The AUA annual meeting 2010 could be considered a landmark meeting for IC with its unprecedented number of presentations and even prestigious plenary sessions devoted to the topic, underlining the attention this syndrome is currently receiving. Nevertheless, confusion, contradiction, inconsistency and lack of agreement still reign supreme. The enigma remains enigmatic!

Our review will cover plenary sessions including the new preliminary guideline and a panel discussion, podium presentation sessions, and Society for Infection and Inflammation in Urology poster presentations.

PLENARY SESSIONS 1

PANEL DISCUSSION: PAINFUL BLADDER SYNDROME: WHAT HAPPENED TO INTERSTITIAL CYSTITIS?

Moderated by Alan J. Wein, MD, with panel members Jorgen Nordling, MD, Christopher Payne, MD, and Deborah Erickson, MD.

Moderator Alan Wein, MD introduced the three speakers:

Jorgen Nordling, MD, (Denmark): The case for changing the nomenclature.

Christopher Payne, MD (USA): The importance of the legacy nomenclature.

Deborah Erickson, MD (USA): How might nomenclature changes affect the clinical approach to the syndrome?

Professor Nordling first explained that ESSIC had agreed no longer to use the name interstitial cystitis, neither alone nor in combinations, but to use the name bladder pain syndrome (BPS) followed by the addition of a type indication. He stated that glomerulations are not specific to IC and the term urgency can only be applied to overactive bladder patients (in its current definition ed.)

Professor Payne then took the stand with an opposing point of view to explain why there are both practical and important philosophical reasons why at this time we need to use interstitial cystitis as part of the name. He stressed that we still lack the knowledge to replace our old ideas with a new comprehensive concept and that until we do have this new knowledge, the legacy should be retained as part of the name until we can move forward to more appropriate nomenclature. We shouldn’t make a huge effort to change the name when we don’t know where we are at. He went on to say that the urothelium has turned out to be an incredibly difficult organ to study. On the subject of glomerulations, Professor Payne said that while clearly not specific, they should not necessarily be dismissed as irrelevant on the basis of one paper. He gave a number of practical reasons for retaining the name IC. When talking to patients, it is important to have a name they can latch on to. While they have the symptoms of a cystitis, it does not appear to be caused by any infectious organism and there may not be inflammation in all patients. There are patients with a clear bladder disorder, with a low capacity under anaesthesia with inflammatory changes seen in biopsy.

Also important are links to the past (research and scientific literature), financial issues with an impact on the patients and physicians as well as disability issues for the patients. He emphasized that the
buzz word today is phenotyping as a potential way forward. As a urologist, he finds it important to ask himself whether the patient has an abnormal bladder and whether the patient responds to bladder therapy. These are really important aspects that create a specific phenotype that we can study. He emphasized the role of the urologist in a multidisciplinary team: the urologist should “captain” the team, exclude confusable diseases and direct both treatment and research. When research provides us with sufficient understanding, new nomenclature can be created based on pathophysiology. Until we have this knowledge, we should not keep changing the name because such changes have a huge impact on the patient and on the system.

Professor Erickson then took the floor to discuss how name changes might affect the clinical approach to this syndrome. It affects several areas: we are no longer looking for a positive finding to diagnose IC but instead we are looking to rule out all other defined causes of the symptoms. This potentially means no diagnostic tests to “rule in” IC: no hydrodistension if you are not looking for glomerulations, no potassium sensitivity test. When you have excluded other potential causes of the symptoms you treat the syndrome. However, distension is helpful to identify Hunner’s lesions which need a specific treatment pathway. However distension can be useful to predict whether a patient who has failed all treatment is likely to do well after a diversion: if their bladder capacity under anaesthesia is very low, they are more likely to do well with no pain after diversion.

How does name change affect treatment? If you are going to treat the bladder, it doesn’t matter what you call it. But the syndrome name is important because it emphasizes that you have to treat all the pain generators not just the bladder and a urologist may not be able to do this alone. With regard to patient counselling, patients need to understand that they may have more than one pain generator.

Professor Erickson said that she really favours interstitial cystitis as a term for the patients to use with others in his or her life. She also referred to the economic implications for the patient, for example insurance coverage and the ability to obtain coverage. Disability is a crucial issue here. IC is a recognised diagnosis for Social Security disability. Obtaining disability in the USA is a long difficult process and without the diagnosis of “IC” this process could be even harder. Treatment coverage is also an important aspect. Treatments such as PPS and DMSO have been approved for “IC” in the USA. Without a diagnosis of IC, will these be reimbursed?

It may be concluded from these three interesting presentations that while the name was changed multiple times in history (probably around 25-30 times), it probably didn’t have such an impact in the days when there was no such thing as medical insurance, treatment reimbursement or social security disability. The world has changed and nomenclature changes can today have far-reaching effects and should not be undertaken lightly.

The second part of the panel discussion concerned whether this is primarily a bladder syndrome associated with pelvic pain or a chronic pain syndrome associated with bladder symptoms? Each of the three panellists was asked to comment briefly.

Professor Nordling expressed the view that it is a pain syndrome (not just a “pelvic pain syndrome” affecting the bladder, emphasizing that the patients need a multidisciplinary approach, and that the urologist will play a central role because the bladder is involved.

