

# 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 26, July 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:

- **AUA 2011 Review of Research and Courses**
- **International Continence Society annual scientific meeting 2011**
- **News from Patient Organisations + Congresses**
- **Websites, Book & Videos**
- **Upcoming Meetings**
- **Research Highlights**
- **Donations & Sponsoring**

## **AUA 2011 REVIEW OF RESEARCH AND COURSES**

A review of research presented at the AUA this year in the field of IC and related topics can be found on our website. [Click here.](#)

Delegates also had a choice of three interesting AUA courses and we will therefore now take the opportunity to pick out just a few useful pointers and tips from each of these:

*- INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A PRIMER AND A WORLD VIEW. Course director Philip Hanno, MD with additional speakers David Burks, MD, Jorgen Nordling, MD and Arndt van Ophoven, MD.*

This course book - which was a reference book in itself - had a very useful background section as well as a detailed diagnostic work-up, with a reminder of the need for thorough exclusion of confusable diseases (while not forgetting of course that patients may have IC + a confusable disease).

It was suggested here that ulcerated "Hunner-type" bladder and non-ulcerated bladder should now be considered and treated as two separate entities. This is also echoed in one of the articles reviewed under the section on new research in this e-newsletter: *ARE ULCERATIVE AND NONULCERATIVE INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME 2 DISTINCT DISEASES? A STUDY OF COEXISTING CONDITIONS. Peters KM, Killinger KA, Mounayer MH, Boura JA. Urology. 2011 Jun 22. [Epub ahead of print].*

On the subject of biopsies, it was explained that it should be borne in mind that one can see completely normal biopsies in non-Hunner-type patients. The same applies to cystoscopies: in the past patients with normal looking bladders were sent home without a diagnosis since it was thought that glomerulations were mandatory. This is not the case now and the bladders of patients with severe symptoms may appear absolutely normal. However, finding a Hunner's ulcer or lesion as it is now more correctly referred to is a positive finding that can confirm the diagnosis of Hunner type IC. There was a reminder of treatment specifically for patients with Hunner's lesion: neodymium YAG-laser, transurethral resection (TUR), coagulation. This kind of surgical destruction of lesions has proven to be very effective in patients with a Hunner-type bladder

On treatment in general, while much attention was paid to pain (“the question is not should the patient receive pain treatment, but why should the patient be left in pain?”), it was nevertheless emphasised that pain management alone does not constitute sufficient treatment, it is simply one component. Patients should also be treated for the underlying bladder-related symptoms.

- *PELVIC PAIN SYNDROMES: PRACTICAL AND MULTIDISCIPLINARY APPROACHES TO DIAGNOSES AND MANAGEMENT.* Course director Robert J. Evans, MD with additional speakers Deborah Erickson, MD. A reminder in this course that when patients with overactive bladder (OAB) fail to respond to OAB (anticholinergic) treatment, IC should be considered.

IC may be being misdiagnosed:

- in women as recurrent UTIs, overactive bladder, endometriosis, dyspareunia.
- in men as prostatitis, epididymia, scrotal pain.

It was emphasised here: do not think that IC is a disease that affects only the middle aged, because it is not. It affects all ages including children. Early diagnosis can avoid unnecessary, inappropriate and invasive treatment, can restore better quality of life and might prevent prolongation and worsening of symptoms.

- *PELVIC PAIN: COMMON CAUSES AND PRACTICAL SOLUTIONS.* Course director Robert Moldwin, MD, with additional speaker Jennifer Fariello, MSN, CRNP.

This course described the increasing prevalence of functional pelvic and vulvar pain and the association with various urological and gynaecological conditions, identifying comorbid conditions that might complicate the diagnosis and the management and care of these patients.

Whatever the name you give it (BPS/IC, PBS/IC, IC/PBS...), this can be described as allodynia of the bladder with/without inflammation. (Allodynia is a painful response to a stimulus that does not usually elicit pain).

On criteria for diagnosis: IC Diagnosis rule - the stricter the criteria...the more homogeneous the patient population but.....the more patients left untreated. This of course presents a dilemma for researchers.

On how to make the diagnosis:

- Typical symptoms
- Lack of other identifiable diseases
- Identify other pain generators
- Confirmatory testing to establish the bladder as a source of symptoms
- If therapy is not effective, consider other diagnosis or co-existing conditions.
- Emphasis on paying attention to co-existing conditions when evaluating any of the chronic pelvic pain syndromes.

A warning was given here about being on the alert for ketamine cystitis caused by ketamine abuse; see more articles on this topic in our Research section of this e-newsletter.

**Diet:** for many patients, diet modification is a mainstay of self-help. The main food/drink groups that may cause irritation of the bladder are: acidic food/drink, caffeinated drinks (especially coffee) and hot spicy foods. However, every patient is individual, not every patient is sensitive to every food and the patient needs to work out what may be causing the irritation through an elimination diet. However, we would add medication to this list since some medicines can irritate the bladder as much as a glass of grapefruit juice.

This course paid considerable attention to pelvic floor dysfunction (PFD). IC patients are particularly at risk of developing this through chronic pain and tight, stressed muscles. Typical symptoms of PFD in IC patients are:

Urinary hesitancy	75%
Decreased force of stream	75%
Sense of incomplete void straining with urination	73%
Straining with urination	70%
Constipation	68%
Dyspareunia	45%
Low back pain	43%
History of urethral dilation	24%

Basic therapy for PFD includes no pushing or straining with urination, avoidance of constipation, warm baths twice a day, with the additional possibility of skeletal muscle relaxants and physical therapy.

## INTERNATIONAL CONTINENCE SOCIETY

### IPBF Booth #51

The 41<sup>st</sup> Annual Scientific Meeting of the International Continence Society (ICS) will be held in Glasgow, United Kingdom, 29 August-2 September 2011. Further information about this meeting can be found at: [www.ics-meeting.com](http://www.ics-meeting.com). The IPBF will have a booth at this meeting (#51), providing conference delegates with up-to-date information on interstitial cystitis and related disorders. If IC patient organisations would like their leaflets to be available for delegates on our info booth in Glasgow, please contact us at [ipbf@dds.nl](mailto:ipbf@dds.nl) as soon as possible.

### ICS Working Lunch to meet Medical and Patient Societies

The ICS plans to organise a working lunch "**ICS meets Continence Societies**" on Thursday, 1 September at 12.30, lasting approximately 45 minutes, to which it has great pleasure in inviting national medical societies, together with national and international patient/consumer organisations, concerned with urinary and faecal incontinence and bladder, bowel and pelvic floor disorders.

The programme for this lunch will include three presentations with time for discussion:

1. An overview of the history and current status of the ICS
2. Affiliation of national continence societies with the ICS and the benefits
3. Continence awareness initiatives of the ICS Continence Promotion Committee (CPC) and its associated patient/consumer organisations.

If you would like to attend this working lunch, please contact Jenny Ellis at the ICS Office on: [jenny@icsoffice.org](mailto:jenny@icsoffice.org) as soon as possible.

For the sake of clarity, the ICS regrets that it is unable to reimburse any costs of attending the ICS annual scientific meeting which will be your own responsibility. [Read online...](#)

### The ICS Public Forum

The 2011 ICS/CPC Public Forum will be held on Friday 2 September at the SECC conference centre in Glasgow, Scotland. A welcome reception with drinks and a light buffet will be held from 18.00-19.00 accompanied by a small consumer-oriented exhibition. The presentations will be held from 19.00-21.00. The Public Forum is a joint venture between the ICS Continence Promotion Committee (CPC) and local patient and professional organisations in the host country. This year the Public Forum will be chaired by the UK Bladder & Bowel Foundation. The Public Forum is a way of focusing the attention of the general public and international medical community on the reality of life for people with urinary, bowel and pelvic floor disorders. It is open to the general public, caregivers and healthcare professionals and provides the perfect opportunity for the ICS and CPC to raise awareness

of all aspects of bladder/bowel incontinence and pelvic floor disorders and to discuss issues of relevance to continence promotion.

