

# 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 27, October 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) and related disorders.*

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

- Review of International Continence Society conference 2011
- IPBF Swedish Toilet Card
- Upcoming Meetings
- Books, Newsletters, Websites etc
- Research Highlights
- Donations & Sponsoring

## INTERNATIONAL CONTINENCE SOCIETY 2011 ANNUAL SCIENTIFIC MEETING IN SCOTLAND A RESOUNDING SUCCESS

While no podium session was dedicated to IC at the ICS annual scientific meeting, 29 August - 2 September 2011 in Glasgow, Scotland, a substantial number of abstracts in this field had been accepted, many of which could be seen there as non-discussion posters, with others available online as "read as title". While they provided a clear indication of just how global IC research has become, they also indicated how little international consensus still exists on the method of diagnosis and on the terminology used which varies from interstitial cystitis to painful bladder syndrome, bladder pain syndrome, hypersensitive bladder syndrome and chronic pelvic pain syndrome as well as many combinations. The research presented concerned basic research, diagnostic techniques, differences between ulcer and nonulcer types of IC, differences and overlaps between OAB and IC, research into the urothelium and new therapies. Abstracts presented as discussion posters can be found in full in *Neurourology and Urodynamics Volume 30 Issue 6 2011*, and all abstracts on the ICS website at [www.icsoffice.org](http://www.icsoffice.org).

**A review of the research related to IC from the Glasgow meeting can be found on the IPBF website at [http://www.painful-bladder.org/pdf/2011\\_ICGlasgow.pdf](http://www.painful-bladder.org/pdf/2011_ICGlasgow.pdf)**

Despite the lack of podium sessions in this field, there were nevertheless several excellent pre-conference workshops on many aspects of chronic pelvic pain including IC.

Webcasts of ICS 2011 can be found at: <http://webcasts.prous.com/ICS2011/html/1-en/home.aspx?section=1>

### "ICS meets Continence Societies" working lunch

An innovation at the ICS conference this year was a working lunch "ICS meets Continence Societies" to which it invited not only national medical societies, but also national and international patient/consumer organisations, concerned with urinary and faecal incontinence and bladder, bowel and pelvic floor disorders. This was remarkably well attended by IC organisations, including the IPBF,

either by patient advocates themselves or by doctors representing them. According to Professor Helmut Madersbacher, the purpose of this first working lunch initiative was to explain what the ICS could offer continence societies around the world and to receive feedback about what they would like to receive from the ICS. As the only international multidisciplinary society that focuses on this field, the ICS is seeking affiliation with other organizations in order to improve management of incontinence care worldwide. Dr Vasan Srini, chair of the ICS Continence Promotion Committee (CPC), of which the IPBF is an associate, discussed the work and aims of the Continence Promotion Committee, explaining that the CPC is dedicated to promoting awareness and prevention across the world, through the establishment of strategic partnerships with worldwide continence groups. The CPC also provides a forum to support the formation of individual public and patient-based organisations in interested countries. If you would like to know more, further information may be obtained from the ICS Office [info@icsoffice.org](mailto:info@icsoffice.org).

#### **IPBF booth at ICS Glasgow**

The IPBF once again organised an information booth at the ICS conference, distributing up-to-date information on IC and related disorders. As is the case every year at the ICS annual meeting, this was a great success with huge interest from all parts of the world, and by nurses and physiotherapists as well as doctors from many different disciplines. As always, the crucial problem is treatment: what to use in which patients? It was clear that most people are now starting to think in “phenotyping” terms and realize that treatment has to be tailored to the individual patient. The surge in interest by physiotherapists is leading to more combined medical/physical therapy concepts.

The next ICS annual scientific meeting will be held in Beijing, China, 15-10 October 2012 ([www.icsoffice.org](http://www.icsoffice.org)).

#### **IPBF NOW ALSO HAS A SWEDISH TOILET CARD FOR DOWNLOADING**

Following many requests, the IPBF now has a toilet card in Swedish. This can be downloaded at <http://www.painful-bladder.org/pdf/TCSwedish.pdf>. The cards can be cut horizontally, folded in the middle and then laminated. We hope that this will prove useful. Toilet cards in a number of other languages can be found at: [http://www.painful-bladder.org/toiletcard\\_other\\_languages.html](http://www.painful-bladder.org/toiletcard_other_languages.html).

#### **CHINESE TOILET CARD?**

Would anyone be willing to help us make a Chinese version of the toilet card?

#### **UPCOMING MEETINGS:**

##### **6TH EUROPEAN CONFERENCE ON RARE DISEASES AND EURORDIS GENERAL ASSEMBLY 23-25 MAY 2012, BRUSSELS, BELGIUM**

The European Conference on Rare Diseases & Orphan Products is an event where everyone from patients, to policy makers, healthcare professionals, industry, researchers and academics are given the opportunity to meet, exchange information and ideas and join together in the fight against rare diseases.

With over 100 speakers, this annual conference covers the latest research, developments in new treatments and information regarding innovations in health care, social care and support at both European and national levels. This is a unique opportunity to network with all stakeholders in the rare disease community. Further details including the programme can be found at <http://www.rare-diseases.eu/2012/About-ECRD>. The EURORDIS General Assembly for members will be held on 23 May 2012.

## 1ST INTERNATIONAL NEURO-UROLOGY MEETING

The 1<sup>st</sup> International Neuro-Urology Meeting will be held 29/30 June 2012, at Balgrist University Hospital, Zurich, Switzerland. This initiative is being organized by the new Swiss Continence Foundation (see <http://www.swisscontinencefoundation.ch/home/intro/default.asp?userlang=EN>)

Programme information can be found at:

<http://www.swisscontinencefoundation.ch/files/Event/Final%20SCF.pdf>

Further information may be obtained from: [info@swisscontinencefoundation.ch](mailto:info@swisscontinencefoundation.ch)

## PELVIC PAIN RETREAT

A comprehensive five-day pelvic pain retreat is to be held at Beaumont Women's Urology Center, Royal Oak, Michigan, USA, 7-11 November, 2011. This unique treatment programme is designed for women over 18 years of age with any of the following issues:

- pelvic pain not associated with periods
- pelvic pain for more than three months
- pain related to pelvic floor dysfunction (tightness of the muscles)
- pelvic pain that may be accompanied by urinary urge or frequency
- pelvic pain that may be accompanied by vulvar pain/burning.

Further information may be obtained from <http://www.beaumont.edu/pelvic-pain-retreat>.

## IAPO 5<sup>TH</sup> GLOBAL PATIENTS CONGRESS

The International Alliance of Patients' Organizations (IAPO) is pleased to announce that registration for the **5<sup>th</sup> Global Patients Congress** is now open for members and invited guests. The Congress will examine how we measure the extent to which patient-centred healthcare is achieved around the world. The Congress will not only highlight examples of best practice, but also examine how meaningful indicators can be developed to measure patient involvement within healthcare systems. This will inform and support the development of participants' advocacy and communications initiatives to promote patient-centred healthcare worldwide. The **5th Global Patients Congress** gives you the opportunity to:

- Network with 200 patients' organizations, academics, government representatives and other stakeholders, from all over the world
- Share best practice and develop practical skills
- Engage with key policy issues that affect patients in the international arena

The Congress will be held at the Renaissance London Heathrow Hotel, UK, 17-19 March 2012. **To register, or for more information, please visit [www.globalpatientscongress.org](http://www.globalpatientscongress.org)**

## BOOKS, NEWSLETTERS, WEBSITES ETC

### **CAMPBELL-WALSH UROLOGY, 10<sup>TH</sup> EDITION (to be shortly released)**

<http://www.campbellsurology.com/> click on your region of the world for further info

Campbell-Walsh Urology, 10th Edition 4 volumes. By Alan J. Wein, MD, PhD(hon), Louis R. Kavoussi, MD, Andrew C. Novick, MD, Alan W. Partin, MD, PhD and Craig A. Peters, MD, FACS, FAAP

### **CHAPTER 12: BLADDER PAIN SYNDROME (INTERSTITIAL CYSTITIS) AND RELATED DISORDERS**

by Philip Hanno, MD provides a complete update and comprehensive overview.

