

REVIEW OF THE AMERICAN UROLOGICAL ASSOCIATION (AUA) ANNUAL MEETING, 4-8 MAY 2013, SAN DIEGO, USA

Jane Meijlink

The AUA this year had quite a lot to offer in the form of courses, research abstracts and special sessions in the field of IC/BPS, CP/CPPS and chronic pelvic pain. A number of abstracts were presented with NIDDK MAPP study feedback. These have been included in the abstract review below.

Where IC/BPS is concerned: the take-home message came over loud and clear that glomerulations are not specific, can occur in other disorders, their significance is as yet unknown, and therefore they should NOT be used for diagnostic purposes. Furthermore, the Hunner's lesion (ulcer) subtype clearly seems to be a different entity to non-lesion disease and it was suggested in San Diego (as previously also in Kyoto) that the historic term interstitial cystitis could perhaps be used for this lesion disease, with bladder pain syndrome being used for non-lesion patients.

ON MONDAY MAY 6, THERE WAS A PODIUM SESSION SPECIFICALLY DEDICATED TO INFECTIONS/INFLAMMATION OF THE GENITOURINARY TRACT: INTERSTITIAL CYSTITIS

The following abstracts were presented:

Abstract #865:

CONSEQUENCES OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME SYMPTOMS ON WOMEN'S WORK PARTICIPATION AND INCOME: RESULTS FROM A NATIONAL HOUSEHOLD SAMPLE.

Megan K. Beckett; Sandra H. Berry; Marc N. Elliott; J. Quentin Clemens

The background to this study was that few studies examine economic consequences of IC/BPS and existing studies have examined women with established diagnoses of IC/BPS, as opposed to those with IC/BPS symptoms. The speaker emphasised that this distinction is important because there is often a long delay in diagnosis of IC/BPS and because due to the lack of objective diagnostic criteria, there is likely to be significant variability between caregivers in assigning a diagnosis of IC/BPS. The purpose of this research was to utilise data from a community sample of women with IC/BPS symptoms to describe differences in work participation and income in relation to measures of bladder symptoms impact and comorbidities and to estimate gains to women's economic outcomes that might be achieved with improved management of pain and symptoms. The RAND Interstitial Cystitis Epidemiology (RICE) Study telephoned 146,231 U.S. households to identify women with symptoms suggestive of IC/BPS. The survey identified 2767 community women age <65 with IC/BPS symptoms. In a telephone interview they assessed demographics (age, race/ethnicity, education, marital status), IC/BPS symptom severity and impact (IC Symptom Index, IC Problem Index, Bladder Symptom Impact questionnaire [BSI-6]), depressive symptomology (Patient Health Questionnaire), 12 self-reported medical co-morbidities, work participation, and income. Multivariate regressions predicted five current work outcomes (current employment, kept from working by pelvic pain, missed work days, days worked with symptoms, and real income change since symptom onset).

A total of 42% of women did not work, 10% of them said that this was because of pain or bladder symptoms. On average, each worker missed 6 days of work/year and worked 37% of workdays with

symptoms. Little change was seen in income levels for working women between diagnosis and interview date, in contrast with gains observed by working women in the general population. ICSI and ICPI and symptom duration were not independently related to any work outcomes. BSI-6, a measure of bladder symptom impact across six quality of life domains (interest in life, energy level, moods, feelings of self-worth, social life, ability to carry out home responsibilities) was the best predictor of work outcomes. Depression and the number of medical comorbidities were also associated with worse work outcomes.

It was concluded that functional status and effective coping mechanisms are better predictors of work participation and productivity than IC/BPS symptoms. Clinical management should include providing psychosocial tools to improve patient coping and self-management and treatment of urinary symptoms. Improved social support and coping might translate into considerable improvement in work outcomes. In summary, IC/BPS is associated with less work participation and levelling of women's long-term earnings.

Abstract #866:

ILEAL CONDUIT WITHOUT CYSTECTOMY MAY BE AN APPROPRIATE OPTION IN THE TREATMENT OF INTRACTABLE BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS

Thomas Norus; Mikkel Fode; Jørgen Nordling

Cystectomy is recommended when performing urinary diversion for intractable Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC). However, at Herlev University Hospital in Copenhagen, Denmark, ileal conduit without cystectomy is the preferred choice of treatment for intractable IC/BPS. This was a retrospective report on their experience with urinary diversion in these patients and their clinical outcome over a period of more than 10 years.

Chart reviews were performed for 23 BPS/IC patients who underwent ileal conduit between 1999 and 2010. The SF-36v2 questionnaire (quality of life), the O'Leary Sant questionnaire (specific BPS/IC symptoms), and the short form McGill pain questionnaire were mailed to all living patients. Fisher's exact test was used to compare outcomes between the cystectomy and the non-cystectomy groups. Twenty patients underwent ileal conduit without cystectomy. Two underwent a subsequent cystectomy due to persistent symptoms. Three patients underwent ileal conduit with concomitant primary cystectomy due to recurrent urinary tract infections preoperatively. All patients reported severe bladder pain and voiding related problems prior to the surgery. Nineteen patients were alive at the time of the study and 15 returned the questionnaires. Twelve responders had been treated with ileal conduit only and 3 had undergone primary cystectomy. All scores on the SF-36v2 questionnaire in both the cystectomy and the non-cystectomy groups were compatible with the health related quality of life in the general population. There was no difference between the cystectomy group and the non-cystectomy group with regard to the proportion of patients who were symptom free after surgery. It was therefore concluded by this group of researchers that ileal conduit without cystectomy may be an appropriate option when performing urinary diversion in BPS/IC patients, without recurrent or intractable urinary tract infections. Subsequent cystectomy can be performed if symptoms persist. Further research is necessary to assess potential preoperative outcome predictors.

