IPBF e-Newsletter and Research Update
Issue 38, January 2015

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

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

- International IC/BPS Patient Survey on Symptoms and Quality of Life
- Meeting Review: PAE/SIP
- Upcoming Events
- Patient Organization News
- Research Highlights
- Donations & Sponsoring

The Board of the International Painful Bladder Foundation would like to wish all its readers around the world a Healthy, Happy, Successful New Year 2015!

INTERNATIONAL IC/BPS PATIENT SURVEY ON SYMPTOMS AND QUALITY OF LIFE

IC/BPS patients around the world are invited to participate in a new online survey study examining “How Pain and IC/BPS symptoms are associated with patient Quality of Life”. This survey, led by Dr Curtis Nickel, Dr Dean Tripp and Dr Robert Moldwin, examines several symptoms of Interstitial Cystitis/ Bladder Pain Syndrome as well as quality of life. In particular, patients are asked questions that focus on their pain experiences, mood, hope, and general questions about how they view their life. Click here to access the survey, where an information letter provides further information. The survey is in the English language.

MEETING REVIEW

PAIN ALLIANCE EUROPE AND SOCIETAL IMPACT OF PAIN (SIP), 17-18 NOVEMBER, 2014, BRUSSELS

The well-attended Pain Alliance Europe (PAE) members’ General Assembly took place at Thon Hotel in Brussels on Monday, November 17, 2014. Patient representatives came from a wide variety of organizations with pain implications from all over Europe. They called for urgent concrete action to prioritize chronic pain at an EU level, to increase public awareness of chronic pain and its visibility, to educate health professionals at all levels and to stimulate research and data collection. It was felt that many proposals have been put forward but no concrete action has been taken at an EU level and this needs to change. It was also felt that there needs to be more sharing of information and cooperation between patient organizations and more cooperation between patient organizations and professionals in order to further their goals. This meeting was followed by a useful networking dinner together with delegates to the SIP Symposium. The following day, the 5th Societal Impact of Pain (SIP) Symposium was held at the SQUARE Brussels Meeting Centre, having been switched from the original...
venue at the European Parliament due to the large number of attendees. There were around 200 delegates, twice the number of the previous year. SIP is an international platform set up in 2010 that provides opportunities for discussion for health care professionals, pain advocacy groups, politicians, insurances, representatives of health authorities, regulators and budget holders. This meeting gives everyone a chance to share thoughts, opinions, plan effective actions and meet key people. This year, the SIP conference had an entirely new (experimental) panel format involving all stakeholders and moderated by the well-known Nick Ross who pointed out that analgesics were first used thousands of years ago. So why are huge numbers of people still suffering huge amounts of pain, he asked? 100 million people in the EU suffer from this and 500 million sick days are lost. The cost is therefore multi billions, with massive utilization of health resources.

Panel discussion topics included:
- Out of sight, out of mind – why the reluctance to see pain as a critical issue?
- Good practice – how do we stimulate innovation and accelerate the replication?
- Outcome of the Italian Presidency’s discussion on Pain and Palliative Care at the informal Ministerial Council.
- What now?
- The future – how can stakeholders advocating for the recognition of pain in Europe work together to ensure change?
- There was also an interview with three patient advocates: making the invisible visible – the experience of living with chronic pain.

A detailed review will be published by the organizers in due course.

### UPCOMING EVENTS

#### 13TH INTERNATIONAL SYMPOSIUM ON SJÖGREN’S SYNDROME
The 13th International Symposium on Sjögren’s Syndrome will be held 19-22 May, 2015 in Bergen, Norway. This will include a meeting of patient organisations.
Further information will be available on [http://www.sicca.org/isss2015/](http://www.sicca.org/isss2015/)

#### EURORDIS Membership Meeting (EMM) 2015 Madrid
The EURORDIS Membership Meeting 2015 will take place at Hotel Rafael Antocha, Madrid, Spain, May 29 and 30.
The draft programme of the EMM 2015 Madrid, hotel and practical information for this meeting as well as the registration form will be available on the [website](http://www.sicca.org/isss2015/) at the beginning of 2015.
This two day event, organised in collaboration with FEDER (Federación Española de Enfermedades Raras), will start with the EURORDIS Annual General Assembly. The meeting’s working language will be English, with simultaneous translation of the Plenary Session on Friday 29 May into Spanish.

#### 2nd WORLD CONGRESS ON ABDOMINAL AND PELVIC PAIN (WCAPP), 11-13 JUNE 2015, NICE, FRANCE
Following the great success of the 1st WCAPP held in Amsterdam, this 2nd multidisciplinary WCAPP (President Dr Jean-Jacques Labat) will be organised 11-13 June 2015 in Nice, France by Convergences PP in collaboration with IPPS and APP-IASP.
Various pathologies concerning organs will be addressed (IC/bladder pain syndrome, chronic prostatitis, endometriosis, pelvic varicose veins, vulvodynia, irritable bowel syndrome, proctalgia fugax, admissions and chronic pelvic pain), as well as less familiar areas such as pudendal nerve pain, musculoskeletal dysfunction, central sensitization and more besides.
It is hoped to be able to organize a patient session again this year.
Further information will be published on [www.pelvicpain-meeting.com](http://www.pelvicpain-meeting.com).

#### 2nd GLOBAL CONGRESS ON LOWER URINARY TRACT DYSFUNCTION 2015
The Second Global Congress on LUTD will be held 24-26 June 2015 in Rome, Italy.
[http://lutd.org](http://lutd.org)
**ESSIC ANNUAL MEETING 2015**
The ESSIC Annual Meeting 2015 will be held in Rome, Italy from Thursday 17 September at 13.00 hours to Saturday 19 September 2015 at 13.30 hours. Further details will follow and will be published on the ESSIC website www.essic.eu

**PATIENT ORGANIZATION NEWS**

**ICA CELEBRATES 30 YEARS!**
Congratulations are due to the Interstitial Cystitis Association (ICA) in America which celebrated its 30th anniversary in 2014. This first IC patient association was started in 1984 by Dr Vicki Ratner and a group of fellow patients to improve healthcare and quality of life for this hitherto neglected group of patients. The ICA also set the ball rolling in the field of research by winning the interest of the NIDDK. Within a decade, it had had a knock-on effect with patient support groups springing up in Germany, the United Kingdom and the Netherlands, gradually expanding around the entire globe and offering information in many different languages.

**TICA (TAIWAN INTERSTITIAL CYSTITIS ASSOCIATION) CELEBRATES 10TH ANNIVERSARY**
In December 2014, TICA celebrated its 10th anniversary with the slogan “Ten Summers of TICA, New future for international collaboration”. TICA is a wonderful communication platform for its members, allowing them to share their IC/BPS experiences. TICA consultant Dr Ming-Hui Lee and his multidisciplinary team provide medical assistance and counselling. The website and mobile APP are also integrated into part of the service including online consulting with immediate help 24hrs a day. During these 10 years, TICA has not only been helping IC/BPS patients, but also Ketamine Cystitis (KC) young patients. KC symptoms are very similar to IC/BPS symptoms, with severe lower urinary tract symptoms including frequency, urgency, and suprapubic pain. The website and mobile service also help teenage KC patients abstain from ketamine dependence. This wonderful 10th anniversary of TICA is another great milestone in the history of IC/BPS patient advocacy and the IPBF sends TICA warmest congratulations. We are filled with admiration for what TICA has achieved for all Chinese speaking patients. But its influence has extended far further, all around the IC/BPS world, through the extensive research being carried out in Taiwan, for which we as patients are deeply grateful. Taiwan doctors can be seen at every urology conference, presenting research into IC/BPS and in recent years also leading the world in research into ketamine cystitis. Knowing that there are doctors in the world who care so much and knowing that there are patients who are willing to devote themselves to helping other patients is a great psychological support to IC/BPS patients and generates a feeling of warmth and comfort. Thank you TICA!