### **NVA NEWS SUMMER 2011 - ARTICLE ON VULVAR PAIN RESULTING FROM ORTHOPAEDIC CAUSES**

NVA News, the newsletter of the National Vulvodynia Association in the US ([www.nva.org](http://www.nva.org)), carried a most interesting article in its Summer 2011 issue on Vulvar Pain Resulting from Orthopaedic Causes

by Deborah Coady, MD and Nancy Fish, MSW, MPH. The article which provides insights into causes of vulvodynia about which we hear little, was adapted from the authors' new book *Healing Painful Sex*, to be published in November 2011 by Seal Press:

**HEALING PAINFUL SEX**

**A WOMAN'S GUIDE TO CONFRONTING, DIAGNOSING, AND TREATING SEXUAL PAIN**

*by Deborah Coady, M.D., and Nancy Fish, M.S.W., M.P.H.*

ISBN-10: 1580053637 ISBN-13: 9781580053631

280 pages, Paperback

Coming November 2011

More information: <http://www.sealpress.com/buy.php?isbn=9781580053631>

**CLINICAL MANAGEMENT OF VULVODYNIA – TIPS AND TRICKS**

*Authors: Alessandra Graziottin, Filippo Murina*

*Published by: Springer-Verlag, 2011*

87 pages

ISBN: 978-88-470-1925-6

This much needed book covers a field – genital/vulvar pain - that has long been neglected and to which many taboos and stigmas are still attached. Currently, it may take years to obtain a diagnosis and even then it can be impossible to find a suitable treatment. While this book is aimed at physicians, there are many patients who will also find it useful and easy to read. In the very first chapter, the authors point out that vulvodynia is not a rare condition and that studies indicate that up to 15% of women attending a gynaecology clinic may have the disorder. Its prevalence may be underestimated, at least in part because some physicians dismiss it as psychological. The book discusses the different types of vulvar pain and its pathophysiology, how to make a diagnosis of vulvodynia and its comorbidities and how to treat it.

**CHRONIC PELVIC PAIN**

*Edited by: Paolo Vercellini*

*Published by Wiley-Blackwell, 2011*

196 pages

ISBN: 978-1-4443-3066-3

This is a practical guide to diagnosing and treating chronic pelvic pain in women. In chapter 1 on the neurobiology of CPP, Jennifer Gunter notes that for many patients with CPP, there may be more than one pain generator in addition to changes in the central nervous system that enhance pain (central sensitization). Chapter 9 by Daniela Wittman and J. Quentin Clemens covers bladder pain syndrome and other urological causes of chronic pelvic pain and there is an interesting final chapter by Cindy Farquhar on alternative treatments for chronic pelvic pain. The many other interesting chapters include endometriosis, gastrointestinal disorders and causes and treatment of dyspareunia where vulvodynia is also discussed.

**WEBSITES:**

<http://orwh.od.nih.gov/health/vulvodynia.html>

A useful website with many suggestions for further information on vulvodynia.

<http://www.drugs.com>

This useful website includes Drugs A-Z . Handy if you want to check out a drug or its side effects for example.

<http://www.ema.europa.eu>

European Medicines Agency (EMA). Good for checking out drugs.

## **RESEARCH HIGHLIGHTS**

### **A REVIEW OF SELECTED RECENT SCIENTIFIC LITERATURE ON INTERSTITIAL CYSTITIS AND RELATED DISORDERS**

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. However, in some cases there may be free access to the full article online.

**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.

### **CONTEMPORARY MANAGEMENT OF THE PAINFUL BLADDER: A SYSTEMATIC REVIEW.**

*Giannantoni A, Bini V, Dmochowski R, Hanno P, Nickel JC, Proietti S, Wyndaele JJ. Eur Urol. 2011 Sep 9. [Epub ahead of print]. PMID: 21920661*

While different types of behavioural, dietary, interventional, pharmacologic, and surgical therapies have been used to treat PBS/IC, because of the paucity of randomised placebo-controlled studies on different treatments, an evidence-based management approach has not yet been developed. The purpose of this study by Giannantoni and colleagues was to critically review and synthesize data from a wide range of current therapeutic approaches to PBS/IC, to quantify the effect size from randomised controlled trials (RCTs), and to reach clinical agreement on the efficacy of treatments for PBS/IC. For this purpose they performed a systematic review of the literature to identify articles published between 1990 and September 2010 on the management of PBS/IC, including articles restricted to the English language published since 1990 to date that reported on oral and intravesical treatment, multimodal or combined treatment, and surgical treatment. They included 7709 adult patients from 29 RCTs and 57 nonRCTs. Meta-analysis of RCTs showed that only cyclosporine A provided a simultaneous great effect size of SMD on ICSI, pain, and frequency. Amitriptyline at different dosages showed a great effect size of SMD on pain and urgency or on ICSI and frequency. The remaining RCTs showed sporadic significant changes in only one of the four considered parameters. The attributed levels of evidence for treatments reported in RCTs were 1b; grades of recommendations ranged from A to C. According to the Jadad score, 11 RCTs were high-quality studies. Meta-analysis of RCTs showed a great heterogeneity in the applied methodologies, clinical outcomes assessed, and the obtained results in different studies. The results from the nRCTs showed that the most frequently adopted treatment is oral pentosan polysulfate and that the use of botulinum A toxin intradetrusorial injections in PBS/IC is increasing. A high heterogeneity in drugs and treatment modalities, clinical outcomes, and obtained results was also found for nRCTs. They concluded however that limited evidence exists for the few treatments for PBS/IC. The lack of definitive conclusions is due to the great heterogeneity in methods used, assessment of symptoms, duration of treatment, and follow-up in both RCTs and nRCTs.

### **SAFETY AND DOSE FLEXIBILITY CLINICAL EVALUATION OF INTRAVESICAL LIPOSOME IN PATIENTS WITH INTERSTITIAL CYSTITIS OR PAINFUL BLADDER SYNDROME.**

*Lee WC, Chuang YC, Lee WC, Chiang PH. Kaohsiung J Med Sci. 2011 Oct;27(10):437-440. Epub 2011 Jul 23. PMID: 21943815*

The purpose of this study from Taiwan was to present a single institution open-label experience with intravesical liposomes (LPs), a mucosal protective agent, in patients with interstitial cystitis/painful bladder syndrome (IC/PBS) and to assess the safety and efficacy on IC/PBS symptoms. A total of 17 symptomatic IC/PBS patients were treated with intravesical LPs (80mg/40mL distilled water) once a week for 4 weeks (n=12) or twice a week for 4 weeks (n=5). The O'Leary-Sant Symptom/Problem score, O'Leary-Sant total Score, and pain score were significantly improved from baseline at both dose regimens with added benefit with the biweekly regimen. The authors conclude that intravesical LP treatment is safe and its efficacy long-lasting. They also feel that large-scale, placebo-controlled studies are warranted to assess the efficacy for this promising new treatment for IC/PBS.

CONTEMPORARY MANAGEMENT OF LOWER URINARY TRACT DISEASE WITH BOTULINUM TOXIN A: A SYSTEMATIC REVIEW OF BOTOX (ONABOTULINUMTOXINA) AND DYSPORT (ABOBOTULINUMTOXINA).

*Mangera A, Andersson KE, Apostolidis A, Chapple C, Dasgupta P, Giannantoni A, Gravas S, Madersbacher S. Eur Urol. 2011 Oct;60(4):784-95. Epub 2011 Jul 13. PMID: 21782318*

Mangera and colleagues from Sheffield report that the use of botulinum toxin A (BoNTA) in the treatment of lower urinary tract dysfunction has expanded in recent years and the off-licence usage list includes neurogenic detrusor overactivity (NDO), idiopathic detrusor overactivity (IDO), painful bladder syndrome (PBS), and lower urinary tract symptoms resulting from bladder outflow obstruction (BOO) or detrusor sphincter dyssynergia (DSD). They note that there are two commonly used preparations of BoNTA: Botox (onabotulinumtoxinA) and Dysport (abobotulinumtoxinA). The purpose of this review study was to compare the reported outcomes of onabotulinumtoxinA and abobotulinumtoxinA in the treatment of NDO, IDO, PBS, DSD, and BOO for adults and children. They note that there is high-level evidence for the use of onabotulinumtoxinA and abobotulinumtoxinA in adults with NDO, but only for abobotulinumtoxinA in children with NDO. Only onabotulinumtoxinA has level 1 evidence supporting its use in IDO, BOO, DSD, and PBS/interstitial cystitis. They identified good-quality studies that evaluated onabotulinumtoxinA for all the indications described above in adults, however this was not the case with abobotulinumtoxinA. Although this does not imply that onabotulinumtoxinA is more effective than abobotulinumtoxinA, they suggest that this should be a consideration when counselling patients on the use of botulinum toxin in urologic applications. They emphasise that the two preparations should not be used interchangeably, either in terms of predicting outcome or in determining doses to be used.

MONTELUKAST FOR SYMPTOM CONTROL OF INTERSTITIAL CYSTITIS.

