

A Review of the American Urological Association (AUA) Annual Conference May 19-24 2007, Anaheim CA, USA

Review by Jane Meijlink

The AUA annual conference, still the world's biggest urology event attended by over 15,000 urologists, healthcare professionals, exhibitors and media from around the world, is a Mecca for researchers presenting cutting-edge science and for health professionals eager to learn about the latest insights in the field of urology. The 2007 conference was held under the palm trees at the Anaheim Convention Center in California's Anaheim, home to the original Disneyland theme park opened by Walt Disney in 1955 and cradle of the Disneyland empire.

Hot topics

While there was once again the usual heavy focus on oncology, hot topics at this meeting included the ground-breaking news on circumcision and HIV transmission published earlier this year in *The Lancet*, and new developments from several centres on tissue engineering and regenerative medicine. Controversy around the world concerning sources and use of stem cells has generated worldwide attention and led developers to seek new sources and applications of stem cells. Special attention was also paid this year to the two opposite ends of the scale: paediatric urology and geriatric urology. The latter mainly concerned the problems of drug use in the elderly patient with urologic disorders, an issue that is also of relevance to PBS/IC.



Painful bladder syndrome/interstitial cystitis

Throughout the conference, a main topic of conversation and behind-the-scenes discussions between IC experts, including the patient representatives attending the conference, was (as one might expect) the issue of nomenclature ("what are we supposed to call this disease?" "Is it essential to change the name right at this moment?") and the complex problem of finding a usable definition for both research and clinical diagnosis. With the current fragmentation of the IC world into regional expert groups each with its own ideas, there is still no global consensus and this is not likely to occur in the immediate future. The provocative use of BPS in the title of this course led to somewhat heated discussions at the AUA! However, despite the nomenclature controversy, this course provided the most up-to-date information on the history of criteria and definition development and took us through recent international developments.

◆ Abstracts – dedicated moderated poster session

During the conference, 27 abstracts were presented on studies that directly or indirectly concerned PBS/IC with many of these presented in a dedicated moderated poster session

on *Infections/Inflammation of the Genitourinary Tract: Interstitial Cystitis* (abstracts 111-136). A study from Germany into botulinum toxin A for IC patients with positive results (abstract 123) suggested that this might prove a useful treatment option. Abstract 127 on EVIDENCE FOR CENTRAL HYPEREXCITABILITY IN PATIENTS WITH INTERSTITIAL CYSTITIS won a Best of Posters AUA 2007 award. Abstract 134 reminded us that before labelling a patient as IC a detailed workup is essential so as not to overlook malignancy. Abstract 299 on GREEN TEA PROTECTS BLADDER CELLS FROM HYDROGEN PEROXIDE-INDUCED INFLAMMATION: POTENTIAL OF HERBAL AGENTS TO TREAT INFLAMMATORY BLADDER DISEASES made one wonder why people still develop inflammatory bladder conditions in countries where green tea is consumed several times a day...

The following abstracts presented at the AUA conference have been briefly summarized here. The full text of these abstracts can be found on the AUA website: <http://www.aua2007.org/content/abstracts/searchabs.cfm>

Abstract 56

SUBSTANCE-P INDUCED EXPRESSION OF CD74 (RECEPTOR FOR MACROPHAGE MIGRATION INHIBITORY FACTOR) ON THE CELL SURFACE OF UROTHELIAL CELLS IN VIVO

Katherine Meyer-Siegler, Pedro Vera.

Substance-P is a neuropeptide that functions as a neurotransmitter and a neuromodulator. These investigators previously showed that substance-P (SP) causes intraluminal macrophage migration inhibitory factor (MIF) release. The aim of this study with rats was to document, in vivo, MIF-CD74 interactions at the urothelial cell surface. According to the investigators, their results indicates that SP upregulates MIF and CD74 in urothelial cells, while bladder MIF released as a consequence of SP treatment interacts with cell surface CD74, suggesting that the previously described MIF-CD74 interaction and the resultant activation of ERK 1/2 is initiated at the urothelial cell surface.

Abstract 68

COMPARISON OF THE ECONOMIC IMPACT OF CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME AND INTERSTITIAL CYSTITIS

J Quentin Clemens, Sheila Brown, Elizabeth Calhoun.

In this study, the authors concluded that both CP/CPPS and IC/PBS have very similar and substantial direct and indirect costs accounting for a large proportion of the total. The direct costs of these conditions are considerably higher than the mean annual costs reported for many other chronic pain conditions such as peripheral neuropathy, low back pain, fibromyalgia and rheumatoid arthritis.