**BELGIAN ICPB – 10 YEARS IN 2015**
On Saturday 22 November 2014, the Belgian IC patient association (ICPB) organized a meeting at Antwerp University Hospital to celebrate the support group’s upcoming 10th anniversary in 2015. Josée De Raas, chairman, has led this support group right from the start, supported and encouraged by Professor JJ Wyndaele. Many thanks are due to both of them for ensuring that Belgian patients are provided with information and patient-to-patient support.

**JOURNALS**

**NEW JOURNAL: TRADITIONAL AND KAMPO MEDICINE**
Bearing in mind the considerable interest by IC/BPS patients in natural and herbal medicine, it was interesting to receive an email advertising a new journal entitled Traditional and Kampo Medicine (TKM). One of the main focuses of this journal is research on Kampo medicine, a Japanese traditional herbal medicine that originated in ancient China and became established in Japan. TKM is dedicated to providing accurate, timely, and significant information on traditional medicine, Kampo medicine and natural medicine for researchers and practitioners in these areas. Contributions may include clinical and basic research on traditional medicine, Kampo medicine and natural medicine, covering pharmacology, pharmacognosy (see http://en.wikipedia.org/wiki/Pharmacognosy), biochemistry and chemistry, as well as clinical applications. Can we think of some way of encouraging the editors-in-chief (Naotoshi Shibahara, MD, PhD, Naoki Inagaki, PhD) to include IC/BPS?

**NEW BLADDER JOURNAL**

*Bladder* is a new international, open-access journal committed to publishing top-quality peer-reviewed articles describing basic laboratory, translational, and clinical investigations in the broad fields of bladder biology and diseases, including benign and malignant conditions. Subject areas covered by *Bladder* include, but are not limited to: anatomy, embryology, development, physiology, neurophysiology and diseases of the bladder and its neighboring organs such as the urethra, ureter, seminal vesicle and pelvic floor. Co-Editors-in-Chief Lori A. Birder, PhD and Toby C. Chai, MD are familiar names to us in the IC/BPS research world. So let’s hope that we see IC/BPS featuring in this new journal very soon.


**ONLINE JOURNAL REMINDER**

**INTERNATIONAL JOURNAL OF UROLOGY (IJU) SPECIAL ISSUE WITH FREE ACCESS**


All articles in this special supplement have free access.

**BOOKS**

**Verborgen Vrouwenleed [in Dutch]**

Author: Marijke C.P. Slieker-ten Hove, PhD
Published by Boekscout.nl Soest, Netherlands
Price: € 20.45
ISBN: 978-94-022-1241-9
Boekscout.nl Soest
Can be ordered from [http://verborgenvrouwenleed.nl/](http://verborgenvrouwenleed.nl/)

The author, Marijke Slieker-ten Hove, is well-known in the international pelvic floor physiotherapy world. This newly published Dutch book on complaints of the pelvic floor, looks at the secret suffering of women caused by bladder and bowel incontinence, prolapse and sexual pain in women and is creating a sensation in the Netherlands. A book that every woman should read. It would be very useful if it could be translated into English.

**BOOK REMINDER**

**Bladder Pain Syndrome, a Guide for Clinicians**

Jørgen Nordling, Jean-Jacques Wyndaele, Joop P van de Merwe, Pierre Bouchelouche, Mauro Cervigni, Magnus Fall (Editors.)
Published by Springer 2013, 365 p.
[Click here for the Content of the book](http://www.springer.com/medicine/urology/book/978-1-4419-6928-6)

**THESIS**

**Research on diagnostic techniques for patients with Chronic Pelvic Pain Syndrome**

By Jörgen Quaghebeur, PhD, Physiotherapist, Osteopath
University of Antwerp, 2014
Includes IC/BPS, noting that in chronic pelvic pain syndromes diagnosis is not easy and treatment options do not always provide the estimated results. There is a need to evaluate methods of diagnosis and management. Questionnaires are evaluated here and it is reported that when the most commonly used questionnaires for symptoms and quality of life are compared, very different results can be found. There is a need for the development of a new or unified questionnaire that allows a good description of symptoms and QoL, with an extended version for research.

WEBSITES

NATIONAL KIDNEY AND UROLOGIC DISEASES INFORMATION CLEARINGHOUSE (NKUDIC) IN THE USA
A useful A-Z list of health topics in the field of kidney and urologic diseases can be found at: http://kidney.niddk.nih.gov/KUDiseases/a-z.aspx. The NIDDK also has downloadable fact sheets, easy-to-read booklets and an awareness and prevention series with links from this A-Z page.

NIDDK PATIENT INFORMATION: DIGESTIVE SYSTEM
Since many IC/BPS patients suffer from irritable bowel syndrome with chronic abdominal pain, cramps, bloating, gas, constipation, and diarrhoea, it is useful to note the following updates:
The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) recently updated its information on The Digestive System and how it works: http://www.digestive.niddk.nih.gov/ddiseases/pubs/yrdd/index.aspx. The NIDDK has free resources about IBS and related digestive disorders available to the public, including:
Irritable Bowel Syndrome
Irritable Bowel Syndrome in Children
Irritable Bowel Syndrome: What You Need to Know (En Español)
What I need to know about Irritable Bowel Syndrome

RESEARCH HIGHLIGHTS

A REVIEW OF SELECTED RECENT SCIENTIFIC LITERATURE ON INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND RELATED DISORDERS
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, chronic pelvic pain (syndrome) or combinations of these. Hunner’s ulcer, Hunner lesion and Hunner Disease are synonymous. When reviewing the article, we generally use the terminology used by the authors.

MAPP NETWORK NEWS

UROLOGICAL CHRONIC PELVIC PAIN SYNDROME SYMPTOM FLARES: CHARACTERISATION OF THE FULL RANGE OF FLARES AT TWO SITES IN THE MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN (MAPP) RESEARCH NETWORK.
The aim of this study from the USA was to describe the full range of symptom exacerbations defined by people with interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome as ‘flares’, and to investigate their associated healthcare utilization and bother at two sites of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Epidemiology and Phenotyping study. Participants completed a flare survey that asked them: 1) whether they had ever had flares (‘symptoms that are much worse than usual’) that lasted <1 h, >1 h and <1 day, and >1 day; and 2) for each duration of flare, to report:
their average length and frequency; their typical levels of urological and pelvic pain symptoms; and their levels of healthcare utilization and bother. The authors compared participants’ responses to their non-flare MAPP values and by duration of flare using generalized linear mixed models. Of 85 participants, 76 (89.4%) completed the flare survey, 72 (94.7%) of whom reported experiencing flares. Flares varied widely in terms of their duration (seconds to months), frequency (several times per day to once per year or less), and intensity and type of symptoms (e.g. pelvic pain vs urological symptoms). Flares of all durations were associated with greater pelvic pain, urological symptoms, disruption to participants’ activities and bother, with increasing severity of each of these factors as the duration of flares increased. Days-long flares were also associated with greater healthcare utilization. In addition to duration, symptoms (pelvic pain, in particular) were also significant determinants of flare-related bother. Their findings suggest that flares are common and associated with greater symptoms, healthcare utilization, disruption and bother. Their findings also show the characteristics of flares most bothersome to patients (i.e. increased pelvic pain and duration), and thus of greatest importance to consider in future research on flare prevention and treatment.

