

# International Painful Bladder Foundation

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

## **IPBF E-Newsletter, Issue 20, March 2010**

*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).*

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

- SUFU Winter Meeting: Review of IC/PBS abstracts and presentations
- IC/PBS Mini-Symposium held in India at USICON
- IAPO's 4<sup>th</sup> Global Patients Congress: a report
- ARACI represented IC/PBS patients at ICORD 2010 in Argentina
- Convergences PP Official Report and Slides online
- ESSIC Annual Meeting Antwerp 20-22 May 2010
- The European Conference on Rare Diseases (ECRD) May 2010 Krakow
- World Continence Week (WCW)
- Current Concepts of Urogenital Pain: PUGO Satellite Symposium at the World Congress on Pain
- Patient Organization News:
  - Patient Organization List
  - International Sjögren's Network
- New Books, websites, etc
- Research Highlights: a review of selected new scientific literature
- Overview of upcoming events

### **SUFU WINTER MEETING, 23-27 FEBRUARY 2010: MANY ABSTRACTS ON IC/PBS AND CHRONIC PELVIPERINEAL PAIN**

This year's SUFU Winter Meeting included many interesting presentations and posters related to interstitial cystitis/painful bladder syndrome and chronic pelvipерineal pain, with studies presented into different methods of treating the pain aspect. Abstracts discussed sacral neuromodulation in IC/PBS patients as well as in patients suffering from both bowel and voiding problems; a study was presented on trying intravesical bupivacaine in IC/PBS patients who have failed to respond to intravesical lidocaine; there was a fascinating look at whether patients and their doctors are speaking the same language when it comes to LUTS terminology and what patients think the term urgency means; a study into the efficacy of using vaginal diazepam for pelvic floor dysfunction pain, IC and/or vulvar pain and much more besides.

A review of selected abstracts can be found on the IPBF website at:

[http://www.painful-bladder.org/pdf/2010\\_SUFU\\_Tampa.pdf](http://www.painful-bladder.org/pdf/2010_SUFU_Tampa.pdf)

## **IC/PBS MINI-SYMPOSIUM HELD IN INDIA AT USICON**

A well-attended mini-symposium on IC/PBS was organized in Agra, India by Dr Nagendra Mishra at the SIU Indian Section Meeting, Session II on 5th February during the 43<sup>rd</sup> Annual Conference of the Urological Society of India (USICON) held 3-7 February 2010 at the magnificent Jaypee Palace Hotel and Convention Centre. Speakers at the IC/PBS mini-symposium included Dr Ajay Singla who discussed recent advances in interstitial cystitis/painful bladder syndrome.

A monograph on IC/PBS written by Dr Mishra was launched on this occasion and immediately proved very popular. Dr Mishra has worked intensively for IC/PBS patients in India for many years. One of the problems has been that many of the drugs used in the Western countries are unavailable in India. It is hoped that this will now start to change.

## **IAPO'S 4TH GLOBAL PATIENTS CONGRESS ON STRENGTHENING HEALTHCARE SYSTEMS GLOBALLY**

Patient advocates called for more meaningful engagement in healthcare design and delivery at the International Alliance of Patients' Organizations' (IAPO) 4th Global Patients Congress in Istanbul, Turkey. Patients' organizations are knowledgeable and motivated to work with information, facts and figures to promote policy change, providing they are involved at decision-making level and treated as equal partners. Patients add value to discussions and decisions by enabling analyses that take into account the reality of what is happening within health systems today. The impact of the global economic situation on healthcare budgets and changing demographics, including a dramatic increase in the number of people with chronic conditions, requires health systems to change and adapt rapidly. Patients must therefore be at the centre of healthcare globally and at the forefront of decision-making.

"We have identified models of patient and public engagement that are successful and can serve as catalysts for further change within healthcare systems. One such model is the European Medicines Agency, where patients play an active role in a number of committees. We strongly advocate that patient engagement should happen in all health systems to the benefit of systems, patients, and thus the public at large." says Hussain Jafri, Chair of IAPO. "Real concerns can be aired and appropriate measures taken that empower patients, health professionals and authorities alike."

The Congress brought together over 100 delegates from around the world, representing patients and other stakeholders in health such as the Council of Europe, the International Council of Nurses (ICN) and the World Health Organization (WHO) to address the subject of Strengthening Healthcare Systems Globally: The Value of Patient Engagement. Patient engagement has been a principal focus of IAPO's work since its foundation.

IAPO advocates for patients and patients' organizations to share the responsibility of healthcare policy-making through meaningful and supported engagement at all levels and at all points of decision making. IAPO is a unique global alliance representing patients of all nationalities across all disease areas and promoting patient-centred healthcare around the world. More information on the Congress can be found at

[www.patientsorganizations.org/congress](http://www.patientsorganizations.org/congress)

(Source: Press release IAPO)

## **ARACI REPRESENTED IC/PBS PATIENTS AT ICORD 2010 INTERNATIONAL RARE DISEASES CONFERENCE HELD IN ARGENTINA**

Liliana Bacchi, president of Asociación Rosarina Afectados Cistitis Intersticial (ARACI) and Beatriz Gomez (vice-president) represented IC/PBS patients from Argentina at the International Conference on Rare Diseases and Orphan Drugs (ICORD) 2010, held 18-20 March this year in Argentina in conjunction with the GEISER Foundation, the umbrella organization for rare diseases throughout Latin American & the Caribbean, of which ARACI is a very active member. The theme of the conference was Global Accessibility and Neglected Diseases. This was a unique opportunity for 53 different disease associations to profile themselves. In addition to attending educational courses and presentations, the ARACI representatives had the opportunity to meet and network with other patient organizations, industry, government authorities, doctors and researchers and the media. The overall aim of the International Conference was to develop constructive international collaborations that will result in diagnostic and treatment advances for patients with rare diseases. Website ARACI: <http://www.araci.org.ar>.

