exhibited markedly reduced bladder histopathology and expression of various inflammatory factor mRNAs. Intravesical DMSO treatment also effectively inhibited bladder inflammation in a spontaneous chronic cystitis model (URO-OVA/OT-I mice). Studies further revealed that DMSO could impair effector T cells in a dose-dependent manner in vitro. Taken together, the authors believe that their results suggest that intravesical DMSO improves the bladder histopathology of IC/PBS patients because of its ability to interfere with multiple inflammatory and bladder cell types.

SACRAL NEUROMODULATION: THERAPY EVOLUTION.

Thompson JH, Sutherland SE, Siegel SW. Indian J Urol. 2010 Jul;26(3):379-84. PMID: 21116359

[Free access article](#)

This review examines the evolution of the technology of sacral neuromodulation (SNM). The authors note that the role for SNM continues to expand as clinical research identifies other applications for this therapy. They conclude that our understanding of SNM, as well as technological advances in therapy delivery, expands the pool of patients for which this form of therapy may prove beneficial. Less invasive instrumentation may even make this form of therapy appealing to patients without refractory symptoms.

URODYNAMIC FINDINGS IN AN AWAKE CHEMICAL CYSTITIS RAT MODEL OBSERVED BY SIMULTANEOUS REGISTRATIONS OF INTRAVESICAL AND INTRAABDOMINAL PRESSURES.

Jin LH, Shin HY, Kwon YH, Park CS, Yoon SM, Lee T. Int Neurourol J. 2010 Apr;14(1):54-60. Epub 2010 Apr 30. PMID: 21120177

The aim of this study from Korea was to investigate the effect of urinary bladder inflammation on bladder function in a rat chemical cystitis model. The authors also histologically confirmed the effects of inflammation in the detrusor on chronically inflamed bladder in rats. They report that overlapping patterns of lower urinary tract symptoms and pelvic pain are common disease characteristics among interstitial cystitis patients. The situation in an animal model of interstitial cystitis is similar, as observed in this study by the histologic and awake cystometric examinations. However, the interstitial cystitis model showed detrusor overactivity during the filling phase without a decrease in bladder capacity and micturition intervals, which differs from the characteristics of overactive bladder patients.

COMPARISON OF VOIDING QUESTIONNAIRES BETWEEN FEMALE INTERSTITIAL CYSTITIS AND FEMALE IDIOPATHIC OVERACTIVE BLADDER.

Kim SH, Oh SJ. Int Neurourol J. 2010 Aug;14(2):86-92. Epub 2010 Aug 31. PMID: 21120217

This retrospective Korean study aimed to find out whether there are any different characteristics in various different voiding symptom questionnaires in the outpatient clinics between interstitial cystitis and overactive bladder. This study showed that some differences among symptom questions in questionnaires did exist between the two groups and that the IC group had much more impaired quality of life than the OAB patients.

TRANSLATION AND LINGUISTIC VALIDATION OF THE KOREAN VERSION OF THE PELVIC PAIN AND URGENCY/FREQUENCY PATIENT SYMPTOM SCALE.

Son HC, Jung YJ, Chang JS, Kim SH, Hong SK, Oh SJ, Parsons CL, Lee KS. Int Neurourol J. 2010 Aug;14(2):112-21. Epub 2010 Sep 1. PMID: 21120221

The purpose of this Korean study was to achieve a linguistic adaptation of the original version of the Pelvic Pain and Urgency/Frequency (PUF) Patient Symptom Scale into the Korean language. Between June 2008 and December 2008, a linguistic adaptation was carried out by 2 native Korean speakers who were also fluent in English. First, the original English version of the PUF was translated into Korean. A panel, which included the 2 translators, reviewed the translations to form a single reconciled forward translation of the Korean version. Then, another bilingual translator, having never seen the original version, back-translated the first draft of the Korean version of the PUF into English, and this back-translation was subsequently assessed for equivalence to the original. The panel discussed all discrepancies and produced a second version. After revising the 2nd version, 10 participants [5 interstitial cystitis (IC) patients and 5 persons from the general population], stratified variously by age, sex, and educational level, answered the PUF and were systematically debriefed afterwards. A summary of the changes from the patient interviews were incorporated into the third version. After the spelling, grammar, layout, and formatting were checked, the third version was verified as the final Korean version of the PUF, without modifications. The multi-step process of forward translation, reconciliation, back-translation, cognitive debriefing, and proofreading of the Korean version of the PUF was completed. It was concluded that the Korean version of the PUF scale may be helpful for screening IC patients in the Korean population and can now be used in Korea.

