

**INTERNATIONAL CONTINENCE SOCIETY
41ST ANNUAL SCIENTIFIC MEETING
29 August - 2 September 2011, Glasgow, Scotland**

**A REVIEW OF RESEARCH ON INTERSTITIAL CYSTITIS, PAINFUL BLADDER SYNDROME,
BLADDER PAIN SYNDROME, HYPERSENSITIVE BLADDER SYNDROME, CHRONIC
PELVIC PAIN SYNDROME AND RELATED TOPICS AND DISORDERS**

Jane Meijlink

While no session was dedicated to this topic at the ICS annual scientific meeting 2011 in Glasgow, a substantial number of abstracts were accepted, many of which could be seen there as non-discussion posters while others are read as title. They provide an indication of how global research has become, but also of how little international consensus still exists on the method of diagnosis and on the terminology used which varies from interstitial cystitis to painful bladder syndrome, bladder pain syndrome, hypersensitive bladder syndrome and chronic pelvic pain syndrome as well as many combinations. The research concerns basic research, diagnostic techniques, differences between ulcer and nonulcer types of IC, differences and overlaps between OAB and IC, research into the urothelium and new therapies.

Abstracts presented as discussion posters can be found in full in *Neurourology and Urodynamics* volume 30 issue 6 2011, and all abstracts on the ICS website at www.icsoffice.org

Discussion Posters

Abstract # 38

INHIBITION OF GLYCINE TRANSPORTER-2 (GLYT-2) IN THE SPINAL CORD AMELIORATES BLADDER OVERACTIVITY AND PAIN SENSATION IN RATS

Yoshikawa S, Oguchi T, Yoshimura N

In order to explore the therapeutic potential of GlyTs for the treatment of OAB and IC/BPS, Yoshikawa and colleagues from Pittsburgh urology department investigated the effects of GlyT inhibitors on bladder activity in cystitis rats treated with cyclophosphamide (CYP) and on nociceptive behaviour induced by intravesical application of resiniferatoxin (RTx). They found that: GlyT-2 inhibitor, not GlyT-1 inhibitor, ameliorated bladder overactivity in rats with cyclophosphamide-induced cystitis; that GlyT-2 inhibitor, not GlyT-1 inhibitor, also inhibited nociceptive behaviour in RTX-treated rats; that the lack of efficacy of GlyT-1 inhibitor might be explained by the proximity of GlyT-1 to glutamate receptors, where glycine has co-agonistic action for excitatory neurotransmission; and that the reductions in GlyTs mRNA shown in CYP-treated rats may indicate a certain biological defence mechanism of glycinergic neurotransmission against excitatory synaptic transmissions in the cystitis condition. The authors are of the opinion that their new findings suggest an important role of spinal glycinergic pathways, enhanced by GlyT-2 inhibitors, in the suppression of bladder overactivity and pain sensation. GlyT-2 inhibitors may have a new therapeutic potential for the treatment of OAB and IC/PBS.

Abstract # 84

SENSATION OF URGENCY; WHICH INSTRUMENTS ARE AVAILABLE AND WHICH DIMENSIONS OF SENSATION DO THEY MEASURE? A SYSTEMATIC REVIEW.

Das R, Buckley J1, Williams M

Adverse sensory experiences such as pain and dyspnoea are multidimensional and include dimensions of intensity, unpleasantness and sensory quality. An understanding of these dimensions has assisted diagnosis and treatment. It has been hypothesized that urinary urgency is a multi-dimensional sensation, yet key questions regarding the nature of this adverse sensation remain unsolved. Recent narrative reviews critique a

selection of instruments used to measure urgency and highlight the difficulty of assessing this poorly understood sensation. This systematic review from the South Australian Sansom Institute for Health Research aimed to (a) identify instruments which have been used to measure either urge or urgency in adults and (b) synthesize the dimensions of sensation measured using these instruments. Das and colleagues concluded that instruments do not consistently indicate which dimension of sensation is assessed, nor do they measure more than one dimension. They therefore ask whether a multi-dimensional instrument is required.

Abstract # 115

APREMILAST: A POSSIBLE NEW TREATMENT FOR VULVAR PAIN—CLINICAL TRIAL RESULTS

Peters K, Carrico D, Boura J

Studies show that more than 14 million women have vulvar pain in the U.S. Vulvar vestibulitis tissue samples show IL-1 β is elevated 2.3-fold, and TNF- α is elevated 1.8-fold over controls [1]. Apremilast is a well tolerated, novel, orally available small molecule that specifically inhibits PDE4 and modulates multiple pro- and anti-inflammatory mediators. However it has not been studied with vulvar pain. Peters and colleagues hypothesis was that Apremilast would be effective in treating vulvar pain. The aims of this study from the William Beaumont Hospital (which received the Best Basic Science Abstract Award) were to evaluate the efficacy, safety and quality of life associated with Apremilast in patients with vulvar pain. They found that it appeared that apremilast may be a useful treatment for vulvar pain, however with a small sample size in an open label trial, statistical significance is difficult to determine and conclusions and conclusions cannot be made. Of note is the improvement in subjects while on the drug over time, with the return to almost baseline levels on all parameters tested when off the drug for one month. They concluded that apremilast needs further study to determine efficacy, safety, dosing and frequency in a randomized controlled trial before efficacy as a treatment for vulvar pain can be determined.

Abstract # 124

EFFECTS OF L-ARGININE ON SINGLE UNIT AFFERENT ACTIVITIES SYNCHRONIZED WITH RHYTHMIC BLADDER CONTRACTIONS IN THE RAT

Aizawa N, Wyndaele J, Homma Y, Igawa Y

It has been reported that nitric oxide (NO) can inhibit the mechanosensitive both A δ - and C-fiber afferent activities during bladder distension in the rat (1). These afferent activities, however, may be enhanced also by bladder contractions (2). To determine the possibility, Aizawa and colleagues from Tokyo and Antwerp established the measurement of single unit mechanosensitive bladder afferent activities (SAAs) synchronized with rhythmic bladder contractions (RBCs), and investigated whether endogenous NO can affect the SAAs in such condition. This study demonstrates that both mechanosensitive A δ - and C-fibers responsive to bladder distension are also responsive to bladder contractions. After L-Arginine administration, the amplitude of RBCs did not change, whereas RBCs disappeared for a while reflected as the increases in TFR and TFP, suggesting that L-Arginine can inhibit the afferent pathway from the bladder, but not the efferent pathway. Moreover, the significant decrease in the peak of FR after L-Arginine administration further supports its selective action on the afferent pathway. These findings may give new insight into the possible mechanism action of L-Arginine/NOS system in inhabiting detrusor overactivity (DO) and overactive bladder syndrome (OAB) since microcontractions are speculated to be responsible for development of DO and OAB (2). The authors' concluded that their results indicate that mechanosensitive afferent activities of both A δ - and C- fibers of the rat bladder are capable of being responsive to both stretch and contractile stimuli. They also suggest that the increased production of endogenous NO, caused by L-arginine administration, can inhibit the activation of mechanosensitive afferent nerves induced by bladder contractions. The authors believe that this is the first direct demonstration of the inhibitory action of L-arginine on SAAs during bladder "contractions".

Abstract # 178

HIGH-DOSE TRANILAST CREATES INTERSTITIAL CYSTITIS WITH INCREASED VESICAL VASCULAR PERMEABILITY IN RATS

Nishijima S, Sugaya K, Kadokawa K, Ashitomi K, Yamamoto H

Nishijima and colleagues from Japan report that tranilast, an anti-allergy agent, rarely induces IC as a side effect in clinical use. Tranilast is also employed for the treatment of keloids and hypertrophic scars because it inhibits collagen synthesis in fibroblasts by blocking the release of transforming growth factor (TGF)- β 1. Therefore, they hypothesized that administration of tranilast might induce IC by inhibiting the activity of bladder fibroblasts along with an increase of vascular permeability. In this study, they examined whether high-dose administration of tranilast could create an animal model of IC and then used the model to assess the relationship between IC

and changes in vascular permeability in the bladder. 50 rats were divided into 4 groups. In the tranilast group, a shorter interval between bladder contractions (urinary frequency) and glomerulation of the bladder wall on bladder distension were observed, suggesting that high-dose tranilast can create an animal model of IC. The significant increase of Evans blue leakage into the bladder wall and thinning of the collagen fiber layer, as well as the decrease of plasma TGF- β 1 in the tranilast group, indicated that tranilast administration had inhibited collagen synthesis in the bladder wall and vessels by blocking TGF- β 1 release from fibroblasts and had also increased vascular permeability in the bladder. Adding carbazochrome to tranilast in the combination group inhibited urinary frequency and the increase of vascular permeability in the bladder wall, supporting the above hypothesis. They concluded that high-dose administration of tranilast can create an IC model in rats. An increase of vascular permeability in the bladder may be one of the causes of IC. Carbazochrome inhibits vascular permeability and may be a potential treatment for IC.