## **CONVERGENCES PP OFFICIAL REPORT AND SLIDES ONLINE**

An official report on the Convergences in Pelviperineal Pain conferences held 16-18 December in Nantes, France will shortly be placed on the Convergences PP website, together with the slide presentations. The report is in French only and will also be published in a French journal. Website: <http://www.convergencespp.org>

## **UPCOMING EVENTS:**

### **ESSIC ANNUAL MEETING: ANTWERP 20-22 May, 2010**

The European Society for the Study of IC/PBS (ESSIC) will be holding its 2010 annual conference in Antwerp, Belgium, 20-22 May 2010 at the Radisson Blu Astrid Hotel, in the heart of Antwerp's famous diamond quarter.

This year, ESSIC has introduced a change from previous years and all scientific presentations will be open to all registered delegates.

On Thursday afternoon, special attention will be paid to the topic of fatigue in what promises to be a very interesting "Fatigue Symposium".

The programme on Friday will kick off with an international round table on definitions, chaired by Professor J.J. Wyndaele with speakers from the USA, Europe and Asia, followed by presentations on questionnaires and symptom scores, endoscopic images of Hunner's lesion, the morphology of the bladder wall and two sessions of scientific presentations/abstracts submitted by participants.

On the Saturday morning, educational courses will be given in English on the ESSIC definition, clinical evaluation, exclusion of confusable diseases and treatment. This will be followed on Saturday afternoon by an educational Pelvic Pain Symposium in Flemish/Dutch for local clinicians including topics such as diet, behaviour, physiotherapy and osteopathy. Registration, venue details and the programme are available on the ESSIC website: <http://symposium.uza.be/essic2010/Pages/home.aspx>

Please note that the deadline for submission of abstracts is 1 May 2010.

## **THE EUROPEAN CONFERENCE ON RARE DISEASES (ECRD) MAY 2010 KRAKOW**

“From Policies to Effective Services for Patients” is the title of the next European Conference on Rare Diseases (ECRD), which will be held 14th and 15th May 2010 in Krakow, Poland. On May 13th, the day before the Conference officially starts, EURORDIS will hold its General Assembly. Several satellite workshops will also take place on May 13th at the same venue, such as the 10th Council of National Alliances, the annual Orphanet Workshop, and the EuroPlan Workshop, which will gather health authorities from all 27 Member States. The biennial European Conference on Rare Diseases is organised by EURORDIS and its partners, and is supported by the European Commission’s Health Programme. It is the most important conference in Europe on rare disease policy and has attracted over 400 participants to each of the three last conferences: ECRD 2003 Paris, ECRD 2005 Luxembourg and ECRD 2007 Lisbon.

For detailed information, please go to: <http://www.eurordis.org/content/preparing-poland> and: <http://www.rare-diseases.eu/2010/index.php>

## **WORLD CONTINENCE WEEK (WCW)**

The 2<sup>nd</sup> World Continence Week will be held 21-27 June 2010. WCW is a project organized by the Continence Promotion committee of the International Continence Society. WCW is aimed at promoting continence awareness worldwide and promoting a multi-disciplinary approach to treatment. Further information may be obtained by contacting:

[info@icsoffice.org](mailto:info@icsoffice.org).

NB: Why don’t we have a World IC/PBS Day or Week?

## **CURRENT CONCEPTS OF UROGENITAL PAIN (OFFICIAL PUGO SATELLITE SYMPOSIUM OF THE 13TH WORLD CONGRESS ON PAIN)**

A satellite symposium will be organized by PUGO (the Pain of Urogenital Origin Special Interest Group of the IASP) on 29 August 2010 at the Montreal Convention Centre/Palais des Congrès de Montreal at the start of the 13<sup>th</sup> WORLD CONGRESS ON PAIN which will be held 29 August-2 September 2010.

The objectives will be:

- To understand what constitutes urogenital pain
- To discuss the current nomenclature used in describing and researching such painful conditions
- To review the current understanding of the basic science modulating urogenital pain
- To discuss the psychological influences in urogenital pain.

A flier may be downloaded at: <http://indoorcat.org/pugo/events.html>. For further information contact: [margaret.whelan@stees.nhs.uk](mailto:margaret.whelan@stees.nhs.uk)

Registration is via the World Congress on Pain Registration web page: <http://www.iasp-pain.org/Montreal>

## **PATIENT ORGANISATION NEWS**

### **IPBF WEBSITE PATIENT ORGANIZATION LIST**

The IPBF has a list of non-profit patient support groups and contacts worldwide for IC/PBS and related disorders on its website:

[http://www.painful-bladder.org/globalgroups\\_etc.html](http://www.painful-bladder.org/globalgroups_etc.html)

If you note any errors in the information on this page or if you know of other groups anywhere in the world, however small, please let us know so that we can try to keep the list as up-to-date as possible.

### **INTERNATIONAL SJÖGREN'S NETWORK**

An International Network for Sjögren's syndrome was recently set up. If any IC patient is looking for a Sjögren's syndrome support group in their country, please go to:

<http://www.sjogrens.org/home/get-connected/isn>

### **NEW BOOKS, WEBSITES, etc**

#### **NVA ONLINE TUTORIAL: VULVODYNIA: INTEGRATING CURRENT KNOWLEDGE INTO CLINICAL PRACTICE.**

The National Vulvodynia Association (NVA) of the USA recently announced the release of the 4<sup>th</sup> edition of its CME/CE accredited online tutorial for health care professionals entitled: Vulvodynia: Integrating Current Knowledge into Clinical Practice. The tutorial, free to all viewers, is a self-guided presentation on the epidemiology, differential diagnosis, treatment and etiology of vulvodynia. This edition includes the latest research findings and additional content on vulvodynia prevalence and comorbid disorders. To access the tutorial, please visit: <http://learnprovider.nva.org>.