Abstract #867:

ANALYSIS OF THE MECHANISM OF CROSS-SENSITIZATION BETWEEN THE COLON AND BLADDER VIA TRPA1 RECEPTOR STIMULATION IN THE COLON OR BLADDER IN RATS

Akira Furuta; Yusuke Koike; Takehito Naruoka; Nozomu Furuta; Yasuyuki Suzuki; Shin Egawa; Naoki Yoshimura

30-43% of patients diagnosed with interstitial cystitis/bladder pain syndrome (IC/BPS) exhibit symptoms for irritable bowel syndrome (IBS). Correspondingly, 26-56% of patients diagnosed with

IBS also have symptoms of IC/BPS. However, while the pathogenesis of IC/BPS and IBS has mostly been studied independently, few investigators have examined multi-organ interactions. Therefore, this group of researchers from Tokyo and Pittsburgh analyzed the mechanism underlying cross-sensitization between the colon and bladder via transient receptor potential (TRP) A1 receptor stimulation in the colon or bladder in a rat study. They examined changes in colon and bladder activity after the application of allyl isothiocyanate (AI, 100mM, 300ul), a TRPA1 activator, into the colon or bladder in an awake condition. Inhibitory effects of the pretreatment of HC-030031 (HC, 3mg/kg i.v.), a TRPA1 inhibitor, on colon-to-bladder cross-sensitization induced by AI instilled in the colon were also examined. They also examined whether colon-to-bladder cross-sensitization was mediated by the hypogastric (sympathetic) or pelvic (parasympathetic) nerves using bilateral hypogastric or pelvic nerves transection near the internal iliac vessels. Their findings suggested that colon-to-bladder cross-sensitization via TRPA1 stimulation in the colon is mediated through the pelvic nerves innervating the colon. However, the TRPA1 receptor expressed in the bladder does not seem to participate in bladder-to-colon cross-sensitization. These findings are consistent with the report that TRPA1 is expressed in lumbosacral colon afferent neurons but not in lumbosacral bladder afferent neurons (La JH, Neuroscience 186;179-87, 2011).

Abstract #868:

PHENOTYPE DIRECTED MANAGEMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

J. Curtis Nickel; Karen Irvine-Bird; Daniel Shoske

A flexible therapeutic strategy for Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) patients using an individualized phenotype directed treatment plan based on clinically based UPOINT categorization has been advocated, instead of the traditional algorithmic approach. Curtis Nickel, MD and colleagues initiated such a treatment plan in their specialized IC/BPS clinic and have assessed the benefits in their patients during the first two years since implementation. 100 consecutive patients diagnosed with IC/BPS referred to a specialized tertiary IC/BPS clinic with at least one follow-up post-treatment visit (patients assessed for consultation only were excluded) were categorized according to their UPOINT status (Urinary, Psychosocial, Organ Specific, Infection, Neuropathic/non-bladder, Tenderness of pelvic floor) were treated according to previously presented and published individualized phenotype based treatment plan. Patients were assessed at baseline and up to 2 years with validated symptom scores (interstitial cystitis symptom score or ICSI; pain urgency frequency questionnaire or PUF), as well as pain and voiding assessments. They observed no correlation between the number of domains and ICSI decrease as points or %. There was no difference in baseline ICSI (symptom severity) and predicted outcome. They found that almost 50% of previously treated patients referred to a tertiary IC/BPS clinic, regardless of complexity of condition (measured by number of UPOINT domains) experienced clinically significant improvement using an individualized phenotype directed therapeutic approach. There was a disconnect between patient satisfaction and measured outcome. What was the reason for this? Nickel suggested that it was because patients had been previously treated (similar to the ICDB); for many the last visit was a flare visit; they have only started pain mapping; appropriate therapies were too expensive; they did not measure other important domains of IC/BPS such as quality of life, activities, psychosocial improvement and satisfaction.

They concluded that ICSI, ICPI, PUF and VAS Pain/Urgency Scales do not appear to accurately measure clinically perceptible success in a pain-centred chronic urological disease with systemic manifestations. They felt that should consider examining: quality of life (general and disease specific), psychosocial impact and coping; measuring changes in Life Activity level; and Patient Satisfaction.

He ended by saying that in a syndrome where cure may not be possible in all patients, amelioration of symptoms, improvement of quality of life and increase in life activities is a successful outcome.

UPOINT Treatment:

U: antimuscarinics, pyridium, bladder retraining
 P: education, coping, CBT, TCAs, anxiolytics
 O: pyridium, intravesical GAGs, DMSO, bicarb, lidocaine, PPS, quercetin
 I: antimicrobials
 N: amitriptyline, gabapentinoids, system specific therapies, referral
 T: physiotherapy, exercise, muscle relaxants, injection therapy.

Abstract #869:**TREATMENT RESPONSE TO NEUROMODULATION IN INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS) PATIENTS ACCOMPANY DECREASE IN URINE CHEMOKINES**

Michael Chancellor; Pradeep Tyagi; Jayabalan Nirmal; Don Bui; Kenneth Peters

Chemokines are responsible for paracrine signalling [= a form of cell-cell communication] within the bladder and for also assisting in communication between the bladder and neurons innervating the bladder. Therefore, Michael Chancellor, MD and colleagues from Beaumont hypothesized that chronic neuromodulation from InterStim implant at the spinal cord level in IC/PBS patients will cause downstream changes in chemokine signalling, which will be reflected in the differences of chemokine levels measured at the baseline and at the end of treatment. Speaking about chemokines as biomarkers, he explained that biomarkers are the transcript/protein derived from the disease locus. Chemokines are constitutively expressed by the bladder and neurons. They increase pain by suppressing opioid and enhancing vanilloid receptor responses. Opioid receptors are involved in neuromodulation (Tai et al, 2012).

Patients with a confirmed diagnosis and a long history of IC/PBS undergoing Interstim participated in this study. Mid- stream urine and symptom scores IC symptom problem index (ICSPI index) were collected at baseline and at 24 weeks after implant. Collected urine was analyzed for presence of cytokines and chemokines by Luminex xMAP analysis. IC/PBS patients responding favourably to neuromodulation showed a corresponding decrease in urine levels chemokines. The decline in urinary chemokines with Interstim appears to correlate with a decreased ICSPI score. The decrease in chemokines in relation to symptoms suggests reduced afferent hyperexcitability. These results support the hypothesis for the action of chemokines as downstream effectors of neuromodulation response in the bladder. Temporal changes in urine chemokines may serve as non-invasive treatment predictors.