Abstract # 179

ENHANCED BLADDER PAIN IN CYCLOPHOSPHAMIDE-INDUCED CYSTITIS IN RATS- INVOLVEMENT OF PELVIC NERVE AND HYPOGASTRIC NERVE SENSITIZATION

Oguchi T, Yokoyama H, Yoshikawa S, Nishizawa O, Yoshimura N

The etiology of BPS/IC is not well known and there is no appropriate animal model of the disease. On the other hand, cyclophosphamide (CYP)-induced cystitis is recognized as chemical cystitis that has an inflammatory status without bacterial infection. Although CYP cystitis is different from BPS/IC, it similarly shows frequent urination and bladder pain. Oguchi and colleagues from Pittsburgh, USA and Shinshu, Japan therefore investigated whether chronic CYP cystitis enhances bladder pain sensation induced by C-fiber activation in rats. Furthermore, they evaluated the contribution of pudendal nerves, pelvic nerves, and hypogastric nerves to pain behaviour in chronic CYP cystitis in a rat study.

They found that chronic CYP cystitis increases pain behaviour such as licking and freezing induced by RTX-mediated C-fiber stimulation, indicating that chronic cystitis induces bladder hyperalgesia. However, they found that bladder capacity following RTX was not different in control and CYP rats, suggesting that it is not a suitable parameter of bladder hypersensitivity in chronic cystitis. Bladder pain (freezing) in normal rats depends on pelvic nerve activation, but not significantly on hypogastric nerves. In chronic cystitis, both pelvic and hypogastric nerves contribute to enhanced bladder pain sensation, but the contribution of pelvic nerves is still dominant. Urethral pain (licking) depends on pudendal nerve activation in normal and cystitis rats. The authors concluded that chronic CYP leads to enhanced bladder pain induced by C-fiber activation due to sensitization of both pelvic and hypogastric nerve afferents while bladder pain in the normal condition predominantly depends on pelvic nerve afferent activation. Consequently, they are of the opinion that the CYP-induced chronic cystitis model could be suitable for the study of mechanisms and new therapies for chronic bladder pain which is also seen in BPS/IC.

Abstract #186

THE ROLE OF THE UROTHELIUM IN POTASSIUM SENSITIVITY TESTING IN THE CLINIC.

Gooch L J, Daly D M, Chapple C R, Grundy D

Gooch and colleagues from Sheffield, UK note that potassium sensitivity testing (high K⁺) for diagnosis in patients with bladder disorders is controversial, although it is considered predictive of increased urothelial permeability. As such high K⁺, as it diffuses across a leaky urothelium, is considered to directly depolarise sensory nerve endings. However, in this mouse study they hypothesised that high K⁺ may act at the level of the urothelium to release mediators that modulate afferent sensitivity indirectly. The aim of this mouse research was to understand the effect of urothelial mediator release on afferent nerve firing, with the hypothesis that stimulating the release of mediators from the urothelium will alter afferent nerve sensitivity. They concluded that these data demonstrate that high K⁺ stimulates the release of urothelial factor(s) that down regulated bladder afferent sensitivity. Urothelial damage with PS abolishes this inhibitory response and unmask an excitatory effect. Inhibition of inhibitory mediators with the inhibitory cocktail reduced the inhibitory response of high K⁺ instillation. High K⁺ exposure does not affect bladder compliance. Spontaneous nerve firing is significantly inhibited by high K⁺ exposure, a phenomenon that is unaffected by denudation of the urothelium suggesting that spontaneous nerve firing and mechanosensitivity are not mediated by the same mechanisms. The potassium sensitivity test in patient may reveal information on the ability of the urothelium to modulate afferent sensitivity, rather than a simple test of permeability. The authors are of the opinion that further exploitation of the urothelial/neuronal inhibitory pathways offers an exciting, new direction for therapy of bladder pathology.

Non discussion posters

Abstract # 334

CHRONIC INFLAMMATION BUT NOT UROTHELIUM DYSFUNCTION IN PATIENTS WITH OVERACTIVE BLADDER SYNDROME

Liu H T, Lin H, Kuo H C

Liu and colleagues from Taiwan report that recent investigations have linked overactive bladder syndrome (OAB) with chronic inflammation. Urinary nerve growth factor, cytokines and serum C-reactive protein have been demonstrated to increase in patients with OAB and interstitial cystitis/ painful bladder syndrome (IC/PBS). Previous reports have suggested that IC/PBS is associated with increased activated mast cell numbers in the bladder and disruption of the barrier function of the urothelium. However, they note that there has been no study investigating the mast cell activation and urothelium barrier dysfunction in OAB. Since there are similarities in the inflammatory protein expression between OAB and IC/PBS, this study explored the infiltration of mast cells and the distribution of protein involved in barrier function by immunohistochemical assessment of E-cadherin and ZO-1 in the bladder tissue of patients with OAB and IC/PBS. Bladder wall biopsies were performed in 27 patients with OAB, 18 patients with IC/PBS, and 19 patients with stress urinary incontinence but without urgency frequency symptoms and served as controls. In this study, patients with OAB and IC/PBS all had significantly greater number of mast cells in the bladder wall compared with controls. The bladder biopsies from IC/PBS patients reported previously have confirmed the involvement and presence of mast cells in the detrusor. Mast cells have been considered as crucial effector cells for the immune response implicated in the pathogenesis of IC/PBS. Bladder mast cell activation has been reported as a characteristic pathological finding in a subset of IC/PBS patients. Measurement of surrogate mast cell-related products in urine has been previously studied to assess the disease extent in patients. Since patients with OAB and IC/PBS all had elevated mast cell activities compared with that of the controls in this study, the authors believe that it is possible that a common pathway of chronic inflammation exists in the pathogenesis between these two diseases. They concluded that the results of this study suggest that both IC/PBS and OAB are associated with chronic inflammation and the role of bladder tissue mast cells in the pathogenesis and pathophysiology of OAB and IC/PBS is worthy of further investigation.

Abstract # 373

QUESTIONNAIRE SURVEY ON ASSOCIATION OF IRRITABLE BOWEL SYNDROME WITH OVERACTIVE BLADDER

Matsumoto S, Kakizaki H

Matsumoto and Kakizaki from Asahikawa Medical University note that previous studies have shown that OAB and IBS occur concurrently in a high frequency. Animal experiments have also shown that hyperesthesia of the bladder is seen in a colitis-induced colon-hyperalgesia model and that colon hyperalgesia is seen in a cyclophosphamide-induced cystitis model (animal OAB model). In addition, the colon and the bladder are reported to share in part common afferent nerve projections, suggesting the presence of a neural cross-talk between the two organs. This raises the possibility that both OAB and IBS may share the common pathologic features. In this study, the authors investigated the concomitant occurrence of OAB and IBS among the Japanese population through a questionnaire survey via the Internet concerning defecation habits and storage symptoms. Questionnaires were sent via the Internet to men and women aged 20 to 79 years, and they obtained a total of 10,000 valid responses (1,000 each from men and women in their 20s, 30s, 40s, 50s, and 60s and older). They found that a high proportion (33.3%) of Japanese OAB patients had concomitant IBS. In accordance with previous epidemiological studies, the prevalence of OAB increased with age, while the prevalence of concomitant IBS decreased with age. Severity of OAB was not related with the prevalence of concomitant IBS. They concluded from this survey that there is substantial overlapping between OAB and IBS, suggesting etiological linkage between the two diseases. However, because the prevalence of OAB and IBS differs depending on age, underlying etiologies may not be identical. Based on these results, it is extremely important to evaluate defecation habits when diagnosing and treating OAB. This study only focused on the association of IBS with OAB (storage symptoms). The authors are of the opinion that further detailed studies need to be conducted to examine the relationship between IBS and lower urinary tract symptoms and the impact of concomitant IBS on treatment outcome of OAB.

Abstract #482

INTRAVESICAL INSTILLATION OF NOCICEPTIN/ORPHANIN FQ (N/OFFQ) IN PATIENTS WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS): RESULTS FROM A PILOT STUDY

Del Popolo G, Celso M, Mencarini M, Neli F, Del Corso F, Lazzeri M

The purpose of this study from Italy was to examine the safety, the tolerability and the efficacy of intravesical instillation of the natural occurring peptide nociceptin/orphanin FQ (N/OFQ) for the treatment of interstitial cystitis/painful bladder/Chronic Pelvic Pain Syndrome (IC/PBS).

23 (21/2 f/m) subjects (mean age 55.8 ± 17.78 years – median 55) with IC/PBS consented to receive twice a week, for 4 weeks, intravesical instillation of the natural occurring peptide N/OFQ (1mg/10ml saline). All the patients completed the treatment. No significant adverse event was recorded in any of the patients during the treatment and after 3 months. The authors are of the opinion that their preliminary results seem to suggest that N/OFQ is able to elicit an inhibitory effect on LUTS and pain in patients with IC/PBS. They believe that this is the first evidence of such an effect, but that further randomised placebo controlled trials are mandatory to confirm their data.