Abstract 117

INCREASED EFFICACY AND POTENCY OF CARBACHOL IN INDUCING INCREASES IN INTRACELLULAR CALCIUM [CA²⁺] AND OUTWARD POTASSIUM CURRENTS (I_o) IN INTERSTITIAL CYSTITIS (IC) BLADDER UROTHELIAL CELLS (BUC): EVIDENCE OF PERSISTENT PHENOTYPIC ALTERATION OF CULTURE.

Gopal N. Gupta, Mingkai Li, Yan Sun, Michael Gold, Marc Simard, Toby C. Chai.

Bladder urothelial cells (BUC) may play a role in bladder sensory transduction on account of the fact that they are able to release neurotransmitters and express receptors typically associated with sensory neurons. The investigators examined whether BUC respond to carbachol stimulation using electrophysiologic differences in human BUC from patients with IC compared to controls. They found that carbachol induced an increase in BUC [CA²⁺] through extracellular calcium stores which results in increased outward potassium. In addition, BUC in IC patients were clearly different in their response to carbachol compared to normal BUC. The authors concluded that bladder urothelial cells could play a central role in the pathogenesis of IC.

Abstract 118

CHANGES IN SYMPTOMS AND URINARY HB-EGF, EGF AND ANTIPROLIFERATIVE FACTOR DURING CHRONIC NEUROMODULATION FOR REFRACTORY INTERSTITIAL CYSTITIS.

Kenneth M. Peters, Richard C. Bennett, Ibrahim A. Ibrahim, Kristopher Koch, Chen-Ou Zhang, Susan K. Keay.

Urinary markers (APF and HB-EGF), voiding frequency and urgency have been shown to be significantly altered following 5 days of acute percutaneous sacral neuromodulation for refractory IC (Chai, 2001). This study examined symptom scores and urinary markers during chronic neuromodulation up to 6 months in 11 patients. However, despite significant improvements, there was no normalization in urinary frequency and the volume of urine voided. Only transient changes were seen in APF, EGF and HB-EGF in individual patients. The results suggest that urinary markers for IC do not generally change with chronic neuromodulation.

Abstract 119

URINARY IL-6 AND EGF LEVELS IN PATIENTS WITH PBS/IC TREATED WITH CYCLOSPORINE OR PENTOSAN POLYSULFATE SODIUM.

Jukka Sairanen, Kristina Hotakainen, Teuvo Tammela, Ulf-Hakan Stenman, Mirja Ruutu.

Cyclosporine (CyA) is an immunosuppressive agent known to affect the inflammatory cells in autoimmune diseases. Pentosan polysulfate sodium (PPS) is an FDA approved drug for PBS/IC. Patients (15 women, 3 men in the CyA group, 14 women and 2 men in the PPS group) were randomised to either CyA or PPS treatment. Disease activity was measured by determining IL-6 and EGF in urine and comparing the results with objective evaluation of treatment response in PBS/IC patients who fulfilled NIDDK criteria. A significant clinical response was observed in 72% of the patients on CyA treatment but only 6% of those receiving PPS. The peridermal growth factor (EGF) decreased significantly during treatment with CyA, but the reduction in IL-6 was not statistically significant. In the patient group treated with PPS, the marker levels did not change. CyA was therefore associated with clinical response and also a reduction in the urinary concentrations of EGF.

Abstract 120

NITRIC OXIDE AS A MARKER FOR EVALUATION OF TREATMENT EFFICACY OF CYCLOSPORINE IN PATIENTS WITH CLASSIC INTERSTITIAL CYSTITIS.

Ingrid Ehren, Margit Vrba, Pierre Lafolie.

A previous study has shown Nitric Oxide (NO) to be a marker for inflammatory disorders in the bladder including classic IC. The aim of this study was to evaluate whether NO measurement can also be used as a marker for treatment response in patients with classic IC treated with cyclosporine. According to the investigators, the results show that measurement of NO formation can be used not only as a marker for classic IC but also for objectively evaluating response to treatment with cyclosporine in this patient group, suggesting measurement of NO formation could be a useful tool in assessing classic IC.

Abstract 121

EVALUATION OF SYMPTOMS IN PATIENTS WITH INTERSTITIAL CYSTITIS TREATED WITH CYCLOSPORINE A.

Jamil Chade, Antonio Lucon, Daher Chade, Miguel Srougi.