The Public Forum is a *free* event open to 250 participants of the general public, including caregivers and healthcare professionals. You don't have to be registered for the Annual Scientific Meeting to be able to attend the Public Forum. [Read more...](#)

## **NEWS FROM PATIENT ORGANIZATIONS:**

### **IAPO 5TH GLOBAL PATIENTS CONGRESS RENAISSANCE LONDON HEATHROW HOTEL, 17–19 MARCH 2012**

The International Alliance of Patients Organizations is pleased to announce that the 5th Global Patients Congress will be held at the Renaissance, London Heathrow Hotel, 17–19 March 2012. The theme of this congress will be: Achieving Patient-Centred Healthcare: Indicators of Progress and Success. The 5th Global Patients 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 examine how meaningful indicators can be developed to measure patient involvement within healthcare systems. To register your interest in attending the congress and to receive further updates please email: [info@globalpatientscongress.org](mailto:info@globalpatientscongress.org). For general enquiries, please contact: International Alliance of Patients' Organizations, Email: [info@patientsorganizations.org](mailto:info@patientsorganizations.org), Website: [www.patientsorganizations.org](http://www.patientsorganizations.org).

### **- 11<sup>TH</sup> INTERNATIONAL SYMPOSIUM ON SJÖGREN'S SYNDROME" WILL INCLUDE MEETING OF COLLABORATING PATIENT ORGANISATIONS**

The 11th International Symposium on Sjögren's Syndrome will be held in Athens, Greece, 28 September-1 October 2011. This symposium aims to:

- Discuss the most recent scientific contributions in clinical and pathogenetic aspects of the disease
- Educate physicians and basic scientists willing to work with the disease
- To provide a forum for ideas exchange and potential collaboration.

High on the agenda will be discussion of the need for new criteria for diagnosing Sjögren's syndrome.

A meeting of collaborating patient organisations in this field (ISN) will also be held during the symposium. Further information about the symposium: <http://www.sjogrensymposium-athens2011.org/>. Information for patient organisations interested in participating in the network: Maggy Pincememin, email: [afgs-maggypincemin@orange.fr](mailto:afgs-maggypincemin@orange.fr).

## **WEBSITES, BOOKS AND VIDEOS**

### **CLINICAL TRIALS WEBSITES**

A reminder that if you want to check out what clinical trials are in progress or what stage they are at, go to the Clinicaltrials.gov website in the US:

<http://www.clinicaltrials.gov/ct2/search>

Type "interstitial cystitis, painful bladder syndrome, bladder pain syndrome" into the search bar and you will receive a list of current studies.

For Europe, you need to go to the European Medicines Agency Website for the clinical trials register: <http://www.ema.europa.eu> or go directly to the register page with search engine: <https://www.clinicaltrialsregister.eu/>

## **BOOK ON CHRONIC PELVIC PAIN**

*Chronic Pelvic Pain*

*Edited by Paolo Vercellini*

*Published by Wiley-Blackwell, 2011*

*ISBN: 978-1-4443-3066-3*

This book is written for gynaecologists as part of the Gynaecology in Practice series, but is an interesting and informative read for anyone involved in this complex topic. There are many potential causes of chronic pelvic pain and this book provides help in identification and diagnosis. All forms of treatment are covered, including a chapter on Alternative Treatments. There is a whole chapter on bladder pain syndrome and other urological causes of chronic pelvic pain by Daniela Wittman and J. Quentin Clemens.

## **IC-HOPE PRODUCES DVD FOR PATIENTS**

Cathy Simone from IC-Hope has produced a DVD by patients for patients in which patients tell about their experiences. Go to <http://www.ic-hope.com> for further information.

## **UPCOMING MEETINGS**

### **BRIEF CALENDAR OVERVIEW OF SELECTED UPCOMING MEETINGS IN 2011 and 2012**

#### **August**

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

#### **September**

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

#### **October**

- SOCIETE INTERNATIONALE D'UROLOGIE (SIU) Annual Congress, ICC Berlin 16-20 October

### **2012**

#### **February**

- EUROPEAN ASSOCIATION OF UROLOGY ANNUAL CONGRESS  
24-28 February, Paris, France

#### **March**

- INTERNATIONAL ALLIANCE OF PATIENTS' ORGANIZATIONS (IAPO)  
5<sup>th</sup> Global Patients Congress  
17-19 March, Renaissance London Heathrow Hotel, London UK

#### **May**

- ESSIC Annual Meeting, either 3-5 or 10-12 May,  
Porto, Portugal

- AMERICAN UROLOGICAL ASSOCIATION (AUA)  
19-24 May, Atlanta, GA, USA

#### **October**

- INTERNATIONAL CONTINENCE SOCIETY (ICS)  
15-19 October, Beijing, China

## **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.

#### GUIDELINE:

##### AUA GUIDELINE FOR THE DIAGNOSIS AND TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

*Hanno PM, Burks DA, Clemens JQ, Dmochowski RR, Erickson D, Fitzgerald MP, Forrest JB, Gordon B, Gray M, Mayer RD, Newman D, Nyberg L Jr, Payne CK, Wesselmann U, Faraday MM. J Urol. 2011 Jun;185(6):2162-70. Epub 2011 Apr 16. PMID: 21497847*

This article is a summary of the AUA Guideline for the diagnosis and treatment of IC/BPS. According to the panel, IC/BPS is best identified and managed through use of a logical algorithm as is presented in this Guideline. In the algorithm, the panel identifies an overall management strategy for the IC/BPS patient. However, the Panel notes that this document constitutes a clinical strategy and is not intended to be interpreted rigidly. The most effective approach for a particular patient is best determined by the clinician together with the patient. In other words, treatment needs to be customized per patient. The Panel emphasises that methods of diagnosis and treatment can be expected to change as the evidence base grows in the future. Furthermore, as scientific knowledge evolves and improves, the strategies presented here will require updating.

Please note that the full text of the AUA Guideline can be read online at:

[http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/ic-bps/diagnosis\\_and\\_treatment\\_ic-bps.pdf](http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/ic-bps/diagnosis_and_treatment_ic-bps.pdf)

#### KETAMINE AND THE BLADDER:

##### RECREATIONAL KETAMINE: FROM PLEASURE TO PAIN.

*Wood D, Cottrell A, Baker SC, Southgate J, Harris M, Fulford S, Woodhouse C, Gillatt D. BJU Int. 2011 Jun;107(12):1881-4. doi: 10.1111/j.1464-410X.2010.10031.x. Epub 2011 Feb 14. PMID: 21314885*

Ketamine is a so-called 'dissociative anaesthetic' that acts as a glutamatergic N-methyl-d-aspartate antagonist and is used clinically for anaesthesia and analgesia. Even when used clinically, it can have some strange side effects such as out-of-body sensation, hallucinations, nightmares and confusion.

In this paper from the United Kingdom, the authors note that it is precisely this dissociative sensation, known on the street as the 'K Hole', that attracts users. It is also cheap compared to alcohol, particularly in Asian countries where it is produced on a large scale. It is not only used as a street drug, but also in social circles recreationally. This review takes a look at the literature on the relationship between ketamine and urinary tracts symptoms, reporting that there is very little literature in this field. The authors note that an increasing number of UK urologists are seeing these patients and that they have formed a collaboration interested in understanding the pathology and establishing an effective treatment pathway for these patients. When used as a recreational drug (in often significantly higher doses than when used clinically), individuals using have developed urinary tract symptoms including a small painful bladder, ureteric obstruction, papillary necrosis and hepatic dysfunction. There has even been one report of ketamine-induced cystitis in a 13 year old. If the doctors are unaware of the ketamine abuse, these patients are often given treatment for urinary

tracts infections or IC/PBS. The authors report that their research has shown a clear link between ketamine abuse and damage to the urothelium. On the basis of their continued work and development with patients who are ketamine users, the authors suggest assessment and treatment that includes cessation of ketamine use and adequate analgesia to overcome symptoms. They emphasise that it is important for medical practitioners who encounter patients with these symptoms to ask about recreational drug use. Patients identified as suffering from this syndrome will need to be referred to a urological unit with an interest in the treatment of this specific condition. This is a most interesting paper and highly recommended for those interested in this growing problem.

KETAMINE EFFECTS ON THE UROGENITAL SYSTEM-CHANGES IN THE URINARY BLADDER AND SPERM MOTILITY.