Abstract #483

INCREASED EXPRESSION OF TRPA1, TRPV2, ASIC1 AND CXCL9 MRNA IN BLADDER TISSUE FROM PATIENTS WITH ULCER-TYPE INTERSTITIAL CYSTITIS

Nomiya A, Tagaya M, Oyama T, Kawai Y, Takagaki K, Nisimatsu H, Aizawa N, Fujimura T, Igawa Y, Homma Y

In this study from Tokyo, Nomiya and colleagues assessed the differential expression of the human transient receptor potential (TRP) channel gene transcripts, acid sensing ion channel (ASIC), nerve growth factor (NGF), uroplakin 3A (UPK3A) and chemokine (C-X-C motif) ligand 9 (CXCL9) in bladder tissue in IC patients and controls. Patients with IC scheduled for hydrodistension or with non-invasive bladder cancer (as controls) undergoing transurethral resection were enrolled under informed consent. Diagnosis of IC was based on the Japanese clinical guidelines for interstitial cystitis and hypersensitive bladder syndrome. The authors found that among the TRP channels, TRPA1 and TRPV2 showed significantly increased mRNA expression in non-ulcerative portions of ulcer-type IC compared with controls. In the same portions, a significant increase in the mRNA expression of ASIC1 and CXCL9 and a decrease in the mRNA expression of UPK3A were observed. Also, in ulcerative portions of ulcer-type IC, a significant increase in TRPV2 and CXCL9 and a significant decrease in UPK3A were found as compared with controls. However, no significant difference was observed in non-ulcer-type IC tissue, suggesting a distinct pathophysiology or disease entity between these two types of IC. They concluded that TRPA1, TRPV2, ASIC1, CXCL9 and UPK3A in the bladder may play a role in the pathophysiology of ulcer-type IC, and as such they are potential targets for novel therapy.

Abstract # 484

AUTONOMIC SYMPATHETIC SYSTEM IS OVERACTIVE IN PATIENTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.

Pinto R, Lopes T, Silva J, Silva C, Dinis P, Cruz F

The role of autonomic nervous system in the development of BPS/IC has been ignored during the last few years in favour of other pathologic mechanisms. However, some forms of chronic pain, as the chronic regional pain syndrome, have a relevant participation of the sympathetic system. In what concerns BPS/IC patients, high levels of urinary catecholamines have been reported before indicating an adrenergic overactivity. Furthermore, chronic bladder inflammation promotes nerve fiber sprouting. Finally, Onabotulinum Toxin A injection in the trigone of BPS/IC patients showed a decrease in pain and frequency, raising the possibility that impairment of sympathetic fibers, almost exclusively located in the trigone, play a role in such improvement. Taken together, these data may suggest that an abnormal sympathetic activity may occur in BPS/IC patients. In this study from Porto, Portugal, the activity of the autonomic sympathetic nervous system in patients with Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC) was evaluated. BPS/IC patients were treated with intra-trigonal injection of Onabotulinum type A, 100 U injected in 10 trigonal sites. O'Leary Sant Score, Visual Analogue Scale (VAS) for Pain and QoL from IPSS were assessed in these patients before and 1 month after treatment. Blood samples and 24 hour urine were collected 1 month after treatment for norepinephrine measurements. The results of this study show an increase in sympathetic activity in patients with BPS/IC. In particular the high excretion of urinary norepinephrine suggests that lower urinary tract is under an intense adrenergic stimulation which may affect the urothelium and the bladder nociceptive fibres, as both express alpha1 receptors. After treatment with OnaBotulinum Toxin A urinary norepinephrine decreased suggesting that local modulation of sympathetic activity might occur under the influence of the neurotoxin. It is well known that OnaBotulinum toxin A prevents the neurotransmitter release from sympathetic fibers. The authors conclude that the eventual role of the sympathetic fibers, in particular those innervating pelvic organs including the bladder, should be further evaluated in order to clarify their contribution to BPS/IC.

Abstract # 485**EFFICACY OF A NARROW-BAND IMAGING CYSTOSCOPY FOR THE DETECTION AND TREATMENT OF HUNNER'S LESIONS IN PATIENTS WITH PAINFUL BLADDER SYNDROME/ INTERSTITIAL CYSTITIS**

Kajiwara M, Oki M, Kobatake K, Miyamoto K, Masumoto H, Inoue S, Kobayash K, Ohara S, Teishima J, Matsubara A

In this study from Hiroshima, Kajiwara and colleagues report that the current diagnostic and therapeutic standard for painful bladder syndrome/ interstitial cystitis (PBS/IC) is cystoscopic examination with hydrodistension, usually with white-light imaging cystoscopy (WLI). It is often not easy to diagnose as having PBS/IC by conventional WLI even if clear ulcerative formations such as Hunner's lesions/ulcers are present. Narrow band imaging cystoscopy (NBI) is a novel method, which might improve the detection rate of Hunner's lesions. The purpose of this study was to determine prospectively whether NBI improves the detection rate and the number of Hunner's lesions of PBS/IC over WLI in cases suspected of having PBS/IC, and whether NBI-assisted transurethral fulguration (TUF) of Hunner's lesions have a treatment efficacy and reduce PBS/IC recurrence rate. PBS/IC can be classified into Hunner's lesions/ulcers (ulcerative subtype) and non-ulcer disease (non-ulcerative subtype). The detection rate of Hunner's lesions by WLI is 10 to 50%. Hunner's lesions could easily be overlooked or misdiagnosed as carcinoma in situ by WLI. NBI is an optical image enhancement technique designed for endoscopy to enhance the contrast between mucosal surfaces and microvascular structures without the use of dyes. This technique is based on the phenomenon that the depth of light penetration into the mucosa increases with increasing wavelength. Since these specific wavelengths are strongly absorbed by haemoglobin, the vascular structures appear dark brown or green against a pink or white mucosal background. Because Hunner's lesions usually consist of small capillaries and submucosal vessels, it is speculated that they may be well visualized and appeared as dark brownish or green areas. T. Ueda demonstrated that NBI makes it possible to easily detect Hunner's lesions. This study demonstrated the same results. In this study, WLI overlooked about 30% of Hunner's lesions. The residual or overlooked Hunner's lesions may consequently lead to early recurrence of PBS/IC symptoms, in up to 45% of patients. Transurethral endoscopic resection (TUR) or TUF of the Hunner's lesions is applicable in ulcerative subtype of IC/PBS, which leads to symptomatic resolution for one year or longer in about half of patients. Because NBI makes it possible to easily detect Hunner's lesions, it is speculated that NBI-assisted TUF would improve TUR/TUF quality for PBS/IC patients with Hunner's lesions. According to the authors, this study demonstrated that NBI is an accurate diagnostic new tool for ulcerative subtype of PBS/IC without the need for hydrodistension and that NBI-assisted TUF is effective in relieving symptoms in PBS/IC patients with Hunner's lesions. They believe that NBI may be considered an effective diagnosis and treatment tool for patients with suspected symptoms of PBS/IC.

Abstract # 486**DIFFERENTIAL GENE EXPRESSION IN CELLS SLOUGHED IN THE URINE IN INTERSTITIAL CYSTITIS SUBJECTS**

Benson K, Fiegen M, Hansen K, Eyster K.

This study was based on the hypothesis that cells obtained from urine can be used to determine whether there is differential gene expression in patients with IC.

They had two specific aims:

1. To determine whether intact RNA could be extracted from cells found in urine specimens. For this purpose, catheterized urine specimens were obtained at the time of evaluation and total RNA was extracted.
2. To confirm differential gene expression between non-affected controls and IC patients. For this purpose, they compared RNA extracted from cells found in urine samples from 18 test subjects and 10 control subject using whole human genome DNA microarray technology.

Their study reveals with real time RT-PCR evaluation that viable RNA is indeed recoverable from cells sloughed in the urine when suspended in TRI reagent. Additionally they have shown RNA stability when suspended in TRI reagent across a variety of temperatures from -80°C to 27°C. DNA microarray analysis demonstrated a total of 21 named genes expressed differentially with greater than a 2 fold difference. Several new findings were revealed with this study. The study confirms that RNA may be extracted from cells shed in the urine of IC subjects. The authors have also shown that cellular RNA from shed bladder cells is stable, when suspended in TRI reagent, across a wide variety of temperatures. This finding will make it potentially easier to collect and store specimens. They have also shown differential gene expression in IC patients sloughed uroepithelial cells. The differences in gene expression are not dramatic as seen in other studies of cultured IC bladder cells. This

may represent a different aspect of the disease and warrants further investigation. Analysis of cells in the urine may play a defining role in identifying IC patients in the future.