**RELATIONSHIP BETWEEN CHRONIC NON-URINARY ASSOCIATED SOMATIC SYNDROMES (NUAS) AND SYMPTOM SEVERITY IN UROLOGICAL CHRONIC PELVIC PAIN SYNDROMES: BASELINE EVALUATION OF THE MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN (MAPP) STUDY.**


Krieger and colleagues report data from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) network to: (1) identify participants having either (a) urologic chronic pelvic pain syndromes (UCPPS) only or (b) chronic functional non-urological associated somatic syndromes (NUAS) in addition to UCPPS, (2) characterize these two subgroups, and (3) explore these two subgroups using three criteria: (a) the MAPP eligibility criteria, (b) self-reported medical history, or (c) RAND interstitial cystitis epidemiologic (RICE) criteria. Self-reported cross-sectional data were collected from men and women with UCPPS including: predominant symptoms, symptom duration and severity, NUAS symptoms, and psychosocial factors. Of 424 UCPPS participants, 162 (38%) had NUAS: 93 (22%) irritable bowel syndrome, 15 (4%) fibromyalgia, 13 (3%) chronic fatigue syndrome, and 41 (10%) with multiple syndromes. Among 233 females, 103 (44%) had NUAS compared to 59 (31%) of 191 males (p = 0.006). Participants with NUAS had more severe urological symptoms, and more frequent depression and anxiety. Of 424 participants, 228 (54%) met RICE criteria. Among 228 RICE-positive participants, 108 (47%) had NUAS compared to 54 (28%) of 203 RICE-negative patients with NUAS. It was concluded that NUAS represent important clinical characteristics of UCPPS. Participants with NUAS have more severe symptoms, longer duration and higher rates of depression and anxiety. RICE-positive patients are more likely to have NUAS and more severe symptoms. Because NUAS are more common in women, future studies need to account for this potential confounding factor in UCPPS.

**IC/BPS DIAGNOSIS AND TREATMENT**

**AUA IC/BPS GUIDELINE UPDATE**

**AMERICAN UROLOGICAL ASSOCIATION GUIDELINE: DIAGNOSIS AND TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME**


Free access, click on title.

Click here for Press Release

The AUA has updated its guideline on interstitial cystitis/bladder pain syndrome, reflecting new insights and published data. There is free access to the full text, while the press release lists the main changes.

**PRETREATMENT FEATURES TO INFLUENCE EFFECTIVENESS OF INTRAVESICAL HYALURONIC ACID INSTILLATION IN REFRACTORY INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.**

International Painful Bladder Foundation
The purpose of this study by Kim and colleagues from Seoul, Korea was to determine the efficacy of intravesical hyaluronic acid (HA) instillation in treating patients with refractory interstitial cystitis/painful bladder syndrome (IC/PBS) and to identify any related factors that influence its therapeutic effect. Thirty-three female IC/PBS patients who demonstrated poor or unsatisfactory responses to previous treatments between December 2010 and October 2012 were enrolled. Despite previous treatments, the enrolled patients had visual analogue scale (VAS) pain scores ≥4 and total scores (symptom and bother scores) ≥13 on the pelvic pain and urgency/frequency (PUF) questionnaire and ≥12 on the O'Leary-Sant interstitial cystitis symptoms index (ICSI)/problems index (ICPI). All patients received once weekly intravesical instillations of 40-mg HA diluted in 50-mL saline for 4 weeks. The efficacy of the HA instillation was evaluated by comparing the mean changes in the scores of the VAS and questionnaires from baseline to 4 weeks after treatment. Improvement was defined as a ≥2 decrease in the VAS. The authors also investigated the effects of the presence of Hunner lesion and previous treatment modalities on the therapeutic outcome of HA instillation. Twenty patients (61%) showed improvements. Previous treatment modalities did not affect the efficacy of HA instillation and the presence of Hunner lesion was unrelated to outcomes. No complications were observed. According to the authors, their results show that intravesical HA instillation is an effective and safe treatment for patients with refractory IC/PBS. Previous treatment modalities and presence of Hunner lesion do not affect the efficacy of HA instillation.

**BOTULINUM TOXIN IN UROLOGY: A REVIEW OF CLINICAL POTENTIAL IN THE TREATMENT OF UROLOGIC AND SEXUAL CONDITIONS.**


Chung from Australia reports that in recent years there has been an increased interest in the use of botulinum neurotoxin (BoNT) to treat medical conditions refractory to conventional treatment. This article provides an overview of the clinical use and efficacy of BoNT in the treatment of various urologic and sexual conditions. BoNT has been accepted and/or explored as novel treatment for various lower urinary tract and sexual dysfunctions such as overactive bladder/detrusor overactivity (DO), detrusor-sphincter dyssynergia (DSD), benign prostatic hyperplasia, interstitial cystitis/painful bladder syndrome, chronic pelvic pain and more recently premature ejaculation. BoNT-A has received regulatory approval for use in neurogenic DO and overactive bladder, but its use remains unlicensed in other lower urinary tract conditions such as non-neurogenic lower urinary tract symptoms in men with benign prostatic hyperplasia, bladder pain syndrome and DSD. Published literature shows that BoNT can be effective in carefully selected patient groups, has minimal adverse event profile and is generally well tolerated by many patients. However, many questions remain unanswered and larger scale multi-institutional studies are required to determine the key factors in BoNT treatment success.

**ELECTROSURGICAL MANAGEMENT OF HUNNER ULCERS IN A REFERRAL CENTER’S INTERSTITIAL CYSTITIS POPULATION.**


The purpose of this study was to characterize electrocautery (EC) as a valid treatment option in interstitial cystitis (IC) patients with Hunner ulcers (HUs). From 1997 to 2013, a single urologist’s IC population was retrospectively reviewed to identify HU patients as well as their demographics, operative characteristics, and response to a 2-page questionnaire evaluating parameters of their experience with EC. Descriptive statistics, Pearson chi-square test, Student t test, and Pearson coefficient were used. Two hundred fourteen EC procedures were performed in 76 patients (87% women; mean age, 66 ± 1.67 years). Fifty-one patients (69%) who underwent multiple EC had mean initial bladder capacity of 438.62 ± 27.90 mL and final bladder capacity of 422.40 ± 30.10 mL. Mean number of EC procedures was 2.98 ± 0.25 (range, 1-11). Mean time between sessions was 14.52 ± 1.34 months (range, 1-121 months). Fifty-two patients (68%) completed our questionnaire, with 13.54 ± 1.28 years of symptoms and 10.66 ± 0.96 years since diagnosis. Ranking IC...
treatments, 37 patients (84%) reported EC most beneficial. On a 0-10 (none to worst possible) scale before and after EC, frequency improved from 9.04 ± 1.30 to 3.65 ± 2.75 (P <.001), urgency from 8.40 ± 2.38 to 3.28 ± 2.71 (P <.001), and pain from 8.62 ± 2.36 to 2.68 ± 2.55 (P <.001). Overall, 89.6% of patients noted some degree of symptom improvement after EC; 56.3% of patients had marked improvement. A total of 98% of patients would undergo EC again. It was concluded that EC of HU is an effective and safe procedure with high patient satisfaction that does not diminish bladder capacity.

**MULTIPLE SENSITIVITY PHENOTYPE IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.**


Free access, click on title.

Phenotypic differentiation of patients with interstitial cystitis/bladder pain syndrome (IC/BPS) may improve our understanding of the condition, as well as the development of patient-specific treatment strategies. Fuoco and colleagues from Canada identified a distinct subgroup of IC/BPS patients with a multiple sensitivity phenotype. They defined patients with this IC/BPS associated multiple sensitivity syndrome as having at least 3 confirmed allergies/sensitivities to medications and/or environmental factors and a diagnosis of IC/BPS. These IC/BPS patients identified with a multiple sensitivity phenotype (cases) were compared to age-matched IC/BPS patients with few or no allergies (controls) at a 1:2 ratio. Comparisons were undertaken using standardized case assessment parameters (age, duration of symptoms, medical history, Interstitial Cystitis Symptoms Index [ICSI] and pelvic pain and urinary urgency/frequency [PUF] symptom scores, and urinary, psychosocial, organ specific, infection, neurologic/systemic, tenderness [UPOINT] categorization). The study consisted of 17 cases and 34 age-matched controls; the mean age was 55 and 56 years, respectively. There was statistically more medication and environmental allergies in the cases versus controls. Cases reported more concomitant illnesses and number of bodily systems affected. The prevalence of irritable bowel syndrome and fibromyalgia was higher in the case group. Additionally, there were more reported psychiatric diseases, allergic/immune diseases, and pulmonary diseases in the case group. UPOINT classification differed with more patients in the case group being categorized in the psychosocial and neuropathic/systemic domains. Total UPOINT classification (out of 6) was also higher in cases than controls. The authors concluded that they have characterized a distinct phenotypic group of patients with IC/BPS and multiple sensitivities. The authors report that the limitations of their study include the retrospective case-control matching design, biases in phenotype definition, single centre patient recruitment, and the lack of follow-up. Furthermore, it should also be mentioned that the authors did not look specifically at the patient’s cystoscopic assessments and therefore made no distinction between lesion and non-lesion disease, the reason being that many patients at this centre do not undergo cystoscopy. Hopefully this will be done in any follow-up. However, the observation of this specific phenotype suggests that further research in this group may help develop targeted therapeutic strategies for patients with a concomitant multiple sensitivity syndrome and IC/BPS.