*Traut JL, Macdonald ES, Spangler ML, Saxena S. Ann Pharmacother. 2011 Sep;45(9):e49. Epub 2011 Aug 23. PMID: 21862713*

The purpose of this study from Kansas was to describe the effects of montelukast, a leukotriene receptor antagonist commonly used in the treatment of allergic rhinitis and asthma, on the symptoms of interstitial cystitis (IC). The authors describe a case of a 64-year-old male with a history of IC with previous trials of solifenacin, dutasteride, and tamsulosin and little improvement in IC symptom reduction. When montelukast 10 mg was initiated for allergic rhinitis symptoms, a substantial improvement in urinary urgency and pain during therapy was noted. This improvement subsequently disappeared when montelukast was stopped. Currently, montelukast is Food and Drug Administration approved for use in the treatment and prevention of mild-to-moderate asthma and exercise-induced asthma, as well as treatment of seasonal and perennial allergic rhinitis. While montelukast treatment did not cure the patient's IC, it improved his quality of life through substantial symptomatic relief, including less pain and urgency. The author concludes that montelukast may be an effective treatment option in the management of interstitial cystitis and that further research is needed to substantiate this novel use.

*Comment: this use of montelukast for treating IC was described in several publications in 2001 by Bouchelouche K. and colleagues from Denmark.*

IMPACT OF INTRAVESICAL HYALURONIC ACID AND CHONDROITIN SULFATE ON BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.

*Porru D, Leva F, Parmigiani A, Barletta D, Choussos D, Gardella B, Daccò MD, Nappi RE, Allegri M, Tinelli C, Bianchi CM, Spinillo A, Rovereto B. Int Urogynecol J. 2011 Sep 9. [Epub ahead of print]. PMID: 21904840*

This study from Italy looked at intravesical instillations of hyaluronic acid (HA) and chondroitin sulfate (CS) based on the supposition that they may lead to regeneration of the damaged glycosaminoglycan layer in interstitial cystitis/bladder pain syndrome (IC/BPS). Twenty-two patients with IC/BPS received intravesical instillations (40 ml) of sodium HA 1.6% and CS 2.0% in 0.9% saline solution (IALURIL®, IBSA) once weekly for 8 weeks, then once every 2 weeks for the next 6 months. On the basis of their results, Porru and colleagues concluded that this treatment appeared to be effective and well tolerated in IC/BPS in this preliminary study.

CORE LOWER URINARY TRACT SYMPTOM SCORE (CLSS) FOR THE ASSESSMENT OF FEMALE LOWER URINARY TRACT SYMPTOMS: A COMPARATIVE STUDY.

*Fujimura T, Kume H, Tsurumaki Y, Yoshimura Y, Hosoda C, Suzuki M, Fukuhara H, Enomoto Y, Nishimatsu H, Homma Y. Int J Urol. 2011 Sep 23. doi: 10.1111/j.1442-2042.2011.02848.x. [Epub ahead of print]. PMID: 21951201*

Fujimura and colleagues from Tokyo, Japan recently developed the core lower urinary tract symptom score (CLSS) questionnaire to address 10 important lower urinary tract symptoms (LUTS). The aim of this study was to evaluate the performance of the CLSS in women compared with the International Prostate Symptom Score (IPSS) and Overactive Bladder Symptom Score (OABSS). Three hundred and eighteen treatment-naïve consecutive female patients, including 48 controls, completed the three questionnaires. Quality of life (QOL) was determined as per the IPSS QOL Index. The clinical diagnoses were overactive bladder, mixed incontinence, stress incontinence, pelvic organ prolapse, interstitial cystitis, bacterial cystitis, underactive bladder, and "other". Simple statistics and the relationship between symptom scores and poor QOL (QOL Index  $\geq 4$ ) were examined. They found that all symptom scores were significantly increased in symptomatic women. The CLSS described the symptom profiles of patients with distinct conditions. The scores of corresponding symptoms on the three questionnaires were significantly correlated. Multivariate logistic regression modelling proved five CLSS symptoms (daytime frequency, nocturia, urgency incontinence, straining, and urethral pain) to be independent predictors of poor QOL, with hazard ratios ranging from 2.0 to 4.2. The IPSS included only two (urgency and straining) significant symptoms. The authors conclude that the IPSS alone does not fully evaluate female LUTS, with a possible negative impact on QOL. They believe that using the CLSS questionnaire would enable a simple and comprehensive assessment of female LUTS.

POTENTIAL FACTORS THAT CAN BE USED TO DIFFERENTIATE BETWEEN INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME AND BLADDER OVERSENSITIVITY IN WOMEN.

*Kuo YC, Kuo HC. Int J Clin Pract. 2011 Sep 26. doi: 10.1111/j.1742-1241.2011.02767.x. [Epub ahead of print]. PMID: 21951755*

Kuo and colleagues from Taiwan note that there is considerable overlap between symptoms of interstitial cystitis/painful bladder syndrome (IC/PBS) and bladder oversensitivity, thereby making it difficult to differentiate between the two based on symptoms alone. They investigated factors that could potentially be used to differentiate between IC/PBS and bladder oversensitivity in women. Video-urodynamic study (VUDS) results in women with lower urinary tract symptoms (LUTS) were retrospectively analysed. Patients classified as having increased bladder sensation (IBS) were selected for analysis. A potassium chloride (KCl) test was performed and pain or urgency elicited was considered positive response. Cystoscopic hydrodistension demonstrating glomerulations was considered to be a diagnosis of IC/PBS; otherwise bladder oversensitivity was diagnosed. LUTS, urodynamic variables and results of the KCl test were used to predict IC/PBS in these women. On the basis of their results, they concluded that a diagnosis of IC/PBS can be made without cystoscopic

hydrodistension in women with increased bladder sensation, having storage symptoms, a CBC ≤ 350ml, a positive KCl test result and a VAS score ≥ 2.

SYMPTOM PROFILE VARIABILITY OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME BY AGE.

*Rais-Bahrami S, Friedlander JI, Herati AS, Sadek MA, Ruzimovsky M, Moldwin RM. BJU Int. 2011 Aug 24. doi: 10.1111/j.1464-410X.2011.10481.x. [Epub ahead of print]. PMID: 21883848*

Rais-Bahrami and colleagues from the Arthur Smith Institute for Urology note that there is a huge variability of symptoms in patients diagnosed with interstitial cystitis and painful bladder syndrome because these diagnoses represent a very heterogeneous patient population. They report that younger patients are being diagnosed with these pain syndromes, without any specific investigation into the symptoms they experience. They found that patients diagnosed with interstitial cystitis and painful bladder syndrome have variable clinical symptom profiles depending on the age at the time of their diagnosis. Dyspareunia, external genitalia pain, urgency, frequency and dysuria were more common in younger patients whereas nocturia, urinary incontinence and the presence of Hunner's ulcers were more common in older patients. The authors suggest that better defining symptom profiles for patients at the time of evaluation may potentially aid in more accurate and expedited diagnosis of these conditions, particularly in the youngest patient population which is being recognized more commonly in recent times. The purpose of this study was to investigate the clinical profile differences among patients with interstitial cystitis/painful bladder syndrome (IC/PBS) based upon age at the time of diagnosis from childhood into the geriatric age group. They analysed 268 patients seen between 1990 and 2008 was performed divided into three age groups: under 30 years, over 30 years but less than 60 years, and over 60 years of age at time of diagnosis. Patient demographics, disease characteristics and IC/PBS-associated symptoms were compared across the three groups. On the basis of their results, they concluded that patients with IC/PBS analysed across a wide spectrum of ages at time of diagnosis portrayed a unique symptom profile pattern. Patients diagnosed at the youngest ages experienced significantly more urinary urgency, frequency, dysuria, dyspareunia and pain in their external genitalia, while older patients had higher rates of nocturia, urinary incontinence and Hunner's ulcer disease.

VOIDING DYSFUNCTION IN THE FEMALE PATIENT: IS THE "SYNDROME" PARADIGM VALID?

*Tunuguntla HS, Tunuguntla R, Barone J, Kanagarajah P, Gousse AE. Curr Urol Rep. 2011 Oct;12(5):377-80. PMID: 21728066*

Tunuguntla and colleagues report that voiding dysfunction in the female patient significantly affects the patient's quality of life, it is poorly understood, has varied etiology and clinical presentation, and lacks standard definitions with no consensus on diagnostic criteria. It consists of a constellation of symptoms involving both phases of the micturition cycle. Appropriate diagnosis and treatment of female lower urinary tract symptoms (LUTS) is of paramount importance. However, the differentiation of female LUTS into various syndromes is currently controversial. Despite new and remarkable advances in elucidating the pathophysiology of LUTS, there is sparse scientific evidence that provides linkage between voiding symptoms and their underlying pathology. Although the underlying root cause for all of these symptoms remains underappreciated, a SYMPTOM BASED APPROACH, rather than a syndrome based one is more appropriate and effective in the evaluation/treatment and offers a better quality of life for women with voiding dysfunction and lower urinary tract symptoms. This article comprehensively reviews the commonly encountered female non-neurogenic LUTS (overactive bladder, interstitial cystitis, and painful bladder syndrome); discusses the contemporary management of these syndromes and emphasizes a symptom-based approach to the condition [Note: there is an error in the abstract].