Abstract # 487

EFFECT OF HERPES SIMPLEX VIRUS VECTOR-MEDIATED GLYCINE RECEPTOR GENE THERAPY ON BLADDER OVERACTIVITY AND NOCICEPTION

Oguchi T, Yokoyama H, Funahashi Y, Nishizawa O, Goins W F, Goss J R, Glorioso J C, Yoshimura N

Bladder pain syndrome/interstitial cystitis (BPS/IC) is a serious disease whose main symptoms are bladder pain and frequent urination. Glycine is an inhibitory neurotransmitter which can affect bladder function. Oguchi and colleagues examined the effects of gene transfer of glycine receptors (GlyR) using replication-deficient herpes simplex virus (HSV) vectors on bladder overactivity and pain behaviour induced by intravesical application of resiniferatoxin (RTx) in rats. The authors found that GlyR vector inoculation to the bladder wall intensifies the exogenous and endogenous glycine-mediated therapeutic effects on bladder overactivity and nociception, respectively, in rats with RTx-induced cystitis. Thus, HSV vector-mediated glycine receptor (GlyR) expression in bladder sensory pathways with glycine administration might be effective for treating BPS/IC symptoms such as bladder pain and frequent urination. In addition, systemic administration of inhibitory transmitters such as glycine in combination with local HSV gene therapy of their receptors could enhance the drug-receptor interaction in HSV-infected target organs and their afferent pathways, and avoid systemic side effects.

Abstract # 488

VISCERAL PAIN RESPONSE IN BALB-C MICE IMMUNIZED WITH UROPLAKIN UP3B AS A MURINE MODEL FOR INTERSTITIAL CYSTITIS

Izgi K, Ozer A, Isariyawongse J, Bicer F, Daneshgari F, Altuntas C

Izgi and colleagues note that little progress has been made in elucidating the pathophysiology or treatment of IC/PBS. They recently reported a method of inducing bladder-specific autoimmunity that manifests IC/PBS symptoms. The aim of this study was to induce autoimmunity in a mouse bladder with uroplakin UP3b peptide and to examine its phenotype. They found that a peptide motif of UP3b is recognized by MHC H2-D. Immunization of BALB-C mice with UP3b induces an immunogenic response that phenotypically manifests as increased visceral pain response, increased micturition frequency, and decreased output per micturition. This phenotype is similar to that observed in IC/PBS patients and according to the authors may qualify this animal model as a candidate model for IC/PBS.

Abstract # 489

EFFECT OF REPEATED INTRAVESICAL BOTULINUM TOXIN A INJECTIONS ON TREATMENT OF REFRACTORY INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME---PRELIMINARY RESULTS

Kuo Y, Shie J, Liu H T, Kuo H C

Kuo and colleagues from Taiwan report that although botulinum toxin A (BoNT-A) injection seems promising in treating symptoms of IC/PBS, long term results have not provided a successful outcome. This study evaluated the effects of repeated intravesical BoNT-A injections plus hydrodistension on treatment of IC/PBS refractory to conventional treatment. A prospective study was performed in a urological referral centre. Patients with IC/PBS who have failed conventional treatments were enrolled. They received intravesical injection of 100 U of BoNT-A (onabotulinumtoxinA, Allergan, Irvine, CA, USA) immediately followed by cystoscopic hydrodistension under intravenous general anaesthesia. Repeated BoNT-A injection and hydrodistension were performed at 6 months after the first treatment if they felt recurrence of baseline symptoms and desired further treatment. The BoNT-A injection plus hydrodistension was repeated every 6 months up to 4 times or until patients declared that their symptoms had been alleviated. They found that the effect of repeated intravesical BoNT-A injection plus hydrodistension on treatment of refractory IC/PBS is promising and durable with acceptable adverse effects.

Abstract # 490

URINE ALKALINISATION BY CITRATES IMPROVES PAIN AND OTHER SYMPTOMS IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME. ASSESSMENT OF URINE PH USING COMPACT PH METERS AT EVERY VOIDING.

Ueda T, Yoshida T, Tanoue H, Ito M, Yoshimura N

Acidic urine may play a role in the development of symptoms in patients with interstitial cystitis/bladder pain syndrome (IC/BPS) because activation of afferent C-fibres can be triggered by excessive H⁺ ions in acidic urine. The aims of this study from Ueda and colleagues from Kyoto and Pittsburgh were to evaluate the precise data

of urine pH value and pain intensity and efficacy of the alkalinisation therapy. A compact pH meter was used to measure the pH and the intensity of pain was recorded at every voiding. They also investigated sleep disturbance in this study. Thirty-four participants were enrolled in this study, and thirty (twenty-five females, five males, age 56.6 ± 15.8) were selected based on symptoms recorded in 2-day voiding diaries and urine pH of each voiding during the screening period. Spot urine tests using the pH meter before treatment with the citrates revealed that many patients had urine pHs lower than 5.2, which is the lower limit of the urine pH test paper previously used. After the treatment, the urine pH at each voiding was increased, and the number of patients with urine with low pH was also decreased. After the treatment with citrates, the mean urine pH was significantly increased from 5.6 to 6.0. Most symptoms improved. The volume per voiding and the maximum voided volume increased significantly. With respect to sleep disturbance, a small improvement was observed in the PSQI and ESS, but the improvement was not significant. The authors are of the opinion that the symptoms of IC/BPS may be related to an attack of H⁺ ions to TRPV1 or the acid-sensing ion channels expressed at the termini of afferent C-fibres located underneath the bladder mucosa. This study demonstrated that the urine at every voiding was alkalinised, and the systemic acid-base balance was adjusted by the administration of citrates. As a result, most symptoms of IC/BPS were improved, suggesting that acidic urine and/or a disturbance in the systemic acid-base balance in the upper stream may cause some symptoms of IC/BPS. Although a reduction in sleep disturbance was observed in their previous study, this effect was not clear in this study. Because the presence of a sleep disturbance was not one of the inclusion criteria of this study, a statistical power may be low. In this study, the urine pH at every voiding was measured by patients using a compact pH meter, allowing the authors to evaluate precisely the elevation of urine pH after the administration of citrates throughout the day. The results of this study suggest that urine alkalinisation could be an effective way to reduce the symptoms of patients with IC/BPS.

Abstract # 491

THE ALTERATION OF GLOMERULATION AND ANGIOGENIC MOLECULES CHANGE AFTER BOTULINUM TOXIN A THERAPY IN INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME

Shie J, Liu H T, Kuo Y, Kuo H C

Shie and colleagues from Taiwan note that glomerulation of bladder mucosa after cystoscopic hydrodistension (HD) has been regarded as one of the requisite criteria for the diagnosis of interstitial cystitis/painful bladder syndrome (IC/PBS). Previous studies have found that botulinum toxin A (BoNT-A) not only inhibited the release of acetylcholine and norepinephrine, but also resolved clinical symptoms of IC/PBS. The authors report that they have observed that the HD induced glomerulation decreased in grade after repeated BoNT-A injections. This study investigated the mechanism of action for IC/PBS patients with symptomatic and cystoscopic improvements after intravesical BoNT-A injections, such as bladder glomerulation and inflammation. Twenty-five women with characteristic symptoms of IC/PBS and glomerulation after cystoscopic HD were enrolled in this study. Bladder biopsies at three sites were taken immediately after cystoscopic HD for the diagnosis of IC/PBS. All patients were previously untreated for IC/PBS before the bladder procedure. Bladder specimens with grade 2 to 3 glomerulation without ulceration were used in this study. The bladder tissue specimens at baseline and after intravesical BoNT-A injection were investigated by immunofluorescence, protein array, western blotting and ELISA for the mast cell activity and angiogenic protein expression. The authors report that intravesical BoNT-A injections in IC/PBS bladders improved clinical symptoms and decreased the grade of glomerulation. Protein analysis revealed a decrease in inflammatory and angiogenic protein expression in IC/PBS bladders. They are of the opinion that these findings provide evidence that BoNT-A intravesical injection can decrease inflammation and improve bladder glomerulation in patients with IC/PBS.

Abstract # 492

PAINFUL BLADDER SYNDROME ASSOCIATED WITH SEXUAL DYSFUNCTION MAY LEAD TO SUICIDE ATTEMPTS

Sumerova N, Tsibulja O, Kovilina M, Malkhasjan V

Sumerova and colleagues carried out a study into whether the symptoms of PBS - pain, urgency and frequency that often lead to a disturbance in sleeping patterns and psychological distress - and dyspareunia may provoke suicidal thoughts in the patients. They concluded that the combination of these symptoms may provoke suicidal thoughts in the patients. They suggest that PBS patients should be assessed for sexual dysfunction and given adequate treatment. PBS patients suffering from extreme pain and sexual dysfunction have a relatively high risk of attempting suicide (up to 5%). Such patients should not only be treated by urologists, but should also be assessed and receive treatment from a psychiatrist, as well as a consultation and adequate treatment from a sexual therapist.