These researchers reported on their experience with cyclosporine A for IC in a study with 2 male patients and 34 female patients fulfilling NIDDK criteria. Diagnosis was made on the basis of voiding diary, urodynamic evaluation, cystoscopic examination and bladder biopsy. Symptoms were measured using the O'Leary-Sant IC symptoms index. The dose given was 1.5 mg/kg CyA twice daily. Since their study indicated good tolerance, safety and produced promising results, they concluded that CyA presents a new alternative for treatment of IC.

Abstract 123

TREATMENT OF INTERSTITIAL CYSTITIS WITH BOTULINUM TOXIN A.

Stefan Carl, Sebastian Laschke.

This was a pilot study from Germany to determine the effectiveness of botulinum toxin A (BoNT-A) in 29 IC patients diagnosed on the basis of NIDDK criteria. 2 patients suffered from temporary haematuria, 3 patients had residual urine greater than 100 cc, 1 patient had urinary retention and had to learn intermittent self-catheterization. The investigators concluded from their study that BoNT-A is effective in the management of IC and that the results suggest that BoNT-A has a nociceptive effect on bladder afferent pathways in IC patients and gives symptomatic and functional improvement. No systemic side effects were observed by this group of researchers during and after treatment.

Abstract 124

IDENTIFICATION OF AUTOANTIBODIES AS BIOMARKERS OF INTERSTITIAL CYSTITIS USING THE "REVERSE CAPTURE" AUTOANTIBODY MICROARRAY.

Robert Caiazza jr, Oliver Tassinari, Joshua Ehrlich, Daniel Cramer, Michael O'Leary, Brian Liu.

While the cause of IC is unknown, it appears that autoimmunity may play a role in initiating or sustaining the chronic inflammatory response evident in this condition. The presence of inflammation in IC allows the body's immune response to be exploited as a means of identifying IC biomarkers. The researchers recently reported the development of a novel 'reverse capture' antibody microarray platform for antibody profiling (Nat protocols 1:452-460, 2006). The objectives of this study were to perform a preliminary 'proof-for-principle' study on the use of this platform for the study of IC and to test its ability to identify potential biomarkers of IC. According to the researchers, the microarray experiments showed consistent capture of native antigens by the array slides and consistent differential autoantibody reactivity profiles. They believe that their results suggest that the 'reverse capture' platform has the ability to consistently detect differential autoantibody profiles between IC patients and controls and demonstrated that there are at least 25 antigens that may be used as biomarkers for IC. They conclude that the serum autoantibody repertoire of IC patients can be used to identify autoantibody signatures as biomarkers of IC.

Abstract 125

DMSO EFFECT ON BLADDER INFLAMMATION AND URINARY GLYCOAMINOGLYCANS EXCRETION AFTER PROTAMINE SULFATE INDUCED CYSTITIS.

Roberto Soler, Homero Bruschini, Jose Truzzi, Niels Camara, Joao Martins, Juliana Dreyfuss, Maria Seixas, Helena Nader, Miguel Srougi, Valdemar Ortiz.

In an experimental rat model of IC induced by protamine sulfate (PS) to study the effect of DMSO on bladder inflammation and GAG urinary excretion, the investigators found that intravesical instillation caused bladder inflammation and DMSO significantly reduced the inflammatory process on both the 1st and 7th days after the injury to the urethelium. On the other hand, this drug provoked mild inflammation in normal mucosa which could explain the flare-up of symptoms that some patients say they initially experience. DMSO treatment did not influence urinary S-GAG excretion.

Abstract 126

ANTI-PROLIFERATIVE FACTOR'S (APF) EFFECT ON PURINERGIC SIGNALING IN NORMAL HUMAN BLADDER UROTHELIAL CELLS.

Yan Sun, Susan K Keay, Toby C Chai.

Cultured IC bladder urothelial cells produce anti-proliferative factor (APF) and also manifest increased purinergic signaling by releasing high quantities of adenosine triphosphate (ATP) when stimulated with exogenous ATP and expressing increased ATP receptor. The investigators' aim was to determine whether APF treatment of normal bladder urothelial cells can alter purinergic signaling phenotype to that of IC bladder urothelial cells.

They found that APF treatment converted the purinergic signaling phenotype of normal bladder urothelial cells, in terms of ATP-stimulated ATP release (ASAR) and ATP receptor

(P2X3) expression, to that of IC bladder urothelial cells. Suramin significantly blocked APF's effect on normal bladder urothelial cells. The authors believe that this suggests a link between APF and purinergic signaling. In addition, suramin can be contemplated as a therapeutic agent to block the effect of APF on bladder epithelial cell ASAR.