**METABOLOMICS INSIGHTS INTO PATHOPHYSIOLOGICAL MECHANISMS OF INTERSTITIAL CYSTITIS.**


Free access, click on title.

Interstitial cystitis (IC), also known as painful bladder syndrome or bladder pain syndrome, is a chronic lower urinary tract syndrome characterized by pelvic pain, urinary urgency, and increased urinary frequency in the absence of bacterial infection or identifiable clinicopathology. IC can lead to long-term adverse effects on the patient’s quality of life. Therefore, early diagnosis and better understanding of the mechanisms underlying IC are needed. Metabolomic studies of biofluids have become a powerful method for assessing disease mechanisms and biomarker discovery, which potentially address these important clinical needs. However, limited intensive metabolic profiles have been elucidated in IC. The article is a short review on metabolomic analyses that provide a unique fingerprint of IC with a focus on its use in determining a potential diagnostic biomarker associated with symptoms, a response predictor of therapy, and a prognostic marker.

*Note: If you are wondering what “metabolomics” means, go to Wikipedia: [http://en.wikipedia.org/wiki/Metabolomics](http://en.wikipedia.org/wiki/Metabolomics)*
URINARY METABOLITE PROFILING COMBINED WITH COMPUTATIONAL ANALYSIS PREDICTS INTERSTITIAL CYSTITIS-ASSOCIATED CANDIDATE BIOMARKERS.


Interstitial cystitis/painful bladder syndrome is a chronic syndrome of unknown etiology that presents with bladder pain, urinary frequency, and urgency. The lack of specific biomarkers and a poor understanding of underlying molecular mechanisms present challenges for disease diagnosis and therapy. The goals of this study by Wen and colleagues from Korea were to identify noninvasive biomarker candidates for IC from urine specimens and to potentially gain new insight into disease mechanisms using a nuclear magnetic resonance (NMR)-based global metabolomics analysis of urine from female IC patients and controls. Principal component analysis (PCA) suggested that the urinary metabolome of IC and controls was clearly different, with 140 NMR peaks significantly altered in IC patients compared to that in controls. On the basis of strong correlation scores, fifteen metabolite peaks were nominated as the strongest signature of IC. Among those signals that were higher in the IC group, three peaks were annotated as tyramine, the pain-related neuromodulator. Two peaks were annotated as 2-oxoglutarate. Levels of tyramine and 2-oxoglutarate were significantly elevated in urine specimens of IC subjects. An independent analysis using mass spectrometry also showed significantly increased levels of tyramine and 2-oxoglutarate in IC patients compared to controls. Functional studies showed that 2-oxoglutarate, but not tyramine, retarded growth of normal bladder epithelial cells. These preliminary findings suggest that analysis of urine metabolites has promise in biomarker development in the context of IC.

ADDING A SEXUAL DYSFUNCTION DOMAIN TO UPOINT SYSTEM IMPROVES ASSOCIATION WITH SYMPTOMS IN WOMEN WITH INTERSTITIAL CYSTITIS AND BLADDER PAIN SYNDROME.


The aim of this study from Guangzhou, China was to examine whether adding a sexual dysfunction domain to urinary, psychosocial, organ specific, infection, neurologic or systemic, and tenderness (UPOINT) system improves the association with interstitial cystitis and bladder pain syndrome (IC/BPS) symptom severity due to a high prevalence of sexual dysfunction in women. A total of 90 Chinese women with IC/BPS were prospectively collected and classified in each domain of the UPOINT system. Symptom severity was measured using the Interstitial Cystitis Symptom Index (ICSI). The sexual function was evaluated using the Female Sexual Function Index (FSFI). Clinically relevant associations were calculated. The percentage of patients positive for each domain were 90 of 90 (100%), 33 of 90 (37%), 88 of 90 (98%), 21 of 90 (23%), 36 of 90 (40%), 38 of 90 (42%), 62 of 90 (69%) for the urinary, psychosocial, organ specific, infection, neurologic or systemic, tenderness, and sexual dysfunction, respectively. Liu and colleagues report that there were significant associations between the number of domains and ICSI and FSFI scores. After adding a sexual dysfunction domain to create a modified UPOINTS system, the association between the number of domains and symptom severity was improved. The presence of sexual dysfunction had a significant impact on the ICSI scores, pain scores, and quality of life index scores. Significantly reduced FSFI scores were found in patients who had positive psychosocial, organ specific, and tenderness domains. According to the authors, this study demonstrated sexual dysfunction was an important component of IC-BPS phenotype, and adding a sexual dysfunction domain to the UPOINT system improved the association with IC/BPS symptom severity.

INTRAVESICAL INSTILLATION OF PENTOSAN POLYSULFATE ENCAPSULATED IN A LIPOSOME NANOCARRIER FOR INTERSTITIAL CYSTITIS.


Free access, click on title.

Lander and See from Nevada determined the effect of intravesical instillation of pentosan polysulfate encapsulated in liposomes for refractory interstitial cystitis patients. This was an open label uncontrolled study. Subjects were recruited from a private urology practice. Inclusion criteria included patients who met NIDDK criteria for Interstitial Cystitis (IC) and who were responding poorly to conventional treatments. Exclusion criteria included evidence of a urinary tract infection, bladder cancer, or other forms of chronic cystitis. Patients received 400 mg of Pentosan Polysulfate (PP) encapsulated into liposomes as an intravesical instillation performed every 2 weeks for 3 months. Baseline and post treatment outcome measures were
obtained that included the O'Leary-Sant Interstitial Cystitis Symptom and Problem Questionnaire and the Pelvic Pain and Urgency/Frequency Patient symptom Scale tests. A total of 37 instillations were used and no adverse events occurred. Clinically significant decreases in symptom scores greater than 50% were seen in virtually all outcome measures at 3 month follow up. All subjects reported remarkable subjective improvement in pain symptoms marked by decreased use of narcotics and increased enjoyment of daily activities. No patients developed systemic symptoms or poor tolerance of the instillations. Intravesical Pentosan Polysulfate encapsulated into liposomes can significantly decrease frequency, urgency, pain and improve quality of life for two months after deployment. Additional studies are needed to determine cellular effects of glycosaminoglycan restoration, ideal doses, dosing intervals, safety and cost-effectiveness of this therapy.

A NEW PARADIGM IN CHRONIC BLADDER PAIN.

The concept of visceral pain has moved from organ-centered disease to a conceptualization based on pathophysiological mechanisms, integrating psychosocial and sexual dimensions. The terms painful bladder syndrome and bladder pain syndrome have been coined to include all patients with bladder pain. There is substantial overlap between IC/BPS and other pelvic/abdominal pain syndromes IC/BPS is likely to be underdiagnosed and undertreated in both men and women IC/BPS requires a multidisciplinary team approach toward management.