Abstract # 493**PELVIC ORGAN CROSS-SENSITIZATION MODULATES EXPRESSION AND RELEASE OF NEUROPEPTIDES AND NEUROTROPHIC FACTORS IN THE URINARY BLADDER OF FEMALE RATS: ROLE OF THE ESTROUS CYCLE***Northington G, Pan X, Mathai T, Asfaw T, Wein A, Malykhina A*

Painful bladder syndrome and interstitial cystitis affect women more often than men suggesting the role of ovarian hormones in pain perception and transmission. The underlying mechanisms regulating pain fluctuations within a menstrual cycle in women are not fully understood. Recent studies suggested that pelvic organ cross-sensitization triggered by pathology in one of the pelvic organs can lead to functional changes in adjacent organs. It was demonstrated that inflammation of the distal colon causes the development of a neurogenic bladder. Northington and colleagues from Pennsylvania hypothesized that changes in ovarian hormones associated with the estrous cycle would result in changes in the expression of bladder neuropeptides in female rats after colonic inflammation. The objective of this study was to identify major neurotransmitters/neuropeptides released in the bladder during rising and falling estrogen phases of the estrous cycle using an animal model of a neurogenic bladder. Their secondary aim was to determine if similar differences in urinary neuropeptides and neurotransmitters were noted among premenopausal women with and without bladder pain. The authors report that active colonic inflammation triggers an increased release of neurotrophic factors and neuropeptides during proestrus phase in the female rat bladder. The absence of similar differences noted in urinary neuropeptide expression between women with and without bladder pain may, in part, be explained by the fact that they were not examined with respect to their menstrual cycle phase (luteal vs. follicular). The menstrual cycle in women with bladder pain may be an important factor in urinary neuropeptide and neurotransmitter expression. Taken together, these data suggest that ovarian hormones may modulate painful sensations in women with bladder pain of neurogenic origin and further research is required to fully elucidate these mechanisms.

Abstract # 494**CORRELATION WITH URINARY EPITHELIUM AND PRIMARY SYMPTOMS IN INTERSTITIAL CYSTITIS: INVESTIGATION OF SCANNING ELECTRON MICROSCOPY***Yokoyama T, Fukumoto K, Hara R, Fujii T, Jo Y, Miyaji Y, Nagai A*

Yokoyama and colleagues from Kawasaki investigated associations between bladder epithelium and urinary symptoms for patients with interstitial cystitis by using scanning electron microscopy (SEM). Bladder tissue biopsies were obtained during routine diagnostic evaluation from macroscopic normal posterior wall of 13 patients with IC (9 females and 4 males with a ranged of 19 to 80 year-old) from November 2008 to January 2011, and examined by HE staining, astra blue staining for mast cell, and SEM. Three pathology features were noted (1) mast cell counts in lamina propria on astra blue stain (2) loss of urothelium on H.E. stain and SEM (3) inflammation in lamina propria on H.E. stain. Symptoms were evaluated before treatment by IPSS, QOL index, and O'Leary and Sant score. In patients with IC, histological findings were varied. The disruption of outer layer of urothelium was clearly observed in all patients by SEM even in macroscopic normal finding area. Moreover the degree of urothelial disruption and symptom were not correlated with the degree of inflammation. Their concluding message was that the urothelium may play a pivotal role in IC symptoms and that new therapy should be investigated targeting urothelium protection.

Abstract # 495**THE USE OF CYSTISTAT® (HYALURONIC ACID) VS URACYST® (CHONDROITIN) BLADDER INSTILLATIONS IN THE TREATMENT OF INTERSTITIAL CYSTITIS: A PROSPECTIVE AUDIT***Lines H, Lingam K, Holden A, Hardwick A*

Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS) currently has no defined aetiology, however defects in the glycosaminoglycan (GAG) layer which line the urothelium have been associated with the condition. Several treatments targeted at replenishing the GAG layer have been produced. The audit aimed to determine whether intravesical hyaluronic acid (Cystistat®) or chondroitin sulphate (Uracyst®) were effective treatments for reducing the symptoms associated with IC/PBS and improving the quality of life of patients with the condition. In a prospective audit, 80 patients (age range 21-82yrs) attending a UK Urogynaecology unit with symptoms of IC/PBS received either Cystistat or Uracyst intravesical instillations weekly for 1 month, and then monthly for a further 2 months, according to the manufacturers' instructions. Patient outcomes were assessed before, 1 month into and 3 months into treatment using the Parsons Pelvic Pain and Urgency/Frequency (PUF) Patient Symptom Scale, the O'Leary-Sant validated Interstitial Cystitis Symptom Index and Problem Index (ICSI and

ICPI), a standard 3-day voiding diary and the Rand Health SF-12 Quality of Life questionnaire. Comparisons were then made between scores at each time point and cohorts.

Overall 77 patients (96.25%) completed the full 3 months of treatment. 3 patients (3.75%) withdrew, 2 due to worsening of symptoms and 1 failure to attend. Scores from the PUF Patient Symptom Scale were significantly reduced after 3 months of treatment with both treatments. ICSI and ICPI scores and average 24-hour voiding frequency were also significantly reduced in both cohorts. SF-12 quality of life scores showed significant increases in those receiving Uracyst whereas the increase was not significant in the Cystistat cohort. No statistically significant difference was seen between the two drugs. In the Cystistat arm, 4 (10.3%) patients were discharged due to resolution of symptoms, and 16 (41%) felt the treatment was helping and requested to continue with treatment, with 13 (38.2%) and 16 (42.1%) in the Uracyst arm respectively.

Abstract # 496

EXAMINING PHENOTYPICAL DIFFERENCES IN WOMEN WITH ULCERATIVE INTERSTITIAL CYSTITIS, NON-ULCERATIVE INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND CONTROLS

Peters K, Killinger K, Mounayer M, Boura J

According to Peters and colleagues from the William Beaumont Hospital, characteristic differences in women with and without bladder pain syndrome/interstitial cystitis (BPS/IC) have been described. However, variations between the ulcerative (ULC) and non-ulcerative (N-ULC) subtypes have not been fully explored even though distinct differences exist in clinical presentation and response to treatment. To identify similarities and differences in each subtype, they evaluated comorbidity prevalence, abuse history, and urinary, psychological, and pain symptoms in women with ULC or N-ULC BPS/IC, and controls without BPS/IC. Their data from this study provide further support for a higher prevalence of comorbid diagnoses and symptoms in women with BPS/IC compared to controls. However, their findings also suggest that key differences exist between women with BPS/IC categorized by cystoscopic subtype. Women with N-ULC BPS/IC experience more emotional issues and diffuse comorbid symptoms/conditions whereas in the ULC subtype symptoms and characteristics are more localized to the bladder. These findings suggest that N-ULC IC/PBS may be more centrally mediated than ULC. The authors conclude that the possibility that these two BPS/IC subtypes are in actuality two distinct conditions cannot be ruled out. More research is needed to determine the temporal relationship between comorbid conditions and BPS/IC and whether each subtype represents a different physiological reaction to a similar stressor or are actually different disease entities altogether. The comorbidities assessed were: anxiety disorder, asthma, bipolar disorder, cluster headaches, chronic fatigue syndrome, chronic low back pain, Crohn's disease, depression, diabetes mellitus, endometriosis, fibromyalgia, frequent bladder infections, heart disease, irritable bowel syndrome, systemic lupus erythematosus, Lyme disease, migraine, multiple sclerosis, Parkinson disease, rheumatoid arthritis, restless legs syndrome, schizophrenia, sinusitis, Sjögren's syndrome, temporomandibular joint disorder, thyroid disease, ulcerative colitis, vulvodynia.

Abstract # 497

BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: IS THIS CONDITION ASSOCIATED WITH A SYMPATHETIC DYSFUNCTION?

Pinto R, Charrua A, Taylor A M W, Barros S, Tavares C, Ribeiro-da-Silva A, Avelino A, Cruz C D, Cruz F

In this study from Portugal, Pinto and colleagues aimed to investigate the effect of a chronic adrenergic stimulation of naive rats in their bladder morphology and function, as well as the effect of chronic bladder inflammation on the activity of the bladder sympathetic system. Chronic adrenergic stimulation induced signs similar to the ones observed in BPS/IC patients. Therefore, future studies should investigate sympathetic dysfunction in patients with BPS/IC. In addition, chronic adrenergic stimulation of naive rats may constitute a new, valuable experimental model to study BPS/IC in rodents.

Abstract # 498

ACID-SENSING CHANNELS IN HUMAN BLADDER: EXPRESSION, FUNCTION AND ALTERATIONS DURING BLADDER PAIN SYNDROME

Monastyrskaya K, Sánchez-Freire V, Blanchard M, Kessler T M, Kuhn A, Kellenberger S, Burkhard F C

To examine the possible role of H⁺-activated acid-sensing ion channels (ASICs) in pain perception, Monastyrskaya and colleagues from Switzerland characterized their expression in bladder dome biopsies of Bladder Pain Syndrome (BPS) patients and controls, in cultured human urothelium and in urothelial TEU-2 cells. Cold cut biopsies from the bladder dome were obtained in 8 asymptomatic controls and 28 patients with symptoms of BPS. ASIC expression was analyzed by QPCR and immunofluorescence. The channel function was measured by electrophysiology. Several types of ASICs are expressed in human bladder and TEU-2 cells, where

their levels are regulated during urothelial differentiation. An up-regulation of ASIC2a and -3 in BPS suggests their involvement in increased pain and hyperalgesia. A down-regulation of TRPV1 mRNA levels might indicate a different regulatory mechanism, controlling its expression in human bladder. The authors concluded that ASICs 2a and 3 may be involved in pain and hyperalgesia in Patients with BPS.