Abstract 127

EVIDENCE FOR CENTRAL HYPEREXCITABILITY IN PATIENTS WITH INTERSTITIAL CYSTITIS.

Christian O Twiss, Lisa Kilpatrick, Veronica Triaca, Valerie A Arboleda, Michelle Craske, Hana Ibrahimovic, Shlomo Raz, Emeran A Mayer, Edward Ornitz, Larissa V Rodriguez, Bruce D Naliboff.

This poster presentation won a Best of Posters AUA 2007 award.

Pain in IC appears to have significant central and neuropathic components, as well as involvement of central modulatory pathways including those involving the limbic system. The startle blink reflex (SBR) is a defensive involuntary eye-blink in response to sudden intense stimuli. To test the hypothesis that IC patients have upregulation of central pain modulation pathways, the investigators compared the SBRs of healthy controls with those of IC patients.

SBRs were examined for 6 female IC patients and 19 healthy females under threat and safe periods. During threat periods subjects would possibly receive aversive electrical stimulation to their bladder region.

These preliminary data indicate that IC patients have significantly greater SBRs than controls during baseline and during the non-imminent threat periods of the study. The investigators believe that this is objective evidence that IC patients may have upregulation of limbic responses involved in anxiety and stress leading to altered pain perception and abnormal modulation of afferent pain signals. Further investigation is needed to determine whether this upregulation is a causative agent or a secondary effect of the IC disease process.

Abstract 128

AN ALTERED DIFFERENTIATION PROGRAM IN THE UROTHELIUM OF INTERSTITIAL CYSTITIS PATIENTS

Robert Hurst, Paul Hauser, Gennady Slobodov, Daniel Culkin.

According to the authors, strong evidence supports urothelial dysfunction as at least being involved in producing the symptoms of IC. The object of this study was to better define the state of differentiation in the IC bladder using cytokeratins as markers for specific, terminal urothelial differentiation.

It was concluded that cytokeratin 18 (KRT 18) was expressed in simple single-layered epithelia, further demonstrating a difference in the umbrella cell layer and the intermediate and basal layers. KRT 20 was only expressed in umbrella cells in normal epithelium. The lack of expression in many IC urothelia or its inappropriate expression in non-umbrella cells demonstrates an alteration in the differentiation program in IC urothelium. The entire bladder may or may not be affected. While the causes are still unknown, the nature of the epithelial dysfunction is becoming clearer. The umbrella cell layer fails to form, resulting in failure of its barrier function.

Abstract 129

SIALIC ACID CONTENT OF URINARY TAMM-HORSFALL PROTEIN IS REDUCED IN INTERSTITIAL CYSTITIS PATIENTS.

C. Lowell Parsons, Mahadevan Rajasekaran, Marianne Chenoweth, Paul Stein.

Normal urine contains cationic factors that can injure bladder epithelium and are neutralized by Tamm-Horsfall protein (THP). In order to test the hypothesis that THP from IC patients has an electrochemical abnormality that reduces its capacity to neutralize cationic urinary toxic factors, the authors compared sialic acid content and zeta potential from urinary THP of IC patient and control subjects. They believe that their findings support the concept of THP as a urinary protective factor whose protective

function appears to reside in the sialic acid content and is compromised in individuals with IC. According to the authors, this is a potentially significant development in the understanding of IC pathogenesis.

Abstract 130

A CASE-CONTROL STUDY OF MEDICAL CO-MORBIDITIES IN WOMEN WITH INTERSTITIAL CYSTITIS

J Quentin Clemens, Richard Meenan, Maureen O'Keefe Rosetti, Teresa Kimes, Elizabeth Calhoun.

While previous studies in this field have used patient self-reported information and are therefore subject to bias, the aim of this study was to use coded physician diagnoses to compare IC patients with matched controls in order to identify and accurately quantify risk factors associated with IC.

It was concluded that, compared with controls, women with IC were more likely to be assigned 23 specific ICD-9 diagnoses, involving multiple organ systems. The high odds ratios indicate very large, clinically meaningful differences between the groups. Many of these conditions appear to indicate the presence of other unexplained physical symptoms.

