International Painful Bladder Foundation

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

IPBF e-Newsletter and Research Update

Issue 28, January 2012

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:

The International Painful Bladder Foundation would like to wish all its e-Newsletter readers a Happy and Healthy New Year, to thank its sponsors for their valuable support and to express gratitude to its medical advisory board members for all their help and advice throughout 2011.
During the holidays, we have been especially thinking of our colleagues and IC patients in Christchurch New Zealand who were subjected to yet more earthquakes and even more damage in December 2011. Dot Milne, IPBF board member, chair of the New Zealand patient support group and herself living in Christchurch, has managed to keep a newsletter going, organise meetings and keep everyone's spirits up, despite all the continuing natural disasters. We send them our best wishes.

MULTIDISCIPLINARY BRAINSTORMING NIH/NIDDK MEETING ON MEASUREMENT OF URINARY SYMPTOMS (MOMUS)

A most interesting and thought-provoking brainstorming meeting was held by the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) at the National Institutes of Health in Bethesda, USA, 14-15 November 2011, and was attended by an impressive array of speakers and participants including urologists, gynaecologists, researchers, basic scientists, epidemiologists, psychologists, biostatisticians, anaesthesiologists, with representatives from the pharma industry, U.S. Food and Drug Administration (FDA), the Centres for Medicare and Medicaid Services, and the Agency for Healthcare Research and Quality and last but certainly not least the all-important patients and advocacy groups.
The objectives of this meeting were defined by the NIDDK as to:

- *Discuss the uses and shortcomings of current symptom-based instruments in research of LUTD.*
- *Disseminate state-of-the-art methodology to improve patient reported outcomes (PRO) of LUTD symptoms.*
- *Discuss the validation and qualification process of new measurement tools, and patient phenotyping.*
- *Align the new LUTD symptom measurement tool among involved parties.*

In other words, a better tool for measuring urinary symptoms and pain needs to be found. This meeting also included much about interstitial cystitis with IC patients also participating.
For a more detailed review of this meeting, go to the IPBF website or click here.

NIDDK MAPP RESEARCH NETWORK HOME PAGE

The NIDDK's Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network embraces a systemic—or whole-body—approach in the study of IC/PBS and CP/CPPS. In addition to moving beyond traditional bladder- and prostate-specific research directions, MAPP Network scientists are investigating potential relationships between these two urological syndromes and other chronic conditions that are sometimes seen in IC/PBS and CP/CPPS patients, such as irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome. If you would like to follow developments online, please click here.

NVA AND VULVODYNIA RESEARCH

Although we include some latest research on vulvodynia in this IPBF e-newsletter, the **National Vulvodynia Association (NVA)** in the USA issues an excellent quarterly newsletter on research in the wide field of vulvar pain. For further information, please go to their website at www.nva.org. Highly recommended for patients and professionals who wish to keep up to date with developments and new insights in this field.

UPCOMING MEETINGS:

EAU CONFERENCE 24-28 FEBRUARY 2012, PARIS, FRANCE

The Annual Congress of the European Association of Urology (Eau) will be held at the Palais des Congrès de Paris, 24-28 February 2012. ESU courses include ESU Course 11 on Painful Bladder/Chronic Pelvic Pain, in men and women chaired by Professor JJ Wyndaele and ESU Course 2 on Female Pelvic Floor Problems, chaired by Dr EJ Messelink. Poster Session 23 will be dedicated to Chronic Pelvic Pain Syndrome. On the Sunday, the programme also includes a state-of-the-art lecture on Female Sexual Dysfunction by Dr A. Graziottin. For further information, go to http://www.eauparis2012.org/

IAPO 5TH GLOBAL PATIENTS CONGRESS

The International Alliance of Patients' Organizations (IAPO) is pleased to announce that registration for the **5th 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**

ESSIC ANNUAL MEETING 2012, 10-12 MAY 2012, PORTO, PORTUGAL

This year, the ESSIC Annual Meeting will be held 10-12 May, 2012 in Porto, Portugal. The theme of this meeting will be PAIN. Other topics will include harmonisation of guidelines and nomenclature, phenotyping (including MAPP) and pain from a patient perspective. A course on clinical diagnosis and management will be given on Saturday 12 May. Detailed information, including topics and speakers, is available on the home page of the ESSIC website: www.essic.eu.

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 1st International Neuro-Urology Meeting will be held 29-30 June 2012, at Balgrist University Hospital, Zurich, Switzerland. This exciting new initiative is being organized by the new Swiss Continence Foundation and features many top speakers from the neuro-urology world.
For information and registration, see
http://www.swisscontinencefoundation.ch/veranstaltungen/intro/detail.asp?IDEvent=1)
Programme information can be found at:
http://www.swisscontinencefoundation.ch/files/Event/Final%20SCF.pdf
Further information may be obtained from: info@swisscontinencefoundation.ch

IASP 14th WORLD CONGRESS ON PAIN, 27-31 AUGUST, 2012, MILAN, ITALY

The International Association for the Study of Pain (IASP) will be organising the 14th @World Congress on Pain, 27-31 August 2012 at Milan Convention Centre, Italy. Information can be found at: http://www.iasp-pain.org/Content/NavigationMenu/WorldCongressonPain2/14thWorldCongressonPain/default.htm and details of the programme at: http://www.iasp-pain.org/Content/NavigationMenu/WorldCongressonPain2/14thWorldCongressonPain/CongressSchedule/default.htm.

BOOKS, NEWSLETTERS, WEBSITES ETC

BOTULINUM TOXIN IN UROLOGY

Authors: Michael B. Chancellor & Christopher P. Smith
Publisher: Springer-Verlag 2011, hardcover, pp. 207
ISBN 978-3-642-03579-1, e-ISBN 978-3-642-03580-7
This book will be a very welcome addition to the urology library since it is the first book on the use of botulinum toxin (BoNT) in the genitourinary tract and is written and edited by two leading pioneers

in the field, Michael Chancellor and Christopher Smith. An introductory section discusses the biology, pharmacology, and safety of BoNT in the lower urinary tract. This is followed by a detail description of applications of BoNT in the bladder and the prostate and pelvic floor, with reviews of the latest clinical series and techniques of BoNT injection in both adults and children. The book closes by looking at non-genitourinary uses of BoNT and addressing issues of health economics as well as providing insights from international experts. This is a practical, hands-on book that also includes appendices with easy to read instructions for patients undergoing bladder and prostate BoNT injections and specific nursing procedural issues. For further information, click here.

BOOK ON SJÖGREN´S SYNDROME ON IPBF WEBSITE NOW WITH SOME CHAPTERS IN DUTCH

Many of you will already be familiar with the book by Dr Joop P van de Merwe on many different aspects of Sjögren´s syndrome, available chapter by chapter, on the IPBF website. Much of the information is relevant to many autoimmune conditions and also includes information on IC. Some of these chapters have now been translated into Dutch and will therefore be very useful for Dutch and Flemish patients and professionals. Click here for further information or go to the home page www.painful/bladder.org and click on associated disorders.

IPBF BROCHURE UPDATE

The IPBF brochure on Interstitial Cystitis Diagnosis and Treatment has once again been updated and can be found via http://www.painful-bladder.org/IPBF_publications.html or by going directly to the pdf file at http://www.painful-bladder.org/pdf/Diagnosis&Treatment_IPBF.pdf.

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. Click on the title to go to the PubMed abstract or to the full article in the case of free access.

Terminology: different published articles use different terminology, for example: interstitial cystitis, painful bladder syndrome, bladder pain syndrome, hypersensitive bladder syndrome, chronic pelvic pain (syndrome) or combinations of these. When reviewing the article, we generally use the terminology used by the authors.

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. 2012 Jan;61(1):29-53. Epub 2011 Sep 9. PMID: 21920661

Free access

Although we reviewed this article last time, we are mentioning it again in this issue in order to draw attention to the fact that it is now a free access article, together with an editorial and a response by the authors. Click on the title to go to the pdf.

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. They concluded 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.

THE FUTURE OF PHARMACOLOGIC TREATMENT FOR BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: LESSONS FROM A META-ANALYSIS

Cruz F. Eur Urol. 2012 Jan;61(1):54-5. Epub 2011 Sep 28.PMID: 21975250

Editorial, Free Access

In this editorial, F. Cruz notes that the article by Giannantoni et al provides overwhelming evidence for urgent profound reflection on the direction of study into BPS/IC. He also comments that a fundamental step in the understanding of BPS/IC is agreement on a single, clear definition.