**IC NATURALLY: A natural remedy approach to treatment of Interstitial Cystitis**

*By Diana Brady MA CNC*

*Paperback: 240 pages*

*Publisher: Diana Brady, MA, CNC; 1st edition (November 9, 2009)*

*ISBN-10: 1441588922*

*ISBN-13: 978-1441588920*

Diana Brady, who is a nutrition counsellor and consultant as well as being an IC patient for the past 25 years, has written this very readable book on a natural approach to IC. With seven interesting chapters, it is a detailed, illustrated guide to IC, with a description of IC, a history and description of natural remedies, mechanisms of pain, diet and IC, natural remedies to treat IC symptoms, underlying health issues and much more besides. This book is a useful addition to the IC patient's library. If you feel you have tried endless drug treatment to no avail, this book will give you plenty of ideas for self-help. Further details are available at: <http://www.icnaturally.com/>

#### **COPING WITH CANDIDA**

*By Shirley Trickett*

*Sheldon Press, Second Edition 2007*

*128pp*

*ISBN: 978-1-84709-012-6*

Coping with Candida has become a classic book on the subject of candida. In this new edition, author Shirley Trickett explains how candida really works, how it causes problems, why it seems to be on the increase, and, most important, how to get it out of your life. As well as details on chronic candidiasis, allergies and food intolerance, and cleansing a toxic colon, she also includes valuable information on the latest research, including the links between candida, chronic fatigue, and the infection borrelia.

Further details: <http://www.sheldonpress.co.uk/books/9781847090126.html>

## **OVERCOMING TIREDNESS AND EXHAUSTION**

*By Fiona Marshall*

*Sheldon Press, 2008*

*128pp*

*216 x 135 mm*

*ISBN: 978-0-85969-964-8*

Tiredness and fatigue are problems that IC patients have to deal with on a daily basis. Those who have IC accompanied by an autoimmune disease may have to battle with severe chronic fatigue. Communicating this problem to your doctor may form a struggle all of its own. Fiona Marshall writes that a study published in the *British Medical Journal* showed that “61 per cent of patients perceived the cause of their tiredness to be physical, while 57 per cent of doctors viewed the problem as psychological. Generally, it seems that patients view tiredness as important because it affects their quality of life and can be disabling, whereas doctors do not, because by itself tiredness doesn’t present specific enough grounds for diagnosis.” This book takes a look at:

- How to measuring tiredness
- Reasons for fatigue including medical causes such as diabetes, thyroid and cardiac problems
- Improving your energy
- Improving your sleep
- Nutritional issues
- How your doctor can help
- Complementary remedies

Further details: <http://www.sheldonpress.co.uk/books/9780859699648.html>

## **PHARMACOLOGY OF PAIN**

*Editors: Pierre Beaulieu, David Lussier, Franck Porreca, Anthony H. Dickenson*

*Published by IASP Press® 2010*

*International Association for the Study of Pain*

*ISBN: 978-0-931092-78-7*

This book, published by the International Association for the Study of Pain (IASP) and aimed at professionals, provides a complete review of the pharmacology of pain, including mechanisms of drug actions, clinical aspects of drug usage, and new developments. It describes the different systems involved in the perception, transmission and modulation of pain and discusses the available options for pharmacological treatment of pain. Pharmacology of Pain is a particularly useful resource for: basic researchers and clinicians,

including physicians, dentists, pharmacists, nurses, and physical therapists, other professionals in the field of pain research and treatment and students and trainees.

Further details from the IASP website: [www.iasp-pain.org](http://www.iasp-pain.org)

Direct link to ordering page: [http://www.iasp-](http://www.iasp-pain.org/AM/Template.cfm?Section=Home&TEMPLATE=/CM/ContentDisplay.cfm&CONTENTID=10397)

[ain.org/AM/Template.cfm?Section=Home&TEMPLATE=/CM/ContentDisplay.cfm&CONTENTID=10397](http://www.iasp-pain.org/AM/Template.cfm?Section=Home&TEMPLATE=/CM/ContentDisplay.cfm&CONTENTID=10397)

### **UROTODAY CAUTI CENTER FOR CATHETER ASSOCIATED URINARY TRACT INFECTION**

Urotoday ([www.urotoday.com](http://www.urotoday.com)) has a new online resource aimed at combating urinary tract infection caused by catheterisation. This is important information on patient safety for everyone: [http://www.urotoday.com/cauti\\_center/index.html](http://www.urotoday.com/cauti_center/index.html)

### **UROTODAY MULTIMEDIA PRESENTATION SERIES ON INDWELLING URINARY CATHETERS AND CATHETER-ASSOCIATED URINARY TRACT INFECTIONS**

Part one of this series of three presentations by Diane K. Newman, RNC, MSN, CRNP, FAAN on catheter-associated urinary tract infections is now available online.

You will need to log in to the UroToday website if you are already a registered user. If not yet registered, sign up by registering for free.

[http://www.urotoday.com/46/browse\\_categories/urinary\\_incontinence\\_ui/indwelling\\_urinary\\_catheters\\_and\\_catheterassociated\\_urinary\\_tract\\_infections\\_cautis\\_part\\_1\\_of\\_302262010.html](http://www.urotoday.com/46/browse_categories/urinary_incontinence_ui/indwelling_urinary_catheters_and_catheterassociated_urinary_tract_infections_cautis_part_1_of_302262010.html)

## **RESEARCH HIGHLIGHTS**

### **A REVIEW OF SELECTED NEW 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. 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.

### **DEVELOPMENT, VALIDATION AND TESTING OF AN EPIDEMIOLOGICAL CASE DEFINITION OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.**

*Berry SH, Bogart LM, Pham C, Liu K, Nyberg L, Stoto M, Suttorp M, Clemens JQ. J Urol. 2010 Mar 18. [Epub ahead of print]. PMID: 20303099*

In this RAND Corporation study that forms part of the RAND Interstitial Cystitis Epidemiology study, the authors explain that one of the big problems has been the lack of a standard case definition for interstitial cystitis/painful bladder syndrome for patient screening or epidemiological studies. They therefore developed a case definition for interstitial cystitis/painful bladder syndrome with known sensitivity and specificity and compared this definition with other definitions used in epidemiological studies for IC /PBS.