Abstract #870:**WHAT HELPS AND WHY? PREDICTING PATIENT OUTCOMES IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME (IC/BPS) WITH PAIN APPRAISALS AND BEHAVIOURAL COPING STRATEGIES.**

Dean A. Tripp; J. Curtis Nickel; Jillian Mulroy; Laura Katz; Michel Pontari; Robert Moldwin; Mayer Robert; Lesley Carr; Ragi Doggweiler; Claire Yang; Nagendra Mishra; Jorgen Nordling

The previous IC/BPS analysis of this research group correlated pain, quality of life (QoL), and psychosocial adjustments with other associated conditions, and catastrophising and behavioural coping strategies (sedentary resting in reaction to pain) have been found to predict pelvic pain outcomes for men and women. However, no study has examined a comprehensive list of pain appraisal and behavioural coping strategies as mechanisms in the relationship between pain and QoL in these patients. From a self-regulation perspective, appraisals and coping responses of patients suffering from IC/BPS are important in advancing patient management. 190 female patients with IC/BPS were recruited from tertiary care urology clinics and completed questionnaires (demographics, O'Leary Sant, McGill Pain Questionnaire, SF12, Chronic Pain Coping Inventory, Pain Catastrophizing Scale). The data was examined for univariate and multivariate normality, and a

missing values analysis was conducted. Associations of validated pain appraisals (e.g. catastrophising) and behavioural coping strategies (e.g., illness focused coping) with outcomes of pain and QoL in IC/BPS were examined. Factor reduction was conducted and resulting variables were input into multivariable mediation models. The study gave new insights into mechanisms of pain and QoL relations and indicated that symptoms (pain) may be physically/mentally disabling through behavioural & cognitive mechanisms. The findings were similar to those in CPO/CPPS. These results suggest that catastrophic appraisals and illness-focused behavioural coping act as mechanisms driving the negative association between pain and QoL indices. These results further support an expanding science emphasizing the importance of biopsychosocial pain/QoL models in Urology.

Abstract #871:

EFFECT OF HERPES SIMPLEX VIRUS (HSV) VECTOR-MEDIATED INTERLEUKIN 4 GENE THERAPY ON ENHANCED BLADDER PAIN BEHAVIOR IN RATS WITH CYCLOPHOSPHAMIDE (CYP)-INDUCED CYSTITIS

Tomohiko Oguchi; Hitoshi Yokoyama; Yasuhito Funahashi; Osamu Nishizawa; Satoru Yoshikawa; William F Goins; James R Goss; Joseph C Glorioso; Naoki Yoshimura

Oguchi and colleagues examined whether subacute chemical cystitis increases pain behaviour in rats induced by nociceptive bladder stimuli and whether gene therapy using replication-deficient HSV vectors expressing an anti-inflammatory cytokine IL-4 (S4IL4) in the bladder can suppress bladder overactivity and bladder pain behaviour enhanced by chemical cystitis. Saline or CYP was injected to female SD rats. Two days later, in a conscious condition, 0.3µM RTx (0.3ml, 1 min) was injected to the bladder through a urethral catheter to evaluate nociceptive behaviors such as licking (lower abdominal licking) and freezing (motionless head-turning), which were counted and recorded every 5 seconds for 15 minutes. Urine volume and frequency were recorded simultaneously. They found that licking behaviour was not enhanced. Freezing behaviour (pain) was significantly increased in CYP cystitis rats compared to controls. The average voided volume per micturition after RTx was also significantly decreased in CYP cystitis rats compared to controls. Subacute chemical cystitis, low concentration RTx, which usually does not elicit pain behavior in normal rats, induced bladder pain behavior and reduced bladder capacity, indicating bladder hypersensitivity after cystitis. HSV vector-mediated IL-4 gene therapy reduced bladder overactivity and pain behaviour in this cystitis model, suggesting that anti-inflammatory IL-4 gene therapy could be a new strategy for treating bladder pain and/or urinary frequency in patients with BPS/IC.

Abstract #872:

CLINICAL RESPONSE TO INTRA-TRIGONAL ONABOTULINUM TOXIN A INJECTIONS IS NOT RELATED TO THE PRESENCE OF ULCERS IN BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS PATIENTS

Rui Pinto; Tiago Lopes; João Silva; Carlos Silva; Paulo Dinis; Francisco Cruz

This team recently showed that intra-trigonal Onabotulinum toxin A (OnaBotA) injection provides prolonged relief of bladder pain in Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC) patients. Since injections were not performed in the lesion/ulcerative area, they investigated if the toxin provided a different symptomatic outcome and duration of effect in the two phenotypes of BPS/IC, the lesion/ulcerative and the non-lesion/ulcerative form. 10 ulcerative (Ulc) and 14 non-ulcerative (NUlc) BPS/IC patients were evaluated at presentation and 1 month after intra-trigonal injection of 100U of OnaBotA. A 10-point Visual Analogue Scale (VAS) was used to quantify pain. Frequency and nocturia in a 3-day voiding chart, O'Leary-Sant Score (OSS), QoL and duration of the effect were evaluated. Urinary norepinephrine was accessed by ELISA. The symptom relief brought by trigonal OnabotA suggests that pain is not directly related with the lesions/ulcers themselves. They could not find symptomatic differences between those two phenotypes, challenging the traditional view that Ulc BPS/IC patients have a more symptomatic form of the disease.

Abstract #873:

CORRELATING GENE EXPRESSION PROFILES IN BLADDER UROTHELIUM WITH CLINICAL AND HISTOLOGICAL PARAMETERS FOR PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

David Koslov; Brandy Hood; Tristan Keys; Stephen Walker; Robert Evans; Gopal Badlani; Karl-Erik Andersson

The exact mechanisms for the etiology and pathophysiology of Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) remain unknown. Clinical diagnosis is mainly symptom based, but some tissue and urine based markers have been reported. A means of relating clinical symptomatology and diagnostic test results (cystoscopy, bladder biopsy) with markers of disease severity is desirable. The objective of this pilot study was to correlate symptom severity and operative findings of non-ulcer/lesion type IC/BPS with urothelial gene expression profiles. Bladder urothelium samples were collected from patients at our institution and stored in our prospectively maintained tissue bank. At the time of tissue collection, patients completed O'Leary Sant and PUF questionnaires. Bladder capacity during hydrodistension and cystoscopic findings were recorded, and urothelial mast cell counts were also obtained. Four groups, based on clinical and histological parameters, were chosen for analysis: 1) low bladder capacity, high O'Leary Sant/PUF symptom score, mast cell count between 35-75 cells/hpf; 2) normal capacity, high symptom score, mast cell count between 22-25 cells/hpf; 3) normal capacity, high symptom score, mast cell count between 36-50 cells/hpf, and severe glomerulations; and 4) patients undergoing cystectomy for end stage IC/BPS. Control samples (group 5) came from patients without IC/BPS. Biopsy tissues were homogenized and mRNA was extracted and purified. Gene expression profiles for each of 16 samples (3 in each group 1-3 and control; 4 in Group 2) were generated using Agilent G3 Human GE 8x60k microarrays; statistical analyses were conducted to identify correlations and differential gene expression within and between these groups. Principal component analysis on unfiltered data indicated distinct grouping of gene expression profiles for patients in group 4 whereas groups 1-3 showed significant overlap with the control group. It was concluded that gene expression profiles seem to be a promising tool for subcategorizing IC/BPS patients and may give valuable pathophysiological information. Microarray seems a promising approach to better understanding of IC/BPS. The results suggest different biological processes in lesion/ulcer and non-lesion/ulcer IC. There appear to be subtle differences in gene expression profiles of non-lesion/ulcer patients. Next steps include: increase patient enrolment to more accurately delineate specific genes; further evaluate grouping scheme on non-lesion/ulcer patients; collect peripheral blood for gene analysis, less invasive biomarkers.