REPLY FROM AUTHORS RE: FRANCISCO CRUZ. THE FUTURE OF PHARMACOLOGIC TREATMENT FOR BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: LESSONS FROM A META-ANALYSIS. EUR UROL 2012;61:54-55.

Giannantoni A, Bini V. Eur Urol. 2012 Jan;61(1):56-7. Epub 2011 Oct 18. PMID: 22018674

Author reply

In their response to the editorial by Cruz, the authors write that “the lesson we learned in performing this review was that we still need to understand the pathoph6ysiology of the disease, to reach a more comprehensive classification system and to establish a more appropriate and standardized diagnostic modality. Finally there is the urgent need to identify an effective and safe treatment modality.”

THE BLADDER PAIN/INTERSTITIAL CYSTITIS SYMPTOM SCORE: DEVELOPMENT, VALIDATION, AND IDENTIFICATION OF A CUT SCORE

Humphrey L, Arbuckle R, Moldwin R, Nordling J, van de Merwe JP, Meunier J, Crook T, Abraham L. Eur Urol. 2012 Feb;61(2):271-9. Epub 2011 Oct 18. PMID: 22050826

The authors note that there was a need to develop and validate a patient-reported symptom-based instrument for clinical trial eligibility of bladder pain/interstitial cystitis patients. They therefore developed this Bladder Pain/Interstitial Cystitis Symptom Score (BPIC-SS). The study took place in three stages: Stage 1: Qualitative concept elicitation (CE) interviews were conducted with IC/BPS patients in France (n=12), Germany (n=12), and the United States (US) (n=20), and overactive bladder (OAB) (n=10) patients in the US for comparison. Stage 2: Cognitive debriefing (CD) interviews were performed with US IC/BPS patients (n=20). Stage 3: An observational study with 99 IC/BPS, 99 OAB, and 100 healthy participants in the US was used to perform item reduction, identify cut scores, and validate the measure. A cut score was defined using logistic regression and receiver operating characteristic curves. Psychometric properties, including test-retest reliability, were assessed. The observational study also included the Pelvic Pain and Urgency/Frequency Patient Symptom Scale, the Interstitial Cystitis Symptom Index, a Clinician Global Impression of Severity, and a Patient Global Impression of Change as well as the BPIC-SS. In CE, reported symptoms were bladder pain, persistent urge to urinate, and high urinary frequency. In CD, 13 items were deleted, and 15 were retained. Based on validation analyses, qualitative findings, and clinical relevance, the instrument was reduced to eight items that had strong sensitivity (0.72) and specificity (0.86) with a cut score ≥19 to determine clinical trial inclusion. Psychometric properties were strong. It was concluded that the BPIC-SS is a reliable, valid, and appropriate questionnaire to select bladder pain/interstitial cystitis patients for clinical trials.

NOCTURIA AND QUALITY OF LIFE: RESULTS FROM THE BOSTON AREA COMMUNITY HEALTH SURVEY.

Kupelian V, Wei JT, O'Leary MP, Norgaard JP, Rosen RC, McKinlay JB. Eur Urol. 2012 Jan;61(1):78-84. Epub 2011 Sep 10. PMID: 21945718

Free access

Nocturia or night-time voiding is common in the elderly, but also among patients with a painful or hypersensitive bladder. It has frequently been described as leading to sleep loss, daytime fatigue, and reduced quality of life (QOL). The purpose of this study was to investigate the association of nocturia with QOL and depressive symptoms among men and women in the form of a population-based epidemiologic survey of urologic symptoms among persons aged 30-79 yr. A multistage stratified cluster sample design was used to randomly sample 5503 residents of Boston, MA, USA.
Nocturia was defined as a self-report of two or more voiding episodes nightly or having to get up to urinate more than once nightly "fairly often," "usually," or "almost always." QOL was assessed using the physical and mental health component scores of the 12-Item Short-Form Survey (SF-12). Depression was assessed using the Center for Epidemiological Studies Depression Scale. Multiple linear and logistic regression methods were used to model the nocturia and QOL association and to control for confounders. The authors found that nocturia is associated with decreased QOL and with an increased prevalence of depressive symptoms in both men and women.

NOCTURIA AND QUALITY OF LIFE.
Wyndaele JJ. Eur Urol. 2012 Jan;61(1):85-7. Epub 2011 Sep 28.PMID: 21963053
Editorial, Free access
In his editorial, JJ Wyndaele notes that Nocturia can have different causes, that it can induce sleep fragmentation and that it may therefore lead to the problem of shortage of sleep. Sufficient sleep is a prerequisite for normal functioning, while shortage of sleep can lead to side effects, which may be dangerous. It can lead to general ill health, negative quality of life and serious personal, psychological and social consequences.

Note: More can be found related to this topic in the IPBF brochure Interstitial Cystitis: Diagnosis & Treatment, Chapter 7: Fatigue in IC Patients.

ADMISSIONS RELATED TO INTERSTITIAL CYSTITIS IN JAPAN: AN ESTIMATION BASED ON THE JAPANESE DIAGNOSISPROCEDURE COMBINATION DATABASE.
Sugihara T, Yasunaga H, Horiguchi H, Nakamura M, Nomiya A, Nishimatsu H, Matsuda S, Homma Y. Int J Urol. 2012 Jan;19(1):86-9. doi: 10.1111/j.1442-2042.2011.02883.x.Epub 2011 Nov 1. PMID: 22044558
In this study from Japan, Sugihara et al estimated the incidence of admissions related to interstitial cystitis in Japan using a national administrative claims database, the DiagnosisProcedure Combination database, which included information for 53.6% of urological training hospitals certified by the Japanese Urological Association. ´**Admissions related to interstitial cystitis**´ was defined as those cases whose ICD-10 code for the main reason for admission was N301 (interstitial cystitis) between 2007 and 2009. Among 8.42 million inpatient cases, 784 female and 212 male patients with interstitial cystitis were identified. The ratio of females to males was 3.69 and the median age was 67 years (range 5-92 years). The admission incidence (per 100,000 person-years) in females and males was estimated to be 1.35 (95% confidence interval 1.25-1.46) and 0.37 (0.31-0.42), respectively. This incidence is low compared with other reports. The authors are of the opinion that possible reasons for this finding include racial difference, clinical examination methods, lack of outpatient data and poor healthcare coverage of interstitial cystitis.

FINE STRUCTURAL CHARACTERIZATION OF CHONDROITIN SULFATE IN URINE OF BLADDER PAIN SYNDROME SUBJECTS.
Maccari F, Buzzega D, Galeotti F, Volpi N. Int Urogynecol J. 2011 Dec;22(12):1581-6. Epub 2011 Aug 2. PMID: 21809155.
Free Access
In this study from Modena, Italy, Maccari and colleagues noted that in previous esearches, urine GAG levels were found increased, decreased, or similar between BPS and controls. Additionally, no study is available on the structure characterization of urinary chondroitin sulfate (CS) in BPS patients.

No significant differences were obtained for total amount of GAGs, absolute content of CS and HS, and their relative percentages. Moreover, no differences were observed for CS structure confirming similar urine CS composition in BPS subjects and controls. This study found no significant differences of BPS and control urine GAG levels and CS structure to allow use of these parameters as diagnostic markers for BPS diagnosis.

THE ROLE OF SODIUM HYALURONATE AND SODIUM CHONDROITIN SULPHATE IN THE MANAGEMENT OF BLADDER DISEASE.