*Tan S, Chan WM, Wai MS, Hui LK, Hui VW, James AE, Yeung LY, Yew DT. Microsc Res Tech. 2011 May 11. doi: 10.1002/jemt.21014. [Epub ahead of print]. PMID: 21563274*

A study from Hong Kong, China looking at the effects of long-term administration of ketamine in mice. Different doses of ketamine were injected into male ICR mice to determine the optimal dosage for studying the toxicity of long-term administration on the urinary bladder and sperm motility. At and above 40 mg/kg I.P. injection, mice had almost no hind limb movement during a swimming test. Subsequently, 30 mg/kg was used as the dose for the study. Apoptosis in the bladder epithelium was observed initially in the 3-month ketamine treated mice and the number of apoptotic cells was significantly different between the 3-month and 6-month ketamine treated mice and the control. The relative thickness of muscular layers in the bladder wall also decreased significantly when the 6-month treated mice and the control were compared. Sirius red staining revealed increase of collagen in the urinary bladder of the treated mice, most evidently 6 months after ketamine treatment. In addition, the sperm motility was studied and there was a statistically significant difference between the control and ketamine treated groups in the percentages of sperms which were motile. This suggested that the chronic administration of ketamine also affected the genital system.

THEME: KETAMINE USE AND ABUSE.

Davey M. Emerg Med J. 2011 Jul;28(7):552. PMID: 21700744

No abstract available.

IC/PBS/BPS/HBS:

ARE ULCERATIVE AND NONULCERATIVE INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME 2 DISTINCT DISEASES? A STUDY OF COEXISTING CONDITIONS.

*Peters KM, Killinger KA, Mounayer MH, Boura JA. Urology. 2011 Jun 22. [Epub ahead of print]. PMID: 21703668*

Coexisting conditions associated with interstitial cystitis/painful bladder syndrome (IC/PBS) have not been fully explored by IC/PBS subtypes. In this study, the authors compared comorbid diagnoses/symptoms in women with ulcerative (ULC) and nonulcerative (N-ULC) IC/PBS and controls. Adult women with IC/PBS and controls without IC/PBS completed a mailed survey assessing for 21 diagnoses. IC/PBS subtype was determined by hydrodistension reports. Standardised questionnaires assessed IC/PBS symptoms (Interstitial Cystitis Symptom/Problem Indexes [ICSI-PI]) and for undiagnosed fibromyalgia, irritable bowel syndrome, and depression (Symptom Intensity Score [SIS]; Rome III Functional Bowel Questionnaire; Center for Epidemiologic Studies Depression Scale [CES-D]). Notable differences in the number of comorbid diagnoses and symptoms were seen between IC/PBS subtypes and controls. The authors emphasise that subtypes should continue to be evaluated individually to ascertain other similarities and differences.

ON THE NATURE OF BLADDER SENSATION: THE CONCEPT OF SENSORY MODULATION.

*De Wachter SG, Heeringa R, van Koeveeringe GA, Gillespie JJ. Neurourol Urodyn. 2011 Jun 9. doi: 10.1002/nau.21038. [Epub ahead of print]. PMID: 21661031*

In this literature review, De Wachter and colleagues begin with a most significant statement: "Healthy people normally do not dwell upon their bladder", because going to the toilet is an essential and everyday event. However, when the system goes wrong, it dominates and complicates the life of those affected and may cause strong sensations and abnormal desires to void, sometimes resulting in incontinence. The authors remind us that a considerable amount of work has focused on this problem and produced ideas and concepts on the nature of bladder sensations. In this paper, however, they argue the necessity to return to first principles and a re-examination of the problem, suggesting that "focus groups" should be used to identify relevant bladder sensation and what triggers 'bladder' behaviour. They explain that it is their intention to stimulate debate and generate further research in the field in order to understand better the physiology of bladder sensation and the pathology of increased urge, frequency and incontinence. They conclude that a review of the literature on bladder sensation and the established ideas suggests that we might be missing something and the problem of normal and increased sensation and of urgency may be much more complex. Very interesting article on bladder sensation, well worth reading. If you like this, you will also enjoy the following related article.

NORMAL BLADDER SENSATIONS IN HEALTHY VOLUNTEERS: A FOCUS GROUP INVESTIGATION.

*Heeringa R, de Wachter SG, van Kerrebroeck PE, van Koeveeringe GA. Neurourol Urodyn. 2011 May 23. doi: 10.1002/nau.21052. [Epub ahead of print]. PMID: 21608021*

The purpose of this study from Maastricht was to describe the bladder sensations experienced during non-invasive rapid bladder filling in a controlled setting in healthy volunteers. During the focus group sessions, with constant focus on their bladder, all participants experienced their bladder sensation as a continuous progression. Healthy subjects describe their bladder sensation(s) as a "pressure" and a "tingling" sensation, but a terminology ranging from no sensations to an absolute need to void was used by all participants and better describes the pattern in which the need to void develops in healthy volunteers. The authors concluded that by using focus group research it is possible to describe the development of normal bladder sensation and to refine terminology used by healthy participants. Their findings show that two types of bladder sensations are reported spontaneously by healthy uninitiated volunteers, pressure and a tingling sensation, of which the first develops in a continuous manner. The pattern in which the absolute need develops is described by the terms: no sensation, weak awareness, stronger awareness, weak need, stronger need and absolute need to void.

AUTOIMMUNITY TO UROPLAKIN II CAUSES CYSTITIS IN MICE: A NOVEL MODEL OF INTERSTITIAL CYSTITIS.

*Altuntas CZ, Daneshgari F, Sakalar C, Goksoy E, Gulen MF, Kavran M, Qin J, Li X, Tuohy VK. Eur Urol. 2011 Jun 28. [Epub ahead of print]. PMID: 21719190*

Based on the hypothesis that deficits in urothelial cell layers and autoimmune mechanisms may play a role, the purpose of this study was to examine whether immunisation of mice with recombinant mouse uroplakin II (rmUPK2), a bladder-specific protein, would provoke an autoimmune response sufficient to create an IC phenotype. The authors note that a possible autoimmune etiopathogenesis for IC continues to trigger interest with increasing reports on the association between IC and other autoimmune diseases and reports of higher incidence of autoantibodies in patients with IC. They suggest that further investigation is warranted into whether the chronic inflammation and consequent tissue damage expose bladder tissues to further noxious stimuli, thereby eventually leading to an autoimmune response. RmUPK2 complementary DNA was generated, transferred into a bacterial expression vector, and the generated protein was purified. Eight-week-old SWXJ female mice were immunized with rmUPK2 protein via subcutaneous injection of 200µg of rmUPK2 protein in 200µl of an emulsion. The authors report that their findings showed that a bladder-specific

autoimmune response sufficient to induce inflammation and EAC occurs in mice following immunization with rmUPK2. EAC mice displayed significant evidence of urinary frequency and decreased urine output per void. Further phenotype characterization of EAC mice should include evidence for pain and/or afferent hypersensitivity, and evidence of urothelial cell layer damage.

CYSTITIS, CO-MORBID DISORDERS AND ASSOCIATED EPITHELIAL DYSFUNCTION.

*Birder LA, Hanna-Mitchell AT, Mayer E, Buffington CA. Neurourol Urodyn. 2011 Jun;30(5):668-72. doi: 10.1002/nau.21109. PMID: 21661011*

This interesting review article provides examples of various animal models studied in relation to PBS/IC including those incorporating chronic stress, thought to produce features that share similarities to that of PBS/IC patients, whose symptoms are often exacerbated by various stressors. It also provides evidence that PBS/IC patients exhibit abnormalities within the bladder epithelium (or urothelium), even though it has not been possible to demonstrate a consistent relationship of such changes with symptom severity. The authors note that the lack of a validated biomarker and a well-defined etiology for this syndrome gives rise to a number of complications, including diagnostic confidence, choice of appropriate animal models to study basic mechanism with the goal toward treatment, and rational therapies. It is also increasingly clear that PBS/IC patients often overlap or share symptoms with other persistent pain disorders. These include for example irritable bowel syndrome (IBS), non-cardiac chest pain, fibromyalgia, and even overactive bladder syndrome (OAB). The authors report that alterations in epithelial signalling/barrier function have also been described in patients diagnosed with a wider variety of syndromes, including functional and inflammatory bowel disorders such as IBS, gastrointestinal esophageal reflux disease (GERD), and asthma, suggesting that changes within the epithelium (barrier as well as signalling functions) may be a common occurrence that may contribute to peripheral mechanisms of hypersensitivity in a number of disorders.