SLEEP DISTURBANCES AND NOCTURNAL SYMPTOMS: RELATIONSHIPS WITH QUALITY OF LIFE IN A POPULATION-BASED SAMPLE OF WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

The aim of this study from Pittsburgh was to characterize the nature and impact of sleep disturbances on quality of life (QOL) in women with interstitial cystitis/bladder pain syndrome (IC/BPS). Participants were 3,397 women from a telephone probability survey who met IC/BPS symptom criteria. Sleep quality, duration, and IC/BPS nocturnal symptoms (i.e., trouble sleeping due to bladder pain, urgency, or needing to use the bathroom), general QOL (mental and physical health and sexual functioning), and IC/BPS QOL impairment were assessed via self-report during telephone interview. Over half of the sample reported poor sleep quality, sleep duration ≤ 6 hours, or trouble sleeping due to IC/BPS symptoms. After covariate adjustment, short sleep duration was significantly associated with greater IC/BPS QOL impairment and poorer self-reported physical health. Poor sleep quality was significantly associated with greater IC/BPS QOL impairment, poorer self-reported physical health, and greater sexual dysfunction. IC/BPS nocturnal symptoms were significantly associated with greater IC/BPS impairment, poorer physical health and mental health, and greater sexual dysfunction, after covariate adjustment. After further adjustment for IC/BPS nocturnal symptoms, we found that poor sleep quality and short sleep duration were independent correlates of poor self-reported physical health. It was concluded that poor sleep quality and short sleep duration, as well as disorder-specific sleep disturbances, are highly prevalent in women with IC/BPS and are associated with poorer disease-specific and general QOL.

ASSOCIATED DISORDERS

RISK OF ASSOCIATED CONDITIONS IN RELATIVES OF SUBJECTS WITH INTERSTITIAL CYSTITIS.

Urological chronic pelvic pain syndrome includes interstitial cystitis/painful bladder syndrome (IC/PBS), a chronic bladder pain condition of unknown etiology. Interstitial cystitis/painful bladder syndrome can co-occur with a number of associated conditions such as irritable bowel syndrome and fibromyalgia. The purpose of this study was to estimate the heritability of approximately 20 associated conditions in first-degree relatives (and if appropriate, second- and third-degree relatives) of patients with IC/PBS to identify shared genetic contributions for the disease combinations. Allen-Brady and colleagues from the USA used the Utah Population Database, a unique population-based genealogical database that has been linked to electronic health records.
for the University of Utah Health Sciences Center back in 1994. Interstitial cystitis/painful bladder syndrome probands were identified by the International Classification of Diseases, Ninth Revision code for chronic interstitial cystitis and had genealogy information for 12 of their 14 immediate ancestors. The authors calculated excess risk of an associated condition in relatives of patients with IC/PBS using relative risk estimates. They identified 248 IC/PBS probands. They found that 2 associated conditions, myalgia and myositis/unspecified (fibromyalgia) as well as constipation, were in significant excess in the patients with IC/PBS themselves, their first-degree relatives, and their second-degree relatives. The excess risk among relatives between IC/PBS and these associated conditions also held in the converse direction. Excess risk of IC/PBS was observed in the first- and second-degree relatives in probands with myalgia and myositis/unspecified (fibromyalgia) and in probands with constipation. These results suggest that myalgia and myositis/unspecified (fibromyalgia) as well as constipation are likely to share underlying genetic factors with IC/PBS.

UROTHELIUM

GLYCOXYLATION OF UROPLAKINS. IMPLICATIONS FOR BLADDER PHYSIOPATHOLOGY.

Urothelium, a specialized epithelium, covers the urinary tract and act not only as a barrier separating its light from the surrounding tissues, but fulfils an important role in maintaining the homeostasis of the urothelial tract and well-being of the whole organism. Proper function of urothelium is dependent on the precise assemble of highly specialized glycoproteins called uroplakins, the end products and differentiation markers of the urothelial cells. Glycosylation changes in uroplakins correlate with and might reflect progressive stages of pathological conditions of the urothelium such as cancer, urinary tract infections, interstitial cystitis and others. In this review we focus on sugar components of uroplakins, their emerging role in urothelial biology and disease implications. The advances in our understanding of uroplakins changes in glycan moieties composition, structure, assembly and expression of their glycovariants could potentially lead to the development of targeted therapies and discoveries of novel urine and plasma markers for the benefit of patients with urinary tract diseases.

MARKERS

[THE ROLE OF URINARY MARKERS IN THE ASSESSMENT AND FOLLOW-UP OF LOWER URINARY TRACT DISORDERS: A LITERATURE REVIEW.] [Article in French]

The purpose of this study from France was to conduct a literature review on the role of urinary biomarkers in the initial assessment and follow-up of lower urinary tract symptoms. A literature review was conducted in August 2014 using the Medline/Pubmed database limiting the search to work in English or French. Most studies were of level of evidence 2 or 3 (prospective cohort, controlled or not) and mainly about overactive bladder and bladder pain syndrome. Nerve Growth Factor (NGF) was the most studied and apparently the most promising in the evaluation of overactive bladder (OAB) and neurogenic detrusor overactivity (NDO). Urinary levels of ATP, prostaglandin E2 (PGE2), Brain-Derived Neurotrophic Factor (BDNF) and some cytokines were also significantly higher in most studies in patients with NDO or OAB. Epidermal Growth Factor (EGF), Heparin-Binding EGF (HBEGF) and Antiproliferative Factor (APF) were the most studied urinary markers in bladder pain syndrome, with a significant increase (EGF APF) or decrease (HBEGF) in cases of interstitial cystitis (compared to healthy controls). The urinary N-terminal-telopeptide (NTx) could be predictive of a failed mid-urethral sling. However, few studies reported the diagnostic values of the markers, their association with urodynamic parameters were rarely evaluated and the existence of a publication bias is likely. No randomized controlled study has so far compared the urinary markers to urodynamic evaluation. It was concluded that in the future, urinary markers could complete or replace urodynamic examination. However, to date, there is no high level of
evidence study comparing these markers to urodynamics and their use can therefore not be recommended in daily practice.

**CYSTECTOMY**

**THE ROLE OF CYSTECTOMY FOR NON-MALIGNANT BLADDER CONDITIONS: A REVIEW**


Free access, click on title.

Few studies have adequately addressed the indications, efficacy, and quality-of-life for cystectomy performed for non-malignant bladder conditions. Patients with debilitating non-malignant bladder conditions who have failed all previous conservative therapies may undergo various forms of cystectomy, including partial, simple or radical cystectomy. Chong and colleagues from Richmond, Virginia provide a review of the current literature and recommendations for cystectomy for various non-malignant bladder conditions. They report that data from the final review suggest that common benign indications for cystectomy are interstitial cystitis/painful bladder syndrome (IC/PBS), neurogenic bladder, hemorrhagic/radiation cystitis, infectious diseases of the bladder and miscellaneous conditions of the bladder such as endometriosis and total refractory incontinence. The most common perioperative complications include urinary tract and wound infections. Efficacy of cystectomy in patients with IC/PBS is greater than 80%, while efficacy in patients with neurogenic bladder is greater than 90%. Finally, improved urinary quality-of-life has been demonstrated in patients with neurogenic bladder post-cystectomy. They conclude that cystectomy for non-malignant conditions can be considered for patients who have failed previous conservative therapy. The limited data in existence suggests fertility can be adequately preserved after cystectomy in younger males. The data regarding the forms of urinary diversion suggests no significant advantage between any of the major forms of urinary diversion. Finally, while newer pharmacologic and technological advances are widely used in the treatment of various benign urological conditions, their role in preventing or treating refractory benign bladder conditions have not been fully characterized.