[BLADDER PAIN SYNDROME--A UROLOGICAL-GYNECOLOGICAL PROBLEM].

[Article in Polish]

*Zabkowski T, Bortnowski L, Zieliński H. Ginekol Pol. 2011 Mar;82(3):210-3. PMID: 21735690*



Noting that bladder pain syndrome remains a great challenge for urologists, both in diagnostics and treatment, Zabrowski and colleagues from Warsaw propose that a cause could be urothelium dysfunction resulting in the destruction of the protective glycosaminoglycan layer/barrier protecting the urothelium from bacteria adhesion and penetration of toxic substances/by bacteria. They report that attempts to find the right method of treatment led to the introduction of hyaluronic acid, which alleviated bladder pain syndrome and its symptoms. Hyaluronic acid reacting with glycosaminoglycans on the bladder decreases penetrability of irritant substances. Their patients were treated with 4-8 weekly instillations comprising 40 mg of hyaluronic acid in 50 ml NaCl solution for 1-2 months. After the last instillation, therapy is repeated for the next 6-8 months with one instillation monthly. They conclude from their results that this form of treatment is successful in alleviating painful symptoms from the bladder.

SIMPLE CYSTECTOMY: OUTCOMES OF A NEW OPERATIVE TECHNIQUE.

*Rowley MW, Clemens JQ, Latini JM, Cameron AP. Urology. 2011 Aug 1. [Epub ahead of print]. PMID: 21813168*

Rowley and colleagues from the University of Michigan urology department present an efficient technique for simple cystectomy. Urinary diversion for benign indications is a relatively rare procedure. However, diversion alone without accompanying cystectomy results in a significant risk of complications. The authors retrospectively reviewed their institutional experience with this simple cystectomy technique, which included 23 patients from 2007-2010 performed by 3 surgeons. There were 14 females and 9 males. All patients had exhausted all other possible conservative therapies. Indication for the procedure included neurogenic bladder and resulting complications in 9 patients, complications from prostate radiation therapy in 5 patients, refractory interstitial cystitis in 5 patients, and refractory incontinence in 4 patients. There were no complications noted intraoperatively or postoperatively specifically attributed to the cystectomy portion. The authors concluded that the simple cystectomy technique presented here, in most cases of urinary diversion for benign indications, can be performed quickly with minimal blood loss and complications.

INCREASED EXPRESSION OF HYPOXIA-INDUCIBLE FACTOR-1A AND VASCULAR ENDOTHELIAL GROWTH FACTOR ASSOCIATED WITH GLOMERULATION FORMATION IN PATIENTS WITH INTERSTITIAL CYSTITIS.

*Lee JD, Lee MH. Urology. 2011 Aug 1. [Epub ahead of print]. PMID: 21813166*

The purpose of this study from Taiwan was to examine whether hypoxia occurs in the bladders of patients with interstitial cystitis (IC) by monitoring the expression of hypoxia-inducible factor-1 (HIF-1) and VEGF. Previous studies have reported that bladder perfusion is decreased in patients with IC. Hypoxia induces overexpression of vascular endothelial growth factor (VEGF), which has been reported to be associated with the formation of glomerulations in patients with IC. The study group consisted of 32 patients with IC, and the control group of 8 volunteers. They obtained bladder biopsies from both groups and studied the expression of HIF-1 $\alpha$  and VEGF proteins by immunoblotting and immunohistochemical and double immunofluorescent staining. Data were analyzed using the Mann-Whitney U test. They report increased expression of HIF-1 $\alpha$  in bladder tissue and overexpression of VEGF in umbrella cells from patients with IC. They suggest that these events may be associated with glomerulation formation during hydrodistension in IC bladders. They consequently believe that these molecular findings could offer the therapeutic mechanism for hyperbaric oxygenation application to patients with IC.

POTENTIAL TARGETING OF SIGLECS, MAST CELL INHIBITORY RECEPTORS, IN INTERSTITIAL CYSTITIS.

*Park CS, Bochner BS. Int Neurourol J. 2011 Jun;15(2):61-3. Epub 2011 Jun 30. PMID: 21811694*

Free full text

Park and colleagues from Korea note that mast cell increases and activation are detected in interstitial cystitis (IC), and their proinflammatory mediators are felt to contribute to regional pelvic pain and inflammatory pathophysiology. They suggest that immunoreceptor tyrosine-based

inhibition motif-containing sialic acid-binding immunoglobulin-like lectins (Siglecs) expressed in mast cells could be evaluated as in vivo signalling regulators capable of inhibiting IC-related mast cell activation.

ENHANCED UROTHELIAL EXPRESSION OF HUMAN CHORIONIC GONADOTROPIN BETA (HCGB) IN BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS (BPS/IC).

*Schwalenberg T, Stolzenburg JU, Thi PH, Mallock T, Hartenstein S, Alexander H, Zimmermann G, Hohenfellner R, Denzinger S, Burger M, Horn LC, Neuhaus J. World J Urol. 2011 Aug 30. [Epub ahead of print]. PMID: 21877171*

Schwalenberg and colleagues from Leipzig University Hospital notes that while BPS/IC is associated with urothelial lesions, pathomechanisms of urothelial damage and factors for urothelial restoration are unknown. hCG is a factor for cellular differentiation, angiogenesis and immune competence of the endometrium during pregnancy. Since clinical observations demonstrate improvement of BPS/IC symptoms during pregnancy or during infertility treatment with hCG, the authors' research aims were to examine the expression of hCG and luteinizing hormone receptor (LHR) in the urothelium of BPS/IC patients and compare the levels of hCG $\beta$  with healthy controls. They found constitutive expression of hCG $\alpha$ , hCG $\beta$  and LHR in healthy controls. hCG $\beta$  was significantly upregulated in BPS/IC patients in CLSM. PCR analysis revealed higher levels of hCG $\beta$ 7 than hCG $\beta$ 5 in controls and BPS/IC patients. They conclude that the constitutive expression of hCG and LHR speaks in favour of functional signalling in urothelial cells without any association with either pregnancy or tumour. They show for the first time that hCG $\beta$  is upregulated in BPS/IC urothelium and that hCG $\beta$ 7 is the dominant splice variant in those cells. They believe that their findings imply a major role of hCG for urothelial integrity and a disturbance of hCG signalling in the case of BPS/IC. They therefore conclude that hCG could gain therapeutical relevance in the future.

INDIVIDUAL RECEPTOR PROFILING AS A NOVEL TOOL TO SUPPORT DIAGNOSIS OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS (BPS/IC).

*Neuhaus J, Schulte-Baukloh H, Stolzenburg JU, Speroni di Fenizio P, Horn LC, Ruffert H, Hartenstein S, Burger M, Schulze M, Schwalenberg T. World J Urol. 2011 Oct 4. [Epub ahead of print]. PMID: 21969132*

Dysregulation of neurotransmitter receptors may contribute to bladder overactivity (OAB) symptoms. To address the question whether specific receptor expression patterns are associated with bladder pain syndrome/interstitial cystitis (BPS/IC), Neuhaus and colleagues from Leipzig University Hospital examined the expression of muscarinic, purinergic and histamine receptors in the detrusor. They found that M2, P2X1, P2X2 and H1 were significantly upregulated in BPS/IC patients, and H2 was occasionally highly overexpressed. There was no significant correlation between receptor protein and gene expression, implying posttranslational mechanisms being responsible for the altered receptor expressions. On the basis of individual receptor profiles, upregulated receptors could be targeted by monotherapy or combination therapy with already approved receptor inhibitors, thereby promoting tailored therapy for patients suffering from BPS/IC-like symptoms.

INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND NONBLADDER SYNDROMES: FACTS AND HYPOTHESES.

*Warren JW, van de Merwe JP, Nickel JC. Urology. 2011 Aug 17. [Epub ahead of print]. PMID: 21855966*

No abstract is available for this commentary paper on IC/BPS and nonbladder syndromes (NBSs). Noting that since the 19th century, searches for the pathogenesis of IC/BPS have concentrated on the bladder, Warren and colleagues note that recent work has shown that patients with IC/BPS are more likely than controls to have syndromes with symptoms beyond the bladder and even beyond the pelvis. These findings suggest that research into IC/BPS etiology should not focus only on the bladder. They conclude that NBSs are associated with IC/BPS and with each other and might provide important clues to the pathogenesis of IC/BPS. Additional cross-sectional studies will be useful to

generate hypotheses about the pathogenesis of IC/BPS. They emphasize, however, that prospective studies will likely be necessary to test these hypotheses.