Damiano R, Cicione A. Ther Adv Urol. 2011 Oct;3(5):223-32. PMID: 22046200

Free Access

According to Damiano and colleagues from Italy, the bladder epithelium is not only a simple defence against infections, but it is also a specialized tissue regulating complex bladder functions and playing an active role in the pathogenesis of many bladder diseases. They believe that there is strong evidence that different chronic inflammatory bladder diseases, such as recurrent urinary tract infection (UTI), chemical or radiation cystitis and painful bladder syndrome/interstitial cystitis (PBS/IC), can be pathophysiologically linked in the first step of the disease to the loss of the glycosaminoglycan (GAG) mucous layer independently of the original cause of the inflammatory process. The aim of this article was to review the current evidence on the clinic applications of GAGs in urology, with particular emphasis on the therapeutic use of hyaluronic acid (HA) and chondroitin sulphate (CS). A comprehensive electronic literature search was conducted in May 2011 using the Medline database. Three studies supported the decrease of the rate of recurrent UTIs by restoring the GAG layer, showing a significant reduction of UTI rates and a prolonged median time to recurrence after HA intravesical instillations in women with recurrent UTI. We provide higher level evidence by reporting a prospective, randomized, double-blind, placebo-controlled study on the use of intravesical HA and CS in women with recurrent UTIs. A significant reduction of 77% in the UTI rate per patient per year versus placebo was observed at the end of the study. Nine studies were published between 2002 and 2011 on the use of HA and CS to treat PBS/IC. Three of them evaluated the use of GAGs bladder instillation to prolong the effects of bladder hydrodistension. In the other six studies the efficacy of HA bladder instillations to reduce symptoms score was assessed. Preliminary studies support data on the role of HA-CS in detrusor overactivity, nonbacterial cystitis and urological malignancies. Few data are available regarding the mode of action of HA-CS or its effectiveness in the management of bladder diseases. The major issue in interpreting the available evidence regarding HA-CS is that most of the reported studies are nonrandomized and without a control arm. HA-CS may be considered for further studies, including randomized, controlled trials with adequate power.

ALKALINIZED LIDOCAINE AND HEPARIN PROVIDE IMMEDIATE RELIEF OF PAIN AND URGENCY IN PATIENTS WITH INTERSTITIAL CYSTITIS.

Parsons CL, Zupkas P, Proctor J, Koziol J, Franklin A, Giesing D, Davis E, Lakin CM, Kahn BS, Garner WJ. J Sex Med. 2011 Nov 14. doi: 10.1111/j.1743-6109.2011.02542.x. [Epub ahead of print]. PMID: 22082303

It has previously been reported in an open-label study that the combination of alkalinized lidocaine and heparin can immediately relieve the symptoms of urinary urgency, frequency, and pain associated with interstitial cystitis (IC). This combination has also been reported to relieve pain associated with sex in patients with IC. The aim of the present study by C.L. Parsons and colleagues was to corroborate these findings in a multicentre prospective, double-blind, crossover, placebo-controlled trial. Each participant met all of the clinical NIDDK criteria (excluding cystoscopy) for IC. The results indicate that the combination of alkalinized lidocaine and heparin provides up to 12 hours of relief from urgency and pain associated with IC. This combination provides significant immediate relief of symptoms for patients with IC.

[INTRAVESICAL THERAPY OF HEPARIN AND LIDOCAINE FOR INTERSTITIAL CYSTITIS : A CASE REPORT].

[Article in Japanese]

Matsuo T, Shida Y, Hayashida Y, Sakai H. Hinyokika Kiyo. 2011 Sep;57(9):513-6. PMID: 22075614
Matsuo and colleagues from the Department of Urology, Kamigoto Hospital, Japan report a case of IC treated with intravesical instillation of heparin and alkalized lidocaine. A 64-year-old woman presented with urinary frequency and urgency with suprapubic pain. She underwent intravesical treatment with combined heparin and alkalinized lidocaine for IC, since prior medical treatments (imipramine, solifenacin, suplatast tosilate, and kampo extracts) and hydrodistention of bladder had little or no effect on her symptoms. A 50 ml solution containing 20,000 units of heparin, 200 mg of lidocaine and 7% sodium bicarbonate was administered intravesically twice a week for 12 months. The O'Leary-Sant IC symptom index score and IC problem index score improved from 20 to 8 and from 16 to 8, respectively, and her bladder capacity increased from 90 ml to 300 ml. Intravesical instillation of combined heparin and lidocaine was useful in the treatment of IC.

GLOBAL CONCEPTS OF BLADDER PAIN SYNDROME (INTERSTITIAL CYSTITIS).
Nordling J, Fall M, Hanno P. World J Urol. 2011 Nov 5. [Epub ahead of print]. PMID: 22057291
Nordling and colleagues note that bladder pain syndrome (BPS), commonly referred to as "interstitial cystitis", is no longer considered a rare disorder. It may affect up to 2.7% of the adult female population (Ueda et al. in Int J Urol 10:1-70, 2003) with up to 20% of cases occurring in men. The last two decades have seen a worldwide effort to try to standardize its nomenclature, definition, diagnosis, and treatment algorithm. The literature has been reviewed. In this article, they detail current terminology, diagnostic approaches and treatment. Standard therapies are discussed, and a section that concentrates on the management of the subset of patients with a Hunner's lesion is highlighted. They conclude that BPS is no longer considered primarily a bladder disease, but rather one of a number of chronic pain syndromes that is distinguished by being manifest through bladder-related symptoms. A distinct subgroup of patients with Hunner's lesion has specific characteristics, and successful treatment of this subgroup is available.

FROM URGENCY TO FREQUENCY: FACTS AND CONTROVERSIES OF TRPS IN THE LOWER URINARY TRACT.
Skryma R, Prevarskaya N, Gkika D, Shuba Y. N Rev Urol. 2011 Oct 4;8(11):617-30. doi: 10.1038/nrurol.2011.142. PMID: 21971315
The members of transient receptor potential (TRP) superfamily of cationic ion channels represent universal sensors, which convert multiple exogenous and endogenous chemical and physical stimuli into electrical and functional cellular responses. TRPs are widely distributed in many different tissues, and expression of numerous TRP types has been reported in lower urinary tract (LUT) tissues, neuronal fibres innervating the bladder and urethra, and epithelial and muscular layers of the bladder and urethral walls, where they are mainly involved in nociception and mechanosensory transduction. As such, they represent attractive targets for treating LUT disorders. Although information on the functional significance of many of the TRP proteins in the LUT remains very limited, compelling evidence has accumulated for a pivotal role of TRPV1, TRPV2, TRPV4, TRPM8, and TRPA1 in normal and pathological LUT function, mainly as sensors of stretch and chemical irritation. Further studies into these and other TRPs in the LUT will facilitate the development of improved therapeutic strategies to target these channels in LUT disorders.

EVIDENCE OF BLADDER OVERSENSITIVITY IN THE ABSENCE OF AN INFECTION IN PREMENOPAUSAL WOMEN WITH A HISTORY OF RECURRENT URINARY TRACT INFECTIONS.
Arya LA, Northington GM, Asfaw T, Harvie H, Malykhina A. BJU Int. 2011 Nov 30. doi: 10.1111/j.1464-410X.2011.10766.x. [Epub ahead of print]. PMID: 22129305
Arya *et al* remind us that urinary tract infections (UTIs) have been considered in the aetiology of interstitial cystitis/painful bladder syndrome (IC/PBS). Prior studies have described symptoms and laboratory tests suggestive of UTI at the onset of IC/PBS as well as a significant history of childhood recurrent UTIs. However, the mechanism by which recurrent UTIs contribute to the development of IC/PBS is not clear. This study from Philadelphia shows that women with recurrent UTI suffer from

bladder oversensitivity. The authors believe that their findings may have useful clinical implications. Women with bladder oversensitivity complain of urinary frequency which is often misdiagnosed as an infection and treated with unnecessary antibiotics. Additionally, there are no effective therapies for bladder oversensitivity. The authors suggest that women with recurrent UTI should undergo prompt evaluation and treatment of episodes of infection to prevent the development of bladder oversensitivity. Their findings also provide a possible mechanism for the development of IC/PBS. Whether women with recurrent UTI are at increased risk for developing IC/PBS in the future will need to be confirmed in future studies. They concluded from their findings that in the absence of an infection, premenopausal women with a history of recurrent UTI have significantly greater urinary frequency, lower average voided volume and a lower threshold of bladder sensitivity than controls.

BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS IN TWIN SISTERS.