SPONTANEOUS BLADDER RUPTURE FOLLOWING CYSTOSCOPY WITH HYDRODISTENTION AND BIOPSY IN A FEMALE PATIENT WITH INTERSTITIAL CYSTITIS

*Platte RO, Parekh M, Minassian VA, Poplawsky D. Female Pelvic Medicine & Reconstructive Surgery:May/June 2011 Volume 17 Issue 3 pp 149-152*

A case is reported here of remote spontaneous rupture of urinary bladder following cystourethroscopy with hydrodistension and a bladder biopsy in a patient with interstitial cystitis. This required abdominal exploration with cystorrhaphy. The authors believe that this case emphasizes a unique and dangerous complication of this procedure in a patient with interstitial cystitis.

NERVE GROWTH FACTOR IN BLADDER DYSFUNCTION: CONTRIBUTING FACTOR, BIOMARKER, AND THERAPEUTIC TARGET.

*Ochodnický P, Cruz CD, Yoshimura N, Michel MC. Neurourol Urodyn. 2011 Apr 21. doi: 10.1002/nau.21022. [Epub ahead of print]. PMID: 21520250*

A review from Amsterdam that aims to summarize the current experimental and clinical evidence for a role played by NGF in the urinary bladder. Experimental administration of NGF elicits states of increased sensation, urgency, and bladder hyperreflexia, resembling pathologies associated with bladder overactivity and inflammatory pain, such as in overactive bladder syndrome (OAB) and interstitial cystitis/painful bladder syndrome (IC/PBS). They found strong experimental evidence of a direct causal role of NGF in rodent models of bladder outlet obstruction, spinal cord injury, diabetic bladder dysfunction, and interstitial inflammation. In humans, there are attempts to use urinary NGF levels as a diagnostic marker in various forms of OAB and IC/PBS. However, there are still several unresolved issues in NGF-related bladder dysfunction requiring further investigation. Furthermore, successful experimental treatment approaches, such as NGF sequestering proteins or modified NGF antibodies, still need to be translated into clinical treatment of bladder disorders.

[NORMALIZATION OF PROLIFERATION AND TIGHT JUNCTION FORMATION IN BLADDER EPITHELIAL CELLS FROM PATIENTS WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME BY D-PROLINE AND D-PIPECOLIC ACID DERIVATIVES OF ANTIPROLIFERATIVE FACTOR.](#)

*Keay S, Kaczmarek P, Zhang CO, Koch K, Szekely Z, Barchi JJ Jr, Michejda C. Chem Biol Drug Des. 2011 Jun;77(6):421-30. doi: 10.1111/j.1747-0285.2011.01108.x. Epub 2011 Apr 27. PMID: 21352500*

Interstitial cystitis/painful bladder syndrome (IC/PBS) is a chronic bladder disorder with epithelial thinning or ulceration, pain, urinary frequency and urgency, which still eludes reliably effective therapy. The authors have already reported that IC/PBS bladder epithelial cells make a glycopeptide antiproliferative factor or 'APF' (Neu5Ac $\alpha$ 2-3Gal $\beta$ 1-3GalNAc $\alpha$ -O-TVPAVVVA) that induces abnormalities in normal cells similar to those in IC/PBS cells in vitro, including decreased proliferation, decreased tight junction formation, and increased paracellular permeability. Dr Susan Keay and colleagues screened inactive APF derivatives for their ability to block antiproliferative activity of asialylated-APF ('as-APF') in normal bladder cells and determined the ability of as-APF-blocking derivatives to normalize tight junction protein expression, paracellular permeability, and/or proliferation of IC/PBS cells. Only two of these derivatives blocked as-APF antiproliferative activity in normal cells. Both of these antagonists also 1) significantly increased mRNA expression of ZO-1, occludin, and claudins 1, 4, 8, and 12 in IC/PBS cells by qRT-PCR; 2) normalized IC/PBS epithelial cell tight junction protein expression and tight junction formation by confocal immunofluorescence microscopy; and 3) decreased paracellular permeability of (14) C-mannitol and (3) H-inulin between confluent IC/PBS epithelial cells on Transwell plates, suggesting that these potent APF antagonists may be useful for the development as IC/PBS syndrome therapies.

[COMPARISON BETWEEN JAPANESE AND NON-JAPANESE FEATURES OF LUPUS CYSTITIS BASED ON CASE REPORTS INCLUDING NOVEL THERAPY AND A LITERATURE REVIEW.](#)

*Nishizaki Y, Tamaki H, Yukawa S, Matsui Y, Okada M. Intern Med. 2011;50(9):961-8. Epub 2011 May 1. PMID: 21532217*

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This study from Japan was carried out to determine the characteristics of lupus cystitis and to compare those of Japanese cases with those of non-Japanese cases. It found that Lupus enteritis, female gender, and positive anti-dsDNA antibody are risk factors for lupus cystitis. Japanese cases showed older age, a higher prevalence of vomiting and a lower prevalence of CNS involvement. The authors also report the efficacy of the novel use of cetirizine hydrochloride for lupus cystitis refractory to corticosteroid.

[THE AFFERENT SYSTEM AND ITS ROLE IN LOWER URINARY TRACT DYSFUNCTION.](#)

*Daly DM, Collins VM, Chapple CR, Grundy D. Curr Opin Urol. 2011 Jul;21(4):268-74. PMID: 21537194*

Lower urinary tract disorders such as overactive bladder syndrome (OABS) and interstitial cystitis/painful bladder syndrome (IC/PBS) are debilitating conditions with serious adverse effects on quality of life. Common to both OABS and IC/PBS are the sensory symptoms of urgency and frequency, implicating the afferent system in the aetiology of these disorders. Understanding the role that afferent pathways play in the function of the lower urinary tract is therefore the focus of much current research. This review from Sheffield UK aims to provide an insight into the recent advances in this field. The authors refer to recent findings which show that sensory transduction in the bladder is not only mediated by direct activation of the afferents via a host of receptors and ion channels located on the afferent terminal, but also may be attributed to the interplay between the urothelium and the release of urothelially derived mediators. Recent studies provide compelling evidence to support this concept and highlight the complex nature of the bladder afferent system. They summarise by saying that recent studies provide further evidence that afferent control of the bladder may be dependent on integration of excitatory and inhibitory mediators from the urothelium such as ATP and nitric oxide. A number of studies have examined the role cholinergic and adrenergic mechanisms play in bladder afferent function, and several new potential mechanisms involving the cannabinoid receptors and transient receptor potential channels have emerged as areas which

warrant further investigation. They conclude that better understanding of afferent mechanisms in the bladder will hopefully lead to more effective treatments of lower urinary tract disorders.

THERAPEUTIC TARGETING OF TRP CHANNELS - THE TR(I)P TO PAIN RELIEF.

*Eid SR. Curr Top Med Chem. 2011 Jun 14. [Epub ahead of print]. PMID: 21671881*

Following the cloning and characterization of the transient receptor potential vanilloid 1 (TRPV1), a growing body of research has identified the important role of TRPV1 and related channels in different physiological functions, including temperature transduction and pain signalling. As a result, there has been a great deal of interest by the pharmaceutical industry to develop small molecule modulators of the activity of these channels for potential therapeutic use. While most of the efforts have focused on examining the role of TRPV1 in nociception, more recent work has begun to assess the therapeutic utility of targeting other TRP channels. This article is aimed at providing an introduction to the promising new developments and findings as well as emerging challenges in the targeting of the thermoTRP family of receptors for clinical therapeutic use. It focuses on current efforts from the pharmaceutical industry to develop highly potent and efficacious compounds that modulate TRP channel function and highlights recent drug discovery activities around the transient receptor potential vanilloid family members TRPV1, TRPV3, and TRPV4, the transient receptor potential ankyrin family member TRPA1, and the transient receptor potential melastatin family member TRPM8. The majority of the work presented here focuses on recent findings in the development of TRP modulators for pain indications. The increasing number of small biotech and pharmaceutical companies pursuing targets in these families of ion channels highlights the perceived importance of these targets in the treatment of a variety of disease states including inflammatory and neuropathic pain, urinary incontinence, painful bladder syndrome, and even types of prostate cancer.