Abstract #874:

THE ROLE OF URINARY CATIONS IN INTERSTITIAL CYSTITIS

C. Lowell Parsons; Timothy Shaw; Paul Zupkas; Sulabha Argade

Bladder epithelial dysfunction has been shown in interstitial cystitis (IC) patients. Urinary cations have been reported to injure the GAG layer causing an epithelial leak and are toxic to cultured urothelial cells, thus they have been called toxic factors (TF). The current study was conducted to isolate and identify these TFs from crude urine employing solid-phase extraction (SPE), quantified in both IC patients and control subjects by reverse phase-high performance liquid chromatography (RP-HPLC). Parsons and colleagues have isolated and identified major cationic metabolites in IC patients using a simple protocol and reported its cytotoxicity to urothelial cells. The biological significance of these findings is substantial. The identification of these toxic factors provides both new insights into the root cause of IC and a framework for the development of new therapeutic strategies.

Abstract #875:

TREATMENT WITH A CB2 AGONIST DECREASES SEVERITY OF ESTABLISHED CYSTITIS

Zunyi Wang; Peiqing Wang; Dale Bjorling

The etiology and pathogenesis of painful bladder syndrome remain unknown, and effective treatments are lacking. Cannabinoids exert potent analgesic and anti-inflammatory effects. Cannabinoid receptor 2 (CB2) is expressed in the bladder, particularly in urothelial cells, and bladder inflammation increases CB2 expression. Wang and colleagues investigated whether treatment with the selective CB2 agonist GP1a ameliorates severity of cystitis and referred hyperalgesia in mice after induction of cystitis by acrolein. Cystitis was induced by intravesical instillation of acrolein (a metabolite of cyclophosphamide; 0.5 mM, 200 µl) in female C57 mice. Forty-eight hours later the mice were sacrificed and bladders were collected for histological analysis. They found that treatment with a selective CB2 agonist after induction of cystitis reduced the severity of acrolein-induced cystitis and also attenuated mechanical hyperalgesia and increased urination frequency associated with cystitis. Their data indicate that CB2 activation inhibits bladder inflammation and associated bladder hyperreactivity and visceral pain. Selective CB2 agonists represent a potential therapeutic option for patients with painful bladder disorders.

Abstract #876:

VOIDING DYSFUNCTION PHENOTYPING OF WOMEN WITH CHRONIC PELVIC PAIN SYNDROMES: RESULTS FROM THE ICEPAC TRIAL

Elias Veizi; Adonis Hijaz; Firouz Daneshgari; Thomas Chelimsky

Interstitial cystitis/Bladder pain syndrome (IC/BPS) and myofascial pelvic pain (MPP) are two of the most common forms of chronic pelvic pain (CPP). Cross-organ sensitization in the pelvis complicates the clinical diagnosis and treatment of IC/BPS as part of general CPP. The aim of the ICEPAC trial is to study the autonomic nervous dysfunction in patients with interstitial cystitis and myofascial pain and to assess the signature phenotypes of pain and voiding dynamic changes. ICEPAC supported by NIH-NIDDK was designed by an interdisciplinary team. Enrolment will include 76 women with IC, 76 women with myofascial pelvic pain disorder (MPP), 38 1st degree female relatives of IC subjects without pelvic pain, and 38 healthy age-matched women. Besides a detailed screening visit with comprehensive assessment of dysautonomias, pain intensity and disability scores, voiding dysfunction phenotype is assessed by Uroflow and a voiding diary. VAS scores, frequency, voiding volumes, flow parameters and timed flow assessment data are collected and analysed. This preliminary quantitative evaluation of voiding diary and uroflow metrics reveals distinct voiding phenotypes in IC and MPP. The decrease in Qmax in IC cluster in comparison with con and MPP could be an indication of the internal sphincter autonomic dysfunction while the prolonged voiding duration and avg flow in MPP patients could indicate external sphincter hypertonicity [incomplete relaxation]. Further details on voiding dysfunction could lead toward a better understanding of the pathogenesis in IC versus other pelvic floor dysfunction syndromes. These findings could lead to mechanistic treatment paradigms in specific entities of IC/BPS versus MPP.

SESSION: URODYNAMICS/INCONTINENCE/FEMALE UROLOGY: BASIC RESEARCH (I)

Abstract #28:

MOLECULAR EVIDENCE OF THE NOVEL HCN2 GENE AS NEW DIAGNOSTIC AND TREATMENT FOR INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME

Vikas Tyagi; Pradeep Tyagi; Jayabalan Nirmal; Samreen Ahmed; Kenneth Peters; Naoki Yoshimura; Michael Chancellor

It is estimated that between three and eight million women in America are affected by interstitial cystitis/painful bladder syndrome (IC/PBS). HCN2 carry an inward current called Ih that is important for driving the repetitive firing of pain fibres, which makes them a promising drug target. Recent

research has shown that mice which had the HCN2 gene deleted had decreased neuropathic pain. Tyagi and colleagues hypothesized that the pain symptoms suffered by IC/PBS patients may be initiated by HCN2-driven action potential firing in pain-sensitive nerve endings. They obtained human bladder biopsies from organ donors without urinary problems and patients with urinary symptoms including interstitial cystitis, overactive bladder and incontinence. Findings from this study reveal the identification of increased HCN2 expression in the bladder of Interstitial Cystitis/Painful Bladder Syndrome over normal bladder tissue. HCN2 may play an important role in the pathogenesis of IC/PBS and reveal new mechanism of action and pathophysiology. The HCN2 may present a new avenue to diagnosis and therapeutic target. In summary, this is a surprising new discovery of a novel gene that is critical for chronic pain and lays the groundwork for the development of new drugs to treat chronic pain by blocking HCN2. In addition, the discovery can lead to new understanding for the underlying mechanism of IC/PBS disease and lead to potential discovery of new method to treat IC/PBS without altering normal urination.