According to Professor Payne, it is both the bladder and generalised pain. He emphasised how important it is to identify sub-groups and to ask is it the bladder, is it some other pain generator or is it both? If patients seem to have multiple issues, they may need multidisciplinary treatment, but he emphasised that it is not good for patients to be shunted around from specialist to specialist unnecessarily. A very important aspect is the whole process of excluding confusable diseases. The goal of treatment should be to obtain and maintain complete remission.

Finally Professor Erickson stressed that if it is primarily a bladder disorder, you should focus research more on bladder-specific treatments. But if it is primarily a pain syndrome with bladder symptoms,
you should focus more on the systemic problem. She concluded that we don’t know which is primary, but both theories suggest lines of further investigation and new treatment development.

The panellists were finally asked about diagnostic tests or markers that they use or see coming in the future or whether they rely on recognising it when they see it. Professor Nordling said there were no reliable diagnostic tests but that the important thing for the future is to classify patients by phenotyping or identifying sub-types and see if they respond to different treatments and have different prognoses.

Professor Payne agreed with this approach and the focus on exclusion of confusable diseases. This means that simple patients may require history physical exam, while complicated patients may need a whole battery of tests.

Professor Erickson expressed the hope that a reliable marker will be found in the future.

This panel session is available as a webcast:


PLENARY SESSIONS 2

PRELIMINARY AUA GUIDELINE INCLUDES THE NAME INTERSTITIAL CYSTITIS

(please note that the final version of the guideline is expected to be published later this year)

Philip Hanno, MD presented the preliminary AUA guideline on what the AUA proposes to call interstitial cystitis/bladder pain syndrome (abbreviated as IC/BPS, with no difference made between the two). This is certainly going to be quite a mouthful as a term and as might be expected there was already some dissension to be heard behind the scenes at the AUA meeting. However, inclusion of the term IC at the beginning means that official recognition of the term interstitial cystitis by health and social security authorities will continue, and this is good news for the patients and patient support groups everywhere.

The proposed definition is as follows:

“An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6 weeks’ duration, in the absence of infection or other identifiable causes.” This is the definition proposed at the SUFU meeting in 2008. (Neurourol Urodyn. 2009;28(4):274-86).

Where diagnosis and treatment strategies are concerned, Professor Hanno explained that there is really insufficient evidence in the scientific literature on which to base this and it had therefore been necessary to base this on expert opinion and clinical principles. The guideline panel is proposing the following principles for treatment:

- begin with conservative treatment, reserving less conservative treatment for when symptoms are not adequately controlled;
- surgery (other than fulguration of Hunner’s lesions) should be reserved for end-stage, small fibrotic bladders or in cases where more conservative treatments have been tried and failed and the quality of life for the patient is poor;
- the initial type and level of treatment depend on the severity of symptoms, on the judgement of the clinician and on patient preference;
- treatment that is ineffective should be stopped once a clinically meaningful interval has elapsed;
- multiple, simultaneous treatments may be considered if it is in the best interests of the patient. Reassessment to document efficacy is essential;
- pain management should be continuously assessed for effectiveness; a multidisciplinary approach should be considered if necessary;
• reconsider the diagnosis if no improvement is observed after multiple treatments have been tried.

Patient education and self-care practices are recommended, including behavioural modification, stress management and suitable manual therapy. However, Professor Hanno emphasized that Kegel and pelvic floor strengthening exercises should be avoided. The treatments recommended in this guideline are limited since they are based on evidence from studies published in scientific literature, expert opinion and therapies available in the USA. The latter may differ from clinical practice in other parts of the world. Some of the treatments recommended in this guideline may be considered controversial in view of contradictory study results which are always a problem with IC studies and trials. The treatments put forward are largely those approved or commonly used in the USA and therefore may not be fully applicable to the rest of the world.

It should be emphasized that this guideline is not yet final and is still undergoing peer review. The guideline panel comprises: D. Burks, Q. Clemens, R. Dmochowski, D. Erickson. M.P. Fitzgerald, J. Forrest, B. Gordon (ICA), M. Gray, P. Hanno, R. Mayer, D. Newman, L. Nyberg, C. Payne and U. Wesselman. It is hoped to publish the final version towards the end of 2010 in the Journal of Urology and on the AUA website. We will then be able to give you much more detail.

This presentation is available as a webcast:

PLENARY SESSIONS 3: LATE-BREAKING NEWS

NERVE GROWTH MONOCLONAL ANTIBODIES FOR THE TREATMENT OF INTERSTITIAL CYSTITIS
Presented by Robert Evans, MD

Dr Evans began by saying that this has been a watershed year for interstitial cystitis with the RAND Interstitial Cystitis Epidemiology (RICE) study and the UPOINT clinical phenotyping for IC/PBS and CP/CPPS breaking patients down into 6 different domains. However, IC often remains extremely difficult to treat and patients may end up on long-term narcotic treatment for the pain. Tanezumab – a monoclonal antibody against nerve growth factor currently undergoing trials – has so far shown some promise for the treatment of chronic bladder pain in patients with IC/PBS. Phase Ila proof of concept study has now been completed with good results and a phase Iib dose-ranging trial is about to start soon. According to Dr Evans: “If you can block nerve growth factor, you can potentially decrease pain. There are now monoclonal antibodies being tested, not only for the treatment of IC/PBS, but for other pain states as well”. (Nerve growth factor (NGF) mediates inflammatory and immune response after injury, initiating hypersensitivity). In a phase II trial, tanezumab has been shown to reduce pain and urgency in IC patients, but did not reduce frequency. It was generally safe and well tolerated. In phase Iib, 300 patients will participate in 18 countries and 150 sites and will be randomized, double blinded, placebo controlled. Other potential disease areas for anti-NGF studies include osteoarthritis, low back pain/sciatica, neuropathic pain, fibromyalgia, colitis/IBS and more. It is hoped that in the future urologists will have the option of offering IC patients an anti-NGF monoclonal antibody injection every 8 weeks for pain control.