Tunitsky E, Barber MD, Jeppson PC, Nutter B, Jelovsek JE, Ridgeway B. J Urol. 2012 Jan;187(1):148-52. Epub 2011 Nov 16. PMID: 22088343

In this study from Cleveland, Ohio, Tunitsky and colleagues determined the genetic contribution of and associated factors for bladder pain syndrome using an identical twin model. Multiple questionnaires were administered to adult identical twin sister pairs. The O'Leary-Sant Interstitial Cystitis Symptom and Problem Index was administered to identify individuals at risk for bladder pain syndrome. Potential associated factors were modelled against the bladder pain syndrome score with the twin pair as a random effect of the factor on the bladder pain syndrome score. Variables that showed a significant relationship with the bladder pain syndrome score were entered into a multivariable model. In this study, 246 identical twin sister pairs (total 492) participated with a mean age (± SD) of 40.3 ± 17 years. Of these women 45 (9%) were identified as having a moderate or high risk of bladder pain syndrome (index score greater than 13). There were 5 twin sets (2%) in which both twins met the criteria. Correlation of bladder pain syndrome scores within twin pairs was estimated at 0.35, suggesting a genetic contribution to bladder pain syndrome. Multivariable analysis revealed that increasing age (estimate 0.46 [95% CI 0.2, 0.7]), irritable bowel syndrome (1.8 [0.6, 3.7]), physical abuse (2.5 [0.5, 4.1]), frequent headaches (1.6 [0.6, 2.8]), multiple drug allergies (1.5 [0.5, 2.7]) and number of self-reported urinary tract infections in the last year (8.2 [4.7, 10.9]) were significantly associated with bladder pain syndrome. Bladder pain syndrome scores within twin pairs were moderately correlated, implying some genetic component. Increasing age, irritable bowel syndrome, frequent headaches, drug allergies, self-reported urinary tract infections and physical abuse were factors associated with higher bladder pain syndrome scores.

COMPARISON OF AN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME CLINICAL COHORT WITH SYMPTOMATIC COMMUNITY WOMEN FROM THE RAND INTERSTITIAL CYSTITIS EPIDEMIOLOGY STUDY.

Konkle KS, Berry SH, Elliott MN, Hilton L, Suttorp MJ, Clauw DJ, Clemens JQ. J Urol. 2011 Dec 14. [Epub ahead of print]. PMID: 22177158

The RAND Interstitial Cystitis Epidemiology survey estimated that 2.7% to 6.5% of United States women have urinary symptoms consistent with a diagnosis of interstitial cystitis/bladder pain syndrome. In this study, Konkle and colleagues describe the demographic and clinical characteristics of the symptomatic community based RAND Interstitial Cystitis Epidemiology cohort, and compare them with those of a clinically based interstitial cystitis/bladder pain syndrome cohort. Participants in this study included 3,397 community women who met the criteria for the RAND Interstitial Cystitis Epidemiology high sensitivity case definition, and 277 women with an interstitial cystitis/bladder pain syndrome diagnosis recruited from specialist practices across the United States (clinical cohort). Questions focused on demographic information, symptom severity, quality of life indicators, concomitant diagnoses and treatment. The authors found that the average symptom duration for both groups was approximately 14 years. Women in the clinical cohort reported worse baseline pain and maximum pain, although the absolute differences were small. They concluded from their findings that the RAND Interstitial Cystitis Epidemiology community cohort was

remarkably similar to an interstitial cystitis/bladder pain syndrome clinical cohort with respect to demographics, symptoms and quality of life measures. In contrast to other chronic pain conditions for which clinical cohorts typically report worse symptoms and functional status than population based samples, the authors' data suggest that many measures of symptom severity and functional impact are similar, and sometimes worse, in the RAND Interstitial Cystitis Epidemiology cohort. These findings suggest that interstitial cystitis/bladder pain syndrome is significantly burdensome, and likely to be underdiagnosed and undertreated in the United States.

GENE EXPRESSION ANALYSIS OF URINE SEDIMENT: EVALUATION FOR POTENTIAL NONINVASIVE MARKERS OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Blalock EM, Korrect GS, Stromberg AJ, Erickson DR. J Urol. 2011 Dec 16. [Epub ahead of print]. PMID: 22177197

The purpose of this study by Blalock and colleagues from Kentucky was to determine whether gene expression profiles in urine sediment could provide noninvasive markers for IC/BPS with and/or without Hunner lesions. They collected and centrifuged fresh catheterized urine from 5 controls, and 5 Hunner lesion-free and 5 Hunner lesion bearing patients. Three biologically likely hypotheses were tested, including 1) all 3 groups are distinct from each other, 2) controls are distinct from the 2 types combined of patients with IC/BPS and 3) patients with Hunner lesion IC/BPS are distinct from controls and patients with nonHunner-lesion IC/BPS combined. For statistical parity an unlikely fourth hypothesis was included, that is that patients with nonHunner-lesion IC/BPS are distinct from controls and patients with Hunner lesion IC/BPS combined. Analysis supported selective up-regulation of genes in the Hunner lesion IC/BPS (hypothesis 3), which were primarily associated with inflammation. They found that the inflammatory profile was statistically similar to that reported in a prior Hunner lesion IC/BPS bladder biopsy study. Gene expression analysis of urine sediment was feasible in this pilot study. Expression profiles failed to discriminate nonHunner-lesion IC/BPS from controls and they are unlikely to be a noninvasive marker for nonHunner-lesion IC/BPS. In contrast, patients with Hunner lesion had increased proinflammatory gene expression in urine sediment, similar to that in a prior microarray study of bladder biopsies. If these preliminary results are validated in future research, they may lead to a noninvasive biomarker for Hunner lesion IC/BPS.

VALIDATION OF A QUALITY-OF-LIFE SCALE FOR WOMEN WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.

Bogart LM, Suttorp MJ, Elliott MN, Clemens JQ, Berry SH. Qual Life Res. 2011 Dec 7. [Epub ahead of print]. PMID: 22146841

The aim of this study from Boston was to validate a disease-specific scale to measure the impact of symptoms of BPS/IC. Participants for the study were drawn from the RAND Interstitial Cystitis Epidemiology (RICE) Study, a telephone probability survey of 146,231 US households. The RICE BSI-6 ($\alpha = 0.92$) was significantly related to greater symptom severity, worse general mental- and physical-health-related QoL, more severe depression symptoms, and lower perceived control over life in general and over BPS/IC symptoms (P values < .05). It was also associated with less use of distancing coping ($P < .05$). The authors concluded from their findings that the RICE BSI-6 shows excellent internal consistency and strong convergent validity and that it can be used to examine the effects of psychosocial and treatment interventions on QoL among women with BPS/IC.

INTRAVESICAL CHONDROITIN SULFATE INHIBITS RECRUITMENT OF INFLAMMATORY CELLS IN AN ACUTE ACID DAMAGE "LEAKY BLADDER" MODEL OF CYSTITIS.

Engles CD, Hauser PJ, Abdullah SN, Culkin DJ, Hurst RE. Urology. 2011 Nov 30. [Epub ahead of print]. PMID: 22137543

In this rat study, Engles and colleagues from Oklahoma University Health Science Center investigated whether a physiologic effect of "glycosaminoglycan (GAG) replenishment therapy" altered recruitment of inflammatory cells in an acute bladder damage model. In clinical practice, it has been shown that replacement of the GAG layer with intravesically administered GAGs is an effective

therapy for interstitial cystitis in at least some patients. Intravesically administered chondroitin sulfate was previously shown to bind to and restore the impermeability of surface-damaged ("leaky") urothelium to small ions. In the present study, rat bladders were damaged with 10 mM HCl. Negative control bladders were treated with phosphate-buffered saline. On the following day, the animal bladders were treated with 20 mg/mL chondroitin sulfate in phosphate-buffered saline, and the negative and positive controls were treated with phosphate-buffered saline alone. At 2 and 4 days after treatment with chondroitin sulfate, the rats were killed, and sections of their bladders were analyzed using toluidine blue staining for mast cell immunohistochemical labeling using antibodies against CD45 for lymphocytes and myeloperoxidase for neutrophils. The authors concluded from their results that they have demonstrated for the first time that intravesical GAG replenishment therapy also produces a physiologic effect of decreasing recruitment of inflammatory cells in an acute model of the damaged bladder. These findings support the use of intravesically administered GAG for bladder disorders that result from a loss of impermeability, including interstitial, radiation, and chemical cystitis, and possibly others as well.

ASSOCIATION OF NEUROPATHIC PAIN WITH BLADDER, BOWEL AND CATASTROPHIZING SYMPTOMS IN WOMEN WITH BLADDER PAIN SYNDROME.