"URO-ABDOMINOPLASTY": A NOVEL ADAPTATION OF ABDOMINAL CONTOURING FOR REVISION OF COMPLICATED UROSTOMIES.

*Mickute Z, Chen YA, Som R, Malata CM. Ann Plast Surg. 2011 May 27. [Epub ahead of print. PMID: 21629097*

The purpose of this study from Cambridge, UK, with 3 female patients and 1 male was to describe the indications, surgical technique and outcomes of abdominoplasty as a novel tool for revising complicated urostomies. Ileal conduits had been previously performed for cervical carcinoma, bladder carcinoma, interstitial cystitis, and neuropathic bladder. A postal questionnaire was used to establish pre- and post-abdominoplasty stoma function. The authors report that their centre has successfully used abdominoplasty for the purpose of improving urostomy dysfunction of intractable mechanical leakage by creating a flatter surface for appliance fitting. They note that uro-abdominoplasty widens the reconstructive repertoire of plastic surgeons and can be considered in those who have exhausted conservative or simpler surgical solutions.

NOCTURIA IN INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.

*Warren JW, Horne L, Diggs C, Greenberg P, Langenberg PW. Urology. 2011 Jun;77(6):1308-12. PMID: 21624590*

Another interesting and welcome study from Dr JW Warren and his Baltimore team aimed at exploring the roles of pain and urgency in the nocturia (night-time voiding) of patients with interstitial cystitis/painful bladder syndrome (IC/PBS). Until now, very little attention has been focused on nocturia specifically in IC/PBS patients other than documenting the number of voids per night. This was a longitudinal study of incident IC/PBS cases, in which the Maryland team assessed the associations of the presence and severity of nocturia with the presence and severity of pain and urgency, using multivariate analyses when necessary. They also very simply asked the IC/PBS patients what they felt was causing them to wake in the night. The multivariate analyses revealed associations of urgency with the presence and severity of nocturia and of bladder pain with the severity of nocturia. Direct queries of patients with IC/PBS about urgency and the reasons for awakening

demonstrated that bladder pain might have played a twofold role: directly in awakening a large minority of patients and possibly indirectly in the majority by generating the sensation of urgency. They concluded that these findings are consistent with urinary urgency and bladder pain each being in the causal pathway leading to nocturia in patients with IC/PBS. The authors note that their study did have some limitations as it did not take into account IC/PBS treatment, fluid intake or voided volumes.

HYPERBARIC OXYGEN THERAPY FOR PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS RESISTANT TO CONVENTIONAL TREATMENTS: LONG-TERM RESULTS OF A CASE SERIES IN JAPAN.

*Tanaka T, Nitta Y, Morimoto K, Nishikawa N, Nishihara C, Tamada S, Kawashima H, Nakatani T. BMC Urol. 2011 May 24;11(1):11. [Epub ahead of print]. PMID: 21609485*

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A pilot study was carried out in Japan to evaluate the efficacy and safety of hyperbaric oxygen (HBO) therapy in PBS/IC patients with severe symptoms who had failed to respond to any previous treatment. HBO treatment (2.0 ATA for 60 minutes/day x 5 days/week for 2 or 4 weeks) was given to 11 PBS/IC patients. Seven of the 11 patients showed persistent improvement in symptoms during the 12 months after HBO treatment. Two responders, who received an additional course of HBO 12 and 13 months after the initial treatment have remained improved for over 2 years. As side effects, there was 1 case of transient eustachian tube dysfunction and 3 cases of reversible exudative otitis media as a consequence of HBO treatment. The authors concluded that HBO is a good treatment for PBS/IC patients who fail to respond to conventional therapy. It was well tolerated and provided maintained improvement of pain, urgency, and urinary frequency for at least 12 months.

DIAGNOSIS AND TREATMENT OF INTERSTITIAL CYSTITIS IN ADOLESCENTS.

*Yoost JL, Hertweck SP, Loveless M. J Pediatr Adolesc Gynecol. 2011 May 19. [Epub ahead of print]. PMID: 21600805*

Interstitial cystitis can also affect children and adolescents in whom diagnosis may either be missed completely or delayed. This review of the literature focuses on diagnosing IC in younger patients and on what treatment modalities are appropriate and effective for this age group.

DEPRESSIVE DISORDERS AND PANIC ATTACKS IN WOMEN WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: A POPULATION-BASED SAMPLE.

*Watkins KE, Eberhart N, Hilton L, Suttorp MJ, Hepner KA, Clemens JQ, Berry SH. Gen Hosp Psychiatry. 2011 Mar-Apr;33(2):143-9. Epub 2011 Feb 18. PMID: 21596207*

This paper from the RAND CORPORATION reports on the population prevalence of probable depressive disorders and current panic attacks in women with BPS/IC symptoms and describes their characteristics and access to care. A telephone screening of 146,231 households was carried out and telephone interviews were held with women with BPS/IC symptoms. A weighted probability sample of 1469 women who met the criteria for BPS/IC was identified. The authors found that over one third of the sample had a probable diagnosis of depression, and 52% reported recent panic attacks. Women with a probable diagnosis of depression or current panic attacks reported worse functioning and increased pain and were less likely to work because of bladder pain. In this community-based sample, rates of probable current depression and panic attacks are high, and there is a considerable unmet need for treatment. The authors are of the opinion that their findings suggest that clinicians should be alert to complaints of bladder pain in patients seeking treatment for depressive or anxiety disorders and to complaints of emotional or personal problems in patients seeking treatment for painful bladder symptoms.

PREVALENCE OF SYMPTOMS OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS AMONG ADULT FEMALES IN THE UNITED STATES.

*Berry SH, Elliott MN, Suttorp M, Bogart LM, Stoto MA, Eggers P, Nyberg L, Clemens JQ. J Urol. 2011 Jun 15. [Epub ahead of print]. PMID: 21683389*

This study from the RAND CORPORATION provides the first population based symptom prevalence estimate to our knowledge among United States adult females in which 2 case definitions were developed and validated to identify bladder pain syndrome/interstitial cystitis symptoms. The authors found that bladder pain syndrome/interstitial cystitis symptoms are widespread among United States women and associated with considerable disability. These results suggest bladder pain syndrome/interstitial cystitis may be underdiagnosed.

#### P2X RECEPTORS IN HEALTH AND DISEASE.

*Burnstock G, Kennedy C. Adv Pharmacol. 2011;61:333-72. PMID: 21586364*

Changes in the expression of P2X receptors have been characterized in many pathological conditions of the cardiovascular, gastrointestinal, respiratory, and urinogenital systems and in the brain and special senses. The therapeutic potential of P2X receptor agonists and antagonists is currently being investigated in a range of disorders, including chronic neuropathic and inflammatory pain, depression, cystic fibrosis, dry eye, irritable bowel syndrome, interstitial cystitis, dysfunctional urinary bladder, and cancer.

#### DEVELOPMENT OF A MUCOADHESIVE NANOPARTICULATE DRUG DELIVERY SYSTEM FOR A TARGETED DRUG RELEASE IN THE BLADDER.

*Barthelmes J, Perera G, Hombach J, Dünnhaupt S, Bernkop-Schnürch A. Int J Pharm. 2011 Jun 24. [Epub ahead of print]. PMID: 21726619*

The purpose of this study from Austria using porcine urinary bladders was to develop a mucoadhesive nanoparticulate drug delivery system for local use in intravesical therapy of interstitial cystitis, since only a small fraction of drug actually reaches the affected site by conventional treatment of bladder diseases via systemic administration. Chitosan-thioglycolic acid (chitosan-TGA) nanoparticles (NP) and unmodified chitosan NP were formed via ionic gelation with tripolyphosphate (TPP). Trimethoprim (TMP) was incorporated during the preparation process of NP. Then, the mucoadhesive properties of NP were determined in porcine urinary bladders and the release of TMP among simulated conditions with artificial urine was evaluated. The authors concluded that by using the method described in this article, chitosan-TGA NP might be a useful tool for local intravesical drug delivery in the urinary bladder.