[A CASE OF BLADDER CANCER ARISING AFTER AUGMENTATION CYSTOPLASTY USING ILEAL PATCH FOR INTERSTITIAL CYSTITIS]. [Article in Japanese]


A 62-year-old man, who was refractory to repeated hydrodistentions for interstitial cystitis, underwent augmentation cystoplasty using ileal patch. Pathological examination revealed no malignancy. Computed tomography (CT) scan showed multiple pelvic and para-aortic lymph-node swellings at 14 months after the operation. CT-guided lymph-node biopsies and transurethral bladder biopsies revealed invasive urothelial carcinoma with lymph node metastasis. In patients with symptoms of interstitial cystitis, bladder cancer should be kept in mind despite negative findings of cytology and bladder biopsies.

**KETAMINE ABUSE AND THE BLADDER**

**BIOLOGICAL EFFECT OF KETAMINE IN UROTHELIAL CELL LINES AND GLOBAL GENE EXPRESSION ANALYSIS IN THE BLADDERS OF KETAMINE-INJECTED MICE.**


Shen and colleagues from Taiwan note that while ketamine is used clinically for anaesthesia, it is also abused as a recreational drug. Previously, it has been established that ketamine-induced bladder interstitial cystitis is a common syndrome in ketamine-abusing individuals. As the mechanisms underlying ketamine-induced cystitis have yet to be revealed, the present study investigated the effect of ketamine on human urothelial cell lines and utilized a ketamine-injected mouse model to identify ketamine-induced changes in gene expression in mice bladders. In the in vitro bladder cell line assay, ketamine induced cytotoxicity in a dose- and time-dependent manner. Ketamine arrested the cells in G1 phase and increased the sub-G1 population, and also increased the barrier permeability of these cell lines. In the ketamine-injected mouse model, ketamine did not change the
body weight and bladder histology of the animals at the dose of 30 mg/kg/day for 60 days. Global gene expression analysis of the animals' bladders following data screening identified ten upregulated genes and 36 downregulated genes induced by ketamine. A total of 52% of keratin family genes were downregulated, particularly keratin 6a, 13 and 14, which was confirmed by polymerase chain reaction analysis. Keratin 14 protein, one of the 36 ketamine-induced downregulated genes, was also reduced in the ketamine-treated mouse bladder, as determined by immunohistochemical analysis. This suggested that cytotoxicity and keratin gene downregulation may have a critical role in ketamine-induced cystitis.

FIBROMYALGIA

WHAT IS IN A NAME? COMPARING DIAGNOSTIC CRITERIA FOR CHRONIC FATIGUE SYNDROME WITH OR WITHOUT FIBROMYALGIA.
This study from Ghent, Belgium had two objectives. (1) to compare objective and self-report measures in patients with chronic fatigue syndrome (CFS) according to the 1994 Center for Disease Control (CDC) criteria, patients with multiple sclerosis (MS), and healthy controls, and (2) to contrast CFS patients who only fulfill CDC criteria to those who also fulfill the criteria for myalgic encephalomyelitis (ME), the 2003 Canadian criteria for ME/CFS, or the comorbid diagnosis of fibromyalgia (FM). One hundred six participants (48 CFS patients diagnosed following the 1994 CDC criteria, 19 MS patients, and 39 healthy controls) completed questionnaires assessing symptom severity, quality of life, daily functioning, and psychological factors. Objective measures consisted of activity monitoring, evaluation of maximal voluntary contraction and muscle recovery, and cognitive performance. CFS patients were screened whether they also fulfilled ME criteria, the Canadian criteria, and the diagnosis of FM. CFS patients scored higher on symptom severity, lower on quality of life, and higher on depression and kinesiophobia and worse on MVC, muscle recovery, and cognitive performance compared to the MS patients and the healthy subjects. Only one difference was found between those fulfilling the ME criteria and those who did not regarding the degree of kinesiophobia (lower in ME), while comorbidity for FM significantly increased the symptom burden. CFS patients report more severe symptoms and are more disabled compared to MS patients and healthy controls. Based on the present study, fulfillment of the ME or Canadian criteria did not seem to give a clinically different picture, whereas a diagnosis of comorbid FM selected symptomatically worse and more disabled patients.

The ACR 1990 fibromyalgia classification criteria are based on widespread pain and tenderness. In 2010 new criteria were proposed, focusing more on multiple symptoms and these, latterly, were modified to require only self-report. The current study aimed to determine the population prevalence of fibromyalgia, and to compare differences in prevalence, using the alternative criteria. Methods A cross-sectional survey was conducted. Questionnaires, including items on pain, symptoms, and rheumatological diagnoses were mailed to 4600 adults in northeast Scotland. Participants with chronic widespread pain, or who met the modified 2010 criteria, plus a sub-sample of other participants were invited to a research clinic. Attendees completed an additional questionnaire, and a rheumatological examination, and were classified according to the ACR 1990, 2010 and modified 2010 criteria. The prevalence of each was calculated, weighting back to the target population by age, sex and area of residence. Of 1604 questionnaire participants, 269 were invited and 104 (39%) attended the research clinic, of whom 32 (31%) met ≥1 of the fibromyalgia criteria. The prevalence of fibromyalgia using the 1990, 2010 and modified 2010 criteria was 1.7% (95%CI: 0.7-2.8%); 1.2% (0.3-2.1%); and 5.4% (4.7-6.1%), respectively. The female/male ratio was 13.7 to 4.8 and 2.3, respectively. It was concluded that fibromyalgia prevalence varies with the different classification criteria - specifically, prevalence is higher, and a greater proportion of men are identified, with the modified 2010 criteria, compared to those requiring clinician input. This has important implications for the use of the new criteria both in research and in clinical practice.
Primary Sjögren syndrome is a systemic autoimmune disease characterized by mouth and eye dryness, pain, and fatigue. Hydroxychloroquine is the most frequently prescribed immunosuppressant for the syndrome. However, evidence regarding its efficacy is limited. The purpose of this study from France was to evaluate the efficacy of hydroxychloroquine for the main symptoms of primary Sjögren syndrome: dryness, pain, and fatigue. From April 2008 to May 2011, 120 patients with primary Sjögren syndrome according to American-European Consensus Group Criteria from 15 university hospitals in France were randomized in a double-blind, parallel-group, placebo-controlled trial. Participants were assessed at baseline, week 12, week 24 (primary outcome), and week 48. The last follow-up date for the last patient was May 15, 2012. Patients were randomized (1:1) to receive hydroxychloroquine (400 mg/d) or placebo until week 24. All patients were prescribed hydroxychloroquine between weeks 24 and 48. The primary end point was the proportion of patients with a 30% or greater reduction between weeks 0 and 24 in scores on 2 of 3 numeric analog scales (from 0 [best] to 10 [worst]) evaluating dryness, pain, and fatigue. At 24 weeks, the proportion of patients meeting the primary end point was 17.9% (10/56) in the hydroxychloroquine group and 17.2% (11/64) in the placebo group. Between weeks 0 and 24, the mean (SD) numeric analog scale score for dryness changed from 6.38 (2.14) to 5.85 (2.57) in the placebo group and 6.53 (1.97) to 6.22 (1.87) in the hydroxychloroquine group. Hydroxychloroquine had no efficacy in patients with anti-SSA autoantibodies, high IgG levels, or systemic involvement. During the first 24 weeks, there were 2 serious adverse events in the hydroxychloroquine group and 3 in the placebo group; in the last 24 weeks, there were 3 serious adverse events in the hydroxychloroquine group and 4 in the placebo group. It was concluded that among patients with primary Sjögren syndrome, the use of hydroxychloroquine compared with placebo did not improve symptoms during 24 weeks of treatment. Further studies are needed to evaluate longer-term outcomes.