Cory L, Harvie HS, Northington G, Malykhina A, Whitmore K, Arya L. J Urol. 2011 Dec 14. [Epub ahead of print]. PMID: 22177143

In this study from Philadelphia, Cory and colleagues determined if there is an association of neuropathic pain with urinary, bowel and catastrophizing symptoms in women with bladder pain syndrome. Female patients with a diagnosis of bladder pain syndrome completed validated questionnaires to assess neuropathic pain, urinary and bowel symptoms, quality of life and pain catastrophizing. Women were dichotomized into neuropathic pain and non-neuropathic pain groups. Urinary and bowel symptoms, pain catastrophizing and quality of life scores were compared between the 2 groups using parametric and nonparametric tests. The authors found that in women with bladder pain syndrome the presence of neuropathic pain is significantly associated with the severity of bladder and bowel pain, urinary urgency and diarrhoea. Women with features of neuropathic pain also have worse pain catastrophizing and quality of life than those without features of neuropathic pain.

GENDER SPECIFIC PELVIC PAIN SEVERITY IN NEUROGENIC CYSTITIS.

Rudick CN, Pavlov VI, Chen MC, Klumpp DJ. J Urol. 2011 Dec 16. [Epub ahead of print]. PMID: 22177208

IC/PBS is a chronic bladder inflammatory disease of unknown etiology that is often regarded as neurogenic cystitis. The condition is associated with focal inflammation, urothelial lesions, voiding dysfunction and pain in the pelvic/perineal area. Approximately 90% of patients with the condition are women, suggesting the possibility of hormonal involvement in IC/PBS. Rudick and colleagues from Chicago examined the basis of gender specific pelvic pain in a mouse model of neurogenic cystitis that recapitulates features of IC/PBS and in which pelvic pain is mediated by mast cell histamine. The data from their findings suggest that pelvic pain in mice with murine neurogenic cystitis is mediated by gender specific responsiveness to mast cells while pelvic pain severity is modulated by genetic factors.

CHILDHOOD SEXUAL TRAUMA IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A CASE CONTROL STUDY.

Nickel JC, Tripp DA, Pontari M, Moldwin R, Mayer R, Carr LK, Doggweiler R, Yang CC, Mishra N, Nordling J. Can Urol Assoc J. 2011 Dec;5(6):410-5. doi: 10.5489/cuaj.11110. PMID: 22154637

Free Access

In this study from Canada, the authors wanted to determine and compare the prevalence and impact of childhood traumatic events, with an emphasis on childhood sexual abuse, on patient symptoms, quality of life and other biopsychosocial parameters. Questionnaires were completed by 207 IC/BPS

patients and 117 controls matched for age, partner status and education. It was found that before 17 years of age, the IC/BPS cases reported higher prevalence of "raped or molested" compared to controls (24.0% vs. 14.7%; p = 0.047). Within the IC/BPS group, cases reporting previous sexual abuse endorsed greater sensory pain, depression and poorer physical quality of life at the present time compared to IC cases without a sexual abuse history. In the controls only, those reporting previous sexual abuse endorsed more depression, anxiety, stress, social maladjustment poorer mental quality of life in the present time. When the analysis was corrected for potential multiple comparison error, none of the findings remained significant in either the IC/BPS or control groups. Childhood traumatic events, in particular sexual abuse and extreme illness, are reported as more common in IC/BPS patients than controls. Early trauma, such as the occurrence of sexual abuse, is associated with some differences in patient adjustment (e.g., pain, quality of life, depression) but this impact appears to be, at most, very modest.

BOTULINUM TOXIN

INCREASED LEVELS OF SV2A BOTULINUM NEUROTOXIN RECEPTOR IN CLINICAL SENSORY DISORDERS ANDFUNCTIONAL EFFECTS OF BOTULINUM TOXINS A AND E IN CULTURED HUMAN SENSORY NEURONS.

Yiangou Y, Anand U, Otto WR, Sinisi M, Fox M, Birch R, Foster KA, Mukerji G, Akbar A, Agarwal SK, Anand P. J Pain Res. 2011;4:347-55. Epub 2011 Oct 18. PMID: 22090803

Free Access

According to Yiangou and colleagues from Imperial College London, Hammersmith Hospital, London, there is increasing evidence that botulinum neurotoxin A may affect sensory nociceptor fibers, but the expression of its receptors in clinical pain states, and its effects in human sensory neurons, are largely unknown. The authors studied synaptic vesicle protein subtype SV2A, a receptor for botulinum neurotoxin A, by immunostaining in a range of clinical tissues, including human dorsal root ganglion sensory neurons, peripheral nerves, the urinary bladder, and the colon. They also determined the effects of botulinum neurotoxins A and E on localization of the capsaicin receptor, TRPV1, and functional sensitivity to capsaicin stimuli in cultured human dorsal root ganglion neurons. Image analysis showed that SV2A immunoreactive nerve fibers were increased in injured nerves proximal to the injury (P = 0.002), and in painful neuromas (P = 0.0027); the ratio of percentage area SV2A to neurofilaments (a structural marker) was increased proximal to injury (P = 0.0022) and in neuromas (P = 0.0001), indicating increased SV2A levels in injured nerve fibers. In the urinary bladder, SV2A nerve fibers were found in detrusor muscle and associated with blood vessels, with a significant increase in idiopathic detrusor over-activity (P = 0.002) and painful bladder syndrome (P = 0.0087). Colon biopsies showed numerous SV2A-positive nerve fibers, which were increased in quiescent inflammatory bowel disease with abdominal pain (P = 0.023), but not in inflammatory bowel disease without abdominal pain (P = 0.77) or in irritable bowel syndrome (P = 0.13). In vitro studies of botulinum neurotoxin A-treated and botulinum neurotoxin E-treated cultured human sensory neurons showed accumulation of cytoplasmic vesicles, neurite loss, and reduced immunofluorescence for the heat and capsaicin receptor, TRPV1. Functional effects included dose-related inhibition of capsaicin responses on calcium imaging after acute treatment with botulinum neurotoxins A and E. The authors concluded that differential levels of SV2A protein expression in clinical disorders may identify potential new targets for botulinum neurotoxin therapy. In vitro studies indicate that treatment with botulinum neurotoxins A and E may affect receptor expression and nociceptor function in sensoryneurons.

KETAMINE CYSTITIS

SEXUAL DYSFUNCTION IN WOMEN WITH KETAMINE CYSTITIS: A CASE-CONTROL STUDY.

Jang MY, Long CY, Chuang SM, Huang CH, Lin HY, Wu WJ, Juan YS. BJU Int. 2011 Dec 16. doi: 10.1111/j.1464-410X.2011.10780.x. [Epub ahead of print]. PMID: 22176970

Jang and colleagues note that increasing problems of ketamine-associated cystitis are being seen in daily clinical practice. Extreme ketamine abuse not only damages the bladder and results in bladder wall fibrosis, but also causes bladder mucosa ulcers. The present case-control study investigated clinical symptom severity and sexual dysfunction in women with KC. In total, 29 patients with KC and 27 controls completed the symptoms survey. Participants completed a visual pelvic pain analogue scale, an O'Leary-Sant Interstitial Cystitis Symptom Index and Problem Index questionnaire, a Female Sexual Function Index, and a short form of the Chinese Health Questionnaire-12. Both the Interstitial Cystitis Symptom Index and Interstitial Cystitis Problem Index scores were significantly higher in patients with KC compared to controls ($P < 0.001$). The prevalence of sexual dysfunction was high in patients with KC. There was no significant difference between patients with KC and controls with respect to mental health as evaluated by the Chinese Health Questionnaire-12. The authors concluded that sexual dysfunction and KC symptoms severely impacted on quality of life but that mental health had no significant difference between patients with KC and controls.

KETAMINE USE: A REVIEW.

Morgan CJ, Curran HV; the Independent Scientific Committee on Drugs (ISCD). Addiction. 2012 Jan;107(1):27-38. doi: 10.1111/j.1360-0443.2011.03576.x. Epub 2011 Jul 22. PMID: 21777321

Morgan and Curran from the Clinical Psychopharmacology Unit, Clinical Health Psychology, University College London, London, UK, note that while ketamine remains an important medicine in both specialist anaesthesia and aspects of pain management, its use as a recreational drug has spread in many parts of the world during the past few years. There are now increasing concerns about the harmful physical and psychological consequences of repeated misuse of this drug. The aim of this review was to survey and integrate the research literature on physical, psychological and social harms of both acute and chronic ketamine use. They found that a major physical harm is ketamine induced ulcerative cystitis which, although its aetiology is unclear, seems particularly associated with chronic, frequent use of the drug. Frequent, daily use is also associated with neurocognitive impairment and, most robustly, deficits in working and episodic memory. Recent studies suggest certain neurological abnormalities which may underpin these cognitive effects. Many frequent users are concerned about addiction and report trying but failing to stop using ketamine. The implications of these findings are drawn out for treatment of ketamine-induced ulcerative cystitis in which interventions from urologists and from addiction specialists should be coordinated. Neurocognitive impairment in frequent users can impact negatively upon achievement in education and at work, and also compound addiction problems. Prevention and harm minimization campaigns are needed to alert young people to these harmful and potentially chronic effects of ketamine.