Abstract # 609

CONSECUTIVE CYSTOMETRIES DURING THE SAME SESSION USING 0.9% NORMAL SALINE (NS) FOR TWICE AND 0.2M POTASSIUM CHLORIDE (KCL) IN WOMEN WITH INTERSTITIAL CYSTITIS/ PAINFUL BLADDER SYNDROME (IC/PBS)

Wei Chih C, Ming Huei L, Chiu De C, Ya Ling C, Yi Chang C, Huei Ching W

Recent research has suggested that in healthy volunteers, if cystometry is repeated with 0.9% NS during the same session, the bladder volumes tend to increase by 30-50 ml, and it is the similar findings in the neurogenic bladder patients. Other researchers have proposed that a comparative assessment of cystometric capacity using 0.9% NS and 0.2M KCL suggesting that a decrease in maximum cystometric capacity of more than 30% with KCL compared to NS is indicative of IC/PBS. The aim of this study by Wei Chih and colleagues is to explore differences between IC/PBS patients in urodynamic findings between consecutive 0.9% NS and 0.2M KCL instillation. This was a prospective study for all the urodynamic studies that were done for female patients with IC/PBS symptoms in one centre. IC/PBS patients who were compatible with the NIDDK criteria were included and the urodynamic findings were reported by one physician. The patients were subdivided into two groups. Group 1 consisted of 80 women that 2 consecutive cystometries with NS and KCL were performed. Group 2 consisted of 22 women that performing 3 consecutive cystometries with 0.9% NS for twice and 0.2M KCL. On filling cystometry they recorded and examined variability between volume at first desire to void (FDV), normal desire to void (NDV), strong desire to void (SDV) and maximum cystometric capacity (MCC). The authors found that, similar to those seen in normal volunteers, IC/PBS patients have increased bladder capacity around 32.00 mL to 50.13 mL during the consecutive cystometries with normal saline from first to second. The urodynamic study is not a definitive diagnostic tool for IC/PBS, but it seems a more significant decrease with mean value 49 mL with 3 consecutive cystometry from second normal saline to 0.2M KCL than dual cystometry.

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Abstract # 710

THE DIFFERENCES IN URODYNAMIC CHARACTERISTICS BETWEEN FEMALE PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND OVERACTIVE BLADDER

Lin A, Huang Y, Fan Y, Lin C, Chen K

Interstitial cystitis/bladder pain syndrome (IC/BPS) and overactive bladder (OAB) share some similar symptoms (urgency, frequency and nocturia). Therefore, it has been argued that both conditions might have a similar underlying pathophysiology. In this study from Taiwan, Lin and colleagues try to examine this argument by comparing the urodynamic findings between IC/BPS and OAB in female patients. The urodynamic results were analyzed in 66 consecutive female patients with IC/BPS and 105 female patients with OAB between January 2009 and August 2010. The diagnosis of IC/BPS was based on National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases (NIDDK) criteria. To clearly separate two groups of patients, only OAB wet patients were enrolled. All OAB patients had urgency and urgency incontinence. No OAB patients had bladder-related pain and no IC/BPS patients had urgency incontinence. Symptoms assessment and questionnaires, including International prostate symptom score (IPSS), quality of life (QOL) score and overactive bladder symptom score (OABSS), were performed before urodynamic studies. All patients had been diagnosed and grouped into IC/BPS or OAB based on the clinical features before cystoscopy, potassium chloride sensitivity test and urodynamic investigation (video-urodynamic or conventional pressure-flow study). Urodynamic characteristics were significantly different between patients with IC/BPS and OAB. IC/BPS patients usually are younger with more severe voiding symptoms, slower flow rate and a higher prevalence rate of dysfunctional voiding. The findings of this study suggest that the underlying pathophysiology might be different between IC/BPS and OAB.

Abstract # 761

THE CORRELATION BETWEEN VOIDING SYMPTOMS, BLADDER DIARY AND OBJECTIVE FINDINGS ON URODYNAMIC FINDINGS AND MAXIMUM CYSTOMETRIC CAPACITY DURING HYDRODISTENSION IN FEMALES WITH INTERSTITIAL CYSTITIS/ PAINFUL BLADDER SYNDROME (IC/PBS)

Wei Chih C, Ming Huei L, Chiu De C, Yi Chang C, Ya Ling C, Huei Ching W

Previous studies demonstrated a strong correlation between pain and cystoscopic findings, as an increase in pain with bladder filling was associated with inflammation, ulceration, and smaller bladder capacity. Other studies reported IC/PBS patients with Hunner's patch had lower bladder capacity, lower volumes at first desire to void, and more severe glomerulations. As shown in the above literature review, existing research has lacked the correlation between subjective symptoms and objective findings. Hence in order to help fill this gap, this study from Taiwan investigated the correlation between voiding symptoms and objective findings on bladder diary and urodynamic findings. Fifty female patients who were compatible with the NIDDK criteria were included and all patients were not previously treated for IC/PBS before hydrodistension. These patients were assessed by validated questionnaire including O'Leary-Sant Symptom (ICSI) and Problem Index (ICPI) was used to objectify subjective symptoms. Pelvic Pain and Urgency/Frequency (PUF) questionnaire was also completed and functional bladder capacity was collected from three day bladder diary. The authors employed standardized consecutive filling cystometry and recorded volume at first desire to void (FDV), normal desire to void (NDV), strong desire to void (SDV) and maximum cystometric capacity (MCC). All patients underwent hydrodistension and cystoscopic maximal bladder capacity (MBC) at the intravesical pressure of 85 cm H₂O was measured. These data were analyzed using Pearson correlations and the authors also used the partial correlation to exclude the influence of MBC on the correlation between symptom score, bladder diary and urodynamic findings. They found that IC/PBS patients who suffered from severe symptoms seemed to have no strong correlation with MBC and MCC. However, the authors note that their data suggested that when using partial correlation to exclude MBC influence, ICPI showed a positive correlation with MCC. The interaction between MBC and MCC may be considered.

Abstract # 763

ADAPTATION OF THE QUESTIONNAIRES "THE INTERSTITIAL CYSTITIS SYMPTOM INDEX AND PROBLEM INDEX" AND "PELVIC PAIN AND URGENCY/FREQUENCY (PUF) PATIENT SYMPTOM SCALE" TO THE BRAZILIAN CULTURE

Fernandes MLV, Lopes MHBDM, D'Ancona CAL

Fernandes and colleagues from Brazil note that diagnosis of Painful Bladder Syndrome/Interstitial Cystitis (PBS/IC) is still a challenge due lack of universally accepted criteria; furthermore, the fact that the patient may present few symptoms in the early stages makes it difficult to achieve an accurate result. It can be diagnosed by cystoscopic examination, urodynamics, potassium sensitivity testing, biopsy, laboratory tests and questionnaires. But none is conclusive, and it is believed that a symptom questionnaire to capture and record the presence of all (PBS/IC) symptoms would be useful in helping to establish the diagnosis and that other resources can contribute to a more accurate diagnosis. Since questionnaires are an important aid for the diagnosis of PBS/IC, but are not available in Portuguese in Brazil, it is necessary to translate and validate questionnaires developed, tested and used in other countries, to obtain an accurate diagnosis and, consequently, appropriate treatment and better prognosis. Therefore, the aim of this study was to adapt the questionnaires "The Interstitial Cystitis Symptom Index and Problem Index" and "Pelvic Pain and Urgency/Frequency (PUF) Patient Symptom Scale" to the Brazilian culture. The methodological process of cultural adaptation aims at acquisition of an instrument true to the original, but adapted to the culture of the country where this version will be applied. In this study the researchers opted for the directives developed by the American Academy of Orthopedic Surgeons, which has as a goal the standardization of the method for cultural adaptation of measuring instruments related to health, confirmed by theoretical findings and by the systematic review of published studies regarding the aforementioned methodology. The steps followed in this process were: translation of the original instrument by two different translators (T1 and T2); synthesis of the translations (T1 and T2); backward translation to the language of origin; assessment of the translation by a panel of specialists and pre-test. In order to implement the present study the researchers got the formal authorization from the authors, so they could proceed to the translation and cultural adaptation of the instruments. The instrument "The Interstitial Cystitis Symptom Index and Problem Index" is composed of two indices (symptom and problem) related to urinary symptom and pain symptom. The instrument "Pelvic Pain and Urgency/Frequency (PUF) Patient Symptom scale" covers pelvic pain, including symptoms associated with sexual intercourse, as well as urinary urgency/frequency. Both instruments were analyzed by a specialist committee composed of an urologist, a methodologist, a linguist, a patient with a clinical diagnosis of interstitial cystitis and the researchers. The specialists produced individual considerations for each item in both instruments before of meeting, and the agreement rate in their opinions was calculated based on their answers. With a percentage agreement of 100% among specialists, it was need to amend seven items, including questions and answer choices in the questionnaire "The Interstitial Cystitis Symptom Index and Problem Index". The expression "need to urinate with little or no warning" has been replaced by the word "suddenly", the words "less than once in five" was replaced by "a few times," the word "approximately" was