The table they presented was as follows:

| Diagnosis (ICD-Code) | Cases (%) | Controls (%) | p-value | Odds ratio |
|---|-----------|--------------|----------|------------|
| Other disorders of bladder(596) | 12.1 | 0.7 | <0.00001 | 19.7 |
| Other disorders of urethra & urinary tract (599) | 14.6 | 1.0 | <0.00001 | 17.4 |
| Drug dependence (304) | 2.1 | 0.1 | 0.0009 | 15.3 |
| Gastritis and duodenitis (535) | 1.7 | 0.1 | 0.004 | 12.2 |
| Endometriosis (617) | 4.2 | 0.4 | 0.00001 | 10.4 |
| Late effects of other & unspecified external causes (909) - late effects of child abuse (909.9A) | 3.8 | 0.4 | 0.00006 | 9.3 |
| Other disorders of intestine (569) | 3.3 | 0.4 | 0.0002 | 8.2 |
| Symptoms involving urinary system (788) | 15.5 | 2.8 | <0.0001 | 6.4 |
| Disorders of function of stomach (536) | 6.7 | 1.5 | 0.00003 | 4.6 |
| Other symptoms involving abdomen & pelvis (789) | 7.5 | 2.0 | 0.00003 | 4.1 |
| Functional digestive disorders (564) | 10.0 | 3.1 | 0.00001 | 3.5 |
| Pain and other symptoms associated with female genital organs (625) | 13.8 | 4.3 | <0.00001 | 3.5 |
| Anxiety, dissociative & somatoform disorders (300) | 19.2 | 8.0 | <0.00001 | 2.8 |
| General symptoms (780) | 16.7 | 7.5 | 0.00003 | 2.5 |
| - sleep disturbances (780.5) | 6.7 | 2.8 | 0.006 | 2.5 |
| - other general symptoms | 10.5 | 2.4 | <0.00001 | 4.8 |
| Unclassified disorders of uterus (621) | 22.6 | 10.5 | <0.00001 | 2.5 |
| Diseases of esophagus (530) | 23.0 | 11.4 | 0.00001 | 2.3 |
| - esophageal reflux (530.81) | 21.3 | 11.1 | 0.0001 | 2.2 |
| Symptoms involving head/neck (784) | 11.3 | 5.2 | 0.001 | 2.3 |
| - headache (784.0) | 10.5 | 4.5 | 0.0007 | 2.5 |
| Other disorders involving soft tissues (729) | 18.4 | 9.1 | 0.00008 | 2.3 |
| - myalgia & myositis, unspecified (729.1) | 16.3 | 6.1 | <0.00001 | 3.0 |
| Other & unspecified disorders of back (724) | 15.5 | 7.8 | 0.0005 | 2.2 |
| Other postprocedural states (V45) | 10.5 | 5.0 | 0.003 | 2.2 |
| Adjustment reaction (309) | 10.5 | 5.3 | 0.005 | 2.1 |
| Depressive disorder (311) | 25.1 | 14.4 | 0.0001 | 2.0 |
| Non-specific abnormal findings on radiological and other examination of body structure (793) | 20.5 | 11.9 | 0.0009 | 1.9 |

Abstract 131

IS GLOMERULATION OBSERVED DURING TURP FOR LUTS/BPH A PREDICTOR OF CLINICAL OUTCOME?

Ryoji Furuya, Seiji Furuya, Naoya Masumori, Toshiro Oda, Hiroshi Ogura, Satoshi Takahashi.

This study looked at the incidence and clinical implications of glomerulations at TURP and found that although it is a common finding, the clinical implications related to IC are unknown. Since there are no differences in clinical outcomes after TURP with hydrodistension between patients with and without glomerulations, glomerulations as such may not be a predictor of the clinical outcome of TURP.

Abstract 132

UROPLAKIN III-DELTA4 MESSENGER RNA AS A PROMISING MARKER TO IDENTIFY NONULCERATIVE INTERSTITIAL CYSTITIS.

Yu Zeng, Yoshiyuki Kakehi, Xiu Wu, Yukio Homma, Naoki Yoshimura, Hideaki Iwaki, Susumu Kageyama, Tatsuhiko Yoshiki.

Urothelial dysfunction and other abnormalities are presumed to be involved in IC. Uroplakins (Ups) that are expressed by urothelial cells are thought to play an important role as major barrier proteins on the apical surface of the urothelium. The investigators focused on the expression pattern of Ups in human IC, and evaluated their mRNA levels on bladder biopsy samples from IC patients. The results led the investigators to conclude that although the clinical implications of the over-expression of UP III and III-delta4 in non-ulcerative IC bladders remains to be clarified, from the diagnostic point of viewpoint, UP III-delta4 mRNA is potentially a promising marker for identifying non-ulcerative IC.