Abstract 332:

A SIGNALING NETWORKING EVOKED BY THE INTERSTITIAL CYSTITIS-ASSOCIATED FRIZZLED 8-RELATED ANTIPROLIFERATIVE FACTOR

Sungyong You; Jennifer Anger; Tack Lee; Susan Keay; Michael Freeman; Kim Jayoung

A sialoglycopeptide urinary biomarker is antiproliferative factor (APF), which has been detected in urine from approximately 95% of IC/PBS patients, is a small glycosylated peptide with 100% of homology to frizzled-8 (a receptor of Wnt signalling). A series of publications from this laboratory has previously shown that APF suppresses the proliferation rate of normal bladder epithelial cells through a mechanism that involves p53 and beta-catenin in vitro and in vivo, leading to inflammation, growth arrest, and urothelial permeability. The objectives of this study were (1) to identify the signalling networks altered in response to APF treatment in bladder epithelial cells, and (2) to understand the global network perturbed in IC/PBS in vivo by computational approaches. Chemically synthesized APF (as-APF) was used in combination with the APF-responsive hTERT-immortalized human bladder epithelial cell line, TRT-HU1. Biochemical and functional analysis including western blot, proliferation assay, immunoprecipitation and immunofluorescence staining were performed to identify the regulators of altered gene expression upon APF treatment. This study group reports that their findings suggest that as-APF functions similarly to native APF, and highlights a new mechanism by which the USP2a-MDM2-p53 signalling pathway plays an important role in the APF network. Targeting USP2a, MDM2, p53 and NF- κ B may be relevant in the development of novel therapeutic approaches to block APF signalling.

SESSION: GENERAL & EPIDEMIOLOGICAL TRENDS & SOCIOECONOMICS: QUALITY OF LIFE

Abstract #443:

NON-UROLOGICAL SYNDROMES AND SEVERITY OF UROLOGICAL PAIN SYMPTOMS: BASELINE EVALUATION OF THE NATIONAL INSTITUTES OF HEALTH MULTIDISCIPLINARY APPROACH TO PELVIC PAIN STUDY

John Krieger; Alisa Stephens; J. Richard Landis; Niloofar Afari; Gerald Andriole; J. Quentin Clemens; Karl Kreder; H. Henry Lai; Sean Mackey; Larissa Rodriguez; Anthony Schaeffer; David Williams

Krieger and colleagues report data from the **Multidisciplinary Approach to Pelvic Pain Study (MAPP)** network to: characterize participants having either primarily pelvic pain symptoms or unexplained non-urological somatic syndromes in addition to pelvic pain, with respect to symptoms, psychosocial factors, quality of life, and healthcare utilisation. This multi-site study evaluated men and women with urological pain, including: predominant symptoms, symptom duration and severity, non-urological syndromes, psychosocial factors, and healthcare utilization in individuals presenting with

chronic pelvic pain syndromes. Of 443 participants with urological symptoms, 168 (38%) had symptoms of non-urological syndromes: 96 (22%) irritable bowel syndrome, 16 (4%) fibromyalgia, 13 (3%) chronic fatigue syndrome, and 43 (10%) with multiple syndromes. Among 256 females, 112 (44%) had non-urological syndromes compared to 56 (30%) of 187 males. Patients with non-urological syndromes were younger at diagnosis, had more severe urological symptoms, worse quality of life, and more frequent depression and anxiety. Of 275 patients with urological symptoms only, 188 (68%) were taking prescription medications for their symptoms, compared to 131 (78%) of 168 patients with non-urological syndromes. Of 443 participants, 236 (53%) met RICE criteria. Among the 236 participants who met RICE criteria, 111 (47%) had non-urological syndromes compared to 57 (28%) of 207 patients not meeting RICE criteria with non-urological syndromes. Non-urological syndromes represent important phenotypic characteristics in chronic pelvic pain. Since the prevalence of non-urological syndromes was substantially higher in women, this suggests that there may be gender-specific factors which contribute to the urological pelvic pain symptoms. Patients with both urological and non-urological syndromes had more severe symptoms, decreased quality of life, and higher rates of depression and anxiety. Patients who meet RICE criteria were more likely to have non-urological syndromes and more severe symptoms.

Abstract #444:

SYMPTOMS, HEALTH CARE UTILIZATION, AND BOTHER ASSOCIATED WITH UROLOGIC CHRONIC PELVIC PAIN SYMPTOM FLARES OF VARYING DURATION: RESULTS FROM THE MAPP STUDY

Siobhan Sutcliffe; Graham Colditz; Ratna Pakpahan; Melody Goodman; Gerald Andriole; Henry Lai

Sutcliffe reports that in one of the first studies to describe symptom flares in interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome patients, they identified a larger spectrum of flares than expected, both in terms of duration (ranging from minutes to months) and frequency. They have now extended this study to examine symptoms during flares of varying duration, and their associated health care utilisation and bother. This performed this study at one site of the **Multidisciplinary Approaches to the Study of Chronic Pelvic Pain (MAPP) study**. At their 6-month visit, participants completed an additional flare survey that asked them: 1) whether they had ever had flares (defined as symptoms that are much worse than usual) that lasted <1 hr, >1 hr and <1 day, and >1 day; and 2) for each duration of flare, to report their typical levels of pelvic pain, urgency, frequency, and overall urologic and pelvic pain symptoms; their most bothersome symptom; and their levels of health care utilization and bother. They compared participants' responses by duration of flares and to their baseline MAPP values by generalised linear mixed models. Fifty-two of 60 participants completed the flare survey, 49 of whom reported having flares (94%). Symptoms were worse during a flare than at baseline, with increasing severity of symptoms as the duration of flares increased. Pelvic pain was the most bothersome symptom reported for flares of all duration (86.3-90.5%). As the duration of flares increased, participants were more likely to contact a health care provider, increase or change their medication, not engage in their usual activities, think about their symptoms, and be bothered by their symptoms. Even for flares lasting <1 hr, 68% of participants reported disruption to their usual activities to some degree, and all reported thinking about their symptoms and being bothered by their symptoms during these flares. Their findings suggest that flares are painful, disruptive, bothersome, and associated with greater health care utilisation, particularly long flares but also short flares. Future research should focus on ways in which to prevent and treat this bothersome aspect of urologic chronic pelvic pain syndromes.