**GASTRO-INTESTINAL DISORDERS**

**IRRITABLE BOWEL SYNDROME: A MICROBIOME-GUT-BRAIN AXIS DISORDER?**


Irritable bowel syndrome (IBS) is an extremely prevalent but poorly understood gastrointestinal disorder. Consequently, there are no clear diagnostic markers to help diagnose the disorder and treatment options are limited to management of the symptoms. The concept of a dysregulated gut-brain axis has been adopted as a suitable model for the disorder. The gut microbiome may play an important role in the onset and exacerbation of symptoms in the disorder and has been extensively studied in this context. Although a causal role cannot yet be inferred from the clinical studies which have attempted to characterise the gut microbiota in IBS, they do confirm alterations in both community stability and diversity. Moreover, it has been reliably demonstrated that manipulation of the microbiota can influence the key symptoms, including abdominal pain and bowel habit, and other prominent features of IBS. A variety of strategies have been taken to study these interactions, including probiotics, antibiotics, faecal transplantations and the use of germ-free animals. There are clear mechanisms through which the microbiota can produce these effects, both humoral and neural. Taken together, these findings firmly establish the microbiota as a critical node in the gut-brain axis and one which is amenable to therapeutic interventions.
VISCERAL AND SOMATIC HYPERSENSITIVITY, AUTONOMIC CARDIOVASCULAR DYSFUNCTION AND LOW-GRADE INFLAMMATION IN A SUBSET OF IRRITABLE BOWEL SYNDROME PATIENTS.
Free access to full article.
The pathophysiology of irritable bowel syndrome (IBS) is complex and not fully understood, so the aim of this study from China was to evaluate whether visceral and somatic hypersensitivity, autonomic cardiovascular dysfunction, and low-grade inflammation of the gut wall are associated with diarrhoea-predominant IBS (D-IBS). Sixty-two patients with D-IBS and 20 control subjects participated in the study. Using the ascending method of limits (AML) protocol, Liu and colleagues demonstrated that D-IBS patients had significantly lower sensory thresholds compared with healthy controls. Using diverse methods, especially the ischemic sensitivity test, for the first time in China, they confirmed that D-IBS patients have somatic hypersensitivity. They had a significantly higher systolic blood pressure and heart rate after a cold stimulus, indicative of autonomic cardiovascular dysfunction. Compared with the control group, D-IBS patients had a significantly higher level of calprotectin. They also found significant correlations between visceral and somatic hypersensitivity, visceral hypersensitivity and autonomic cardiovascular dysfunction, and somatic hypersensitivity and autonomic cardiovascular dysfunction. The authors conclude that their findings may provide valuable suggestions for the treatment of D-IBS.

FACTORIAL STUDY OF MOXIBUSTION IN TREATMENT OF DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME.
Free access, click on title.
The aim of this study from Shanghai, China was to identify an appropriate therapeutic regimen for using aconite cake-separated moxibustion to treat diarrhea-predominant irritable bowel syndrome (D-IBS). A factorial design was employed to examine the two factors of moxibustion frequency and number of cones. The two tested frequencies were three or six moxibustion sessions per week, and the two tested doses were one or two cones per treatment. A total of 166 D-IBS patients were randomly divided into four treatment groups, which included each combination of the examined frequencies and doses. The bilateral Tianshu acupoints (ST25) and the Qihai acupoint (RN6) were selected for aconite cake-separated moxibustion. Each patient received two courses of treatment, and each course had a duration of 2 wk. For each group, the scores on the Birmingham irritable bowel syndrome (IBS) symptom questionnaire, the IBS Quality of Life scale, the Self-Rating Depression Scale (SDS), the Self-Rating Anxiety Scale (SAS), the Hamilton Depression (HAMD) scale, and the Hamilton Anxiety (HAMA) scale were determined before treatment, after the first course of treatment, and after the second course of treatment. On the basis of the results achieved in this study, the authors are of the opinion that an aconite cake-separated moxibustion treatment regimen of 3 treatments/wk and 1 cone/treatment appears to produce better therapeutic effects for D-IBS compared with the other tested regimens.
Note: For information on “moxibustion”, see Wikipedia http://en.wikipedia.org/wiki/Moxibustion.

THE SEVERITY OF IRRITABLE BOWEL SYNDROME OR THE PRESENCE OF FIBROMYALGIA INFLUENCING THE PERCEPTION OF VISCERAL AND SOMATIC STIMULI.
Free access, click on title.
Fibromyalgia Syndrome (FMS) is a frequent comorbidity in Irritable Bowel Syndrome (IBS) patients with a higher functional bowel disorder severity index (FBDSI). Tremolaterra and colleagues from Italy tested the possibility that mild to severe IBS patients without FMS would have a graduated visceral and somatic perception, and the presence of FMS would further enhance somatic, but conversely attenuate visceral perception. Our aim was to study visceral and somatic sensitivity in mild IBS patients and in severe IBS patients...
with or without FMS. Eleven mild IBS and 19 severe IBS with and without FMS patients were studied. Somatic and visceral stimuli were applied in each patient by means of electrical stimulations at active and control sites and by means of an electronic barostat in the rectum. Thresholds for discomfort and perception cumulative scores were measured. Mild and severe IBS patients without FMS demonstrated a significantly lower somatic perception cumulative score than severe IBS patients with FMS at active site. Conversely only severe IBS patients without FMS had significantly lower visceral thresholds for discomfort than mild IBS patients and severe IBS patients with FMS. It was concluded that the presence of co-existing FMS or greater FBDSI affects somatic and visceral perception in a graded fashion across IBS patients.

FOOD ALLERGY AND INTOLERANCE

**REVIEW ARTICLE: THE DIAGNOSIS AND MANAGEMENT OF FOOD ALLERGY AND FOOD INTOLERANCES.**

Adverse reactions to food include immune mediated food allergies and non-immune mediated food intolerances. Food allergies and intolerances are often confused by health professionals, patients and the public. The aim of this review from the John Radcliffe Hospital, Oxford was to critically review the data relating to diagnosis and management of food allergy and food intolerance in adults and children. MEDLINE, EMBASE and the Cochrane Database were searched up until May 2014, using search terms related to food allergy and intolerance. An estimated one-fifth of the population believe that they have adverse reactions to food. Estimates of true IgE-mediated food allergy vary, but in some countries it may be as prevalent as 4-7% of preschool children. The most common food allergens are cow's milk, egg, peanut, tree nuts, soy, shellfish and finned fish. Reactions vary from urticaria to anaphylaxis and death. Tolerance for many foods including milk and egg develops with age, but is far less likely with peanut allergy. Estimates of IgE-mediated food allergy in adults are closer to 1-2%. Non-IgE-mediated food allergies such as Food Protein-Induced Enterocolitis Syndrome are rarer and predominantly recognised in childhood. Eosinophilic gastrointestinal disorders including eosinophilic oesophagitis are mixed IgE- and non-IgE-mediated food allergic conditions, and are improved by dietary exclusions. By contrast food intolerances are nonspecific, and the resultant symptoms resemble other common medically unexplained complaints, often overlapping with symptoms found in functional disorders such as irritable bowel syndrome. Improved dietary treatments for the irritable bowel syndrome have recently been described. The authors conclude that food allergies are more common in children, can be life-threatening and are distinct from food intolerances. Food intolerances may pose little risk but since functional disorders are so prevalent, greater efforts to understand adverse effects of foods in functional disorders are warranted.

CHRONIC (PELVIC) PAIN

**EUROPEAN ASSOCIATION OF UROLOGY: GUIDELINES ON CHRONIC PELVIC PAIN 2014.**
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The authors note in the introduction that minor revisions have been made in the 2014 version of the Guidelines on Chronic Pelvic Pain. Chapter 5 ‘Gastrointestinal aspects of chronic pelvic pain’ has been expanded with a section on sacral neurostimulation and percutaneous tibial nerve stimulation, based on a systematic review of the literature using the Embase and Medline databases and the Cochrane Central Register of controlled trials. Minor revisions have also been made in Chapter 8 ‘Psychological aspects of chronic pelvic pain’, also based on a systematic review of the literature in the above databases including PsycINFO.