They set about this by reviewing the literature and performing a structured, expert panel process so as to arrive at an interstitial cystitis/painful bladder syndrome case definition. They then designed a questionnaire aimed at assessing interstitial cystitis/painful bladder syndrome symptoms using this case definition and others used in the literature. This questionnaire was given to 599 women with interstitial cystitis/painful bladder syndrome, overactive bladder, endometriosis or vulvodynia. They calculated the sensitivity and specificity of each definition on the basis of physician assigned diagnoses as the reference standard. Since they found that no single epidemiological definition had high sensitivity and high specificity, it was decided to develop two definitions: one with high sensitivity (81%) and low specificity (54%), and the other with the opposite (48% sensitivity and 83% specificity). It was concluded that no single case definition of interstitial cystitis/painful bladder syndrome provides high sensitivity and high specificity to identify the condition. They are of the opinion that, for **prevalence studies** of interstitial cystitis/painful bladder syndrome, the best approach may be to use two definitions that would generate a prevalence range. The RAND Interstitial Cystitis Epidemiology interstitial cystitis/painful bladder syndrome case definitions, developed through structured consensus and validation, can be used for this purpose. These are as follows:

#### **High Sensitivity Definition Criteria**

(sensitivity 81%, specificity 54% for IC/PBS vs. endometriosis, vulvodynia, and overactive bladder)

Pain, pressure or discomfort in the pelvic area

**AND**

Daytime urinary frequency 10+ OR Urgency due to pain, pressure, or discomfort not fear of wetting

#### **High Specificity Definition Criteria**

(sensitivity 48%, specificity 83% for IC/PBS vs. endometriosis, vulvodynia, and overactive bladder)

Pain, pressure or discomfort in the pelvic area

**AND**

Daytime urinary frequency 10+ OR Urgency due to pain, pressure, or discomfort not fear of wetting

**AND**

Symptoms did not resolve after treatment with antibiotics

**AND**

No treatment with Lupron for endometriosis

#### **Exclusion Criteria**

Bladder cancer, diverticulum of urethra, spinal cord injury, stroke, Parkinsons, multiple sclerosis, spina bifida, cyclophosphamide-cytoxan treatment, radiation treatment to pelvic area, tuberculosis affecting the bladder, cancer of the uterus, ovaries or vagina, genital herpes, pregnancy.

### **A SURVEY OF PRIMARY CARE PHYSICIAN PRACTICES IN THE DIAGNOSIS AND MANAGEMENT OF WOMEN WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.**



*Clemens JQ, Calhoun EA, Litwin MS, Walker-Corkery E, Markossian T, Kusek JW, McNaughton-Collins M; Urologic Pelvic Pain Collaborative Research Network. Urology. 2010 Mar 18. [Epub ahead of print]. PMID: 20303575*

This study looked into patterns of practice of USA primary care physicians (PCPs) caring for patients who have symptoms suggestive of interstitial cystitis/painful bladder syndrome (IC/PBS). The authors developed a case presentation of a woman with typical IC/PBS symptoms and questions concerning etiology, management strategies, and familiarity with this syndrome. This was sent to 556 primary care physicians. 52% responded. 19% of these said that had never seen any such case in their practice, two thirds were able to identify the characteristic symptoms of IC/PBS as being bladder pain or pressure. 90% of the respondents knew that IC/PBS was a non-infectious disease, 76% that it was not a sexually transmitted disease, 61% correctly stated that it was not a psychiatric disease. Although most of them appeared to be familiar with the disease, they did not appear to be caring for many patients with IC/PBS and seemed to be unfamiliar with clinical characteristics and uncertain regarding diagnosis and treatment. It was concluded that the care of IC/PBS patients can probably be improved by more education of primary care physicians. Although this was a USA-based study, the same is likely to apply worldwide.

#### **NEW INSIGHTS IN THE DIFFERENTIAL DIAGNOSIS OF BLADDER PAIN SYNDROME.**

*Schwalenberg T, Neuhaus J, Horn LC, Alexander H, Zimmermann G, Ho Thi P, Mallock T, Stolzenburg JU. Aktuelle Urol. 2010 Mar;41(2):107-118. Epub 2010 Mar 22. PMID: 20309783*

The authors from Leipzig underline the fact that diagnosing BPS/IC is a challenge since there is still considerable discussion about pathogenesis and the definition of clinically relevant parameters. According to Schwalenberg and colleagues, the criteria proposed by the European Society for the Study of Interstitial Cystitis (ESSIC) define a collection of patients based on the hallmark symptom of bladder pain which is heterogeneous, and therefore cannot be given standardised, consistent therapy. Therefore, they are of the opinion that an extended diagnosis based on molecular markers seems to be indicated so as to facilitate individual medical treatment, and also to contribute to clarifying pathogenesis. They feel that this means that taking a bladder biopsy is essential. Diagnosis should be based on three arms: clinical diagnostics, histopathology and molecular diagnostics / protein expression. Examination should ideally include the urothelium, lamina propria, and detrusor musculature. Generation of receptor profiles of the detrusor muscle represents a first attempt to define a diagnostic tool for the individualisation of BPS / IC medical treatment. Extended BPS / IC diagnostics could be realistically integrated into routine patient care within a clinic / laboratory network.