SESSION: INFECTIONS/INFLAMMATION OF THE GENITOURINARY TRACT: KIDNEY & BLADDER (II)

Abstract #1143:

DEVELOPMENT OF BLADDER GLOMERULATIONS AFTER HYDRODISTENSION IN PATIENTS WITH UPPER URINARY TRACT UROLITHIASIS SUGGESTING CROSS TALK AND BLADDER INFLAMMATION OCCUR BETWEEN UPPER AND LOWER URINARY TRACT

Yuan-Hong Jiang; Cheng-Ling Lee; Jia-Fong Jhang; Hann-Chorng Kuo

Development of glomerulations after hydrodistension has been considered a definite diagnosis of interstitial cystitis/bladder pain syndrome (IC/BPS). Urothelial dysfunction and suburothelial inflammation play important role in the IC/BPS bladder. Lower urinary tract symptoms are common in the patients with upper urinary tract (UUT) urolithiasis [urinary stones]. The aim of this study was to investigate the relationship of UUT urolithiasis and bladder inflammation. A total of 42 patients with UUT urolithiasis were enrolled and received hydrodistension before the stone surgery. Bladder tissues from 15 patients who developed glomerulations after hydrodistension were compared with 10 controls. Immunofluorescence (IF) staining of junction protein E-cadherin, and tryptase (indicating mast cell activation) were performed. The IF intensity of E-cadherin was measured using an Image J method. The percentage of activated mast cells were measured and quantified as positive cell per area unit ($4 \mu\text{m}^2$). The mean age was 56 years old for the urolithiasis group and 50 for the controls. Thirty one of the 42 (73.8%) patients developed glomerulations after hydrodistension. Grade 1 glomerulations developed in 19 patients, grade 2 in 11 and grade 3 in 1, no bladder ulcer was noted in these patients. In IF staining, the distribution of E-cadherin in urolithiasis patients was significantly lower than controls. The fluorescence tryptase signals in urolithiasis patients were significantly higher than controls. It was concluded that glomerulations after hydrodistension are not specific for IC/BPS. The incidence of glomerulations in patients with urolithiasis is high. Urothelial dysfunction and suburothelial inflammation in the bladder are observed in patients with UUT urolithiasis, indicating that cross talk of chronic inflammation between UUT and LUT might exist.

Abstract #1147:

APPLICATION OF STATE-OF-THE-ART METHODS TO SEARCH FOR MICROBIAL CONTRIBUTIONS TO THE ETIOLOGY OF UROLOGICAL CHRONIC PELVIC PAIN SYNDROME (UCPPS).

J. Curtis Nickel; Alisa Stephens; Jun Chen; Rachael Melton-Kreft; Tracy Spirk; Josh Earl; Mary O'Toole; J. William Costerton; Adrie van Bokhoven; Chris Mullins; Garth Ehrlich

The presence of microorganisms or an imbalance of the microbial ecology of the lower urinary tract has been implicated in UCPPS. Nickel and colleagues used culture-independent molecular methods to identify the microbiota of the lower urinary tract in men and women with UCPPS. Uniformly collected urine specimens were obtained in UCPPS and age matched healthy controls (including positive controls with CFS, FM, IBS). Baseline urine specimens were obtained from 257 cases (161 female; 96 male) and 261 controls (164 female; 97 male). A total of 136 species (57 genera) were detected in VB1; VB2 contained 109 species (52 genera). Mean VB2 species count per person was 2.50 and 2.29 among female UCPPS patients and controls respectively; 1.33 and 1.08 for males respectively. They report that despite observing some provocative trends, they did not find significant differences in the microbiome detected in lower urinary tract urine specimens from men and women with UCPPS compared to controls using state-of-the-art detection methods.

SESSION: URODYNAMICS/INCONTINENCE/FEMALE UROLOGY: FEMALE UROLOGY (I)

Abstract #1581:

IMPACT OF SYMPTOM DURATION ON BASELINE CHARACTERISTICS OF THE MULTIDISCIPLINARY APPROACH TO PELVIC PAIN (MAPP) STUDY COHORT

Larissa Rodriguez; Alisa Stephens; J Quentin Clemens; Claire Yang; Henry Lai; Deborah Buchwald; Cate Bradley; John Krieger

Symptom severity in patients with urologic chronic pelvic pain syndromes (UCPPS) has been associated with symptom duration. Compared with the general population, UCPPS patients have higher rates of other somatic syndromes, such as fibromyalgia (FM), irritable bowel syndrome (IBS) and chronic fatigue syndrome (CFS), and mental health comorbidities. This MAPP study group hypothesized that UCPPS patients with longer duration of symptoms would also be more likely to report these comorbid conditions. They evaluated cross-sectional associations between symptom duration and 1) symptom severity, and 2) presence of other somatic syndromes and mental health symptoms. Baseline data were analyzed from the MAPP Epidemiology and Phenotyping Study, an NIH-sponsored multi-centre observational study of patients with UCPPS. Patients were stratified by symptom duration as a discrete or continuous variable. Symptom severity was assessed by the Genitourinary Pain Index (GUPI), the IC Symptom and Problem Index, and Likert scales for pelvic pain, urgency and frequency. Depression and anxiety were evaluated with the Hospital Anxiety and Depression Scale (HADS) and stress with the Perceived Stress Scale (PSS). 442 participants were included. Males (not females) with symptoms ≥ 2 years had more severe symptoms than those with < 2 years. When evaluating symptom duration as a continuous variable, adjusting for age and gender, there was an increase in GUPI total and GUPI pain subscale scores for each additional year of symptoms. Females were 62% more likely than males to have other somatic syndromes. On multivariable analysis, there was a significant increase in the likelihood of patients experiencing CFS and FM, but not IBS for each additional year of UCPPS symptoms. It was concluded that females with UCPPS symptoms < 2 years experienced more severe urinary symptoms, higher levels of stress, anxiety and depression than males with symptoms < 2 years. Symptom duration was associated with increased severity of urinary symptoms and risk for concomitant somatic disorders. These findings point to gender-specific differences in the likelihood of comorbid conditions and symptom severity in UCPPS patients with longer symptom duration.

Abstract #1851:

REPEAT ONABOTULINUMTOXINA INJECTIONS PROVIDE BETTER THERAPEUTIC RESULTS THAN SINGLE INJECTION IN TREATMENT OF PAINFUL BLADDER SYNDROME

Cheng-Ling Lee; Yuan-Hong Jiang; Jia-Fong Jhang; Hann-Chorng Kuo

While onabotulinumtoxin-A (BoNT-A) appears to be effective for the treatment of interstitial cystitis/painful bladder syndrome (IC/PBS), long-term follow-up does not show successful outcome after a single injection. The objective of this study was to evaluate the efficacy and safety of repeated intravesical BoNT-A injections for treatment of IC/PBS. Intravesical injection of 100 U of BoNT-A was performed in 81 patients every 6 months for up to 4 times. Patients who received single injection served as active controls. Measured parameters included O'Leary-Sant symptom indexes (ICSi) and problem indexes (ICPI), visual analogue score (VAS), voiding diary variables, urodynamic parameters, maximal bladder capacity under anesthesia, glomerulation grade, and global response assessment. Multiple measurements and Kaplan-Meier analysis were used for success rates among groups. Among 81 patients, 20 received single, 19 received two, 12 received three, and 30 received four injections, respectively. Significantly better success rates were noted in patients who received four injections and three injections, compared to those who received a single injection. Difficult urination was the most common adverse events. It was concluded that repeated intravesical BoNT-A injections were safe and effective for pain relief and they increased bladder capacity and provided a better long-term success rate than a single injection did for treatment of IC/PBS.