Abstract 133

PAINFUL SYMPTOMS AND DECREASED BLADDER CAPACITY ARE SIGNIFICANT PREDICTORS OF CYSTOSCOPIC GLOMERULATION SUGGESTIVE OF INTERSTITIAL CYSTITIS IN ELDERLY MALE PATIENTS WITH LOWER URINARY TRACT SYMPTOMS.

Munekado Kojima, Yasufumi Yada, Yosimasa.

This study was conducted to reveal the prevalence of glomerulations – which have hitherto been considered as a criterion for the diagnosis of IC – in 110 elderly male patients with LUTS and to identify the predictive factors for glomerulations using logistic regression analysis. This study demonstrated that painful symptoms and decreased bladder capacity are significantly associated with glomerulations. These two factors have been considered to be conventional clinical symptoms of IC. Taken together, a considerable number of elderly male patients with LUTS are likely to have IC-like pathological changes in the bladder.

Abstract 134

MALIGNANCY IN AN INTERSTITIAL CYSTITIS REFERRAL POPULATION.

Durwood Neal.

Another important study concerning the risk of overlooking malignancy when diagnosing IC, particularly while there is still controversy about the workup needed for a diagnosis of IC. 2.3% of a referral group of patients were found to have a malignancy. This is considerably higher than the asymptomatic population at large. The author emphasizes that we should not be lulled in labelling patients who have been given the diagnosis of IC without a complete evaluation.

Abstract 135

EFFECT OF THERAPEUTIC SOLUTION ON DYSpareUNIA AND VOIDING SYMPTOMS IN INTERSTITIAL CYSTITIS.

Blayne Welk, Joel Teichman.

Dyspareunia occurs in up to 78% of IC/PBS patients. The authors tested the dyspareunia response of IC/PBS patients treated with intravesical therapeutic solution. It was concluded that intravesical therapeutic solution provides relief from voiding symptoms,

pain, and dyspareunia in IC/PBS patients. According to the authors, the ideal patient for therapy has point tenderness on the anterior vaginal wall only.

Abstract 136

HYDRODISTENSION AND INTROVESICAL INSTILLATION OF SODIUM HYALURONATE UNDER GENERAL ANESTHESIA FOR TREATMENT REFRACTORY INTERSTITIAL CYSTITIS

Imran Ahmad, Nalagatia Sarath Krishna, Robert Meddings.

This retrospective study looked at effectiveness of sequential general anaesthetic hydrodistension and intravesical instillation of sodium hyaluronate for treatment of patients with refractory IC. It was concluded that sequential hydrodistension and sodium hyaluronate under general anaesthesia should be considered for resistant cases of IC, especially those who cannot tolerate it under local anaesthesia.

Abstract 297

DECREASED EXPRESSION OF CLAUDINS 1, 4 AND 8 IN BLADDER EPITHELIAL CELL EXPLANTS FROM INTERSTITIAL CYSTITIS PATIENTS AS COMPARED TO NORMAL CONTROLS.

Chen-Ou Zhang, Li Guo, Susan K. Keay.

The authors of this study into claudin proteins and their significance in relation to tight junction formation and high paracellular resistance concluded that claudin 1, 4, 8 and 12 proteins are expressed by human bladder epithelial cells explants in vitro, and the expression of claudins 1, 4 and 8 is significantly decreased in cells grown from IC patients compared with matched controls. In addition to the decreased ZO-1 and occluding expression, decreased expression of claudins 1, 4, and 8 may also contribute to the leakiness of the bladder epithelial barrier in IC.

Abstract 298

BACTERIAL CYSTITIS IN C57BL/6N MICE INCREASES SENSITIVITY TO THERMAL STIMULI.

Dale E. Bjorling, Wade Bushman, Kyle Boldon, Zun-Yi Wang.

The investigators looked at the effects of bacterial cystitis on somatic nociception. Bacterial cystitis was induced into the bladder of female mice and sensitivity to thermal stimuli applied to the hind paws was determined after instillation of bacteria. According to the authors, the results of their study suggest that the influence of visceral inflammation on somatic sensitivity may be modulated by genetic background.

Abstract 299

GREEN TEA PROTECTS BLADDER CELLS FROM HYDROGEN PEROXIDE-INDUCED INFLAMMATION: POTENTIAL OF HERBAL AGENTS TO TREAT INFLAMMATORY BLADDER DISEASES.

Shelby Morrisroe, Christian Coyle, Brian Philips, William de Groat, Naoki Yoshimura, Michael Chancellor.