replaced by the word "almost" and the word "often" was replaced by "many times". It was necessary to change six items, including title, layout, questions and answer alternatives of the instrument "Pelvic Pain Urgency / Frequency (PUF) Patient Symptom Scale." The expression "sexual act" was substituted for "sex intercourse" and the word "urgency" was replaced by "strong desire", also with a percentage of 100% agreement among experts. A feature of the two questionnaires is that they are self-reported and thus the researchers realized that to achieve cultural equivalence, all of these items need to be changed, in order to make the instruments more easily understandable to the target audience. The use of two translations (T1 and T2) allowed small corrections of referential and generic meaning, which in turn elicited an adequate synthesis of the translations. The specialist committee meeting, although long, elicited the final understanding of the instruments. The connection that came from the healthcare and linguistics professionals was enriched and facilitated by the presence of the representative of the target population (woman with Interstitial Cystitis). All the changed items indicate the need to adapt the questionnaires developed in other countries to the Brazilian culture. In the next step they intend to perform a pre-test among Brazilian patients with interstitial cystitis, using the final questionnaires versions in Portuguese and, consecutively, to investigate the validity and reliability of both instruments. As the instruments are very simple, the authors are of the opinion that they can be useful for healthcare professionals, in different scenarios of practice, promoting multidisciplinary actions. The adaptation of the instruments "The Interstitial Cystitis Symptom Index and Problem Index" and "The Pelvic Pain Urgency/Frequency (PUF) Patient Symptom Scale" to the Brazilian culture was adequately accomplished. The use of a minutely defined methodology was able to produce a Portuguese version that is equivalent to the original in English.

Abstract # 764

CLINICAL OUTCOMES OF SACRAL NERVE STIMULATION IN MEN WITH OR WITHOUT INTERSTITIAL CYSTITIS OR CHRONIC PELVIC PAIN SYNDROME

Griebling T, Woodruff D, Wilson B, Bengston C

Sacral nerve stimulation (SNS) is approved for urinary urgency/frequency, urge urinary incontinence and non-obstructive idiopathic urinary retention. Many patients also have conditions such as interstitial cystitis (IC) or chronic pelvic pain syndrome (CPPS). The literature is lacking regarding results of this type of intervention in this particular population of men. Although IC/CPPS is not a primary indication for SNS, anecdotal reports suggest some patients have symptomatic improvements, but the majority of patients were female. Griebling and colleagues from Kansas examined clinical outcomes of SNS in men using a validated instrument, and compared results in those with and without IC/CPPS. The authors note that to their knowledge, this is the only study to specifically compare voiding outcomes after SNS in men with or without IC/CPPS with a validated instrument. These data demonstrated men implanted with SNS who have concomitant IC/CPPS may not benefit as much as those without this additional diagnosis. These findings should prompt prospective studies into the efficacy of SNS implantation in men with significant IC/CPPS. In addition, these patients should be counselled regarding realistic goals that can be potentially achieved using SNS for voiding symptoms based on presence or absence of IC/CPPS. They conclude that sacral nerve stimulation may be a viable clinical treatment option in men with urinary symptoms associated with IC/CPPS.

Abstract # 765

OUTPATIENT HYDRODISTENSION FOR PATIENTS WITH SUSPECTED PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS

Yoshikawa Y, Moriya Y, Hirabayashi H, Yamaguchi A, Kimura K, Fukatsu A, Kamihira O, Matsuura O

In this study from Komaki, Yoshikawa and colleague evaluated the diagnostic and therapeutic benefits of outpatient hydrodistension for patients with suspected PBS/IC. Seventy-one patients with frequency, urgency or bladder pain with no specific urological disease received outpatient hydrodistension. Hydrodistension was carried out with using NSAIDS, 15 minutes after instillation of 20ml of 4% lidocaine. The instilled saline volume for hydrodistension was determined based on each patient's level of tolerance of urgency and bladder pain. The median instilled saline volume was 430ml (200 to 600ml). No patients were admitted to hospital due to adverse events with hydrodistension. Glomerulation was found in 50 patients, haemorrhage was found in 42 and 15 had Hunner's ulcers. After hydrodistension, we instructed the patients on diet modification (regulation of spicy foods, caffeine, alcohol etc.). 58 (81.7%) patients had no need of another session of hydrodistension due to worsening of symptoms. The authors concluded that cystoscopy with hydrodistension under local anaesthesia in an outpatient clinic is an effective and safe procedure for PBS/IC patients. Furthermore, the economic burden is less than the procedure under general or spinal anaesthesia. The authors concluded that

outpatient hydrodistension under local anaesthesia may provide diagnostic and therapeutic value in selected patients.

Abstract #766

INTRA VESICAL INJECTION OF BOTULINUM A TOXIN (BTX-A) IN THE MANAGEMENT OF PAINFUL BLADDER SYNDROME /INTERSTITIAL CYSTITIS (A RANDOMIZED CONTROL STUDY)

Yassin M, Saffan A, Shaker H, Mourad S, Gamal M

With the wide spread use of BTX-A in lower urinary tract dysfunction including painful bladder syndrome and with encouraging results from some small pilot studies, Yassin and colleagues from Ain Shamas University assessed the efficacy of BTX-A intravesical injection in patients with PBS/IC who did not respond to any of the conventional treatment modalities. This study began in March 2008 and included 28 patients (23 women and 5 men), who were randomly divided into 2 groups: G1, 18 patients (16 women & 2 men) were injected with 200U of BTX-A diluted in 20ml normal saline, while G2, 10 patients (7 women & 3 men) were injected with normal saline only. Submucosal injection was done under GA after cystoscopic examination & hydrodistension in both groups with video recording of the injection sites in a similar mapping in both groups. 16 patients from G1 reported significant improvement at 1, 3 & 6 months follow up, mean VAS score significantly reduced, decreased frequency ($p < 0.001$) with increased bladder capacity 28% at three months follow up. One patient only in G2 reported subjective improvement which was non-significant. No side effects were detected in any patient. The authors concluded that intravesical BTX-A injection is a very effective measure in the management of painful bladder syndrome/interstitial cystitis, significantly reducing bladder pain, urinary frequency and improving bladder capacity but it is still a short term management and reinjection has to be considered.

Abstract # 767

BLADDER ENDOMETRIOSIS: EFFECTIVENESS OF THE CLINICAL EVALUATION AND DIAGNOSTIC TESTS FOR AN ACCURATE TREATMENT.

Garcia-Rojo D, Hannaoui N, Vicente E, Prera A, Pubill J, Abad C, Gonzalez-Sala J, Martos R, Muñoz J, Barrio M, Gual J, Prats J

The incidence of bladder endometriosis is generally considered to be around 1% or less of endometriotic patients. Bladder endometriosis is often not diagnosed during laparoscopy, because it is a disease involving the vesical detrusor and therefore may not be visible on the peritoneum covering the bladder. In this setting, the identification of a group of patients at a higher risk for this condition becomes necessary. The American Urologic Association Symptom Index (AUASI) is a questionnaire which was originally created to assess the severity of benign prostatic hyperplasia, but has been found to accurately describe lower urinary tract symptoms in women. Fedele et al. partially modified this questionnaire with the aim of assessing the presence of specific catamenial symptoms related to bladder endometriosis in patients with a high suspicion index for this disease. The aim of this study by Garcia-Rojo and colleagues from Sabadell hospital was to evaluate the effectiveness of preoperative exams and the treatment of patients with bladder endometriosis. Urinary tract endometriosis is an uncommon pathologic finding. Most of the cases in this hospital had urinary symptoms with a high score on the modified AUASI questionnaire. The use of transvaginal ultrasound in patients with endometriosis can minimize the risk of neglecting bladder endometriotic lesions during surgery. The cystoscopic evaluation in catamenial phase is very important for the assessment of these lesions. But the limits of the cystoscopic evaluation must be considered, as there is often no involvement of the mucosa. However, in the majority of cases there is a fixed protuberance that deforms the inner bladder profile and that undermines the mucosa, presenting with bluish-reddish areas that are suggestive of endometriosis. Surgery is the treatment of choice. While this study had limitations due to being a retrospective study with a small number of cases, the authors believe that the questionnaire evaluated in the present study showed an excellent diagnostic accuracy in the preoperative diagnosis of bladder endometriosis. The cystoscopic evaluation in catamenial phase is very important for the management of bladder endometriosis. Partial cystectomy is the treatment of choice.

Abstract # 768

EFFECTIVENESS OF ACUPUNCTURE AND MOXIBUSTION THERAPY FOR THE TREATMENT OF REFRACTORY INTERSTITIAL CYSTITIS

Inoue K, Katayama Y, Shitamura T, Nose K, Kamoto T

The primary aim of the management of interstitial cystitis (IC) is to decrease its symptoms. Acupuncture plus moxibustion [traditional Chinese medicine technique] is a neuromodulatory therapy available in Japan. The objective of this study by Inoue and colleagues from Miyazaki University Faculty of Medicine was to assess the

efficacy of this treatment for patients with refractory IC after hydrodistension. Patients who had previous conservative medical treatment, e.g. hydrodistension, intravesical instillation of dimethylsulfoxide or oral medication (e.g. suplatast tosilate, anticholinergics), which at best achieved short symptomatic relief, were enrolled.