CYSTITIS AND KETAMINE ASSOCIATED BLADDER DYSFUNCTION.

García-Larrosa A, Castillo C, Ventura M, Lorente JA, Bielsa O, Arango O. Actas Urol Esp. 2011 Sep 26. [Epub ahead of print]. PMID: 21955556

Free Access (in Spanish with English abstract)

The purpose of this study from Barcelona was to analyze the prevalence of lower urinary tract symptoms (LUTS) in 13 recreational ketamine users and evaluate its relationship with the consumption pattern. The authors analyzed the presence of LUTS, gross haematuria and lumbar spine pain. The ketamine usage pattern was recorded: initiation, administration route, dose in the last month and frequency of usage. On the basis of their results, the authors concluded that there seems to be a relationship between the picture with the dose and frequency of consumption, since there are factors that reinforce the hypothesis that this action of the drug is due to the harmful effect on the urothelium. The process to identify it on time should be known, since the only known effective measure is to stop the consumption in the initial phases.

CHRONIC PELVIC PAIN

UROLOGIC CHRONIC PELVIC PAIN.

Potts JM, Payne CK. Pain. 2011 Dec 5. [Epub ahead of print]. PMID: 22153018

Topical Review

Urologic chronic pelvic pain (UCPP), primarily interstitial cystitis (IC)/painful bladder syndrome (PBS) in men and women, and chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS) in men, were initially regarded as bladder and prostate diseases. Decades of research have failed to establish infectious or other clear etiologies; in fact, bladder/prostate inflammation is uncommon. Most patients are best characterized as having a functional somatic syndrome (FSS). Current theory focuses on hyperesthesia/allodynia and pelvic floor muscle dysfunction (PFD). The authors propose that urologic chronic pelvic pain syndromes are best considered as FSS and not as a urological condition. A logical approach focused on individualized therapy for patients with FSS is warranted to improve patient care and to reduce the burden to the healthcare system.

PAIN

TARGETING THE VISCERAL PURINERGIC SYSTEM FOR PAIN CONTROL.

Burnstock G. Curr Opin Pharmacol. 2011 Oct 28. [Epub ahead of print]. PMID: 22036885

Experimental evidence is presented by Burnstock from the Autonomic Neuroscience Centre, University College Medical School, London, UK to support the hypothesis that purinergic mechanosensory transduction can initiate visceral pain in urinary bladder, ureter, gut and uterus. In general, physiological reflexes are mediated via P2X3 and P2X2/3 receptors on low threshold sensory fibres, while these receptors on high threshold sensory fibres mediate pain. Potential therapeutic strategies are considered for the treatment of visceral pain in such conditions as renal colic, interstitial cystitis and inflammatory bowel disease by purinergic agents, including P2X3 and P2X2/3 receptor antagonists that are orally bioavailable and stable in vivo and agents that modulate ATP release and breakdown.

CENTRAL PAIN MECHANISMS IN CHRONIC PAIN STATES - MAYBE IT IS ALL IN THEIR HEAD.

Phillips K, Clauw DJ. Best Pract Res Clin Rheumatol. 2011 Apr;25(2):141-54. PMID: 22094191

This is an interesting article from Michigan in which Phillips and Clauw investigate mechanisms underlying chronic pain which differ from those underlying acute pain. In chronic pain states, central nervous system (CNS) factors appear to play particularly prominent roles. In the absence of anatomical causes of persistent pain, medical sub-specialities have historically applied wide-ranging labels (e.g., fibromyalgia (FM), irritable bowel syndrome, interstitial cystitis and somatisation) for what now is emerging as a single common set of CNS processes. The hallmark of these 'centrally driven' pain conditions is a diffuse hyperalgesic state identifiable using experimental sensory testing, and corroborated by functional neuroimaging. The characteristic symptoms of these central pain conditions include multifocal pain, fatigue, insomnia, memory difficulties and a higher rate of co-morbid mood disorders. In contrast to acute and peripheral pain states that are responsive to non-steroidal anti-inflammatory drugs (NSAIDs) and opioids, central pain conditions respond best to CNS neuromodulating agents, such as serotonin-norepinephrine reuptake inhibitors (SNRIs) and anticonvulsants.

INCIDENCE AND IMPACT OF PAIN CONDITIONS AND COMORBID ILLNESSES.

Davis JA, Robinson RL, Le TK, Xie J. J Pain Res. 2011;4:331-45. Epub 2011 Oct 10. PMID: 22090802

Free Access

Individuals with pain often present with more than one painful condition. The purpose of this study was to characterize the rates of comorbidity, pain medication use, and health care costs for 23 selected pain conditions in a large health plan using administrative claims data from 2005 to 2007.

Eligible patients included 1,211,483 adults with at least one pain condition during the one-year study period. Pain condition cohorts were classified based on the first diagnosis present in the claims during the study period. Musculoskeletal pain conditions were among the most prevalent cohorts including low back pain, osteoarthritis, and fibromyalgia. Cancer pain was the least prevalent cohort. Conditions with the lowest illness severity included migraine and painful bladder syndrome cohorts, while cohorts with diabetic neuropathy, human immunodeficiency virus (HIV)-associated pain, and cancer pain were the most severe. Across cohorts, the mean number of comorbid pain conditions ranged from 1.39 (for cancer pain and migraine) to 2.65 (for multiple sclerosis pain). High rates of mental health conditions were found in cohorts with HIV-associated pain and multiple sclerosis pain (42.59% and 34.78%) and were lowest among cohorts with rheumatoid arthritis and psoriatic arthropathy (12.73% and 13.31%), respectively. Rates of sleep disorders ranged from 5.47% (for painful bladder syndrome) to 11.59% (for multiple sclerosis pain). Overall, patients averaged 3.53 unique pain medications during the study period. Considerable annual total health care costs were observed in the cancer pain cohort and the lowest costs were observed in the postherpetic neuropathy, surgically-induced pain, migraine, and irritable bowel syndrome cohorts. Costs attributed to pain were highest among the multiple sclerosis, HIV, and cancer pain cohorts. The highest pharmaceutical costs were observed in the HIV cohort. These findings underscore the heterogeneity of patients with pain in terms of burden of illness, costs to the health care system, and the complexity of commonly co-occurring disorders.

FIBROMYALGIA

THE PREVALENCE OF FIBROMYALGIA IN OTHER CHRONIC PAIN CONDITIONS.

Yunus MB. Pain Res Treat. 2012;2012:584573. Epub 2011 Nov 17. PMID: 22191024

Free Access

Central sensitivity syndromes (CSS) include fibromyalgia syndrome (FMS), irritable bowel syndrome, temporomandibular disorder, restless legs syndrome, chronic fatigue syndrome, and other similar chronic painful conditions that are based on central sensitization (CS). CSS are mutually associated. In this paper, prevalence of FMS among other members of CSS has been described. An important recent recognition is an increased prevalence of FMS in other chronic pain conditions with structural pathology, for example, rheumatoid arthritis, systemic lupus, ankylosing spondylitis, osteoarthritis, diabetes mellitus, and inflammatory bowel disease. Diagnosis and proper management of FMS among these diseases are of crucial importance so that unwarranted use of such medications as corticosteroids can be avoided, since FMS often occurs when RA or SLE is relatively mild. CSS diseases are based on a neurochemical pathology, and they are not psychological or psychiatric illnesses. Associated psychosocial issues, as may be present in any chronic disease, including RA or SLE or cancer should be addressed. CSS conditions are mutually associated, and a particular patient may have several of them. Multiple symptoms in these patients have a demonstrable pathophysiological basis and do not represent somatization. It is most important that FMS is suspected in all chronic diseases with structural pathology, for example, RA, SLE, OA, and AS, so that proper diagnosis and management can be undertaken

NEUROBIOLOGY UNDERLYING FIBROMYALGIA SYMPTOMS.