#### ROLE OF PURINERGIC SIGNALING IN VOIDING DYSFUNCTION.

*Sun Y, Chai TC. Curr Bladder Dysfunct Rep. 2010 Aug 26;5(4):219-224. PMID: 21572572*

Purinergic signalling is a term that relates to adenosine triphosphate binding to its receptor (purinergic receptors such as P2X and P2Y subtypes). This pathway has been implicated in bladder functional disorders related to interstitial cystitis/painful bladder syndrome, neurogenic bladder secondary to spinal cord injury, lower urinary tract symptoms, diabetes, and aging. Purinergic signalling occurs at multiple sites, including the central nervous system, peripheral motor and sensory nerves, detrusor smooth muscle, and the bladder urothelium. The authors suggest that future pharmacologic agents to treat bladder functional disorders may be able to target purinergic signalling at one or more of these sites.

#### A MULTI-SITE STUDY CONFIRMS ABNORMAL GLYCOSYLATION IN THE TAMM-HORSFALL PROTEIN OF PATIENTS WITH INTERSTITIAL CYSTITIS.

*Parsons CL, Proctor J, Teichman JS, Nickel JC, Davis E, Evans R, Zupkas P, Phillips C, Shaw T, Naidu N, Argade S. J Urol. 2011 May 13. [Epub ahead of print]. PMID: 21571325*

In this study from San Diego, urine samples from 41 controls and 48 patients with interstitial cystitis from a total of 5 North American sites were obtained in blinded fashion as to participant status. The authors report that these multisite data validate that abnormal glycosylation of Tamm-Horsfall protein occurs in patients with interstitial cystitis and may have a role in interstitial cystitis causation.

#### WHEN TO SUSPECT INTERSTITIAL CYSTITIS.

Whitmore KE, Theoharides TC. *J Fam Pract.* 2011 Jun;60(6):340-8. PMID: 21647470

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The symptom profile and comorbidities associated with this painful condition can make it difficult to diagnose, unless you know what to look for. The authors emphasise that it is often under- or misdiagnosed, both because of the many comorbidities found in patients with the disorder and because its symptoms overlap with those of other common conditions. Since family doctors are often the first practitioners that a patient is likely to consult, it is vital that they are made aware of the condition. This article will certainly to achieve that in the USA.

INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.

French LM, Bhambore N. *Am Fam Physician.* 2011 May 15;83(10):1175-81. PMID: 21568251

Useful overview of diagnosis and treatment for family physicians.

PAINFUL BLADDER SYNDROME: MANAGEMENT AND EFFECT ON SEXUAL FUNCTION AND QUALITY OF LIFE.

Schmid C, Berger K, Müller M, Silke J, Mueller MD, Kuhn A. *Ginekol Pol.* 2011 Feb;82(2):96-101. PMID: 21568222

The primary aim of this prospective study from Switzerland was to evaluate the effect of the therapeutical management in 69 patients with painful bladder syndrome (PBS)/interstitial cystitis (IC) on sexual function, quality of life and bladder symptoms at a tertiary referral centre. Staged treatment included tetracycline, bladder instillation consisting of heparin, local anaesthetic and sodium-bicarbonate, prednisolon and antihistaminics or instillation with DMSO. Sexual function, quality of life and symptoms were evaluated with validated tools FSFI, King's Health Questionnaire and visual analogue scale (VAS). They found that the patients showed significant improvement regarding sexual function, quality of life and symptoms. Long term follow-up is needed however.

IDIOPATHIC CYSTITIS IN DOMESTIC CATS-BEYOND THE LOWER URINARY TRACT.

Buffington CA. *J Vet Intern Med.* 2011 May 12. doi: 10.1111/j.1939-1676.2011.0732.x. [Epub ahead of print]. PMID: 21564297

The purpose of this review was to summarize research investigations into the various abnormalities present in cats, to compare some of these findings with those identified in human beings, and to discuss how they might modify perceptions about the etiopathogenesis, diagnosis, and treatment of cats with this disease.

MODELS OF INFLAMMATION OF THE LOWER URINARY TRACT.

Bjorling DE, Wang ZY, Bushman W. *Neurourol Urodyn.* 2011 Jun;30(5):673-82. doi: 10.1002/nau.21078. PMID: 21661012

Inflammation of the lower urinary tract occurs frequently in people. With the exception of disorders arising from bacterial causes, initiating causes of inflammatory diseases in humans remain obscure. Animal models have proven useful for investigating and assessing mechanisms underlying symptoms associated with lower urinary tract inflammation and options for suppressing these symptoms. This review discusses various animal models of lower urinary tract inflammation, including feline spontaneous (interstitial) cystitis, neurogenic cystitis, autoimmune cystitis, cystitis induced by intravesical instillation of chemicals or bacterial products (particularly lipopolysaccharide or LPS), and prostatic inflammation initiated by transurethral instillation of bacteria. Animal models will continue to be of significant value in identifying mechanisms resulting in bladder inflammation, but the relevance of some of these models to the causes underlying clinical disease is unclear. This is primarily because of the lack of understanding of causes of these disorders in people. According to the authors, comparative and translational studies are required to better characterize causes of clinical disease in humans and the utility of animal models in studying these causes.

ACTIVATION OF SPINAL EXTRACELLULAR SIGNAL-REGULATED KINASES (ERK) 1/2 IS ASSOCIATED WITH THE DEVELOPMENT OF VISCERAL HYPERALGESIA OF THE BLADDER.

*Lai HH, Qiu CS, Crock LW, Morales ME, Ness TJ, Gereau RW 4th. Pain. 2011 Jun 24. [Epub ahead of print]. PMID: 21705143*

Activation of extracellular signal-regulated kinases (ERK) 1/2 in dorsal horn neurons is important for the development of somatic hypersensitivity and spinal central sensitization after peripheral inflammation. However, data regarding the roles of spinal ERK1/2 in the development of visceral hyperalgesia are sparse. This study investigated the activation of ERK1/2 in the lumbosacral spinal cord after innocuous and noxious distension of the inflamed (cyclophosphamide-treated) and noninflamed urinary bladder in mice. The authors also correlated the spinal ERK1/2 activation to distension-evoked bladder nociception as quantified by the abdominal visceromotor response (VMR). Cyclophosphamide treatment (bladder inflammation) evoked increased bladder hyperalgesia and allodynia to bladder distension, as evident from an upward and leftward shift of the VMR stimulus-response curve compared with that of noninflamed mice. Development of bladder hyperalgesia was associated with robust enhancement of ERK1/2 activation in the dorsal horn and deeper laminae bilaterally in the L6-S1 spinal cord. Functional blockade of spinal ERK1/2 activity via intrathecal administration of the upstream MEK inhibitor U0126 attenuated distention-evoked bladder nociception and caused a significant downward shift of the VMR stimulus-response curve. The authors report that they have provided functional and immunohistochemical evidence that activation of lumbosacral spinal ERK1/2 is associated with the development of primary visceral (bladder) hyperalgesia. They are of the opinion that the results suggest that aberrant processing of visceral nociceptive information at the level of the lumbosacral spinal cord via activation of ERK1/2 signalling may contribute to chronic bladder pain in the context of inflammation. They also state that the observation that MEK/ERK inhibitors are effective in alleviating visceral pain is an exciting one because it may lead to new treatments of functional visceral pain syndromes such as interstitial cystitis or irritable bowel syndrome.

CHRONIC PELVIC PAIN:

SAFETY AND EFFECTIVENESS OF AN INTERNAL PELVIC MYOFASCIAL TRIGGER POINT WAND FOR UROLOGIC CHRONIC PELVIC PAIN SYNDROME.