## CHRONIC PELVIC PAIN

### SACRAL NEUROMODULATION AS A TREATMENT FOR CHRONIC PELVIC PAIN.

Marcelissen T, Jacobs R, van Kerrebroeck P, de Wachter S. *J Urol.* 2011 Aug;186(2):387-93. Epub 2011 Jun 17. PMID: 21683381

Marcelissen and colleagues from Maastricht University Medical Centre in the Netherlands note that a significant number of patients with chronic pelvic pain do not respond to conservative treatment and often no good alternative can be offered except radical surgery. Sacral neuromodulation is a well established therapy for patients with lower urinary tract dysfunction and has also been suggested to be useful in the treatment of chronic pelvic pain. Although currently no Food and Drug Administration approval exists for this indication, several studies have demonstrated promising results. The authors provide an overview of the published literature on sacral neuromodulation as a treatment for chronic pelvic pain. A total of 12 relevant articles were identified. Of these articles 10 mainly addressed the efficacy of sacral neuromodulation in patients with interstitial cystitis/bladder pain. The percentage of patients who responded to test stimulation was reported between 51% and 77%. Of the 10 articles 7 reported treatment outcome after implantation. The duration of follow-up ranged between 5 and 87 months. The mean reduction in pain scores was reported between 40% and 72%. The reoperation rate ranged between 27% and 50% after long-term follow-up. Two articles included patients with miscellaneous urogenital pain syndromes. The success rates after implantation ranged from 60% to 77% with follow-up ranging between 19 and 36 months. They concluded that there is currently insufficient evidence to determine the role of sacral neuromodulation in the treatment of chronic pelvic pain and that larger prospective trials with long-term evaluation are required to determine the ultimate efficacy of this treatment.

### ANTERIOR VAGINAL WALL TENDERNESS (AVWT) AS A PHYSICAL SYMPTOM IN CHRONIC PELVIC PAIN.

Paulson JD, Paulson JN. *JSLs.* 2011 Jan-Mar;15(1):6-9. PMID: 21902934

The aim of this study from Virginia was to see whether the physical presence of anterior vaginal wall tenderness could help narrow down and elucidate diagnoses in a practice focusing on diagnosis and treatment of chronic pelvic pain. The study comprised 284 patients with chronic pelvic pain limited to gynaecologic and lower urinary tract problems. Histories, physical examinations, and endoscopic procedures were performed on each patient. An analysis of this information was conducted. Of the chronic pelvic pain patients, 78% had endometriosis, 81% had interstitial cystitis, and 61% had both concurrently. The sensitivity of anterior vaginal wall tenderness (AVWT) in patients with interstitial cystitis was 95%, and in those with only endometriosis and no interstitial cystitis, the sensitivity was 17%. The positive predictive value for interstitial cystitis was 85%, and for endometriosis it was 67%. The authors concluded that examination of the anterior vaginal wall with an empty bladder at the initial examination can lead one to suspect interstitial cystitis and possibly either concomitant or singular endometriosis and allow the physician to approach the workup accordingly.

### ETIOLOGICAL, DIAGNOSTIC AND THERAPEUTIC CONSIDERATION OF THE MYOFASCIAL COMPONENT IN CHRONIC PELVIC PAIN.

Díaz-Mohedo E, Barón-López FJ, Pineda-Galán C. *Actas Urol Esp.* 2011 Sep 12. [Epub ahead of print]. PMID: 21917358

Free full text: Article in Spanish

The purpose of this study from Spain was to justify the important role played by the myofascial component in the etiology and clinical manifestation of Chronic Pelvic Pain and to encourage a therapeutic approach to this component in intervention protocols. The authors found that chronic pelvic pain and the different conditions associated with it occur with myofascial changes that

may be responsible for the perpetuation of the body symptoms and lack of evolutive resolution of the condition if this component is not approached in a specific way. They concluded that this is a clinical situation with high prevalence and incidence with a significant impact on quality of life and significant financial cost.

[CHRONIC PELVIC PAIN TREATMENT WITH POSTERIOR TIBIAL NERVE STIMULATION.]

Gaj F, Andreuccetti J, Speziali F, Trecca A, Crispino P. Clin Ter. 2011 Jul-Aug;162(4):e111-e114. PMID: 21912811

[Article in Italian]

Gaj and colleagues from Italy note that the technique of percutaneous neuromodulation by electrical stimulation of the tibial nerve (Percutaneous Tibial Nerve Stimulation PTNS) described by Stoller for the treatment of overactive bladder syndrome in the 90s is currently being tested in the treatment of chronic pelvic pain. This Italian study included 35 patients with chronic pelvic pain: 17 were treated with a protocol based on 12 PTNS stimulation sessions performed weekly (Group A), 18 were treated with a protocol based on 12 sessions PTNS stimulation performed 3 times a week (group B). All patients were evaluated before and after treatment, by means of diary quality of life score (I-QoL, SF36) and proctologic examination. At the end of treatment 11/17 patients (63%) in group A and 12/18 patients (67%) in group B were considered a success. Overall, 4/11 (36%) patients in group A and 5/11 (45%) patients in group B recovered completely after treatment. In both groups, patients reported a subjective improvement after 6-8 stimulation sessions. At follow-up 36/8 months there were more complications. The authors conclude that the use of PTNS in the treatment of chronic pelvic pain shows encouraging results in patients not responding to standard pain treatment.

QUALITATIVE RESEARCH AS THE BASIS FOR A BIOPSYCHOSOCIAL APPROACH TO WOMEN WITH CHRONIC PELVIC PAIN.

Souza PP, Salata Romão A, Rosa-E-Silva JC, Candido Dos Reis F, Nogueira AA, Poli-Neto OB. J Psychosom Obstet Gynaecol. 2011 Sep 16. [Epub ahead of print]. PMID: 21919820

Souza and colleagues from Sao Paulo, Brazil report that chronic pelvic pain (CPP) is a highly prevalent clinical condition and is recognized as a public health problem in their country and elsewhere. Although the number of qualitative studies related to the topic is increasing, it is essential that this knowledge be presented in a synthesized manner, grounded in the context of the care provided to patients with CPP, in order to increase the clinical and research applicability of the findings. Little attention is given to CPP in undergraduate courses and in meetings for the continuing education of health professionals, the approach to CPP typically being based on the biomedical model. We believe that qualitative research can provide insights into CPP and form the basis for a bio-psychosocial approach to the condition, which can in turn lead to better results, including resolution of the pain and greater patient/health professional satisfaction. Therefore, they conducted a metasynthesis of seven qualitative studies of CPP, the principal themes of which were as follows: (a) coping with CPP versus secondary gain; (b) the great importance of determining the cause of the pain; (c) expectations regarding the doctor-patient relationship; and (d) gender issues. The authors hope that the present study can aid in restoring the humanistic aspects of CPP treatment.

UNDERSTANDING MULTISYMPTOM PRESENTATIONS IN CHRONIC PELVIC PAIN: THE INTER-RELATIONSHIPS BETWEEN THE VISCERA AND MYOFASCIAL PELVIC FLOOR DYSFUNCTION.

Hoffman D. Curr Pain Headache Rep. 2011 Oct;15(5):343-6. PMID: 21739128

Patients presenting with chronic pelvic pain frequently complain of multiple symptoms that appear to involve more than one organ system, creating diagnostic confusion. The multisymptom presentation of chronic pelvic pain has been frequently described. This article describes four proposed explanations for the clinical observation of multisymptom presentations of patients with chronic pelvic pain. These include the concepts of viscerovisceral convergence; viscerosomatic convergence; hypertonicity of pelvic floor muscles creating visceral symptoms along with somatovisceral convergence and central sensitization with expansion of receptive fields.

UPDATE ON UROLOGIC PELVIC PAIN SYNDROMES: HIGHLIGHTS FROM THE 2010 INTERNATIONAL CHRONIC PELVIC PAIN SYMPOSIUM AND WORKSHOP, AUGUST 29, 2010, KINGSTON, ONTARIO, CANADA.

*Nickel JC, Tripp D, Gordon A, Pontari M, Shoskes D, Peters KM, Doggweiler R, Baranowski AP. Rev Urol. 2011;13(1):39-49. PMID: 21826127*

Free full article

Nickel and colleagues report that Urologic Chronic Pelvic Pain Syndromes (UCPPS), including chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS), and interstitial cystitis (IC)/painful bladder syndrome (PBS), remain some of the most frustrating urologic conditions to understand and manage. The paradigm shift in our understanding that these conditions represent more than an organ-centric medical disease, and our observations that patients presenting with these conditions have multiple different clinical phenotypes has led to a more rational patient-directed multidisciplinary, multimodal therapeutic strategy. These concepts were explored and discussed at an International Pain Day symposium, held on August 29, 2010, in Kingston, Ontario, Canada. This comprehensive review represents an update on urologic chronic pelvic pain based on the proceedings of that meeting. UCPPS is one of the most frustrating and difficult conditions seen in urologic practice. The etiology is uncertain, the diagnosis is one of exclusion, and, based on significant subjective criteria, prediction of progression is not possible, prognosis is unpredictable, and treatment, particularly for chronic patients, is acknowledged as dismal. It is now recognized that successful management of UCPPS is only possible using a multidisciplinary and multimodal pain management approach for chronic noncancer pain. According to the authors, urologists managing male and female patients presenting with UCPPS need to understand that CP and IC/PBS are not the only pelvic pain syndromes that they will see. Other conditions that must be considered in the differential diagnosis include vulvar and urethral pain syndromes, pudendal nerve (and other regional nerve) entrapment, pelvic floor pain, endometriosis, and irritable bowel syndrome (IBS), as well as pain syndromes associated with external genitalia including clitoral, penile, and testicular (scrotal) pain. Furthermore, they note that we now know that these conditions frequently coexist in the same patient.