#### **EFFECT OF AMITRIPTYLINE ON SYMPTOMS IN TREATMENT NAÏVE PATIENTS WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.**

*Foster HE Jr, Hanno PM, Nickel JC, Payne CK, Mayer RD, Burks DA, Yang CC, Chai TC, Kreder KJ, Peters KM, Lukacz ES, Fitzgerald MP, Cen L, Landis JR, Propert KJ, Yang W, Kusek JW, Nyberg LM; Interstitial Cystitis Collaborative Research Network. J Urol. 2010 Mar 17. [Epub ahead of print]. PMID: 20303115*

Although the tricyclic antidepressant amitriptyline is often used in the treatment of IC/PBS patients, scientific evidence to support this largely comes from a clinical trial at one centre and case reports. It was therefore decided to conduct a multi-centre, randomized, double-blind, placebo controlled clinical trial of amitriptyline in IC/PBS patients who had not

received any previous treatment for their IC/PBS (so-called treatment naïve patients). During the study period, dosage was increased from 10 mg to 75 mg once a day. Both groups of patients (drug and placebo) followed a standardised education and behavioural programme. 231 patients (out of a total of 271) completed the programme with a global response assessment after 12 weeks follow-up. It was found that, seen overall, amitriptyline did not show a significant improvement in IC/PBS patients who had received no previous treatments. However, a significantly higher rate of improvement compared to the placebo group was found in the patients who had managed to take at least 50 mg amitriptyline a day.

#### **LONG-TERM RESULTS OF AMITRIPTYLINE TREATMENT FOR INTERSTITIAL CYSTITIS.**

*Hertle L, van Ophoven A. Aktuelle Urol. 2010 Jan;41(S 01):S61-S65. Epub 2010 Jan 21. PMID: 20094958*

This is a prospective open-label study from Münster, Germany, into the safety and efficacy of long-term use of the tricyclic antidepressant amitriptyline in patients with interstitial cystitis (IC). The patients in this study were divided into two groups: group 1 fulfilled NIDDK criteria, group 2 had typical IC symptoms but met at least one of the NIDDK exclusion criteria. The amitriptyline was taken strictly at bedtime. Dosage was self-titrated without a maximum limit. The average was 55 mg, varying from 12.5 to 150 mg. The authors found a significant improvement in IC symptoms in both groups and concluded from the results that long-term use of amitriptyline is feasible, safe and effective as long as care is taken with the dosage to minimise side effects.

#### **ANTIDEPRESSANT DRUGS FOR CHRONIC UROLOGICAL PELVIC PAIN: AN EVIDENCE-BASED REVIEW.**

*Papandreou C, Skapinakis P, Giannakis D, Sofikitis N, Mavreas V. Adv Urol. 2009;2009:797031. Epub 2010 Feb 14. PMID: 20169141*

Free article ONLINE: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2821755/pdf/AU2009-797031.pdf>

The purpose of this study was to evaluate the available evidence for the efficacy and acceptability of antidepressant drugs in the management of urological chronic pelvic pain. Studies were selected through a literature search, including all types of study designs due to the limited evidence. The studies were classified into levels of evidence according to their design. Ten studies were included with a total of 360 patients. Antidepressants reported in scientific literature are amitriptyline, sertraline, duloxetine, nortriptyline, and citalopram. Only four randomized, controlled trials were identified (two for amitriptyline and two for sertraline) with mixed results. The authors concluded that use of antidepressants for the management of chronic urological pelvic pain is not adequately supported by sound randomized, controlled trials. The existing published studies indicate that amitriptyline may be effective in interstitial cystitis. However the authors believe that this could be explained by publication bias. They note that all the above drugs appear to have been generally well tolerated with no serious side effects reported.

#### **CHRONIC PUDENDAL NEUROMODULATION: EXPANDING AVAILABLE TREATMENT OPTIONS FOR REFRACTORY UROLOGIC SYMPTOMS.**

*Peters KM, Killinger KA, Boguslawski BM, Boura JA. Neurourol Urodyn. 2009 Sep 28. [Epub ahead of print]. PMID: 19787710*

The purpose of this study was to evaluate symptoms, complications and patient satisfaction after chronic pudendal nerve stimulation (CPNS) by retrospectively reviewing patients who had received a tined lead placed at the pudendal nerve via the ischial-rectal approach. The majority of the 84 patients had interstitial cystitis/painful bladder syndrome, or overactive bladder. Pudendal response ( $\geq 50\%$  improvement) occurred in 60/84 (71.4%), however 5 of these chose sacral neuromodulation. It was interesting to note that almost all the patients (93.2%) who had failed sacral neuromodulation responded positively to pudendal nerve stimulation and that there was an overall improvement in bladder, pelvic pain, incontinence, urgency, and frequency symptoms. The authors concluded that CPNS is a reasonable alternative in complex patients who have failed to respond to other therapies including sacral neuromodulation. The authors note that further research is necessary to fully assess long-term outcomes and identify predictors of success.

#### **CLINICAL APPLICATIONS OF NEUROSTIMULATION: FORTY YEARS LATER.**

*Mekhail NA, Cheng J, Narouze S, Kapural L, Mekhail MN, Deer T.*

*Pain Pract. 2010 Jan 8. [Epub ahead of print]. PMID: 20070547*

In this review article, Mekhail and colleagues write that neurostimulation has given new hope to many patients suffering from debilitating chronic pain conditions. They look at many pain conditions, including visceral pain. A growing body of literature supports neurostimulation for visceral pain in general and interstitial cystitis in particular. "Considering the strength of evidence, the use of neurostimulation should be encouraged prior to cystectomy", they write. However, according to the authors, patient selection for appropriate methods of neurostimulation is essential in order to ensure safe, successful and cost-effective applications of this form of treatment. One problem the authors have encountered is that use of neurostimulation for visceral pain has been underreported, even though carried out quite extensively, and this makes some healthcare professionals reluctant to use it. Randomized, controlled studies are needed to establish evidence-based clinical practice so that patients with devastating visceral pain can benefit from this potentially useful therapy that can reduce pain, optimise function and improve quality of life for the patient.