According to a preliminary study that looked at the ability of green tea to protect bladder cells from inflammation, herbal agents could be used to treat inflammatory bladder diseases. This study from the University of Pittsburgh found that components of green tea protected bladder cells from damage in culture. Green tea is rich in powerful antioxidants that make it a potential remedy for many medical conditions. It comprises catechins: plant metabolites that give it many anti-oxidative properties. According to Michael Chancellor MD: "We discovered that catechins found in green tea protected both normal and cancerous bladder cells from inflammation when we exposed the cells to hydrogen peroxide. Although further studies are needed, these results indicate herbal supplements from green tea could be a treatment option for various bladder conditions that are caused by injury or inflammation." In the study, normal and cancerous bladder cells were exposed to two major catechin components of green tea, epigallocatechin gallate (EGCG) and epicatechin gallate (ECG), for 23 hours. Both significantly protected cell lines from exposure to hydrogen peroxide which damages or kills cells. The

concentrations of EHCG and ECG used in the study were at levels that may be achieved through dietary intake.

Abstract 1191

BLADDER BOTULINUM TOXIN A INJECTION CAN BENEFIT PATIENTS WITH RADIATION AND CHEMICAL CYSTITIS.

Yao-Chi Chuang, Dae Kyung Kim, Po-Hui Chiang, Michael Chancellor.

This pilot study, funded by the Fishbein Family CURE-IC, focused on the efficacy of botulinum toxin (BoNT-A) in an initial series of 6 patients with radiation cystitis and BCG-induced chemical cystitis. While it looks as though botulinum toxin may be considered for selected patients with refractory radiation cystitis or BCG cystitis, formal clinical trials are needed to investigate this important problem further.

Abstract 1377

EFFECTS OF SACRAL NEUROMODULATION ON THE CENTRAL NERVOUS SYSTEM

Nasim Zabihi, Daniel Silverman, Veronica Triaca, Christian O Twiss, Cheri Geist, Shlomo Raz, Larissa V Rodriguez.

Sacral neuromodulation has been used with some success to treat voiding dysfunction and more recently painful bladder syndrome/interstitial cystitis. The object of this study was to evaluate the effects of sacral neuromodulation on the central nervous system (CNS) by tracking brain activity during sacral neuromodulation. It was concluded that sacral neurostimulation does indeed appear to modulate the CNS. The differences found appear to be a direct result of stimulation and not influenced by patient anticipation. Stimulation resulted in a decrease in activity of anterior cingulate cortex closely associated with somatic sensorimotor functions, and increased activity in anterior cingulate cortex closely associated with visceral sensorimotor function including especially descending pain inhibitory pathways. This may go some way to explaining how sacral neuromodulation works.

Abstract 1476

ABNORMALITIES IN PERICYTE COVERAGE ON BLOOD VESSELS INDUCE GLOMERULATIONS IN PATIENTS WITH INTERSTITIAL CYSTITIS.

Hiroshi Kiuchi, Testuya Takao, Jiro Nakayama, Toshiaki Hirai, Tomohiro Ueda, Kazuhiko Komori, Yasuhiro Matsuoka, Yashushi Miyagawa, Shingo Takada, Tsujimura Akira, Keisuke Yamamoto, Masami Takeyama, Akihiko Okuyama.

While glomerulations were once considered a hallmark of IC bladders, there is now some uncertainty and the mechanism is still unclear. In this study, the investigators hypothesized that reduced pericyte coverage on blood vessels in IC patients may induce glomerulations and sought to explore in more detail the angiogenic profile in IC patients, including VEGF expression, microvessel counts (MVD) and maturation of angiogenesis. The results of the study indicated that over-expression of VEGF did not promote neovascularization in IC patients, but promoted the formation of immature microvessels. The increase in immature vascularization in the bladder suggests a potential role in glomerulations during hydrodistension of the bladder in IC patients.

Also of interest: [tissue-engineering](#)

Abstract 196

TISSUE-ENGINEERED AUTOLOGOUS BLADDERS FOR PATIENTS NEEDING CYSTOPLASTY

Anthony Atala, Stuart B Bauer, Shay Soker, James J Yoo, Alan B Retik.

While patients with end-stage bladder disease can be treated with cystoplasty using gastrointestinal segments, the presence of such segments in the urinary tracts has been associated with many complications. The authors explored an alternative approach using autologous engineered bladder tissues for reconstruction in a small group of 7 patients with myelomeningocele (a type of spina bifida).