Ceko M, Bushnell MC, Gracely RH. Pain Res Treat. 2012;2012:585419. Epub 2011 Oct 27. PMID: 22135739

Free Access

Fibromyalgia is characterized by chronic widespread pain, clinical symptoms that include cognitive and sleep disturbances, and other abnormalities such as increased sensitivity to painful stimuli, increased sensitivity to multiple sensory modalities, and altered pain modulatory mechanisms. Here Ceko and colleagues from Canada relate experimental findings of fibromyalgia symptoms to anatomical and functional brain changes. Neuroimaging studies show augmented sensory processing in pain-related areas, which, together with gray matter decreases and neurochemical abnormalities

in areas related to pain modulation, supports the psychophysical evidence of altered pain perception and inhibition. Gray matter decreases in areas related to emotional decision making and working memory suggest that cognitive disturbances could be related to brain alterations. Altered levels of neurotransmitters involved in sleep regulation link disordered sleep to neurochemical abnormalities. Thus, current evidence supports the view that at least somefibromyalgia symptoms are associated with brain dysfunctions or alterations, giving the long-held "it is all in your head" view of the disorder a new meaning.

OBSERVATION-BASED ASSESSMENT OF FUNCTIONAL ABILITY IN PATIENTS WITH CHRONIC WIDESPREAD PAIN: A CROSS-SECTIONAL STUDY.

Amris K, Wæhrens EE, Jespersen A, Bliddal H, Danneskiold-Samsøe B. Pain. 2011 Nov;152(11):2470-6. Epub 2011 Jun 28. PMID: 21715094

Knowledge about functional ability, including activities of daily living (ADL), in patients with chronic widespread pain (CWP) and fibromyalgia (FMS) is largely based on self-report. The purpose of this study from Denmark was to assess functional ability by using standardised, observation-based assessment of ADL performance and to examine the relationship between self-reported and observation-based measures of disability. A total of 257 women with CWP, 199 (77%) fulfilling the American College of Rheumatology tender point criteria for FMS, were evaluated with the Assessment of Motor and Process Skills (AMPS), an observation-based assessment providing linear measures of ADL motor and ADL process skill ability (unit: logits). A cutoff for effortless and independent ADL task performance is set at 2.0 for the motor scale and 1.0 for the process scale. A total of 248 (96.5%) had ability measures below the 2.00 ADL motor cutoff and 107 (41.6%) below the 1.00 ADL process cutoff, indicating increased effort and/or inefficiency during task performance as well as a potential need of assistance for community living. Mean ADL motor ability measure was 1.07 and was significantly lower in patients diagnosed with FMS than plain CWP (1.02 vs 1.27 logits, P=.001). Mean ADL process ability measure was 1.09 logits and was without difference between FMS and plain CWP (1.07 vs 1.16 logits, P=.064). Only weak to moderate correlations between self-reported functional ability and observation-based AMPS ability measures were observed. The results of the study support the notion of considerable performance difficulties in women with CWP. The everyday life problems are substantial and place the individual at risk of need of support for community living.

See also comment in Pain. 2011 Nov;152(11):2449-50.

THE QUALITY OF WEBSITES ADDRESSING FIBROMYALGIA: AN ASSESSMENT OF QUALITY AND READABILITY USING STANDARDISED TOOLS.

Daraz L, Macdermid JC, Wilkins S, Gibson J, Shaw L. BMJ Open. 2011 Jan 1;1(1):e000152. Epub 2011 Jul 31. PMID: 22021777

According to Daraz and colleagues, patients living with fibromyalgia greatly prefer to access health information on the web. However, the majority of subjects in previous studies strongly expressed their concerns about the quality of online information resources. The purpose of this study from Canada was to evaluate existing online fibromyalgia information resources for content, quality and readability by using standardised quality and readability tools. The first 25 websites were identified using Google and the search keyword 'fibromyalgia'. Pairs of raters independently evaluated website quality using two structured tools (DISCERN and a quality checklist). Readability was assessed using the Flesch Reading Ease score maps. They found that ranking of the websites' quality varied by the tool used, although there was general agreement about the top three websites Fibromyalgia Information, Fibromyalgia Information Foundation and National Institute of Arthritis and Musculoskeletal and Skin Diseases). Content analysis indicated that 72% of websites provided information on treatment options, 68% on symptoms, 60% on diagnosis and 40% on coping and resources. DISCERN ratings classified 32% websites as 'very good', 32% as 'good and 36% as 'marginal'. The mean overall DISCERN score was 36.88 (good). Only 16% of websites met the

recommended literacy level grade of 6-8 (range 7-15). They concluded that higher quality websites tended to be less readable. Online fibromyalgia information resources do not provide comprehensive information about fibromyalgia, and have low quality and poor readability. While information is very important for those living with fibromyalgia, current resources are unlikely to provide necessary or accurate information, and may not be usable for most people.

CHARACTERISTICS OF SUITABLE WORK FROM THE PERSPECTIVE OF PATIENTS WITH FIBROMYALGIA.

Bossema ER, Kool MB, Cornet D, Vermaas P, de Jong M, van Middendorp H, Geenen R. Rheumatology (Oxford). 2011 Oct 22. [Epub ahead of print]. PMID: 22019800

Bearing in mind that the evaluation of work ability of patients with FM is difficult, the aim of Bossema and colleagues from Utrecht, the Netherlands was to investigate the characteristics of suitable work from the perspective of patients with FM. Interviews with patients yielded statements about characteristics of suitable work. Patients individually sorted these statements according to similarity. Hierarchical cluster analysis was applied to these sortings. The hierarchical structure included 74 characteristics of suitable work. The 10 clusters at the lowest level included (i) recovery opportunities, (ii) pace of work, (iii) not too high workload, (iv) keeping energy for home and free time, (v) match between work and capabilities, (vi) development opportunities, (vii) understanding from colleagues, (viii) help from colleagues, (ix) support from management and (x) work agreements with management. According to patients with FM, suitable work is paced in such a way that one can perform the job well and with satisfaction while keeping energy for home and free time and having acknowledgement and help from management and colleagues. The brief suitable work checklist that is provided can help patients with FM to negotiate with employers and job professionals to improve the match between job demands and capabilities.

DEVELOPMENT AND TESTING OF THE FIBROMYALGIA DIAGNOSTIC SCREEN FOR PRIMARY CARE.

Arnold LM, Stanford SB, Welge JA, Crofford LJ. J Womens Health (Larchmt). 2011 Dec 14. [Epub ahead of print]. PMID: 22165952

The Fibromyalgia Diagnostic Screen was developed for use by primary care clinicians to assist in the diagnostic evaluation of fibromyalgia, a disorder that predominantly affects women.The screen was designed to have a patient-completed questionnaire and a clinician-completed section, which included a brief physical examination pertinent to the differential diagnosis of fibromyalgia. The items in the questionnaire were based on patient focus groups and clinician and patient Delphi exercises, which resulted in a ranking of the most common and troublesome fibromyalgia symptoms. One hundred new chronic pain patients (pain > 30 days) and their primary care physicians completed the screen. The patients were grouped as fibromyalgia or non-fibromyalgia by an independent fibromyalgia specialist, who was blind to screen responses. Logistic regression was used to model the probability of fibromyalgia as a function of physician-reported and patient-reported variables. Best subset regression was used to identify a subset of symptoms that were summed to form a single measure. Receiver operating characteristic (ROC) analysis was then used to select thresholds for continuous variables. The symptom and clinical variables were combined to create candidate prediction rules that were compared in terms of sensitivity and specificity to select the best criterion. Two final models were selected based on overall accuracy in predicting fibromyalgia: one used the patient-reported questionnaire only, and the other added a subset of the physical examination items to this patient questionnaire. The authors concluded that a patient-reported questionnaire with or without a brief physical examination may improve identification of fibromyalgia patients in primary care settings.

DELIRIUM SECONDARY TO PREGABALIN.

Hickey C, Thomas B. Gen Hosp Psychiatry. 2011 Dec 14. [Epub ahead of print] PMID: 22177026

More recently, pregabalin has been approved to treat pain associated with fibromyalgia. However, it can have serious neuropsychiatric consequences. Several case reports have documented delirium secondary to pregabalin, usually in older patients with multiple medical comorbidities and

concurrent medications. The authors describe a case of delirium in a young patient without significant medical problems and in the absence of other potentially causal medications. In this case, pregabalin appears to be the single causal etiology for delirium. They recommend clinicians to consider the causal role it may play in any patient who presents with delirium.