*Anderson R, Wise D, Sawyer T, Nathanson BH. Clin J Pain. 2011 May 25. [Epub ahead of print]. PMID: 21613956*

Pelvic muscle tenderness occurs often in patients with urologic chronic pelvic pain syndrome; symptoms frequently can be reduced with pelvic myofascial physical therapy. This open-label pilot study from Stanford evaluated the safety of a personal "wand" that enables patient's self-treatment of internal myofascial trigger points in the pelvic floor and its effect in reducing pelvic muscle tenderness. A specially designed curved wand served as a kind of extended finger to locate and release painful internal myofascial trigger points with an integrated algometer monitoring and guiding appropriate applied point pressure. Patients used the wand several times weekly after education and careful supervision. 113 of the enrolled 157 patients completed 6 months of wand use-106 men and 7 women; 44 patients withdrew before study completion but none for adverse events. Most patients (95.5%) reported the wand as either very or moderately effective in alleviating pain. No serious adverse events occurred. The authors concluded that a multimodal protocol using an internal pelvic therapeutic wand seems to be a safe, viable treatment option in select refractory patients with pelvic pain.

PELVIC FLOOR THERAPIES IN CHRONIC PELVIC PAIN SYNDROME.

*Doggweiler R, Stewart AF. Curr Urol Rep. 2011 May 6. [Epub ahead of print]. PMID: 21547556*

Chronic pelvic pain syndrome is a poorly understood clinical entity associated with urinary symptoms, pelvic floor dysfunction, and multisystem disorders. Treatment of pelvic floor dysfunction is difficult and often frustrating for the patient as well as for the involved physician. The purpose of this review was to update clinicians on the latest research for the treatment of pelvic floor dysfunction in relation to chronic pelvic pain syndrome.

#### COULD CHRONIC PELVIC PAIN BE A FUNCTIONAL SOMATIC SYNDROME?

*Warren JW, Morozov V, Howard FM. Am J Obstet Gynecol. 2011 Apr 14. [Epub ahead of print] PMID: 21620363*

Despite considerable research, the cause of noncyclical chronic pelvic pain (CPP) in many women is unknown: 30% have no identifiable pelvic pathology, and in those who do the relationship of CPP and the pathology is often unclear. Moreover, epidemiologic studies demonstrate that the common findings of endometriosis and adhesions do not greatly increase the odds of having CPP. CPP and the functional somatic syndromes (fibromyalgia, irritable bowel syndrome, and others) share many characteristics including pain as a prominent symptom and comorbidity. For the functional somatic syndromes, the initial focus of etiologic investigations has been on local mechanisms and then on systemic pathogenesis. The authors believe that the research trajectories of the functional somatic syndromes and CPP are converging and that their juncture might reveal an important pathologic mechanism for CPP in some women that is primarily outside the pelvis. This observation would open up new areas of exploration and treatment of CPP. Indeed, the authors note that clinicians appear to be anticipating this possibility and are testing in CPP certain central nervous system medications that have proven useful for functional somatic syndromes.

#### RISK FACTORS FOR CHRONIC PELVIC PAIN IN A COHORT OF PRIMIPARA AND SECONDIPARA AT ONE YEAR AFTER DELIVERY: ASSOCIATION OF CHRONIC PELVIC PAIN WITH AUTOIMMUNE PATHOLOGIES.

*Driul L, Bertozzi S, Londero AP, Fruscalzo A, Rusalen A, Marchesoni D, Di Benedetto P. Minerva Ginecol. 2011 Apr;63(2):181-7. PMID: 21508906*

In addition to genetic and obstetric factors, autoimmunity may also be involved in female chronic pelvic pain (CPP) pathogenesis. The aim of this study from Italy was to determine the prevalence of CPP one year after delivery and to investigate the possible influence of concomitant autoimmune conditions on CPP. On the basis of their findings, they concluded that delivery may highlight CPP symptoms in predisposed women affected by chronic autoimmune pathologies.

#### **FIBROMYALGIA:**

#### SLEEP DISORDERS AND FIBROMYALGIA.

*Roizenblatt S, Neto NS, Tufik S. Curr Pain Headache Rep. 2011 May 20. [Epub ahead of print]. PMID: 21594765*

This article from São Paulo, Brazil concerns sleep disorders and fibromyalgia, but may be of relevance to some IC patients. The authors observe that disordered sleep is such a prominent symptom in fibromyalgia that the American College of Rheumatology included symptoms such as waking feeling unrefreshed, fatigue, tiredness, and insomnia in the 2010 diagnostic criteria for fibromyalgia. Even though sleep recording is not part of the routine evaluation, polysomnography may disclose primary sleep disorders in patients with fibromyalgia, including obstructive sleep apnea and restless leg syndrome. In addition, genetic background and environmental susceptibility link fibromyalgia and further sleep disorders. Among nonpharmacological treatment proposed for sleep disturbance in fibromyalgia, positive results have been obtained with sleep hygiene and cognitive-behavioural therapy. The effect of exercise is contradictory, but overweight or obese patients with fibromyalgia should be encouraged to lose weight. Regarding the approved antidepressants, amitriptyline proved to be superior to duloxetine and milnacipran for sleep disturbances. New perspectives remain with

the narcolepsy drug sodium oxybate, which was recently approved for sleep management in fibromyalgia.

#### VULVODYNIA:

##### INTERSTITIAL CYSTITIS IS ASSOCIATED WITH VULVODYNIA AND SEXUAL DYSFUNCTION - A CASE-CONTROL STUDY.

*Gardella B, Porru D, Nappi RE, Daccò MD, Chiesa A, Spinillo A. J Sex Med. 2011 Jun;8(6):1726-34. PMID: 21477020*

Gardella and colleagues from Pavia, Italy note that dyspareunia and sexual dysfunction are common in women with urological disorders. The study of comorbidity between interstitial cystitis (IC) and vulvodynia seems to be relevant to understand the mechanism generating pain in these conditions. The aim of this study was to conduct a case-control study to evaluate vulvodynia and sexual dysfunction in 47 women with IC compared with 188 age-matched, negative controls. They found an increased prevalence of vulvodynia among women with recently diagnosed IC and that both conditions seem to have profound consequences on women's sexual function. A potential role for sex hormone-dependent mechanisms in the comorbidity of vulvar and bladder pain is proposed, but further research is warranted.

##### VULVODYNIA IN ADOLESCENCE: CHILDHOOD VULVAR PAIN SYNDROMES.

*Clare CA, Yeh J. J Pediatr Adolesc Gynecol. 2011 Jun;24(3):110-5. PMID: 21601807*

The purpose of this literature review study was to define and characterize vulvodynia, diagnostic criteria, causes and pathophysiology, and propose treatment modalities, emphasizing its prevalence in young children, adolescents and young women less than 25 years of age. Little data was found for the period under review. In childhood, vulvar pain is usually found to have a cause and pain characteristics in this group are similar to adults. In adolescents and young reproductive age women, vulvar pain is associated with sexual intercourse or early tampon use. The authors found that women with vulvodynia vary in ages from 16 to 80 years with the majority between the ages of 20 to 50 years and that young women in their teens and early twenties are at the greatest risk of developing vulvodynia. Vulvar pain disorders are important in these groups because early pain syndromes may affect future development of body image, self-esteem, and attitudes toward sexual behaviour and functioning.

##### ALTERED CENTRAL SENSITIZATION IN SUBGROUPS OF WOMEN WITH VULVODYNIA.

*Zhang Z, Zolnoun DA, Francisco EM, Holden JK, Dennis RG, Tommerdahl M. Clin J Pain. 2011 May 17. [Epub ahead of print]. PMID: 21593667*

This study from North Carolina investigated the clinical correlates of central nervous system alterations among women with vulvodynia. According to the authors, altered central sensitisation has been linked to dysfunction in central nervous system-inhibitory pathways (eg,  $\gamma$ -aminobutyric acidergic), and metrics of sensory adaptation, a centrally mediated process that is sensitive to this dysfunction, could potentially be used to identify women at risk of treatment failure using conventional approaches. 12 women with vulvodynia and 20 age-matched controls participated in this study, which was conducted by sensory testing of the right hand's index and middle fingers. The following sensory precepts were assessed: (1) vibrotactile detection threshold; (2) amplitude discrimination capacity (defined as the ability to detect differences in intensity of simultaneously delivered stimuli to 2 fingers); and (3) a metric of adaptation (determined by the impact that applying conditioning stimuli have on amplitude discriminative capacity). Although the participants did not differ on key demographic variables, vibrotactile detection threshold, and amplitude discrimination capacity, the authors found significant differences from controls in adaptation metrics in 1 subgroup of vulvodynia patients. Compared with healthy controls and women with a shorter history of pain, those with a longer history were found to be less likely to have adaptation metrics similar to control

values. The authors conclude by saying that chronic pain is thought to lead to altered central sensitisation, and adaptation is a centrally mediated process that is sensitive to this condition. This article suggests that similar alterations exist in a subgroup of vulvodynia patients.