#### **TRIGONAL INJECTION OF BOTULINUM TOXIN A IN PATIENTS WITH REFRACTORY BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.**

*Pinto R, Lopes T, Frias B, Silva A, Silva JA, Silva CM, Cruz C, Cruz F, Dinis P. Eur Urol. 2010 Mar 6. [Epub ahead of print]. PMID: 20227820*

Most nociceptive bladder afferents are concentrated in the trigone. This study with 26 women with BPS/IC aimed at evaluating the efficacy and tolerability of trigonal injection of botulinum toxin A (BoNTA). Urine concentrations of nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) were also evaluated in this study. No voiding difficulties were observed. The authors report that their study showed that trigonal injection of BoNTA improved lower urinary tract symptoms, including pain and frequency, in all the participating patients. A significant, transient reduction in urinary NGF and BDNF levels was also observed. It was concluded that trigonal injection of BoNTA is safe and effective for this group of patients. Rejections continue to be effective. The study had limitations in the low number of patients and the lack of a placebo control group. The authors recommend that placebo-controlled, dose-escalating studies should be carried out.

### **EXPERIENCE WITH INJECTIONS OF BOTULINUM TOXIN TYPE A INTO THE DETRUSOR MUSCLE.**

*Miyagawa I, Watanabe T, Isoyama T, Honda M, Kobayasi N, Hikita K, Saito M, Hirakawa S. Aktuelle Urol. 2010 Jan;41(S 01):S24-S26. Epub 2010 Jan 21. PMID: 20094947*

The purpose of this study by Miyagawa and colleagues from Japan was to investigate the effects of intravesical injections of botulinum toxin type A into the detrusor muscle in patients with neurogenic overactive bladder (OAB), patients with non-neurogenic overactive bladder and patients with interstitial cystitis between January 2003 and December 2006. Thirty patients were treated with 100 I. U. to 300 I. U. of botulinum toxin A injected into the detrusor muscle and received follow-up after 4, 12 and 36 weeks. In the case of interstitial cystitis: in all four patients the treatments were considered to be ineffective.

### **CXCR3 BINDING CHEMOKINE AND TNFSF14 OVER EXPRESSION IN BLADDER UROTHELIUM OF PATIENTS WITH ULCERATIVE INTERSTITIAL CYSTITIS.**

*Ogawa T, Homma T, Igawa Y, Seki S, Ishizuka O, Imamura T, Akahane S, Homma Y, Nishizawa O. J Urol. 2010 Jan 21. [Epub ahead of print]. PMID: 20096889*

The purpose of this study from Japan was to investigate the genes responsible for ulcerative interstitial cystitis (Hunner's lesion subtype) by DNA microarray analysis and quantitative real-time polymerase chain reaction. The authors found that this method revealed over-expression of genes related to immune and inflammatory responses, including T-helper type 1 related chemokines, and cytokines such as CXCR3 binding chemokines and TNFSF14. They believe that these genes may be potential interstitial cystitis biomarkers. However, from a clinical point of view, measurement of upregulated chemokines in urine may be a better diagnostic tool due to its less invasive nature. Furthermore, immunohistochemical studies to determine chemokine sites and investigate the role of chemokines in IC pathogenesis are needed, and particularly comparative studies of ulcerative and nonulcerative IC.

### **INCREASED NERVE GROWTH FACTOR IN NEUROGENIC OVERACTIVE BLADDER AND INTERSTITIAL CYSTITIS PATIENTS.**

*Jacobs BL, Smaldone MC, Tyagi V, Philips BJ, Jackman SV, Leng WW, Tyagi P. Can J Urol. 2010 Feb;17(1):4989-94. PMID: 20156378*

In recent years we have seen much interest in studying nerve growth factor (NGF) both as a potential diagnostic biomarker for overactive bladder (OAB) as well as a prognostic marker to measure response to treatment in IC/PBS patients. The purpose of this study from Canada was to evaluate urine nerve growth factor (NGF) levels in a normal control group and in patients with several urologic conditions in order to examine NGF's role as a future biomarker and to gain better insight in the relationship between urinary NGF levels and various diseases of the genitourinary tract. The authors found that urinary NGF levels were significantly elevated in patients with neurogenic overactive bladder and IC/PBS regardless of whether they had had previous medical treatment or not. Levels approached significance in patients with OAB wet – most of whom had been on prior treatment – and patients with nephrolithiasis. Future studies with larger groups of patients are needed to further examine the significance of urinary NGF levels in the pathogenesis of a variety of urologic diseases and whether NGF could be used as a diagnostic or prognostic marker for specific urologic diseases. They also suggest that standardisation of urine collection would probably give more consistent results.

### **CORTICOTROPIN-RELEASING HORMONE-RECEPTOR 2 IS REQUIRED FOR ACUTE STRESS-INDUCED BLADDER VASCULAR PERMEABILITY AND RELEASE OF VASCULAR ENDOTHELIAL GROWTH FACTOR.**

*Boucher W, Kempuraj D, Michaelian M, Theoharides TC. BJU Int. 2010 Mar 1. [Epub ahead of print]. PMID: 20201838*

This study investigated the corticotropin-releasing hormone (CRH) receptor (CRH-R) requirement for the effect of acute stress on bladder vascular permeability and release of vascular endothelial growth factor (VEGF). According to the authors, there is increasing evidence that acute stress worsens certain inflammatory disorders, including IC/PBS, which is characterized by pain, variable bladder inflammation, increased expression of bladder vascular endothelial growth factor (VEGF), and many detrusor mast cells. They concluded from their results that acute stress may induce bladder vascular permeability and VEGF release that is dependent on CRH-R2. They are of the opinion that these findings suggest that CRH and VEGF might participate in the pathogenesis of IC/PBS and provide for new therapeutic targets.