Webcast of this session:

PODIUM SESSIONS
Abstract # 118
IDENTIFYING CHRONIC PROSTATITIS/ CHRONIC PELVIC PAIN SYNDROME FOR EPIDEMIOLOGIC STUDIES
J. Quentin Clemens, Lara Hilton, Marika Suttorp, Sandra Berry.
The purpose of this study was to assess the sensitivity and specificity of the definition in the NIH-Chronic Prostatitis Symptom Index (NIHCPSI) used by J. Curtis Nickel and colleagues1) to identify the presence of symptoms indicative of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and subsequently used by many other researchers to report the prevalence of CP/CPPS symptoms. The study showed the sensitivity of the definition to be 70% while the specificity was 91% when compared with BPH patients, and 99% when compared with controls. It was therefore concluded that the Nickel et al case definition seems to have excellent specificity for the purpose of distinguishing CP/CPPS from BPH and controls. The sensitivity is also reasonably high, particularly if you take into account the fact that CP/CPPS is a clinical syndrome without an objective diagnostic marker.

Abstract # 119
DESCRIPTIVE EPIDEMIOLOGY OF UROLOGIC PAIN SYMPTOMS IN MEN AND WOMEN
Jessica Brewer, Carol Link, Paul Eggers, John Kusek, John McKinlay
This longitudinal study examined the epidemiology of symptoms suggestive of IC/PBS and CP/CPPS. The reason for this was that while it is commonly assumed that most non-malignant urologic conditions worsen as people age, data from cross-sectional studies indicate – rather unexpectedly - that the prevalence of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and interstitial cystitis/painful bladder syndrome (IC/PBS) is lower as people grow older. In this study, symptoms suggestive of IC/PBS were defined as pain increasing as the bladder fills and/or pain relieved by urination (fairly often, usually, almost always) for at least 3 months. Symptoms suggestive of CP/CPPS were defined as perineal and/or ejaculatory pain and a Chronic Prostatitis Symptom Index pain score of 4+. The authors present the prevalence, remission, and incidence of IC/PCS and CP/CPPS over 4.7 year period. It was concluded that symptoms suggestive of CP/CPPS and IC/PBS are not reported in over ¾ of the sample after almost five years. The authors therefore recommend that factors that may promote remission of symptoms need to be examined and identified.

Abstract # 605
THE MANAGEMENT OF KETAMINE ASSOCIATED URINARY TRACT PATHOLOGY
Angela Cottrell, David Gillatt, Pete Weinstock, Rachel Ayres, Cathy Stannard, Fergus Law
The urologic consequences of use of the anaesthetic drug ketamine as a recreational drug, which is increasing in popularity, received much attention during this year’s AUA annual meeting with presentations from different parts of the world. Bladder problems caused by recreational ketamine use are now considered one of the confusable diseases when excluding other possible causes of IC/PBS-like symptoms. There is every indication that this form of drug abuse is on the increase since it is a relatively cheap way of getting a “high”. Ketamine is an anaesthetic that when used as a recreational drug induces a state of dissociation, similar to the effects produced by phencyclidine (PCP). Ketamine is known to cause amnesia, impaired motor function, high blood pressure and respiratory problems in addition to severe painful urination, smaller bladder capacity, frequency, urgency, incontinence, and blood in the urine.
According to Cottrell and colleagues from Bristol (the South West of the UK) who are now seeing an increasing number of individuals with this problem, case series around the world have described
severe urinary tract symptoms and pathology associated with chronic use of street ketamine (known by users as “K”). The urologic symptoms can be difficult to manage, especially when illegal use of this drug continues, while little is known about the long-term consequences. The authors describe the strategy used at their centre for management of this group of patients.

Patients with a history of chronic ketamine abuse and urinary symptoms underwent investigations including urine microscopy and culture, baseline blood tests, imaging (renal tract ultrasound or CT scan), cystoscopy and bladder biopsy. If felt to be appropriate, patients were referred to a local pain clinic specializing in drug abuse, with psychiatric support available. The study involved 16 patients (13 male, 3 female), all of whom had a history of ketamine use and severe urologic symptoms. No bacterial growth was observed, cystoscopy revealed a small capacity bladder, erythematous bladders with contact bleeding and ulcerative cystitis. The authors found that urologic effects caused by chronic ketamine abuse can be very severe and difficult to treat. A multidisciplinary approach seems to be the best form of management, including a pain team, drug support team, psychiatrists and urologists.

See also abstract # 1043.