## IRRITABLE BOWEL SYNDROME (IBS)

### DIAGNOSIS AND TREATMENT OF IRRITABLE BOWEL SYNDROME.

*Suares NC, Ford AC. Discov Med. 2011 May;11(60):425-33. PMID: 21616041*

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Irritable bowel syndrome (IBS) is a chronic functional disorder of the gastrointestinal tract. The exact cause is unknown. No medical therapy for IBS has been shown to alter the disease course, and treatment has traditionally been directed towards symptom relief. The aim should be to improve the predominant symptom reported by the patient. This article from Leeds, UK provides a summary of diagnostic criteria for IBS, evidence to support investigations to exclude organic disease, and current and emerging therapies in this field.

### NEW INSIGHTS INTO VISCERAL HYPERSENSITIVITY-CLINICAL IMPLICATIONS IN IBS.

*Zhou Q, Verne GN. Nat Rev Gastroenterol Hepatol. 2011 Jun;8(6):349-55. PMID: 21643039*

Zhou and colleagues note that a subset of patients with IBS have visceral hypersensitivity and/or somatic hypersensitivity. Visceral hypersensitivity might have use as a clinical marker of IBS and could account for symptoms of urgency for bowel movements, bloating and abdominal pain. The mechanisms that lead to chronic visceral hypersensitivity in patients who have IBS are unclear. However, several working models may be considered, including: nociceptive input from the colon that leads to hypersensitivity; increased intestinal permeability that induces a visceral nociceptive drive; and alterations in the expression of microRNAs in gastrointestinal tissue that might be delivered via blood microvesicles to other target organs, such as the peripheral and/or central nervous system. As such, the chronic visceral hypersensitivity that is present in a subset of patients with IBS might be maintained by both peripheral and central phenomena. The theories underlying the development of chronic visceral hypersensitivity in patients with IBS are supported by findings from new animal models in which hypersensitivity follows transient inflammation of the colon. The presence of somatic hypersensitivity and an alteration in the neuroendocrine system in some patients who have IBS suggests that multisystemic factors are involved in the overall disorder. They therefore conclude that IBS is similar to other chronic pain disorders, such as fibromyalgia, chronic regional pain disorder and temporomandibular joint disorder, since chronic nociceptive mechanisms are activated in all of these disorders.

### IRRITABLE BOWEL SYNDROME: COMMON INTEGRATIVE MEDICINE PERSPECTIVES.

*Nahas R. Chin J Integr Med. 2011 Jun;17(6):410-3. Epub 2011 Jun 10. PMID: 21660674*

In this review, the author describes and comments on a number of potentially relevant factors that have been commonly emphasized by practitioners who treat IBS and patients who have the disease. They include gluten and other food allergies, the candida syndrome and biofilm, interference fields and post-infectious IBS, as well as mind-body factors.

### MANAGEMENT OF IRRITABLE BOWEL SYNDROME (IBS) IN ADULTS: CONVENTIONAL AND COMPLEMENTARY/ALTERNATIVE APPROACHES.

*Yoon SL, Grundmann O, Koepp L, Farrell L. Altern Med Rev. 2011 Jun;16(2):134-51. PMID: 21649455*

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Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder with a range of symptoms that significantly affect quality of life for patients. The purposes of this review article are to: (1) address current issues related to IBS, including symptom presentation, diagnosis, and current treatment

options; (2) summarise benefits and side effects of currently available drugs and other symptom management strategies, with an emphasis on commonly used complementary and alternative medicines (CAM) and diet modification; and (3) outline recommendations and future directions of IBS management based on systematic reviews, meta-analyses, and research findings. Since optimal treatment is often delayed due to delay in diagnosis, people with IBS often treat themselves with non-prescribed medication and/or complementary and alternative medicines and by modifying diet and daily activities.

#### VISCERAL HYPERSENSITIVITY IN IRRITABLE BOWEL SYNDROME.

*Kanazawa M, Hongo M, Fukudo S. J Gastroenterol Hepatol. 2011 Apr;26 Suppl 3:119-21. doi: 10.1111/j.1440-1746.2011.06640.x. PMID: 21443723*

In this study from Japan, Kanazawa and colleagues observed that altered central processing, abnormal gastrointestinal motility and visceral hypersensitivity may possibly be an important pathophysiology of irritable bowel syndrome (IBS). These factors affect each other and are probably associated with the development of IBS symptoms. The purpose of this study was to investigate pain perception of the descending colon among different subtypes of IBS. They found that visceral hypersensitivity is common in IBS patients and probably plays a major role in development of the symptoms and that both central and peripheral factors may enhance the pain sensitivity.

#### IRRITABLE BOWEL SYNDROME IN ADULTS: DIAGNOSIS AND MANAGEMENT OF IRRITABLE BOWEL SYNDROME IN PRIMARY CARE [INTERNET].

*Editors: National Collaborating Centre for Nursing and Supportive Care (UK).*

*Source: London: Royal College of Nursing (UK); 2008 Feb. PMID: 21656972*

*National Institute for Health and Clinical Excellence: Guidance.*

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PDF version: <http://www.ncbi.nlm.nih.gov/books/NBK51953/pdf/TOC.pdf>

This guideline may be of interest to those concerned with IBS and covers areas relevant to the diagnosis and management of irritable bowel syndrome (IBS) reflecting the complete patient journey, from the person presenting with IBS symptoms, positive diagnosis and management, targeted at symptom control. The guideline incorporates Cochrane reviews, published NICE clinical and public health guidance, Health Technology Assessment reports, systematic and health economic reviews produced by the National Collaborating Centre for Nursing and Supportive Care. Recommendations are based on clinical and cost effectiveness evidence, and where this is insufficient, the GDG used all available information sources and experience to make consensus recommendations using nominal group technique.

#### **PUDENDAL NERVE:**

#### BENJAMIN ALCOCK AND THE PUDENDAL CANAL.

*Colebunders B, Matthew MK, Broerm N, Persing JA, Dellon AL. J Reconstr Microsurg. 2011 May 27. [Epub ahead of print]. PMID: 21623563*

The anatomy of the pudendal nerve is complex and difficult to visualize. Entrapment of the pudendal nerve is believed to occur in a canal, the pudendal canal or Alcock's canal, yet in the literature this term is used to refer to several different anatomic locations. The authors present a brief history of Benjamin Alcock, and compare Alcock's original description of the pudendal canal with their findings from a cadaveric study. It is concluded that Alcock's canal for the pudendal nerve, as Alcock described it related to the pudendal artery, should be that portion of the pudendal nerve within the obturator internus fascia. This definition now permits future medical and surgical approaches to use the appropriate terminology for this anatomic location.

#### **CANNABINOIDS:**

## CANNABINOIDS FOR PAIN MANAGEMENT.

*Thaler A, Gupta A, Cohen SP. Adv Psychosom Med. 2011;30:125-38. PMID: 21508629*

Cannabinoids have been used for thousands of years to provide relief from suffering, but only recently have they been critically evaluated in clinical trials. This review by Thaler and colleagues provides an in-depth examination of the evidence supporting cannabinoids in various pain states, along with an overview of potential adverse effects. In summary, there is strong evidence for a moderate analgesic effect in peripheral neuropathic and central pain conditions, and conflicting evidence for their use in nociceptive pain. For spasticity, most controlled studies demonstrate significant improvement. Adverse effects are not uncommon with cannabinoids, though most are not serious and self-limiting. In view of the limited effect size and low but not inconsequential risk of serious adverse events, cannabinoids should be employed as analgesics only when safer and more effective medication trials have failed, or as part of a multimodal treatment regimen.

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