**PREVALENCE OF LOWER URINARY TRACT SYMPTOMS AND LEVEL OF QUALITY OF LIFE IN MEN AND WOMEN WITH CHRONIC PELVIC PAIN.**
The aim of this study from Belgium was to evaluate the prevalence of lower urinary tract symptoms and quality of life in patients with chronic pelvic pain syndrome (CPPS). The McGill Pain Questionnaire, Dutch Leiden/Leuven Version (MPQ-DLV), Pain Disability Index (PDI), National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), Interstitial Cystitis Symptom Index (ICSI) and Pelvic Pain and Urinary/Frequency Symptom Scale (PUF) were used, based on their specific properties, to assess the symptoms and impact on the quality of life. Total scores and domains were compared for gender. Results. The studied group (18 male, 17 female) showed a good distribution in gender for age and body mass index. The MPQ-DLV showed significantly higher scores for pain in women for Pain Rating Index - Affective and Total, and Visual Analogue Scale for Pain - Most. Women were less sexually active and had a significantly higher disability and MPQ - Quality of Life. The urinary symptoms showed similar results for gender. It was concluded that a wide variety of symptoms and a negative impact on quality of life were shown. No differences in lower urinary tract symptoms were found between genders. Women were less sexually active than men. Chronic pelvic pain had a significantly higher negative impact on the level of quality of life in women than in men.

LITERATURE REVIEW OF PAIN MANAGEMENT FOR PEOPLE WITH CHRONIC PAIN.
Multimodal approaches toward relieving pain, patients' participation, and improving self-efficacy are important for chronic pain management. The aims of this review from Japan were to identify possible options of nursing strategies for pain management in individuals with chronic pain and to determine the effectiveness of these strategies for pain relief/pain-related problems; therefore, nurses and researchers could consider and/or adopt multimodal chronic pain management strategies. A Systematic Integrated Literature Review was conducted. Published work related to pain management in individuals with chronic pain was identified by searching databases and reviewed. Among the studies reviewed, we identified 35 studies that focused on pain management strategies. In 10 studies, interventions such as integrated and multidisciplinary pain management programs were associated with significant decreases in pain intensity. However, they reported that the long-term effectiveness of pain relief was not satisfactory. Individuals with chronic pain reported that strategies including pharmacotherapy, physical activity, social support from friends and family, acupuncture, heating, rest, diets, or lifestyle changes helped them to effectively manage their pain. The authors identified possible options of pain management strategies and explored effectiveness of chronic pain interventions. The long-term effects of pain relief interventions and social support for individuals with chronic pain require further investigation.

A POSSIBLE LINK BETWEEN DYSMENORRHOEA AND THE DEVELOPMENT OF CHRONIC PELVIC PAIN.
Anecdotally, severe dysmenorrhoea can pre-date the development of chronic pelvic pain (CPP). This study from Australia describes the timeline for the transition from dysmenorrhoea to CPP in a cohort of new patients attending a private gynaecology clinic. In 16.4% of cases, transition occurred within one year, and within 12 years in over 50%. Our study suggests clinicians need to observe women with severe dysmenorrhoea for signs of chronic pain. Further research is needed into the transition from dysmenorrhoea to CPP, and effective early interventions.

BRAIN-DERIVED NEUROTROPHIC FACTOR AS A DRIVING FORCE BEHIND NEUROPLASTICITY IN NEUROPATHIC AND CENTRAL SENSITIZATION PAIN: A NEW THERAPEUTIC TARGET?
Central sensitization is a form of maladaptive neuroplasticity underlying many chronic pain disorders, including neuropathic pain, fibromyalgia, whiplash, headache, chronic pelvic pain syndrome and some forms of osteoarthritis, low back pain, epicondylitis, shoulder pain and cancer pain. Brain-derived neurotrophic factor (BDNF) is a driving force behind neuroplasticity, and it is therefore crucial for neural maintenance and repair. However, BDNF also contributes to sensitization of pain pathways, making it an interesting novel therapeutic
This article presents an overview of BDNF's sensitizing capacity at every level of the pain pathways, including the peripheral nociceptors, dorsal root ganglia, spinal dorsal horn neurons, and brain descending inhibitory and facilitatory pathways. This is followed by the presentation of several potential therapeutic options, ranging from indirect influencing of BDNF levels (using exercise therapy, anti-inflammatory drugs, melatonin, repetitive transcranial magnetic stimulation) to more specific targeting of BDNF's receptors and signaling pathways (blocking the proteinase-activated receptors 2-NK-κβ signaling pathway, administration of phencyclidine for antagonizing NMDA receptors, or blockade of the adenosine A2A receptor). The expert opinion section focuses on combining pharmacotherapy with multimodal rehabilitation for balancing the deleterious and therapeutic effects of BNDF treatment in chronic pain patients, as well as accounting for the complex and biopsychosocial nature of chronic pain.

PLACEBO EFFECTS IN IDIOPATHIC AND NEUROPATHIC PAIN CONDITIONS.

The magnitude of placebo analgesia effect appears to be large in chronic pain patients experiencing hyperalgesic states. So far, placebo effects have primarily been investigated in idiopathic pain conditions, such as irritable bowel pain syndrome, but more recently they have also been investigated in neuropathic pain patients, in which the underlying nerve injury is known. Expected pain levels and emotional feelings are central to placebo effects in both types of pain. They appear to help patients to engage in a mindset for pain relief and activate the pain-modulating system. Furthermore, expectations, emotional feelings, and the experience of pain seem to interact over time, thereby maintaining or enhancing the pain-relieving effect. Expectations and emotional feelings also contribute to the effect of active drugs, and recent studies indicate that drug effects and placebo effects interact in ways that may complicate the interpretations of the findings from clinical trials. It is suggested that expectations and emotional feelings may act as additional or alternative measures in the testing of new pharmacological agents, thereby improving the understanding of the interaction between pharmacological effects and placebo effects, which may have far-reaching implications for research and clinical practice.

VULVODYNIA

CONCURRENT DEEP-SUPERFICIAL DYSpareunIA: PREVALENCE, ASSOCIATIONS, AND OUTCOMES IN A MULTIDISCIPLINARY VULVODYNIA PROGRAM.

Little is known about women with concurrent diagnoses of deep dyspareunia and superficial dyspareunia. The aim of this study from Canada was to determine the prevalence, associations, and outcome of women with concurrent deep-superficial dyspareunia. This is a prospective study of a multidisciplinary vulvodynia programme. Women with superficial dyspareunia due to provoked vestibulodynia were divided into two groups: those also having deep dyspareunia (i.e., concurrent deep-superficial dyspareunia) and those with only superficial dyspareunia due to provoked vestibulodynia. Demographics, dyspareunia-related factors, other pain conditions, and psychological variables at pretreatment were tested for an association with concurrent deep-superficial dyspareunia. Outcome in both groups was assessed to 6 months posttreatment. The level of dyspareunia pain (0-10) and Female Sexual Distress Scale were the main outcome measures. The prevalence of concurrent deep-superficial dyspareunia was 44% (66/150) among women with superficial dyspareunia due to provoked vestibulodynia. At pretreatment, on multiple logistic regression, concurrent deep-superficial dyspareunia was independently associated with a higher level of dyspareunia pain, diagnosis of endometriosis, history of bladder problems, and more depression symptoms, with no difference in the Female Sexual Distress Scale. At 6 months posttreatment, women with concurrent deep-superficial dyspareunia improved in the level of dyspareunia pain and in the Female Sexual Distress Scale to the same degree as women with only superficial dyspareunia due to provoked vestibulodynia. Concurrent deep-superficial dyspareunia is reported by almost half of women in a multidisciplinary vulvodynia program. In women with provoked vestibulodynia, concurrent deep-superficial dyspareunia may be related to endometriosis or interstitial cystitis, and is associated with
depression and more severe dyspareunia symptoms. Standardized multidisciplinary care is effective for women with concurrent dyspareunia.

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