Abstract # 793
VULVAR AND EXTRA-VULVAR PAIN THRESHOLDS IN PATIENTS WITH PROVOKED, LOCALIZED VULVODYNIA
Maureen Basha, Susan Kellogg-Spadt, Monique Ruberu, Sandy Mosiniak, Salim Wehbe, Jennifer Yonaitis Fariello, Amy Rebja Hoffman, John Grothusen, Philadelphia, PA, Kristene Whitmore
Basha and colleagues note that vulvodynia is defined as vulvar pain for a minimum of 6 months in the absence of gross anatomic or neurologic findings and has been shown to be associated with interstitial cystitis (painful bladder syndrome). Provoked, localized, vulvodynia (PLV) is the most common subtype of vulvodynia and is characterized by provoked vestibular pain in response to a non painful pressure/touch stimulus allodynia). The cause of PLV is largely unknown.

The purpose of this study was to determine possible differences in 1) vulvar and forearm mechanical and thermal pain thresholds and 2) self-reported bladder pain in 9 women with PLV compared to 12 controls. PLV patients reported greater bladder pain with activity and intercourse. Vulvar pain thresholds to mechanical and cold stimuli were significantly lower in PLV patients compared to control subjects. Forearm pain thresholds to mechanical and cold stimuli were also lower in PLV patients. No differences in heat pain thresholds were detected at any of the sites. These results indicate that both mechanical and cold allodynia is present within the vulva of the PLV patients investigated in this study. This finding is consistent with neuropathic pain. In addition, significantly higher ICSI/ICPI and VAS scores for bladder pain and reduced pain thresholds at the forearm of these PLV patients indicate altered sensory processing at other pelvic and extra-pelvic sites.

Abstract # 794
6-DAY INTENSIVE PHYSIOTHERAPY AND COGNITIVE BEHAVIOUR CLINIC TREATMENT FOR CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME
Rodney Anderson, David Wise, Tim Sawyer, Patricia Glowe
In this study, an intensive 6-day manual physiotherapy and cognitive behaviour relaxation training appeared to be helpful for the treatment of severe chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) patients exhibiting the phenotype of pelvic musculature tenderness and who had failed to respond to previous therapies. The 125 men in the study underwent myofascial trigger point release and training in paradoxical relaxation for 6 consecutive days, some learning how to carry out the manipulation themselves. Of the men completing the therapy, 68% perceived benefit and stated they would participate again or recommend this therapy to a friend. The authors concluded that CP/CPPS patients with longstanding pain, refractory to traditional treatment, may benefit from focused myofascial trigger point therapy and cognitive behaviour relaxation training. It is anticipated
that refinement of phenotyping and selection of patients should improve the success rate with this form of treatment.

Abstract # 798
PHENOTYPICALLY DIRECTED MULTIMODAL THERAPY FOR CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME: A PROSPECTIVE STUDY USING UPOINT
Daniel Shoskes, Dolinga Robert, Curtis Nickel
Shoskes and colleagues note that chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is most likely to be multifactorial with sub-types (phenotypes). This was why they developed the UPOINT system with six yes/no domains (Urinary, Psychosocial, Organ Specific, Infection, Neurologic/Systemic and Tenderness of muscles). In this study, they treated 100 patients with multimodal therapy based on the UPOINT phenotype (one therapy recommended for each positive domain) and hypothesized that patients would have significant long term symptom improvement. They report that their findings show that multimodal therapy based on phenotypes using the UPOINT system leads to significant improvement in symptoms and quality of life in men with CP/CPPS.

Abstract # 799
CLINICAL PHENOTYPING OF PATIENTS WITH CHRONIC PROSTATITIS-CHRONIC PELVIC PAIN SYNDROME IN TWO SPECIALIZED EUROPEAN INSTITUTIONS
Florian Wagenlehner, Vittorio Magri, Gianpaolo Perletti, Sebastian Schneider, Wolfgang Weidner
The aim of this European study was to correlate the UPOINT phenotyping system to patients’ symptoms in a large database of 1219 CP/CPPS patients from two European centres in Italy and Germany. The authors report that they found a large heterogeneity of clinical phenotypes in this group of patients. They consider that it might be beneficial in the future to include additional phenotypes for further stratification of patients. While the exact role of clinical phenotyping has yet to be evaluated in treatment studies, they consider that a phenotype-oriented treatment might more closely match the underlying etiology than a non-specific treatment and therefore lead to better results.

Abstract # 800
CATASTROPHIZING AND SPOUSAL RESPONSES IN MEN SUFFERING FROM CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME (CP/CPPS)
Dean A. Trip, Jessica Ginting, J. Curtis Nickel, Kathleen J. Propert, John Kusek
This study examined the moderating effect of psychosocial factors such as catastrophizing and spousal responses on the relationship between pain and quality of life (QoL), and pain and disability in 188 men suffering from CP/CPPS. They found that the association between pain and poorer QoL was amplified when examined across higher versus lower levels of catastrophizing. The association between pain and disability was also amplified when female spouses were reported to provide higher levels of solicitous support for males with CP/CPPS than at lower levels.

Abstract # 802
CHRONIC PELVIC PAIN IS ASSOCIATED WITH MAST CELL ACTIVATION AND IS AMENABLE TO MAST CELL DIRECTED THERAPIES
Praveen Thumbikat, Charles Rudick, David Klumpp, Anthony Schaeffer
The etiology and pathogenesis of this pain syndrome remains unknown. In this study, the authors hypothesized that mast cells and factors released by activated mast cells contribute to the pathogenesis of CPPS. They therefore examined clinical samples from CPPS patients for mast cell activation products. Mechanisms of chronic pelvic pain were further defined in an experimental autoimmune prostatitis (EAP) model in mice. Activated factors released by mast cells were significantly increased in expressed prostatic secretions (EPS) from CPPS patients compared to controls. The authors concluded that their results demonstrate that mast cells and their activation
products play an important role in the pathogenesis of chronic pelvic pain and may be involved in pain mechanisms in CP/CPPS. Furthermore, treatments targeting mast cell activation appear to be effective in reducing established pelvic pain in animal models.