DEMYSTIFYING PLEOMORPHIC FORMS IN PERSISTENCE AND EXPRESSION OF DISEASE: ARE THEY BACTERIA, AND IS PEPTIDOGLYCAN THE SOLUTION?

Domingue GJ. Discov Med. 2010 Sep;10(52):234-46. PMID: 20875345

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There is considerable circumstantial evidence linking tissue pleomorphic forms of unknown origin with idiopathic chronic inflammatory, collagen, lymphoproliferative, nephro-urological (including interstitial cystitis and prostatodynia), and neoplastic diseases. Although these forms have been observed in stained tissue histopathologic specimens for many decades, most are ignored and generally regarded as diagnostically insignificant staining artifacts or debris. It is hypothesized that these pleomorphic forms are not staining artifacts/cellular debris, but instead represent various stages in the life cycle of stressed bacteria: cell wall-deficient/defective (often called L-forms) that are difficult-to-culture or nonculturable. Essential to the thesis is that small, electron dense, non-vesiculated L-forms are the central (core) element in bacterial persistence. Depending on the stimulus received, these dense forms might be considered as undifferentiated cells, with the capacity to develop along several different routes. Hence, these altered forms created in vivo take up intracellular and/or extracellular residence; possibly establishing a sort of immune protected parasitic relationship, resisting/surviving phagocytic action, and creating subtle pathologic changes in the host during a prolonged period of tissue persistence. This might translate into an etiology for chronic inflammatory diseases, when the stressed bacteria increase in numbers and overwhelm the normal biological functions of the host. In the last few decades, an increasing percentage of the population has become immunosuppressed. Some mechanisms for this increase are aging; autoimmunity; congenital, metabolic and degenerative disorders; and AIDS. The life of a patient so affected is prolonged by therapy with hormones, antimicrobials, and immunosuppressants. It is therefore not surprising that pleomorphic, dormant, and mutant bacterial populations arise in vivo when bacteria are exposed to agents that interfere with structural components and metabolic processes necessary to survival of the microbe. Recent provocative, microbiological data lend credence to the hypothesis and corroborate the multiplicity of pleomorphic forms that develop during reproduction of L forms in vitro. It is proposed that in vivo persistence of these bacterial elements escape immune surveillance partially, completely, or may integrate with host cell organelles to create bacteria-host-cell-antigen complexes which could provoke immunopathologic consequences. Highly relevant, newly published data on modifications of gene expression, modes of division for stressed bacteria, and the paradoxical finding of peptidoglycan in L-forms are pertinent to the hypothesis that atypical, pleomorphic bacteria are the

organisms operative in persistence and expression of pathology over a wide spectrum of diagnostically troublesome human diseases.

An editorial on this study has been written by Philip Hanno, MD, on the UroToday website, entitled "*Speculation on Infectious Origin of IC/BPS and Other Disorders of Unknown Origin*".

USE OF BOTULINUM TOXIN IN THE TREATMENT OF LOWER URINARY TRACT DISORDERS. CURRENT STATUS.

Mangera A, Chapple CR. Arch Esp Urol. 2010 Dec;63(10):829-841. PMID: 21187564
[Article in English, Spanish]

This review article on the current status of botulinum toxin treatment is available in two versions English and Spanish. The authors note that the role of botulinum toxin in the treatment of lower urinary tract disorders has vastly expanded in the last few years. Produced by the bacterium *Clostridium botulinum*, botulinum toxins are amongst the most potent toxins known to man. The conditions for which it is now being used range from detrusor sphincter dyssynergia, neurogenic and idiopathic detrusor overactivity, painful bladder syndrome and lower urinary tract symptoms from bladder outflow obstruction. According to this review, this treatment is minimally invasive, shows a remarkable efficacy and has effects lasting up to one year. The article reviews the latest scientific and clinical evidence. The authors say that while there is an abundance of evidence supporting the efficacy, safety and tolerability of this treatment and indicating that it has minimal side effects, it is nevertheless clear that much work is still required to understand the mechanism(s) of action of the toxin and more robust placebo controlled randomised trials need to be undertaken to answer the many remaining questions.

The article takes a look at the mechanisms of action including current theories to explain its effects. There are still many questions unanswered regarding how it works, further complicated by the lack of understanding as to how and why urgency is felt. In the review of the different conditions for which botulinum toxin is currently used, the authors note that given the lack of evidence for the use of botulinum toxin in PBS/IC, it should still be considered an experimental treatment.