SESSION: URODYNAMICS/INCONTINENCE/FEMALE UROLOGY: NON-NEUROGENIC VOIDING DYSFUNCTION

Abstract #1955:

COMPARISON OF BASELINE UROLOGIC SYMPTOMS IN MEN AND WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME OR CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME

J. Quentin Clemens; Daniel J. Clauw; Karl J. Kreder; John N Krieger; John W Kusek; H. Henry Lai; Larissa V. Rodriguez; David Williams; Xiaoling Hou; Alisa Stephens; J. Richard Landis

The clinical features characteristic of interstitial cystitis/ bladder pain syndrome (IC/BPS) are similar to those of chronic prostatitis/ chronic pelvic pain syndrome (CP/CPPS). However, no studies have directly compared the clinical characteristics of these syndromes in men and women. The National Institutes of Health **Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP)** network was established in part to apply novel phenotyping strategies to these conditions. To address one of the hypotheses of the network, that IC/BPS and CP/CPPS represent the same underlying condition, this study group compared baseline demographic and urologic symptoms in men and women. A total of 186 men and 254 women with IC/BPS or CP/CPPS were recruited from six clinical centres across the United States. All subjects underwent an intensive in-person phenotyping evaluation that included demographic data and symptom characteristics and severity. After adjustment for age, income and symptom duration, most measures of symptom severity were similar across genders (Table). Mean scores for the IC Symptom Index, IC Problem Index and AUA Symptom score were significantly higher in women than men. The most bothersome single symptom in men was pain in the pubic or bladder area (34%), perineal pain (23%), and urinary frequency (17%), while the most bothersome symptom in women was pain in the pubic or bladder area (59%) and urinary frequency (14%).

While numerous studies have described symptoms of patients with either IC/BPS or CP/CPPS, this is the first study to prospectively recruit men and women with both urologic pain syndromes and to compare these syndromes using the same instruments. Our findings confirm the similarities between these syndromes. Additional information about the pathophysiology of these symptoms is needed to determine if these common urologic pain syndromes truly represent the same underlying condition.

SOCIETY FOR INFECTION AND INFLAMMATION (SIU).

Peripheral Contributions to Organ Hypersensitivity - G.F. Gebhart

Hypersensitivity is a term that keeps cropping up currently, including at the AUA meeting where an interesting talk was given by Dr G.F. Gebhart on Peripheral Contributions to Organ Hypersensitivity at the meeting of the Society for Infection and Inflammation (SIU). Describing the problem, he noted that functional gastrointestinal (GI) disorders (IBS, FD, etc) affect around 20% of people (in developed countries); regarding IC/BPS, he reported a 16% incidence with 94% of patients reporting pain); functional GI disorders and BPS are more common in women; chronic prostatitis represents > 90% of CPPS with around 13% incidence; genitourinary pain in the absence of evidence of a urinary tract infection. He stressed that chronic IBS/BPS/CP contribute to organ cross-sensitisation and chronic pelvic pain syndrome. Asking what's different about visceral pain, he said that while we sense a lot, we feel little: most visceral input is not consciously perceived; the principal conscious sensations are discomfort and pain. Localisation is poor and referral is common. Visceral innervation is unique: organs are innervated by two nerves and also have an intrinsic innervations. He noted that many visceral disorders – IBS, BPS, CP/CPPS, functional dyspepsia – are characterised by organ hypersensitivity, often in the absence of a pathobiological explanation for the discomfort and pain.

Visceral hypersensitivity can result from either peripheral or central mechanisms, and can therefore be modulated at either peripheral or central sites, he said. His suggestion was to focus on the periphery, noting that data indicates that peripheral input underlies maintenance of hypersensitivity in functional disorders. Approximately 25% of visceral endings are “silent”, but awaken he said and asked if this contributes to organ hypersensitivity. Weeks after the insult, mechanically insensitive

afferents (MIAs) are decreased and stretch-responsive afferents are sensitised. Persistent inflammation is not required for afferent fibre sensitisation, he concluded.

Several other presentations at this session included the following:

INTRAVESICAL PENTOSAN POLYSULFATE ENCAPSULATED IN A LIPOSOME NANOCARRIER FOR INTERSTITIAL CYSTITIS

Lander EB, See JR.

The authors noted that there is increasing data supporting GAG barrier restoration therapy for treating IC/BPS. Pentosan polysulfate (PP) has been used extensively both orally and intravesically for GAG restoration therapy. However, inefficient oral absorption and a hostile proton environment with relatively rapid washout diminish the efficacy of barrier restoration therapy. In an effort to improve drug delivery, protect the GAG molecule, prolong dwell times and enable effective urothelial absorption, high quality multi-lamellar liposomes were used to encapsulate the PP instilled intravesically in a group of refractory IC patients. This study included patients with refractory IC confirmed by NIDDK criteria, all of whom had failed either oral and/or intravesical PP therapy. All patients received biweekly intravesical instillations of 400 mg PP homogenized at 16000 rpm with 150 mg of liposomes (50-200 miron). Patients received at least 4 treatments and subjective outcome tools consisted of the O'Leary-Sant and Pelvic Pain Urgency Frequency scores. Eight patients received a total of 37 treatments. No adverse events were recorded. Several patients noted durable and sustained relief of symptoms for more than six months. It was concluded that PP appears to have efficacy in alleviating IC symptoms when delivered intravesically to the urothelium in multi-lamellar liposomes. In some cases, the positive effects lasted for months and still continue. This pilot study showed a trend towards favourable results and warrants further clinical study. Additional studies are needed to determine the cellular effects of barrier restoration with PP in liposomes, ideal dosages and intervals, safety and cost-effectiveness of this treatment.

PREVALENCE OF URINARY TRACT INFECTION IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENTS: A DIAGNOSIS NOT TO OVERLOOK

Waingankar N, Friendlander J, Moldwin R.