Abstract # 1033
SACRAL NERVE ROOT NEUROMODULATION FOR THE TREATMENT OF INTRACTABLE PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS: 14 YEARS EXPERIENCE OF ONE CENTER
Jerzy Gajewski, Ali Alzahrani
The purpose of this retrospective study was to evaluate the long-term success and tolerability of the chronic sacral neuromodulation (SNM) for the control of painful bladder syndrome/interstitial cystitis (PBS/IC) symptoms in 78 patients over a period of 14 years. The explantation rate was 28%, the revision rate 50%. The most common reason for revision was lack of stimulation sensation and worsening of symptoms. The average durability of the pulse generator battery was 93 months. The authors concluded that SNM is an effective treatment to control the symptoms of PBS/IC. It should be considered before any major intervention if conservative measures have failed. It is minimally invasive, safe and has good long term durability. However, the revision rate is high and patients require lifelong follow-up.

Abstract # 1034
TIME-DEPENDENT CHANGES IN BLADDER FUNCTION AND PLANTAR SENSITIVITY IN A RAT MODEL OF FIBROMYALGIA INDUCED BY HYDROCHLORIC ACID INJECTION INTO THE GLUTEUS
Akira Furuta, Yasuyuki Suzuki, Yusuke Koike, Takehito Naruoka, Nozomu Furuta, Shin Egawa, Michael Chancellor, Naoki Yoshimura
Bearing in mind that organ cross-sensitization could be a pathogenesis of bladder pain syndrome/interstitial cystitis (BPS/IC) because BPS/IC often coexists with irritable bowel syndrome and/or fibromyalgia syndrome (FMS), this team from Japan and the USA examined time-dependent changes in bladder function and plantar sensitivity using a rat model of FMS induced by hydrochloric acid (HCl) injection into the gluteus. They concluded from their findings that injection of pH4 HCl into the gluteus can induce both plantar hypersensitivity and urinary frequency, suggesting that somatico-visceral cross-sensitization might be involved in comorbidities of muscular (gluteal) pain in FMS and bladder hypersensitivity in BPS/IC. In addition, treatment of specific tender points outside the bladder could be effective to treat bladder hypersensitive conditions because lidocaine injection into the gluteus normalized bladder function in FMS rats.

Abstract # 1035
RANDOMIZED MULTICENTER CLINICAL TRIAL SHOWS EFFICACY OF MYOFASCIAL PHYSICAL THERAPY IN WOMEN WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS)
Christopher Payne, Mary Pat Fitzgerald, David Burks, J.Curtis Nickel, Emily Lukacz, Karl Kreder, Toby Chai, Phil Hanno, Robert Mayer, Claire Yang, Kenneth Peters, Harris Foster, J Richard Landis, Kathleen Propert, John Kusek
The aim of this multi-centre, randomized, controlled study was to determine the efficacy, safety and tolerability of myofascial physical therapy (MPT) in women with IC/PBS, as compared to an active control of global therapeutic massage (GTM). The 81 women recruited had urinary urgency, frequency and pain present for less than 3 years, plus pelvic floor tenderness on examination. Although blinding was attempted, it was unsuccessful since all subjects were able to correctly guess their treatment group assignment. The patients received 10 weekly standardized treatments over a period of 12 weeks. At week 12, the Global Response Assessment (GRA) was 26% in the global massage group and 59% in the myofascial physical therapy group. Pain was the most common side effect, occurring at similar rates in both groups. There were no serious adverse events reported. This study confirmed the results of a previous study. However, further research is needed to define the role of MPT in a broader IC/PBS population, to define optimal patient selection criteria and optimal treatment parameters, and to define long-term durability.
Abstract # 1036
THE UROTHELIAL CELL-LINE RT4 EXPRESSES A GLYCOSAMINOGLYCAN (GAG) LAYER ON ITS OUTER SURFACE; AN IN VITRO MODEL FOR THE BLADDER GAG-LAYER
Dick Janssen, Jack Schalken, Gerdy ten Dam, John Heesakkers
This aim of this Dutch study was to investigate 3 urothelial cell lines for their suitability as a GAG-layer-model for in vitro testing. This is based on the hypothesis that IC is caused by a decreased ability to construct a normal GAG-layer, a rationale which is applied when giving GAG-replacement therapies. According to the research team, it has proven difficult to examine the contribution of the GAG-layer to the bladder barrier in vivo models. They note that while there is no evidence that GAGs in the bladder actually contribute to the urothelial barrier, some IC patients benefit from GAG replacement therapy. They report that they discovered a highly differentiated urothelial cell line (RT4) that expresses a GAG-layer that resembles the normal urothelial GAG-layer of the bladder. With this cell line, they have constructed an in vitro model that can facilitate research into the urothelial GAG-layer.