*Comment: This free full article includes interesting tables with holistic modalities and for herbal and supplement treatment.*

## **PAIN**

### A NEW DEFINITION OF NEUROPATHIC PAIN

*Jensen TS, Baron R, Haanpää M, Kalso E, Loeser JD, Rice AS, Treede RD. Pain. 2011 Oct;152(10):2204-5. Epub 2011 Jul 18. PMID: 21764514*

Jensen and colleagues from Aarhus University Hospital in Denmark report that IASP (International Association for the Study of Pain) recently published a new definition of neuropathic pain according to which neuropathic pain is defined as “pain caused by a lesion or disease of the somatosensory system” ([www.iasp-pain.org/resources/painDefinition](http://www.iasp-pain.org/resources/painDefinition)). This definition replaces the 17-year old definition that appeared in the Classification of Chronic Pain published by IASP in 1994 [7], which defined neuropathic pain as “pain initiated or caused by a primary lesion, dysfunction, or transitory perturbation of the peripheral or central nervous system”. Even though the definition has not been changed dramatically, there are two important changes in the new version: (1) the word “dysfunction” has been removed and (2) a lesion or disease affecting the nervous system has been specified to be a lesion or disease of the somatosensory system. The authors conclude that a definition of neuropathic pain is only useful if it distinguishes conditions in a clinically meaningful way. If the definition does not provide additional benefit in terms of understanding and treating the condition(s), then there is no reason to keep it. Hopefully, the new definition of neuropathic pain will act as a stimulant to discuss the definition in more detail and provide input for studies that can be used to test the value of the definition.

### HCN2 ION CHANNELS PLAY A CENTRAL ROLE IN INFLAMMATORY AND NEUROPATHIC PAIN

*Edward C. Emery, Gareth T. Young, Esther M. Berrocoso, Lubin Chen, Peter A. McNaughton. Science 9 September 2011: 1462-1466. DOI:10.1126/science.1206243*

The rate of action potential firing in nociceptors is a major determinant of the intensity of pain. Possible modulators of action potential firing include the HCN ion channels, which generate an inward current, *I<sub>h</sub>*, after hyperpolarization of the membrane. The authors found that genetic deletion of HCN2 removed the cyclic adenosine monophosphate (cAMP)–sensitive component of *I<sub>h</sub>* and abolished action potential firing caused by an elevation of cAMP in nociceptors. Mice in which HCN2 was specifically deleted in nociceptors expressing Nav1.8 had normal pain thresholds, but inflammation did not cause hyperalgesia to heat stimuli. After a nerve lesion, these mice showed no neuropathic pain in response to thermal or mechanical stimuli. Neuropathic pain is therefore initiated by HCN2-driven action potential firing in Nav1.8-expressing nociceptors.

See also:

#### UNRAVELING NEUROPATHIC PAIN

*Peter R. Stern. Sci. Signal. 4, ec257 (2011).*

Neuropathic pain results from nerve damage and is evoked by trauma in conditions ranging from shingles and diabetes to cancer chemotherapy, but the mechanisms remain poorly understood. By using gene knockouts in animal models, Emery and colleagues from Cambridge found that a member of the HCN ion channel family is important in both inflammatory and neuropathic pain. This discovery opens up the possibility of developing specific antagonists to treat neuropathic pain.

See also: <http://www.bbc.co.uk/news/health-14837879>

<http://www.empowher.com/wellness/content/scientists-find-gene-controls-chronic-pain>

## **CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME**

### QUERCETIN FOR CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME.

*Shoskes DA, Nickel JC. Urol Clin North Am. 2011 Aug;38(3):279-84. PMID: 21798389*

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a common condition with a heterogeneous origin that responds best to multimodal therapy. The bioflavonoid quercetin has antioxidant and anti-inflammatory effects that have proven useful for treating this condition. Using the clinical phenotype system UPOINT, quercetin can be helpful for those with organ-specific complaints (bladder or prostate) and pelvic floor spasm. This article discusses the current understanding of CP/CPPS and how treatment with quercetin can be used alone or as part of multimodal therapy.

### THE ROLE OF PHENOTYPING IN CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME.

*Mahal BA, Cohen JM, Allsop SA, Moore JB, Bhai SF, Inverso G, Dimitrakoff JD. Curr Urol Rep. 2011 Aug;12(4):297-303. doi: 10.1007/s11934-011-0196-y. PMID: 21533747*

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a chronic pain syndrome identified by the presence of non-infectious pelvic or perineal pain lasting longer than 3 months. Current diagnoses and treatments for the syndrome solely depend on and target symptoms, respectively. Thus far, the mechanistic disturbances responsible for the pathogenesis of CP/CPPS have remained largely elusive and treatments, and therefore, continue to be ineffective. To move toward successful management and treatment of CP/CPPS, it is necessary to elicit the underlying biological mechanisms responsible for the syndrome. Therefore, a phenotyping system that is able to bridge the gap between current symptom-based diagnosis and future mechanistic approaches to diagnosis and treatment is needed. In this article, Mahal and colleagues from Harvard Medical School examine current CP/CPPS phenotyping systems, analyze their utility, and make suggestions for changes in

clinical approaches to the syndrome that would both promulgate a mechanistic understanding and advance treatment approaches.

## IRRITABLE BOWEL SYNDROME

### ALPHA 2 DELTA (A(2)Δ) LIGANDS, GABAPENTIN AND PREGABALIN: WHAT IS THE EVIDENCE FOR POTENTIAL USE OF THESE LIGANDS IN IRRITABLE BOWEL SYNDROME.

*Gale JD, Houghton LA. Front Pharmacol. 2011;2:28. Epub 2011 Jun 9. PMID: 21713059*

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Irritable bowel syndrome (IBS) is a complex disorder that is characterized by abdominal pain and altered bowel habit, and often associates with other gastrointestinal symptoms such as feelings of incomplete bowel movement and abdominal bloating, and extra-intestinal symptoms such as headache, dyspareunia, heartburn, muscle pain, and back pain. It also frequently coexists with conditions that may also involve central sensitization processes, such as fibromyalgia, irritable bladder disorder, and chronic cough. This review from the UK examines the evidence to date on gabapentin and pregabalin which may support further and continued research and development of the  $\alpha(2)\delta$  ligands in disorders characterized by visceral hypersensitivity, such as IBS. The distribution of the  $\alpha(2)\delta$  subunit of the voltage-gated calcium channel, possible mechanisms of action, pre-clinical data which supports an effect on motor-sensory mechanisms and clinical evidence that points to potential benefits in patients with IBS will be discussed.

### NEED FOR A COMPREHENSIVE MEDICAL APPROACH TO THE NEURO-IMMUNO-GASTROENTEROLOGY OF IRRITABLE BOWEL SYNDROME.

*Katiraei P, Bultron G. World J Gastroenterol. 2011 Jun 21;17(23):2791-800. PMID: 21734786*

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Irritable bowel syndrome (IBS) is defined by the Rome III criteria as symptoms of recurrent abdominal pain or discomfort with the onset of a marked change in bowel habits with no evidence of an inflammatory, anatomic, metabolic, or neoplastic process. As such, many clinicians regard IBS as a central nervous system problem of altered pain perception. Here, Katiraei and Bultron from Loma Linda, USA review the recent literature and discuss the evidence that supports an organic based model, which views IBS as a complex, heterogeneous, inter-dependent, and multi-variable inflammatory process along the neuronal-gut axis. They delineate the organic pathophysiology of IBS, demonstrate the role of inflammation in IBS, review the possible differences between adult and pediatric IBS, discuss the merits of a comprehensive treatment model as taught by the Institute of Functional Medicine, and describe the potential for future research for this syndrome.