Although the presence of bacterial cystitis excludes a diagnosis of IC/BPS, many established IC/BPS patients develop intermittent urinary tract infections (UTI), which may cause symptom flares. The aim of this study was to investigate the prevalence and clinical characteristics of UTI in this patient population. Waingankar and colleagues performed a retrospective review of 229 patients with a diagnosis of IC/BPS seen at a single IC/BPS treatment centre between 1990 and 2007. Patient demographics and clinical data including urinalyses and urine cultures were obtained. Recurrent UTI was defined as two or more symptomatic episodes with corresponding abnormalities on urinalysis and urine culture. 177 of the 229 patients were female. 76 patients had had at least one infection since the time of their IC/BPS diagnosis. E.coli was the most commonly isolated organism from urine cultures reviewed, followed by Enterococcus species, Klebsiella species and Proteus species respectively. They found the prevalence of UTI in the IC/BPS population to be 33.2%, which is similar to the rates reported in the literature for the general population. However, IC/BPS patients have a higher prevalence of recurrent UTI than the population at large. The data suggest that one should consider the diagnosis of UTI seriously in the face of symptom flares in this patient population.

THE SCIENCE OF FEMALE PELVIC HEALTH

THIS SESSION WAS PRESENTED BY THE AUA, THE SOCIETY OF URODYNAMICS, FEMALE PELVIC MEDICINE AND UROGENITAL RECONSTRUCTION (SUFU), AND THE INTERNATIONAL CONTINENCE SOCIETY (ICS).

Treatment of lower urinary tract symptoms (LUTS) is mainly based on evaluation of symptoms and exclusion of other objectively demonstrable diseases/disorders. This is because the biologic causes of LUTS are not precisely understood. Better understanding of the pathophysiology underlying LUTS would improve the evaluation and treatment of patients. An important aspect of this would be a better understanding of bladder sensation/afferent signalling. LUTS could also be better understood by biomarker discovery.

This meeting consisted of three sessions:

1. To examine the role of how bladder afferent signalling might be modulated by inflammation, purinergic and TRPV1 signalling pathways.
2. Technological measurements of afferent bladder signals including fMRI and NIRS.
3. Understanding how urinary biomarkers have been used to better understand pathophysiology of kidney diseases and how these researchers can help urologic researchers understand LUTS.

David Klumpp, PhD looked at Host Responses to Bacteriuria and pain responses to e.coli. In their mice studies they have induced chronic pain from transient infections that can exist long after the bacteria have cleared. The pain phenotype is independent of inflammation. He raised the possibility that if the patient is unfortunate enough to get infected with a bad bug + have the wrong genotype/epigenome, this can result in chronic pain. And finally ASB E.coli may possess analgesic activity that could be used for treating either acute or chronic pain.

Anthony Ford, PhD spoke on purinergic pathways and Lower Urinary Tract Signalling in relation to the design and development of P2X3 antagonists for pain and hollow organ sensitisation, comparing the lower urinary tract (LUT) with airways, which are hollow organs showing similar morphology, pathophysiology and pharmacology. Both systems are characterised by poor management of sensory symptoms. Primary afferent neurons are optimal drug targets for irritation, sensitisation and chronic pain. He reported that ATP content is heightened in fluids/tissues from many painful and irritative conditions. Bladder urine concentrations of ATP in patients with painful and overactive bladder significantly exceed those in healthy controls. P2X3 receptors on bladder afferents may convey sensations of pain and urgency and trigger hyperactivity in urological disorders. AF-219 is the first clinical P2X3 antagonist. Its efficacy is comparable to NSAIDs in joint pain, comparable to gabapentin in neuropathic pain and active in models of visceral sensitivity. Studies are underway to determine the benefits of P2X3 antagonism for patients.

Francisco Cruz, MD discussed TRPV1 and afferent signalling in the urinary bladder, reporting that TRPV1 is essential for signalling noxious input and bladder hyperactivity associated with bladder inflammatory conditions. He noted that TRPV1 IR is increased in bladder nerve fibres of IC/BPS patients. NGF and bradykinin are important regulators of TRPV1 expression and function in nerve fibres in the urothelium. TRPV1 may represent a potential target to treat lower urinary tract symptoms in several bladder conditions. Looking at intravesical RTX treatment in IC/BPS patients, he said that since a more stable form of RTX is now available, we may see this achieving a comeback.

Takeya Kitta, MD from Japan presented on Neuroimaging of the Brain from Bladder Stimulation, noting that the micturition reflex is controlled by a complex hierarchy of the central nervous system and that the last three decades have seen great advances in research in the fields of neurourology of the lower urinary tract. Clas Linnman, PhD followed with a talk on functional MRI current findings and future potential, explaining that neuroimaging provides clear in vivo evidence of CNS processes involved in healthy and abnormal bladder control. Imaging protocols, sensitivity and specificity are

improving, he said. This largely confirms preclinical models, with potential to provide mechanistic insight into clinical populations.

AUA COURSES

There were several interesting courses related to IC/BPS and chronic pelvic pain. These can be accessed as webcasts on the AUA website against payment.

<http://www.aua2013.org/webcasts/>

003IC: PRACTICAL AND EFFECTIVE WAYS TO MANAGE UROLOGICAL CHRONIC PELVIC PAIN IN MEN AND WOMEN: Jeannette Potts, MD, Christopher Payne, MD, Rhonda Kotarinos, PT, DPT.

006PG: UROLOGICAL PELVIC PAIN: THE “NUTS AND BOLTS” OF THERAPY: Robert Moldwin, MD, Kristene Whitmore, MD, Robert Evans, MD.

071PG: INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A PRIMER AND A WORLD VIEW: Philip Hanno, MD, David Burks, MD, Jorgen Nordling, MD, Arndt Van Ophoven, MD.

044PG: CONTEMPORARY UROLOGIC MANAGEMENT OF WOMEN WITH SEXUAL DYSFUNCTION: Irwin Goldstein, MD, T. Goldstein, MD, Noel Kim, PhD, Kenneth Peters, MD.

Some points raised in the courses:

There are many problems still varying from definition/epidemiology to etiology, complexity of trial design, placebo issues, therapeutic alternatives and guidelines. Different definitions arise from the fact that we don't know the cause, the symptoms are subjective, leading to different case definitions. We still don't know the etiology, even after so many years of research. There are also many associated disorders, but we don't know how they fit in and whether they make it more likely to get this disorder or whether they are a result of the disorder or both. Trials have been made difficult due to different diagnostic criteria and the propensity for temporary remissions unrelated to therapy. Are we talking about different diseases here? Pelvic floor dysfunction, Hunner's lesion, localised pain syndromes, multifocal pain syndromes, should we be lumping these together when doing drug trials or focusing on individual phenotypes. Hunner's lesion clearly seems to be a different disease. It is therefore not likely that the same treatment will work in both current subtypes. It was repeatedly emphasised that glomerulations are now not to be considered diagnostic.

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