Abstract # 1037
SUBMUCOSAL INJECTION OF TRIAMCINOLONE FOR HUNNER’S ULCER TYPE INTERSTITIAL CYSTITIS
Matthew Thom, Robert Royce, Carl Klutke
This team previously reported immediate pre and post-op changes in symptoms and quality of life measures with injection of endoscopic intralesional steroid in patients with Hunner’s lesion. This subtype of IC requires a different type of management to patient with the non-lesion type. They now present their longer follow-up experience with these patients including length of response. 58 patients underwent cystoscopic evaluation with endoscopic biopsy of lesion(s) to rule out malignancy and submucosal injection of triamcinolone for Hunner’s ulcer type IC. 66% of the patients showed global improvement. They concluded that submucosal injection of triamcinolone for treatment of Hunner’s ulcer type IC offers significant improvement in patient symptoms and quality of life on validated questionnaires. It was found that prior history of urinary tract infection or more than 2 lesions did not affect treatment outcomes. Perioperative complications were limited to mild facial swelling in two patients. Longer follow-up has shown durable response. Repeat injections are well tolerated with no evidence of tachyphylaxis.

Abstract # 1038
ENKEPHALIN GENE THERAPY USING A HERPES SIMPLEX VIRUS VECTOR SUPPRESSES CYTOKINE ELEVATION IN THE BLADDER AND URINE OF RATS WITH CYSTITIS
Hitoshi Yokoyama, Tomohiko Oguchi, Osamu Nishizawa, William Goins, James Goss, Joseph Glorioso, Naoki Yoshimura
According to Yokoyama and colleagues, herpes simplex virus (HSV) is an attractive gene therapy vector because of its natural affinity to primary afferent nerves and the large size of the genome, which can reduce the systemic side effects and accommodate multiple and large genes respectively. This team believes that the result of the present study suggest the possibility that HSV-vector mediated enkephalin gene therapy can reduce the local inflammatory condition through inhibition of production of some cytokines/chemokines in the bladder. They speculate that the release of neuropeptides such as substance P and CGRP from peripheral sensory nerve terminals is reduced by HSV vector-mediated enkephalin gene delivery which could suppress the interaction between the nervous and immune systems. They are of the opinion that the results of this study suggest that 1) the antinociceptive effects of HSV-mediated enkephalin gene therapy in cystitis rats could be in part induced by the bladder and 2) some urine cytokines/chemokines are useful markers to predict the condition of bladder tissue inflammation and its changes after the treatment. They conclude that HSV-mediated enkephalin gene therapy, which can suppress bladder pain and inflammation, might potentially be a useful modality for the treatment of BPS/IC.
Abstract # 1039
SAFETY AND CLINICAL EVALUATION OF INTRAVESICAL LIPOSOME IN PATIENTS WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME
Yao-Chi Chuang, Wei-Chiang Lee, Wei-Chia Lee, Po-Hui Chiang
Liposomes are stable self-assembled phospholipids bubbles filled with water that adhere to a surface such as the bladder mucosa. The purpose of this study was to present a single institution open-label experience with intravesical liposomes (LPs) in 17 IC/PBS patients and to assess the safety and efficacy for IC/PBS symptoms. The patients were treated once a week for 4 weeks or twice a week for 4 weeks. Both courses of treatment were well tolerated and there was no incontinence, retention or unanticipated side effects with either dosage. It was concluded that intravesical treatment with LPs is safe and its effect is maintained for 4 weeks after a course of instillation. Large-scale, placebo-controlled studies are needed to further assess efficacy.

Abstract # 1040
THE PREDICTORS OF SUCCESSFUL HYDRODISTENSION THERAPY IN 399 PATIENTS WITH INTERSTITIAL CYSTITIS IN JAPAN
Hiroshi Hayami, Hideki Enokida, Mari Kawagoe, Masayuki Nakagawa, Seiji Naito, Tetsuro Matsumoto, Jiro Uozumi, Hiromitsu Mimata, Mineo Takei
The aim of this retrospective study from Japan was to look for predictors for successful hydrodistension treatment for IC patients, since its efficacy as a treatment differs between patients. They evaluated 399 IC patients (87 male, 312 female) who had received hydrodistension therapy between 2002 and 2006. Their findings suggest that an instilled volume of greater than 500 mL, age under 60 years and symptom duration of less than 6 months are significant predictors of a successful treatment outcome.

Abstract # 1041
PELVIC FLOOR INJECTION OF BOTULINUM TOXIN A FOR PELVIC PAIN: A RANDOMIZED, CONTROLLED PILOT STUDY
Henry Gottsch, Richard Berger, Jane Miller, Claire Yang, Seattle
Botulinum toxin A (BTX) has been a therapeutic treatment for pain from muscle spasticity and overactivity. The purpose of this randomized controlled pilot study was to test the hypothesis that transperineal injection of BTX improves chronic pelvic pain. 29 men with CPPS and 20 women with IC/PBS completed the study. There was a modest effect of transcutaneous application in men with CPPS, but this effect was not seen in women with IC/PBS.