Preparations, dose, methods of administration and reinjection are all discussed in this article.

Where research is concerned, the authors emphasise that the potential of botulinum toxin in disorders of the lower urinary tract has only been touched upon and that there is still considerable research required.

They conclude that botulinum toxin has a promising future in management of lower urinary tract disorders. However considerable work still needs to be done. Many questions still remain unanswered. For example: what is the appropriate dose range for optimal efficacy? What is the best method of administration? What is the optimal number and site of injection? Should we include the trigone or the external sphincter during injection - if so by how much? Should we use and/or combine different serotypes? And what is the effect of long term treatment?

It is hoped that ongoing placebo controlled randomised controlled trials will produce interesting results. It is emphasised that currently all use of botulinum toxin for urological reasons is off-label and not licensed, therefore caution should be exercised until future large randomised licensing studies are reported.

THE GENETIC AND ENVIRONMENTAL CONTRIBUTION TO THE OCCURRENCE OF BLADDER PAIN SYNDROME: AN EMPIRICAL APPROACH IN A NATIONWIDE POPULATION SAMPLE.

Altman D, Lundholm C, Milsom I, Peeker R, Fall M, Iliadou AN, Pedersen NL. Eur Urol. 2010 Nov 4. [Epub ahead of print]. PMID: 21056533

The aim of this study from Sweden was to empirically assess the genetic and environmental contribution to IC/BPS in a population-based sample of twins, using the Swedish Twin Registry as a data source. The reason behind this study is that the etiology of IC/BPS is still poorly understood. Increasing attention is being paid to the importance of genetic factors, but data so far is of a preliminary nature. The authors concluded that the influence of environmental factors in the development of IC/BPS in women is substantial, whereas genetic influences are of only modest importance for the possibility of developing the disease. According to the authors, a limitation of the study lies in the use of self-reported symptoms to define the disease prototype as BPS is a rather heterogeneous diagnostic term that may encompass different conditions associated with chronic bladder pain. It was not possible to make subdivisions in the absence of confirmation of diagnosis by cystoscopy and histologic findings. They therefore recognise that

the overlap with other types of bladder pain and the age range of their subjects (twins born between 1959 and 1985) may have caused an underestimation of the heritability for classic Hunner's type IC.

AN HTERT-IMMORTALIZED HUMAN UROTHELIAL CELL LINE THAT RESPONDS TO ANTI-PROLIFERATIVE FACTOR.

Kim J, Ji M, Didonato JA, Rackley RR, Kuang M, Sadhukhan PC, Mauney JR, Keay SK, Freeman MR, Liou LS, Adam RM. In Vitro Cell Dev Biol Anim. 2010 Dec 7. [Epub ahead of print]. PMID: 21136194

While studies of the urothelium, the specialized epithelial lining of the urinary bladder, are critical for understanding diseases affecting the lower urinary tract, including interstitial cystitis, urinary tract infections and cancer, the authors note that our understanding of urothelial pathophysiology has been hampered by a lack of appropriate model systems. In this article, they describe the isolation and characterization of a non-transformed urothelial cell line (TRT-HU1), originally explanted from normal tissue and immortalized with hTERT, the catalytic subunit of telomerase. They demonstrate responsiveness of the cells to anti-proliferative factor (APF), a glycopeptide implicated in the pathogenesis of interstitial cystitis. TRT-HU1 carries a deletion on the short arm of chromosome 9, an early genetic lesion in development of bladder cancer. TRT-HU1 urothelial cells displayed growth and migration characteristics similar to the low-grade papilloma cell line RT4. In contrast, they observed marked differences in both phenotype and gene expression profiles between TRT-HU1 and the highly malignant T24 cell line. They suggest that together these findings provide the first demonstration of a non-transformed, continuous urothelial cell line that responds to APF. They believe that this cell line will be valuable for studies of both benign and malignant urothelial cell biology.

URINARY NERVE GROWTH FACTOR LEVELS IN OVERACTIVE BLADDER SYNDROME AND LOWER URINARY TRACT DISORDERS.