Using the patient's own bladder tissue (obtained from biopsy), the researchers grew urothelial and muscle cells and seeded them on collagen-based, bladder-shaped

scaffolds. The bladder constructs were then used for reconstruction and implanted, some with an omental wrap. Overall follow-up (ranging from 22-61 months, mean 46 months) showed a prompt return of bowel function after surgery, preserved renal function, normal mucus production and no urinary calculi. Results were best in those patients where implantation included an omental wrap. It was concluded that engineered bladder tissues, created with autologous cells seeded on collagen-polyglycolic acid scaffolds, and wrapped in omentum after implantation, can be used in patients who need cystoplasty.

◆ Courses on PBS/IC

Since three educational courses (under a variety of names) were presented on IC during the AUA conference, there was no reason for anyone to leave Anaheim without having at least some idea of how to diagnose and treat IC. All the course handouts were available on a CD Rom distributed during the conference.

All the course presenters emphasized that a thorough diagnostic workup is indispensable, that it is important to exclude all other possible causes of the symptoms while bearing in mind that it is possible to have both IC and another confusable disease concurrently (e.g. IC + endometriosis), and that glomerulations are no longer the hallmark of IC, that the severity of glomerulations bears no relation to the severity of the symptoms and that patients who show glomerulations in an early cystoscopy may show no glomerulations in a later cystoscopy.

Course 17 IC: Bladder Pain Syndrome/Interstitial Cystitis: A Primer and an Update. Speakers: Philip Hanno MD (Course director) and David Burks MD.

The provocative use of BPS in the title of this course led to some controversy amongst attendees and colleagues! However, despite the nomenclature controversy, this course provided the most up-to-date information on the history of criteria and definition development and took us through recent international developments.



Philip Hanno explained that where the definition and the triad of symptoms are concerned, what seems simple and obvious may not really be so:

- **frequency** is dependent on individual drinking habits and perspiration and therefore an absolute number of voids may not be meaningful;
- **urgency** is dependent on the definition (on which nobody can agree);
- the site and source of **pain** can be difficult for both the patient and the clinician to determine.

He went on to explain that a definition is critical because it has:

- an impact on how the diagnosis is made
- an impact on the economics of the disease
- an impact on pharmaceutical companies
- an impact on the spending of research dollars
- an impact on who takes care of these patients.

A clear overview of current treatment options was provided by David Burks MD. The course handout included chapter 7 on Painful Bladder Syndrome (Interstitial Cystitis) by Philip Hanno from the Penn Clinical Manual of Urology. This is a very useful reference.

Course 47 MC Plus: Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS): Coordinating a Collaborative Practice. Speakers: John Forrest MD (Course Director), Sandra Seidel APRN.



This course, jointly presented by a urologist and an Advanced Practice Registered Nurse, was designed for the entire multidisciplinary team of doctors and nursing staff in a urology department.

John Forrest gave an overview of developments and definitions and explained that we are dealing with an evolving definition.

Sandra Seidel from SUNA gave a useful checklist of interviewing tips that might lead one to suspect IC:

- Voiding pattern (frequency, urgency, nocturia)
- Pain with intercourse/men painful ejaculation
- Specific problematic foods/drinks
- Flares at certain times
- Co-disorders (endometriosis, fibromyalgia, allergies, IBS, migraine)



Course 103 PG: Pelvic Pain: Diagnosis and Treatment – A Practical Approach. Speakers: Robert Moldwin MD (course director), Fred Howard MD, Ragi Doggweiler MD.

This very useful course was designed to provide participants with a down-to-earth, practical approach to diagnosis and treatment of common causes of pelvic pain such as interstitial cystitis, chronic prostatitis/chronic pelvic pain syndrome, chronic orchalgia, endometriosis, pelvic congestion syndrome, pelvic floor muscle spasm and neuropathic pain. Types of care discussed included behavioural therapies, oral and intravesical treatment, interventional radiological techniques, trigger point injections, neuromodulation, endoscopic/ laparoscopic therapy and more besides. The handout included very clear slides on diagnosis and treatment by urologist Robert Moldwin MD and gynaecologist Fred Howard MD, as well as a very useful text by Ragi Doggweiler MD on pelvic floor muscle dysfunction, neurogenic inflammation and myofascial release and trigger point injection. Many practical tips were given.



Webcasts:

Webcasts from the AUA conference are available to browse through on:

<http://webcasts.prous.com/aua2007/>

Thanks to sponsor

With thanks to the Medtronic Foundation for enabling the IPBF to attend this important urology conference.

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