Abstract # 1042
ENDOTHELIN-1 AS A REGULATOR OF UROTHELIAL CELL PROLIFERATION AND A POTENTIAL URINARY BIOMARKER IN INTERSTITIAL CYSTITIS (IC)
Shaohua Chang, Jaber Alanzi, Philip M. Hanno, Diane K. Newman, Gina M. Northington, Alan J. Wein, Samuel Chacko
The purpose of this study was to investigate whether Endothelin-1 (ET-1) inhibits the proliferation of urothelial cells in vitro. The effect of ET-1 was tested on the cell growth and DNA synthesis in cultured human and rabbit urothelial cells. The team report that results show that ET-1 is increased in urine from IC patients compared to age-matched healthy controls and that ET-1 inhibits urothelial cell proliferation in vitro. Both cell growth rate and new DNA synthesis were reduced by ET-1. They suggest that ET-1-induced inhibition of urothelial cell proliferation may play a role in the pathogenesis of IC which is associated with changes in the urothelial layer, at least in some sub-types of IC/PBS, and that ET-1 might be used as a urinary biomarker to monitor urothelial integrity in IC. Chang and colleagues conclude that information gained from this study might be useful in the development of therapeutic agents for limiting the effects of IC in the urothelium and bladder wall.
THE ASSOCIATION OF PELVIS PAIN, URGENCY AND FREQUENCY SCORE AND BLADDER CAPACITY WITH STREET KETAMINE ABUSE - OBSERVATIONS FROM A PILOT COMMUNITY SURVEY OF YOUNG DRUG ABUSERS.

Siu-king Mak, Tsz-yeung Chan, Bo-bik Wu, See-ming Hou, Kam-hung Yip, Chi-yin Man

This very interesting pilot community survey of street ketamine abuse and its impact on urologic function and physical and psychological status on teenagers and young adults comes from Hong Kong where ketamine abuse currently forms an increasing problem among young people. The study data were also presented to the media at an AUA press conference at the AUA. 66 teenagers and young adults aged 13 to 25 (24% female) were assessed in 6 clinic sessions from July to September 2009. More than 97% of them had a history of ketamine abuse. The first drug abuse started as early as 10 years old. The urologic assessment included a self-reported questionnaire on pelvic pain, urgency and frequency (PUF), uroflowmetry, post-void bladder scan and kidney ultrasound. The team found that ketamine abuse of more than 24 months resulted in a higher PUF symptom score. Abuse more than 5 times a week was associated with smaller bladder capacity. However, the good news was that those who had abstained from ketamine abuse for one year had an improved bladder capacity.

Abstract # 1044
END STAGE BLADDER: DIAGNOSIS AND TREATMENT

Jerry G. Blaivas, Mazyar Ghanaat, Jeffrey P. Weiss, Lorraine M. Liang

Blaivas and colleagues presented a very interesting retrospective observational study of a group of 25 patients (17 women, 8 men) age 20 – 84 years with end stage bladder using a database from 1993-2008. In 19 of these patients, the time from presentation to the development of end stage bladder was 3 – 12 months, in 2 patients it was gradually progressive over years and in 3 was unknown. The purpose of the study was to provide criteria to define end stage bladder, to determine whether patients with end stage bladder evolve from those with painful bladder syndrome, to determine the underlying causes and to assess treatment outcomes. Inclusion criteria were refractory lower urinary tract symptoms for at least 6 months, negative urine culture, marked bladder inflammation on at least 2 cystoscopies at > 3 and bladder biopsy negative for malignancy. They concluded that most patients with end stage bladder do not progress from PBS and are idiopathic. Bladder cancer and colovesical fistula must be excluded. Empiric treatments are rarely effective and the best chance for success is radical surgical treatment.

Abstract # 1506
CHOICE AND OUTCOMES OF ALTERNATIVE THERAPIES IN PATIENTS WITH INTERSTITIAL CYSTITIS (IC) AND CHRONIC PELVIC PAIN (CPP)

Chad Baxter, Roger Bolus, Emeran Mayer, Deborah Ackerman, Larissa V. Rodriguez

Baxter and colleagues report that patients with IC/CPP often seek alternative therapies. The purpose of this study was to look at symptoms and demographics on treatment selection and evaluate alternative therapy outcomes in 223 IC/CPP patients. These patients completed validated questionnaires on pain, quality of life, anxiety and depression, early trauma, physical health and coping strategies and reported on alternative treatments (including prescription, over the counter, physical therapy, massage, yoga, acupuncture, psychiatry/psychology, MD, chiropractic, homeopathy, herbalist, healer, surgery, meditation, and frequency specific microcurrent) up to 6 months prior to enrolment. It was concluded that, while this study had its limitations, alternative therapies did not appear to have a significant impact on symptoms or quality of life in these IC/CPP patients and that there is a need for rigorously designed investigation of alternative treatments before they can be recommended them to patients.

Abstract # 1507
A QUALITATIVE ANALYSIS OF SYMPTOM CLUSTERING AMONG WOMEN DIAGNOSED WITH INTERSTITIAL CYSTITIS/ PAINFUL BLADDER SYNDROME, ENDOMETRIOSIS, VULVODYNIA, AND OVERACTIVE BLADDER
Women go to their doctors with complaints expressed in the form of symptoms. The doctors are then faced with the problem of deciding what diagnosis to assign to clusters of symptoms. In this study, 599 women with diagnoses of interstitial cystitis/painful bladder syndrome (IC/PBS) and/or endometriosis, vulvodynia, or overactive bladder (OAB) were recruited from the clinical practices of urologists and gynecologists across the United States and interviewed by telephone. Subjects who reported pain, pressure or discomfort in the lower abdomen or pelvic area were asked to describe exactly what these sensations felt like. The research team report that most diagnoses were associated with at least one clear and interpretable symptom. For example, endometriosis was associated with cramp, vulvodynia with burning and itching, OAB with incontinence episodes and unproductive urination, and IC/PBS with urgency, pain before and after urination, pain all or much of the time, and pain located in the urinary tract or bladder. They concluded, however, that while some conditions were associated with symptoms that were distinctive, many common symptoms that women describe were associated with many of the conditions. This may make it difficult to assign a clear diagnosis.