### GUT MEMORIES: TOWARDS A COGNITIVE NEUROBIOLOGY OF IRRITABLE BOWEL SYNDROME.

*Kennedy PJ, Clarke G, Quigley EM, Groeger JA, Dinan TG, Cryan JF. Neurosci Biobehav Rev. 2011 Jul 13. [Epub ahead of print]. PMID: 21777613*

The brain and the gut are engaged in continual crosstalk along a number of pathways collectively termed the 'brain-gut axis'. Over recent years it has been becoming increasingly clear that dysregulation of the axis at a number of levels can result in disorders such as irritable bowel syndrome (IBS). With recent advances in neuroimaging technologies, insights into the neurobiology of IBS are beginning to emerge. However the cognitive neurobiology of IBS has remained relatively unexplored to date. In this review, Kennedy and colleagues from University College Cork, Ireland summarise the available data on cognitive function in IBS, specifically addressing three key pathophysiological factors, namely; stress, immune activation and chronic pain, together with other factors involved in the manifestation of IBS. They explore how each of these components may impact centrally, what neurobiological mechanisms might be involved, and consider the implications for cognitive functioning in IBS. They conclude that each factor addressed could significantly impinge on central nervous system function, supporting the view that future research efforts must be directed towards a detailed assessment of cognitive function in IBS.

A PRELIMINARY INVESTIGATION OF THE EFFECTS OF COGNITIVE BEHAVIORAL THERAPY FOR PANIC DISORDER ON GASTROINTESTINAL DISTRESS IN PATIENTS WITH COMORBID PANIC DISORDER AND IRRITABLE BOWEL SYNDROME.

Gros DF, Antony MM, McCabe RE, Lydiard RB. *Depress Anxiety*. 2011 Jul 18. doi: 10.1002/da.20863. [Epub ahead of print]. PMID: 21770001

High comorbidity between panic disorder with/without agoraphobia (PD/A) and irritable bowel syndrome (IBS) has been identified in the literature. These findings have resulted in the recent development of neurobiological models to explain their overlapping symptoms and related origins. This study from South Carolina was a preliminary investigation of the influence of cognitive behavioural therapy (CBT) for PD/A on PD/A patients with and without comorbid IBS. The results demonstrated significant reductions in the symptoms of anxiety, depression, and overall impairment in both patient groups. In addition, PD/A patients with comorbid IBS also experienced reductions in the disability and distress associated with their gastrointestinal symptoms of IBS. They concluded that although additional research still is needed, these preliminary findings suggest that CBT for PD/A can be used to simultaneously treat comorbid symptoms of PD/A and IBS. Implications for the neurobiological models for these comorbid conditions were discussed.

QUALITY OF LIFE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME.

Mönnikes H. *J Clin Gastroenterol*. 2011 Aug;45 Suppl 2:S98-101. PMID: 21666428

Monnikes from Berlin reports that there has been an underestimation of the impact of irritable bowel syndrome (IBS) on an individual's functioning and quality of life (QoL). The general health status of both young and elderly individuals with IBS is generally found to be poorer than that of the general population. Patients with IBS seem to have worse health-related quality of life (HRQoL) than patients with certain other conditions such as gastroesophageal reflux disease, diabetes, and end-stage renal disease. Various disease-specific instruments are now available and are widely used in clinical trials to measure changes in QoL in patients with IBS after treatment intervention. Although few such data are presently available from clinical trials, it seems that patients who have a therapeutic response to therapy for IBS have a corresponding improvement in HRQoL. There seems to be no major differences in HRQoL based on IBS subtype (constipation-dominant or diarrhoea-dominant). However, the severity of bowel symptoms in IBS is associated with a corresponding impact on HRQoL and patients with worse bowel symptoms have a greater diminished QoL compared with patients with milder symptoms. Evidence also indicates that HRQoL in patients with IBS is affected by sex and psychological conditions. Careful consideration of these factors may help to individualize a therapeutic strategy to optimize long-term outcomes.

MAKING A POSITIVE DIAGNOSIS OF IRRITABLE BOWEL SYNDROME.

Dumitrascu DL. *J Clin Gastroenterol*. 2011 Aug;45 Suppl 2:S82-5. PMID: 21666424

Dumitrascu from Romania reports that the traditional diagnostic approach for irritable bowel syndrome (IBS) is to exclude other gastrointestinal conditions, which has led to patients being subjected to excessive testing. However, the development of consensus guidelines, such as Rome III, has enabled physicians to make a positive diagnosis of IBS based on the pattern and nature of symptoms. It is now possible to employ a more rational diagnostic strategy with a reduced need for laboratory testing based on symptom-based approaches aimed at standardizing IBS patient subgroups. Patient outcomes in IBS can be further improved by careful consideration of several diagnostic issues including differentiating between disorders (IBS is 1 of >20 functional gastrointestinal disorders), practical aspects of testing, the indications for colonoscopy, and the need to improve the physician-patient relationship and enhance the patient's adherence to treatment.

See also on IBS: Supplement J Clin Gastroenterol. 2011 Aug;45 Proceedings from the Pan-European Conference on Irritable Bowel Syndrome December 10, 2010 Vienna, Austria:S98-S101.



PROBIOTICS AND PREBIOTICS IN THE MANAGEMENT OF IRRITABLE BOWEL SYNDROME: A REVIEW OF RECENT CLINICAL TRIALS AND SYSTEMATIC REVIEWS.

*Whelan K. Curr Opin Clin Nutr Metab Care. 2011 Sep 1. [Epub ahead of print]. PMID: 21892075*

The aim of this review article from King's College London School of Medicine is to briefly review the aspects of IBS pathogenesis that involve the gastrointestinal microbiota, and then to critically appraise the recent and emerging evidence for the use of probiotics and prebiotics in its management. Recent findings suggest that the increased risk of developing IBS following gastroenteritis and the co-existence of dysbiosis, elevated luminal gas production and immune activation indicate that the gastrointestinal microbiota may be a therapeutic target in IBS. Most systematic reviews indicate that probiotics have a beneficial impact on global IBS symptoms, abdominal pain and flatulence. However, recent trials indicate that different probiotics can improve, have no effect, or even worsen symptoms, confirming that benefits are likely to be strain and symptom-specific. There are no recent clinical trials of prebiotics in IBS, although previous studies indicate potential benefit at lower doses. They conclude that some probiotics have considerable potential in the management of IBS; however, the benefits are likely to be strain-specific. According to Whelan, preliminary studies suggest low doses of prebiotics may improve symptoms of IBS, although further robust clinical trials are required.

DECREASED PAIN INHIBITION IN IRRITABLE BOWEL SYNDROME DEPENDS ON ALTERED DESCENDING MODULATION AND HIGHER-ORDER BRAIN PROCESSES.

*Piché M, Bouin M, Arsenault M, Poitras P, Rainville P. Neuroscience. 2011 Aug 23. [Epub ahead of print]. PMID: 21889972*

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder involving abdominal pain and bowel dysfunction. IBS pain symptoms have been hypothesized to depend on peripheral and central mechanisms, but the pathophysiology is still unclear. The aim of this Canadian study was to assess the contribution of cerebral and cerebrospinal processes to pain inhibition deficits in IBS. Fourteen female patients with diarrhea-predominant IBS (IBS-D) and 14 healthy female volunteers were recruited. Acute pain and the nociceptive withdrawal reflex (R111 reflex) were evoked by transcutaneous electrical stimulation of the right sural nerve with modulation by hetero-segmental counter-irritation produced by sustained cold pain applied on the left forearm. Psychological symptoms were assessed by questionnaires. The authors conclude that their results demonstrate that pain inhibition deficits in female IBS-D patients depend on two potentially separable mechanisms reflecting: (1) altered descending modulation and (2) higher-order brain processes underlying regulation of pain and affect.

## **FIBROMYALGIA**

TIME-DEPENDENT CHANGES IN BLADDER FUNCTION AND PLANTAR SENSITIVITY IN A RAT MODEL OF FIBROMYALGIA SYNDROME INDUCED BY HYDROCHLORIC ACID INJECTION INTO THE GLUTEUS.

*Furuta A, Suzuki Y, Honda M, Koike Y, Naruoka T, Asano K, Chancellor M, Egawa S, Yoshimura N. BJU Int. 2011 Aug 2. doi: 10.1111/j.1464-410X.2011.10258.x. [Epub ahead of print]. PMID: 21810158*

Furuta and colleagues from Japan and Pittsburgh note that bladder pain syndrome/interstitial cystitis (BPS/IC) and fibromyalgia syndrome (FMS) often occur concomitantly. In this study, they found that somatic (gluteus)-to-visceral (bladder) cross sensitization might underlie bladder hypersensitivity in patients with FMS. The purpose of this rat study was to examine the correlation between muscular pain and bladder hypersensitivity in order to clarify the pathogenesis of comorbidity of bladder pain syndrome/interstitial cystitis with other chronic pain conditions such as fibromyalgia syndrome (FMS). They found that HCl injection (pH 4.0) into the gluteus can induce plantar hypersensitivity and urinary frequency for up to 2 weeks after the injection, suggesting that somatic (gluteus)-to-visceral (bladder) cross-sensitization might underlie bladder hypersensitivity in patients with FMS. Moreover, intervention at specific tender points outside the bladder could be

effective in treating urinary frequency because lidocaine injection into the gluteus normalized bladder function in FMS rats for up to 2 weeks.