MULTIPLE CHEMICAL SENSITIVITY

PHYSICIANS' PERCEPTIONS AND PRACTICES REGARDING PATIENT REPORTS OF MULTIPLE CHEMICAL SENSITIVITY.

Gibson PR, Lindberg A. ISRN Nurs. 2011;2011:838930. Epub 2011 Sep 7. PMID: 22007328

Free Access

Ninety physicians practicing in the state of Virginia USA completed a mail survey regarding Multiple Chemical Sensitivity (MCS). Survey questions addressed demographics; familiarity with MCS; etiology; overlapping conditions; accommodations made for patients and practices regarding evaluation, treatment, and referral. A little over half of respondents were familiar with MCS. Under a third had received any medical training regarding chemical sensitivity, only 7% were "very satisfied" with their knowledge, and 6% had a treatment protocol for the condition. Participants cited a range of etiologies and overlapping conditions including asthma, Reactive Airway Dysfunction Syndrome (RADS), Sick Building Syndrome (SBS), Chronic Fatigues Syndrome (CFS), and Fibromyalgia. Physicians infrequently considered chemicals as a cause of illness when seeing new patients. Evaluation techniques included interviews, blood work, immune profiles, and allergy testing. Interventions recommended included chemical avoidance, alterations in the home environment, diet restrictions, the use of air filters, and referrals to outside specialists.

IRRITABLE BOWEL SYNDROME (IBS)

THE IMPORTANCE OF RELATIONSHIPS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME: A REVIEW.

Gerson MJ, Gerson CD. Gastroenterol Res Pract. 2012;2012:157340. Epub 2011 Dec 1. PMID: 22190912

Free Access

Chronic illnesses such as irritable bowel syndrome are not experienced by patients in isolation. They live in a context of relationships, including spouses and partners, other family members, friends and business associates. Those relationships can have an effect, both positive and negative, on the course of illness and may also be affected by the experience of living with a chronic illness like IBS. The authors review the general literature regarding the effect of relationship factors on chronic illness followed by a focus on IBS symptomatology. They then discuss the challenges experienced by partners of IBS patients, followed by the effects of spousal violence, the particular relationship of mothers with IBS and their children, the effects of social support, and the importance of family dynamics and IBS. The final segment includes conclusions and recommendations. The topic, relationships and IBS, may have a significant effect on the lives of IBS patients and deserves more attention than it has received.

IRRITABLE BOWEL SYNDROME - AN INFLAMMATORY DISEASE INVOLVING MAST CELLS.

Philpott H, Gibson P, Thien F. Asia Pac Allergy. 2011 Apr;1(1):36-42. Epub 2011 Apr 26. PMID: 22053295

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Irritable bowel syndrome (IBS) is traditionally defined as a functional disorder - that is the presence of symptoms in the absence of demonstrable pathological abnormalities. In recent times, low grade inflammatory infiltrates in both the small and large bowel of some patients with IBS - often rich in mast cells, along with serological markers of low grade inflammation have focussed attention on IBS as an inflammatory disease. The observation that mast cells often lie in close association to enteric neurons, and in-vitro and in-vivo animal studies demonstrating that mast cell mediators may

influence enteric motility provides a biologically plausible causal mechanism in IBS. Pilot studies on patients with IBS using the mast cell stabiliser sodium cromoglycate ('proof of concept') have been encouraging. The essential question remains why mast cells infiltrate the bowel of IBS patients. A disturbance of the 'brain-gut axis' is the current favoured hypothesis, whereby childhood stress or psychiatric comorbidity act via neuro-immune mechanisms to modulate low grade inflammation. An alternative hypothesis is that food allergy may be responsible. Serum specific IgE, and skin prick tests are not elevated in IBS patients, suggesting type 1 IgE mediated food allergy is not the cause. However questionnaire-based studies indicate THAT IBS patients have higher rates of atopic disease, and increased bronchial reactivity to methacholine has been demonstrated. In this review from Australia, the authors highlight the potential role of mast cells in IBS, and current and future research directions into this intriguing condition.

ENDOMETRIOSIS IN URINARY TRACT

PREVALENCE AND MANAGEMENT OF URINARY TRACT ENDOMETRIOSIS: A CLINICAL CASE SERIES.
Gabriel B, Nassif J, Trompoukis P, Barata S, Wattiez A. Urology. 2011 Dec;78(6):1269-74. Epub 2011 Sep 29. PMID: 21962747

The purpose of this study was to report on the prevalence, surgical management, and outcome of urinary tract endometriosis (UTE) in a cohort of 221 patients undergoing laparoscopic surgery for severe endometriosis. UTE can cause significant morbidity, such as silent kidney or progressive renal function loss. Its frequency is underestimated and data on laparoscopic management are scarce. Between 2007 and 2010, 43 patients were eligible for this single-centre, retrospective study. The inclusion criterion was the presence of UTE (ie, bladder and/or ureteral endometriosis). All patients were operated laparoscopically. The prevalence of UTE was 19.5% (43/221). There was no correlation between bladder and ureteral endometriosis. Ureteral endometriosis was associated with patient's age. Patients with bladder, but not ureteral, involvement complained more frequently about dysuria, hematuria, and urinary tract infections. Intraoperative and magnetic resonance imaging (MRI) findings revealed a moderate to good correlation. UTE was not associated with rectovaginal or bowel endometriosis, but rather with involvement of the uterosacral ligaments. Twenty-two patients with bladder endometriosis were treated by mucosal skinning and 11 patients underwent partial cystectomy. Superficial ureteral excision was performed in 4 patients, whereas resection with ureteroureterostomy was done in 9 patients. There was no difference regarding the intra- and postoperative complications in patients with or without UTE. The authors concluded that in severe pelvic endometriosis, involvement of the urinary tract is quite common. Laparoscopic management is feasible and safe. Because of the lack of specific symptoms, the preoperative diagnosis of ureteral endometriosis still remains a challenge. They suggest that pelvic MRI represents a useful preoperative diagnostic tool.

VULVODYNIA

CHARACTERISTICS OF THE PAIN OBSERVED IN THE FOCAL VULVODYNIA SYNDROME (VVS).
Donders G, Bellen G. Med Hypotheses. 2012 Jan;78(1):11-4. Epub 2011 Oct 29. PMID: 22041052

Symptoms and signs of patients with focal vulvodynia or vulvo-vestibulitis syndrome (VVS) are variable in location and severity. It is not known whether the location of the most severe pain in the vestibulum is linked to the complaints and perhaps a different entity. According to Donders and colleagues from Belgium, clinical gut feeling suggests that two distinct varieties of focal vulvodynia may be either focused at 2 points (5 and 7 o' clock) or at 4 points (5, 7, 1 and 11 o' clock). A questionnaire was filled out by 30 women with focal vulvodynia during 147 visits and checked for completeness by an independent study nurse. Another investigator evaluated the clinical signs of VVS, blinded to the patients´ history or complaints. The visual analogue score (VAS) of pain experienced when attempting sexual contact was used as a marker of severity. Focal vulvar pain was assessed using Q-tip with a score from 1 to 10 on 7 areas of the vestibulum. In addition to pain

during sexual contact, 47% also had pain on inserting a tampon. More than 40% of women have suffered for more than 3years, 70% had to interrupt the act of sexual intercourse mostly or always due to unbearable pain and 25% never had satisfactory sex due to this pain. Feeling deep pain, burning lasting for 12-24h after sexual contact, and stopping attempted intercourse were more prominent in women with high pain scores (VAS): 26% of women with VAS >7 had no sex during the last year versus 6% in the group with low pain score (p=0.004). The authors note that patients suffering from para-urethral pain zones at 1 and 11 o' clock, more often have pain upon deep penetration, and experienced more pain when inserting tampons than patients with only painful areas at 5 and 7 o' clock (p=0.001). They concluded that patients with severe disease display a different panel of complaints than women with less pain. Patients with focal pain at 1 and 11 o' clock have more deep pain sensations, but feel less pain during insertion of tampons. Hence disease with bi-focal disease may have a different ethiopathogenesis that 4-focal disease. They suggest that glands of Bartholin and Skene may be involved in this pathogenenis.

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