### **CXCR3 BINDING CHEMOKINE AND TNFSF14 OVER EXPRESSION IN BLADDER UROTHELIUM OF PATIENTS WITH ULCERATIVE INTERSTITIAL CYSTITIS.**

*Ogawa T, Homma T, Igawa Y, Seki S, Ishizuka O, Imamura T, Akahane S, Homma Y, Nishizawa O. J Urol. 2010 Mar;183(3):1206-1212. Epub 2010 Jan 22. PMID: 20096889*

In this study from Japan, Ogawa and colleagues investigated the genes responsible for ulcerative interstitial cystitis (Hunner's lesion type IC) by DNA microarray analysis and quantitative real-time polymerase chain reaction in order to explore IC etiology and potential biomarkers. Bladder urothelial samples were taken from 8 females and 1 male with ulcerative IC from a site with no lesions and from a normal-looking area in 5 female and 4 male controls. The authors report that their study using DNA microarray analysis followed by quantitative real-time polymerase chain reaction revealed over expression of genes related to immune and inflammatory responses, including T-helper type 1 related chemokines, and cytokines such as CXCR3 binding chemokines and TNFSF14. These genes and their products are suspected to be a cause of ulcerative IC and may be potential IC biomarkers.

### **GENOME-BASED EXPRESSION PROFILING STUDY OF HUNNER'S ULCER TYPE INTERSTITIAL CYSTITIS: AN ARRAY OF 40-GENE MODEL.**

*Tseng LH, Chen I, Wang CN, Lin YH, Lloyd LK, Lee CL. Int Urogynecol J Pelvic Floor Dysfunct. 2010 Mar 4. [Epub ahead of print]. PMID: 20204322*

The purpose of this study from Taiwan was to explore potential molecular mechanisms contributing to the pathogenesis of Hunner's ulcer type interstitial cystitis, comparing global gene expression profiles in bladder epithelial cells from IC patients with Hunner's ulcer with normal controls. Their results indicate that genome-based expression profiling can be used for the diagnostic tests of Hunner's ulcer type IC in clinical practice.

### **DISTRESS IN PATIENTS WITH INTERSTITIAL CYSTITIS: DO ILLNESS REPRESENTATIONS HAVE A ROLE TO PLAY?**

*Heyhoe J, Lawton R. Psychol Health Med. 2009 Dec;14(6):726-39. PMID: 20183545*

This study from the UK investigated the illness perceptions of IC patients and their experience of psychological distress using the Revised Illness Perceptions Questionnaire (IPQ-R) and semi-structured interviews. Forty-four patients with IC attending an out-patient

clinic at a large UK hospital completed a questionnaire booklet comprising of the IPQ-R and the General Health Questionnaire-28 (GHQ-28), while fifteen patients also took part in a follow-up interview. The authors found evidence suggesting that illness perceptions influence psychological well-being in IC patients. Findings concerning the emotional consequences of illness perceptions in IC patients suggest that interventions which help to modify dysfunctional illness perceptions may assist in the prevention of psychological distress.

#### **LOWER URINARY TRACT SYMPTOMS IN WOMEN WITH IRRITABLE BOWEL SYNDROME.**

*Guo YJ, Ho CH, Chen SC, Yang SS, Chiu HM, Huang KH. Int J Urol. 2010;17(2):175 – 181. PMID: 20088875*

The purpose of this study from Taiwan was to investigate lower urinary tract symptoms (LUTS) in 52 women diagnosed with irritable bowel syndrome (IBS) and to evaluate risk factors associated with the psychiatric health of these patients. 55 women without gastrointestinal symptoms were used as controls. The most common lower urinary tract symptoms in patients with IBS were storage symptoms. These patients had significantly higher scores of frequency, nocturia, urge incontinence, lower maximal flow rate and lower voiding volume. Furthermore, the authors found significantly higher storage and total American Urological Association Symptom Index questionnaire scores in the IBS patients. The prevalence of psychiatric health problems in IBS patients (28.8%) was significantly higher than in the control group (20%). In addition, the urinary storage symptom score was significantly correlated with psychiatric morbidity. The authors concluded from the results of this study that LUTS are common in IBS patients and have a negative impact on their psychiatric health. They recommended that healthcare providers should be aware of the psychological consequences of LUTS in these patients and assess LUTS in addition to gastrointestinal symptoms in patients with IBS. Their advice is that specialists in both fields should work together to find better way of managing these patients.

#### **CENTRAL AND PERIPHERAL HYPERSENSITIVITY IN THE IRRITABLE BOWEL SYNDROME.**

*Zhou Q, Fillingim RB, Riley JL 3rd, Malarkey WB, Verne GN. Pain. 2010 Mar;148(3):454-61. Epub 2010 Jan 13. PMID: 20074857*

Many patients with IBS also have a wide range of somatic symptoms including back pain, migraine, heartburn, dyspareunia and muscle pain, suggesting that IBS patients may also suffer from central hyperalgesic dysfunction. Similarly, patients with other chronic pain disorders have been shown to have generalized hyperalgesia. In the case of IBS patients, it had been previously thought that hypersensitivity was limited to the intestines. The purpose of this study was to characterize differences in perceptual responses to a battery of noxious somatic stimuli in IBS patients compared to controls. A total of 78 diarrhoea-predominant and 57 controls participated in the study. A subset of IBS patients demonstrated the presence of somatic hypersensitivity to thermal, ischemic, and cold pressor nociceptive stimuli. The somatic hypersensitivity in IBS patients was somatotopically organized with the lower extremities that share viscerosomatic convergence with the colon demonstrating the greatest hypersensitivity. There were also changes in ACTH, cortisol, and systolic blood pressure in response to the ischemic pain testing in IBS patients when compared to controls. The results of this study suggest that a more widespread alteration in central pain processing in a subset of IBS patients may be present as they display hypersensitivity to heat, ischemic, and cold pressor stimuli.