#### FIBROMYALGIA - SHOULD WE BE TESTING AND TREATING FOR VITAMIN D DEFICIENCY?

*Daniel D, Pirodda MV. Aust Fam Physician. 2011 Sep;40(9):712-6. PMID: 21894281*

Free article

This review from Australia aims to synthesise the evidence regarding any association between vitamin D deficiency and fibromyalgia, addressing whether general practitioners should be testing and treating these patients for vitamin D deficiency. A systematic literature review was performed, using MEDLINE as the primary database, to find and critically appraise all relevant research fulfilling inclusion criteria from January 1990 until September 2010. Results There were conflicting results in the cross sectional studies obtained, with no association in studies using control groups and mixed results in larger population based studies. One adequately powered randomised controlled trial suggests fibromyalgia pain is not improved by vitamin D supplementation. The evidence for an association between fibromyalgia and vitamin D deficiency is inconclusive, with no improvement in pain on supplementation. However, patients with concurrent risk factors for deficiency should be tested and treated for vitamin D deficiency to minimise osteoporosis risk and maximise muscular strength.

#### THE RELATION BETWEEN VITAMIN D DEFICIENCY AND FIBROMYALGIA SYNDROME IN WOMEN.

*Matthana MH. Saudi Med J. 2011 Sep;32(9):925-9. PMID: 21894355*

This prospective study was carried out in Sultan Bin Abdulaziz Humanitarian City, Riyadh, Kingdom of Saudi Arabia from May 2007 to March 2010. One hundred women suffering from fibromyalgia syndrome were included. Blood level of 25-hydroxyvitamin D [25(OH) D] was estimated at initial visit and every 4 weeks until its level exceeded 50 ng/mL. The patients with vitamin D deficiency were treated with ergocalciferol 50,000 IU once weekly until their blood level of 25(OH) D exceeded 50 ng/mL. The number of tender points and the revised Fibromyalgia Impact Questionnaire (FIQR) score were used to assess the fibromyalgia before and after vitamin D repletion. Among the 100 fibromyalgia women, there were 61 women with 25(OH) D deficiency; with vitamin D supplementation, only 42 women showed a significant improvement when their blood level of 25(OH) D became  $\geq 30$  ng/mL, this improvement became more significant when their blood level of 25(OH) D exceeded 50 ng/mL. The author concluded that vitamin D deficiency has to be considered in the management of fibromyalgia syndrome.

### **VULVODYNIA**

#### REPEATED VULVOVAGINAL FUNGAL INFECTIONS CAUSE PERSISTENT PAIN IN A MOUSE MODEL OF VULVODYNIA.

*Farmer MA, Taylor AM, Bailey L, Tuttle AH, Macintyre LC, Milagrosa ZE, Crissman HP, Bennett GJ, Ribeiro-da-Silva A, Binik YM, Mogil JS. Sci Transl Med. 2011 Sep 21;3(101):101ra91. PMID: 21937756*

Provoked vestibulodynia, the most common form of vulvodynia, is a prevalent, idiopathic pain disorder associated with a history of recurrent candidiasis (yeast infections). It is characterized by vulvar allodynia (painful hypersensitivity to touch) and hyperinnervation. Farmer and colleagues from McGill University, Montreal tested whether repeated, localized exposure of the vulva to a common fungal pathogen can lead to the development of chronic pain. A subset of female mice subjected to recurrent *Candida albicans* infection developed mechanical allodynia localized to the vulva. The mice with allodynia also exhibited hyperinnervation with peptidergic nociceptor and sympathetic fibers (as indicated by increased protein gene product 9.5, calcitonin gene-related peptide, and vesicular monoamine transporter 2 immunoreactivity in the vaginal epithelium). Long-lasting behavioural allodynia in a subset of mice was also observed after a single, extended *Candida* infection, as well as after repeated vulvar (but not hind paw) inflammation induced with zymosan, a mixture of fungal

antigens. The hypersensitivity and hyperinnervation were both present at least 3 weeks after the resolution of infection and inflammation. According to the authors, their data show that infection can cause persistent pain long after its resolution and that recurrent yeast infection replicates important features of human provoked vulvodynia in the mouse.

#### DYSAESTHETIC PENOSCROTODYNIA: NOMENCLATURE, CLASSIFICATION, DIAGNOSIS AND TREATMENT.

*Markos AR. Int J STD AIDS. 2011 Sep;22(9):483-7. PMID: 21890542*

Male patients can present with a genital skin burning sensation that bears similarities to vulvodynia. The classification of vulvodynia by International Society for the Study of Vulvovaginal Disease of vulvodynia provides a blueprint for nomenclature and classification of Dysaesthetic penoscrotodynia (DPSD). Recognizing DPSD as generalized, localized, provoked, unprovoked and mixed will enable precise and objective communication between practitioners. Learning from research on the aetiology and management of vulvodynia can improve the care of patients suffering with DPSD. Scope remains for better acknowledgement of DPSD within the medical profession and improvement in its public profile in order to enhance patient care.

#### **SLEEP DISRUPTION**

##### SLEEP DISRUPTION AND INTERSTITIAL CYSTITIS SYMPTOMS IN WOMEN.

*Panzer A, Reishtein J, Shewokis P. Urol Nurs. 2011 May-Jun;31(3):159-65, 172. PMID: 21805753*

Four hundred and seven women with interstitial cystitis participated in a Web-based study. One hundred percent of participants had poor sleep, with a mean sleep quality score of 13.4. This indicates very poor sleep. The predictor variables (nocturia, pain, and urinary urgency) were significant predictors of sleep quality when controlling for confounding variables.

#### **CHRONIC FATIGUE SYNDROME**

##### CHRONIC FATIGUE SYNDROME: UNDERSTANDING A COMPLEX ILLNESS.

*Holgate ST, Komaroff AL, Mangan D, Wessely S. Nat Rev Neurosci. 2011 Jul 27;12(9):539-44. doi: 10.1038/nrn3087. PMID: 21792218*

Chronic fatigue syndrome (CFS) is a debilitating illness that affects many people. It has been marred by controversy, from initial scepticism in the medical community about the existence of the condition itself to continuing disagreements - mainly between some patient advocacy groups on one side, and researchers and physicians on the other - about the name for the illness, its aetiology, its pathophysiology and the effectiveness of the few currently available treatments. The role of the CNS in the disease is central in many of these discussions. Nature Reviews Neuroscience asked four scientists involved in CFS research about their views on the condition, its causes and the future of research aimed at improving our understanding of this chronic illness.

See also: <http://www.bbc.co.uk/news/health-14883651>

BBC: "A deeper understanding of the illness is desired by all involved. Delving into the sub-types of the condition may help in finding causes, which could also have implications for treating each sub-type".

##### IN THE MIND OR IN THE BRAIN? SCIENTIFIC EVIDENCE FOR CENTRAL SENSITISATION IN CHRONIC FATIGUE SYNDROME.

*Nijs J, Meeus M, Van Oosterwijck J, Ickmans K, Moorkens G, Hans G, De Clerck LS. Eur J Clin Invest. 2011 Jul 2. doi: 10.1111/j.1365-2362.2011.02575.x. [Epub ahead of print]. PMID: 21793823*

Central sensitisation entails several top-down and bottom-up mechanisms, all contributing to the hyper-responsiveness of the central nervous system to a variety of inputs. In the late nineties, it was first hypothesised that chronic fatigue syndrome (CFS) is characterised by hypersensitivity of

the central nervous system (i.e. central sensitisation). Since then, several studies have examined central sensitisation in patients with CFS. This study provides an overview of such studies. Various studies showed generalised hyperalgesia in CFS for a variety of sensory stimuli, including electrical stimulation, mechanical pressure, heat and histamine. Various tissues are affected by generalised hyperalgesia: the skin, muscle tissue and the lungs. Generalised hyperalgesia in CFS is augmented, rather than decreased, following various types of stressors like exercise and noxious heat pain. Endogenous inhibition is not activated in response to exercise and activation of diffuse noxious inhibitory controls following noxious heat application to the skin is delayed. According to the authors, the observation of central sensitisation in CFS is in line with current understanding of CFS. The presence of central sensitisation in CFS corroborates with the presence of several psychological influences on the illness, the presence of infectious agents and immune dysfunctions and the dysfunctional hypothalamus-pituitary-adrenal axis as seen in these severely debilitated patients.

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