Liu HT, Chen CY, Kuo HC. J Formos Med Assoc. 2010 Dec;109(12):862-78. PMID: 21195884

This study from Taiwan looks at urinary NGF levels in OAB and lower urinary tract disorders and reviews the latest advances in this field. Although urgency is the core symptom of OAB, patients might have difficulty to distinguish urgency from the urge to void. While a urodynamic study is a useful diagnostic tool to diagnose detrusor overactivity (DO) in patients with OAB, not all OAB patients have DO. They therefore believe that a more objective and non-invasive way of diagnosing and assessing OAB including DO is needed. They note that recent research has focused on urinary biomarkers in assessment of OAB. Urinary nerve growth factor (NGF) level increases in patients with OAB-wet, bladder outlet obstruction, mixed urinary incontinence and urodynamic DO. Urinary NGF levels are correlated with severity of OAB symptoms. In patients with OAB and DO who have been well treated with antimuscarinics or botulinum toxin injection, urinary NGF levels have been shown to decrease significantly in association with reduction of urgency severity. However, not all patients with OAB have an elevated urinary NGF level. It might also be increased in patients with interstitial cystitis/painful bladder syndrome, cerebrovascular accident and lower urinary tract diseases such as urinary tract stone, bacterial infection and urothelial tumor. It is possible to use urinary NGF levels as a bio-marker for diagnosis of OAB as well as for the assessment of therapeutic outcome in patients with OAB or DO.

INTERSTITIAL CYSTITIS AND ENDOMETRIOSIS IN A 12-YEAR-OLD GIRL.

Walid MS, Heaton RL. Arch Gynecol Obstet. 2010 Dec 19. [Epub ahead of print]. PMID: 21170744

This is an interesting single case report on a 12 year old girl with both interstitial cystitis and endometriosis. This case article partly expands on a previous article (*Walid MS, Heaton RL (2010) Interstitial cystitis in adolescent girls: an underestimated problem. Int J Child Adolesc Health 3(3)*) and confirms the authors' earlier observation of the prevalence of IC among younger females. The authors note that while the typical IC patient is generally considered to be a middle-aged woman, IC can also be a source of chronic pelvic pain in young females, adolescents and children and is usually understated by primary care physicians and paediatricians in this category of patients. These young patients may manifest nonspecific lower urinary tract symptoms in their early childhood which progress gradually to IC during their teenage years. They emphasize the importance of IC screening in female children and young teenagers who exhibit symptoms of lower urinary tract irritation that do not go away with conventional treatment. These symptoms may combine with vague chronic/cyclic pelvic pain of gynaecological origin.

Furthermore, the majority of females with endometriosis report symptoms starting in adolescence, which may lead over time to structural defects and infertility. The role of gynaecologists and urologists in diagnosing both diseases is crucial in this category of patients. These young women require adequate evaluation and treatment to protect their fertility and prevent permanent damage to their pelvic organs and bladder. According to the authors: "The comorbid state we see in this patient with both endometriosis and IC is extraordinarily common and suggest a causal relationship". This case report shows that endometriosis symptoms may begin with the first menstrual cycle and so may IC. It illustrates the general problem of ignoring the complaints of young women with chronic/cyclic pelvic pain who may have endometriosis and/or IC. The authors warn that if you fail to diagnose these young patients, they will go on to develop chronic myofascial pelvic pain syndrome with spasm and this is much harder to treat. They conclude that it is important to screen for IC in young patients with endometriosis and vice versa.

SEX DIFFERENCES IN AUTOIMMUNE DISEASE.

Voskuhl RR. *Biol Sex Differ.* 2011 Jan 4;2(1):1. [Epub ahead of print].

Open access article.

Women are more susceptible to a variety of autoimmune diseases including systemic lupus erythematosus (SLE), multiple sclerosis (MS), primary biliary cirrhosis, rheumatoid arthritis and Hashimoto's thyroiditis. This increased susceptibility in females compared to males is also present in animal models of autoimmune diseases such as spontaneous SLE in (NZBxNZW)F1 and NZM.2328 mice, experimental autoimmune encephalomyelitis (EAE) in SJL mice, thyroiditis, Sjogren's syndrome in MRL/Mp-lpr/lpr mice and diabetes in non-obese diabetic mice. Indeed, being female confers a greater risk of developing these diseases than any single genetic or environmental risk factor discovered to date. Understanding how the state of being female so profoundly affects autoimmune disease susceptibility would accomplish two major goals. First, it would lead to an insight into the major pathways of disease pathogenesis and, secondly, it would likely lead to novel treatments which would disrupt such pathways. Since this increased susceptibility in females also applies to IC/PBS, this is a field of research to keep our eyes on.

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