## **FIBROMYALGIA SUPPLEMENT**

In December 2009, the American Journal of Medicine published a supplement on Fibromyalgia. Those with an interest in fibromyalgia may like to look at the following articles:

### **FIBROMYALGIA IS A CONTROVERSIAL DISEASE.**

Clauw DJ. Am J Med 2009;122(12 Suppl):S1-2

### **FIBROMYALGIA: AN OVERVIEW.**

Clauw DJ. Am J Med 2009 Dec;122(12 Suppl):S3-S13. PMID: 19962494

### **DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF FIBROMYALGIA.**

Goldenberg DL. Am J Med 2009;122(12 Suppl):S14-21

### **PATHOPHYSIOLOGY OF FIBROMYALGIA.**

Bradley LA. Am J Med 2009;122(12 Suppl):S22-30

### **STRATEGIES FOR MANAGING FIBROMYALGIA.**

Arnold LM. Am J Med 2009;122(12 Suppl):S31-43

### **FURTHER STRATEGIES FOR TREATING FIBROMYALGIA: THE ROLE OF SEROTONIN AND NOREPINEPHRINE REUPTAKE INHIBITORS.**

Mease PJ. Am J Med 2009;122(12 Suppl):S44-55

## **CLINICAL STUDIES WITH CANNABIS AND CANNABINOIDS online**

### **REVIEW ON CLINICAL STUDIES WITH CANNABIS AND CANNABINOIDS 2005-2009**

Arno Hazekamp, Franjo Grotenhermen. *Cannabinoids* 2010;5(special issue):1-21

A special 21-page article entitled "Review on clinical studies with cannabis and cannabinoids 2005-2009" by Arno Hazekamp from the University of Leiden, the Netherlands, and Franjo Grotenhermen from the Nova-Institut in Huerth, Germany, was published in the IACM online journal CANNABINOIDS on 13 February. The full article can be downloaded at:

[http://www.cannabis-med.org/data/pdf/en\\_2010\\_01\\_special.pdf](http://www.cannabis-med.org/data/pdf/en_2010_01_special.pdf)

## **REVIEW ARTICLES ON NEUROUROLOGY**

*Neurourology and Urodynamics* recently published a number of interesting review articles IN ITS Frontiers in Urology section related to neurourology, innervation of the lower urinary tract and interaction between the brain and the bladder which you may find interesting.

### **THE EMOTIONAL MOTOR SYSTEM AND MICTURITION CONTROL.**

Holstege G. *Neurorol Urodyn.* 2010;29(1):42-8. PMID: 20025036

Like other body movements, micturition is the result of activation of the motor system in the central nervous system. This review explains how the brain and brainstem control micturition, allowing the individual to postpone micturition until time and place are appropriate. Lesions in the pathways from prefrontal cortex and limbic system to the periaqueductal gray probably cause urge-incontinence in the elderly.

### **A DECADE OF FUNCTIONAL BRAIN IMAGING APPLIED TO BLADDER CONTROL.**

*Fowler CJ, Griffiths DJ. Neurourol Urodyn. 2010;29(1):49-55. PMID: 19412958*

Over the last 10 years functional brain imaging has emerged as the most powerful technique for studying human brain function. Although the literature is now vast, including studies of every imaginable aspect of cortical function, the number of studies that have been carried out examining brain control of bladder function is relatively limited. Nevertheless those that have been reported have transformed our thinking. This article reviews that development in the context of emerging ideas of interoception and a working model of brain activity during bladder filling and emptying is proposed.

### **NEURAL CONTROL OF THE LOWER URINARY AND GASTROINTESTINAL TRACTS: SUPRASPINAL CNS MECHANISMS.**

*Drake MJ, Fowler CJ, Griffiths D, Mayer E, Paton JF, Birder L. Neurourol Urodyn. 2010;29(1):119-27. PMID: 20025025*

Normal urinary function depends on a complex system of regulation by the central nervous system (CNS). In the brainstem, the pontine micturition centre (PMC) is a convergence point of multiple influences, representing a co-ordinating centre for voiding. Control by the brain allows voiding to take place if necessary, socially acceptable and in a safe setting.

### **NEURAL CONTROL OF THE LOWER URINARY TRACT: PERIPHERAL AND SPINAL MECHANISMS.**

*Birder L, de Groat W, Mills I, Morrison J, Thor K, Drake M. Neurourol Urodyn. 2010;29(1):128-39. PMID: 20025024*

This review deals with individual components regulating the neural control of the urinary bladder, focusing on factors and processes involved in the two modes of operation of the bladder: storage and elimination. Topics included in this review include: (1) The urothelium and its roles in sensor and transducer functions including interactions with other cell types within the bladder wall ("sensory web"), (2) The location and properties of bladder afferents including factors involved in regulating afferent sensitization, (3) The neural control of the pelvic floor muscle and pharmacology of urethral and anal sphincters (focusing on monoamine pathways), (4) Efferent pathways to the urinary bladder, and (5) Abnormalities in bladder function including mechanisms underlying comorbid disorders associated with bladder pain syndrome and incontinence.

## **OVERVIEW OF UPCOMING EVENTS 2010**

### **25th Annual congress of the European Association of Urology (EAU)**

16-20 April 2010, Barcelona, Spain.

**5<sup>th</sup> European Conference on Rare Diseases**, 13-15 May 2010 Krakow, Poland.

**ESSIC Annual Conference 2010**, 20-22 May 2010, Antwerp, Belgium.

**AUA Annual Meeting 2010**, 29 May - 3 June 2010, San Francisco (CA), USA.

**Joint Meeting of the International Continence Society (ICS) and International Urogynecological Association (IUGA)** "Advancing Incontinence and Pelvic Floor Research and Treatment", 23-27 August 2010, Toronto, Canada.

**13<sup>th</sup> World Congress on Pain**, 29 August-2 September, 2010, Montreal, Canada.



## **PUGO Satellite Symposium: CURRENT CONCEPTS OF UROGENITAL PAIN**

29 August 2010.

*A more detailed list of conferences and events with contact addresses and websites can be found on our website under "Calendar".*

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

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### **The Board of the International Painful Bladder Foundation (IPBF)**

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