Acupuncture and moxibustion therapy was given by applying moxa needles to BL32 and BL33 and performing electroacupuncture on BL34 at 3 Hz for 20 min. The treatment was given once every two weeks. The bladder condition was assessed by the Visual Analogue Scale (VAS) score (scoring 0-10), the O'Leary-Sant Interstitial Cystitis Symptom Index (ICSi), the Problem Index (IPSI), and the maximum voided volume (MVV) on the frequency-volume chart. Patients who had a reduction of VAS score by >2 and an increase of MVV >100 ml were considered responders. Acupuncture and moxibustion therapy resulted in improvement in 20% (2/5) patients with refractory IC, and repeated therapy maintained the therapeutic effects. The authors note that acupuncture and moxibustion treatment is a traditional and relatively noninvasive therapy. Although its precise mechanism of action is unclear, this study suggests that acupuncture and moxibustion treatment may be a therapeutic option for IC. Further studies are needed to clarify the efficacy of acupuncture therapy for IC patients

Abstract # 769

EFFICACY AND SAFETY OF AUGMENTATION ILEOCYSTOPLASTY FOR THE TREATMENT OF INTERSTITIAL CYSTITIS

Lee H S, Ahn J S, Cho W J, Lee H N, Lee Y, Lee K

The aims of this study by Lee and colleagues from Korea were to evaluate the long term efficacy and safety of augmentation ileocystoplasty for severe symptomatic patients with BPS/IC. They prospectively evaluated 26 patients, who had undergone augmentation ileocystoplasty by single surgeon from July 2006 to February 2010 for severe BPS/IC refractory to conservative treatments. Their results showed augmentation cystoplasty decreased pain and frequency and that bladder capacity increased significantly. There was no severe complication with surgery for short term and long term follow up. The finding that in some patients clean intermittent self-catheterization is required after surgical reconstruction is in accordance with previous experience. It was known that clean intermittent, self-catheterization is well accepted by patients because the overall situation is so markedly improved after surgery. The authors conclude that augmentation cystoplasty for severe symptomatic BPS/IC is one of the effective and safe treatment options with a high probability of cure or marked improvement of symptoms.

Abstract # 770

BLADDER PAIN SYNDROME TREATED WITH TRIPLE THERAPY WITH GABAPENTIN, AMITRIPTYLINE, AND A NONSTEROIDAL ANTI-INFLAMMATORY DRUG

Jeong H J, Rho J H, Han D Y

Bladder pain syndrome is a chronic disease that manifests as bladder pain, frequency, nocturia, and urgency. Gabapentin, amitriptyline, and nonsteroidal anti-inflammatory drugs are efficacious treatments for bladder pain syndrome. In this study from Korea, Jeong and colleagues assessed the effect of triple therapy with these drugs in women with bladder pain syndrome. Between May 2007 and May 2010, the conducted a prospective nonrandomized study on 74 patients with bladder pain syndrome. The O'Leary-Sant IC symptom index and problem index and VAS scores improved considerably 1 month after treatment. However, the results at 1, 3, and 6 months after treatment were not significantly different. The authors concluded that triple therapy was sufficiently effective in patients with bladder pain syndrome and caused no significant adverse effects. However, large-scale studies should be performed to verify their findings.

Abstract # 771

COMPARISON OF INTRAVESICAL HYALURONIC ACID INSTILLATION WITH DIFFERENT REGIMENS FOR INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME

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Preliminary studies using intravesical hyaluronic acid instillation have been demonstrated to have benefit in the treatment of interstitial cystitis/painful bladder syndrome (IC/PBS). A loading dose of four weekly instillation of 50ml (40 mg) hyaluronic acid followed by 5 monthly maintaining doses has been suggested. However, the optimal regimen has not been defined yet. Patients might feel improved during the first month, but gradually failed in the maintenance period. The aim of this study by Lai and colleagues from Taiwan was to compare the clinical effectiveness of intravesical hyaluronic acid instillations with different regimens in patients with IC/PBS. In this prospective, randomized, parallel study, 60 patients (age 16-77 years) who were diagnosed to have

IC/PBS, participated. Intravesical hyaluronic acid instillation improved IC/PBS symptoms and improved quality of life. Treatment either with initial four weekly loading doses plus maintaining five monthly doses or regular treatment biweekly for 12 times provided similar results. However, patients in the HA-12 group had better improvement in pain and symptom after treatment although the difference in treatment effect in this study was not statistically significant between two regimens. It was concluded that no significant difference was noted in therapeutic effect between two regimens of HA instillation for IC/PBS patients. Both groups showed significant improvement in symptom score and QoL index.

Abstract # 772

THE CORRELATION BETWEEN POTENTIALLY TRAUMATIC EXPERIENCE AND SUBJECTIVE SYMPTOMS IN WOMEN WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS) IN TAIWAN

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Wei Chih and colleagues from Taiwan note that early stressful experience, such as childhood sexual maltreatment, has been considered as an environment risk factor for IC/PBS. However, the definition and the scope of potentially traumatic experience vary in studies. It is unclear to what an extent this experience prevails in patients with IC/PBS and links to its symptom profile. The purpose of this study was to investigate the traumatic experiences prevalence in IC/PBS patients and correlation between traumatic experience and subjective symptoms. This was a prospective case control study with 50 female patients who were compatible with the NIDDK criteria and these patients were assessed by validated questionnaire including O'Leary-Sant Symptom (ICSI) and Problem Index (ICPI) was used to objectify subjective symptoms. Pelvic Pain and Urgency/Frequency (PUF) questionnaire was also completed and standardized self-report instruments, Chinese Brief Betrayal-Trauma Survey (BBTS) questionnaire was used to measure the prevalence of diverse potentially traumatic experiences (natural disasters, traffic accidents, physical and sexual assaults, emotional maltreatment, and witnessing other negative events) in childhood and adulthood. Subjects were tested individually in two sessions, in order to avoid fatigue. Taiwanese college students selected randomly served as controls. These data were analysed using Pearson correlations. Their results showed that women with IC/PBS endorsed higher incidences on various traumatic experiences except for sexual maltreatment in both childhood and adulthood. Diverse life events prevail in patients with IC/PBS. Nevertheless, potentially traumatic experiences did not reliably predict the symptom profiles of IC/PBS. Only sexual maltreatment by someone close to the patients had negative correlation with subjective symptoms, ICSI. The authors' concluding message was that the prevalence of interpersonal abuse, especially those inflicted by someone close to the patients, was higher in patients with IC/PBS. However, potentially traumatic experiences did not reliably predict the symptom profiles of IC/PBS. The IC/PBS patients with sexual maltreatment by someone close to patients may have lower subjective symptoms.

Abstract # 773

FIVE TEENAGED CASES WITH INTERSTITIAL CYSTITIS-LIKE LOWER URINARY TRACT SYMPTOMS RELIEVED BY HYDRODISTENTION

Torimoto K, Aoki K, Hirayama A, Samma S, Kagebayashi Y, Matsumoto Y, Fujimoto K, Hirao Y

Interstitial cystitis (IC) is often difficult to diagnose because the subjective and objective findings are not nonspecific. Adult cases of IC have been well known for two decades. The symptoms related to IC are compelling urge to urinate that is difficult to postpone, increased urinary frequency, feeling of incomplete emptying and bladder pain. The objective findings related to IC are glomerulations or Hunner's ulcers on cystoscopic examination. In younger cases less than 20 years of age, IC is seldom diagnosed because IC is considered to be a rare disease and the IC-related symptoms are more difficult to be grasped than in adult cases. Torimoto and colleagues from Japan report on 5 teenage cases with interstitial cystitis-like lower urinary tract symptoms (LUTS), which were relieved by hydrodistension (HD). Two of 5 patients were male and the other 3 patients were female. Their chief complaints were increased daytime urinary frequency and increased bladder sensation. They had no symptoms of nocturia or urgency. Only one patient had feeling of incomplete emptying and bladder pain. The onset of symptoms occurred at the age of 12 to 18 years. The symptoms had continued for 0.5 to 96 months although they were treated with antimuscarinics etc. None of them had objective findings of neurogenic bladder or bladder outlet obstruction. HD was performed for all 5 patients. Both the subjective and objective findings were compatible with adult IC in all cases. The LUTS resistant to antimuscarinics were significantly improved by HD. Therefore, the authors believe that the bladder condition in these cases can be considered to be IC. They also observe that there should be a certain prevalence of increased bladder sensation similar to adult IC in paediatric cases. It is possible that only the severe cases have

so far been diagnosed as IC. They believe that we need to keep IC in mind when we examine paediatric patients with bladder storage symptoms.

Reference:

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