Abstract # 1508
TANEZUMAB REDUCES PAIN AND URGENCY IN INTERSTITIAL CYSTITIS: RESULTS OF A PHASE 2 TRIAL
Robert Evans, Robert Moldwin, Nandini Cossons, Amanda Darekar, David Scholfield, Ian Mills
Tanezumab, a humanized antibody specific for nerve growth factor, which has been show to reduce pain in conditions such as osteoarthritis of the knee and low back pain, is currently being investigated for the treatment of interstitial cystitis. This randomized, doubleblind, placebo-controlled study concerns a phase 2 trial to evaluate the safety and efficacy of intravenous tanezumab 200 ug/kg for the treatment of patients with moderate to severe IC. Of the 65 patients enrolled in the study, 34 (91% female) received tanezumab 200 ug/kg, 30 (87% female) received placebo, and 1 patient did not receive treatment. At Week 6, tanezumab produced clinically significant improvements in average daily pain score and urgency episodes per 24 hours versus placebo, but had no significant effect on urinary frequency compared to placebo. 15% of those receiving the drug (3% of those receiving placebo) had paraesthesia as a side effect. The next phase of trials will begin soon.

Abstract # 1509
EARLY LIFETIME TRAUMA IMPACTS SYMPTOM SEVERITY OF INTERSTITIAL CYSTITIS AND CHRONIC PELVIC PAIN
Chad Baxter, Roger Bolus, Emeran Mayer, Deborah Ackerman, Larissa V. Rodriguez
This study investigated the impact of early life trauma on symptom severity and quality of life in 223 adult patients with interstitial cystitis (IC) and chronic pelvic pain (CPP), using the UCLA database of patient-reported, validated questionnaires. It was concluded that early lifetime traumatic events, particularly emotional trauma, may significantly impact patient perception of disease and disease severity in IC and/or CPP patients.

Abstract # 1511
PREVALENCE AND PREDICTORS OF SEXUAL DYSFUNCTION AMONG WOMEN WITH SYMPTOMS OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS)
Laura M. Bogart, Marika Suttorp, J. Quentin Clemens, Sandra H. Berry
As part of the RAND Interstitial Cystitis Epidemiology Study (RICE), this team examined the prevalence of sexual dysfunction, and the relationship of IC/PBS symptom severity to sexual dysfunction in a national representative sample of women with IC/PBS symptoms. 146,246 households with telephones were contacted to identify those with a female aged 18 or over who had bladder symptoms. Women who had a current partner were asked to what extent they had experienced general sexual dysfunction due to physical health in the past 12 months and IC/PBS-specific sexual dysfunction symptoms in the past four weeks. It was concluded that women with...
IC/PBS symptoms experience very high levels of sexual dysfunction, which may be exacerbated by IC/PBS symptoms.

Abstract # 1589
ELEVATION OF SERUM C-REACTIVE PROTEIN AND URINARY NERVE GROWTH FACTOR LEVELS IN PATIENTS WITH OVERACTIVE BLADDER AND INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME IMPLIES CHRONIC INFLAMMATION IN THE URINARY BLADDER
Shiu-Dong Chung, Hsin-Tzu Liu, Hann-Chorng Kuo
C-reactive protein is a protein found in the blood, the levels of which rise in response to inflammation. The purpose of this study from Taiwan was to elucidate the association of C-reactive protein (CRP) and OAB or IC/BPS and the correlation of elevated CRP and urinary nerve growth factor (NGF) levels in these patients. Although there was no correlation between plasma CRP and urinary NGF levels, they concluded that elevated plasma CRP and urinary NGF levels are associated with the presence of LUTS from patients with OAB or IC/BPS. They are of the opinion that these data support the association between chronic inflammation of the urinary bladder and LUTS due to OAB or IC/BPS and provide new insights into the underlying mechanisms that warrant further investigation.

Abstract # 1590
DISCRIMINATION OF OAB FROM IC/PBS BY MULTIVARIATE DATA MODELING OF URINARY PROTEINS
Pradeep Tyagi, Vikas Tyagi, Don Bui, Harvey Qu, Kenneth Peters, Yao-Chi Chuang, Hann-Chorng Kuo, Naoki Yoshimura, Michael Chancellor
While there appears to be an overlap between the symptoms of overactive bladder (OAB) and the symptoms of Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS), there is an absence of diagnostic tools for objective classification. According to the authors, recent studies suggest the association of inflammation with both diseases. In this study with 39 IC/PBS patients and 17 OAB patients, they hypothesized that mechanistic differences in paracrine signalling mechanisms underlying OAB and IC/PBS may be orchestrated by distinct chemokines or cytokines. They concluded that the findings of this study supported their hypothesis of mechanistically distinct inflammatory pathways underlying the two diseases and believe that analysis of urine in larger groups of OAB and IC/PBS patients followed long-term will reduce the number of variables required in their predictive model and further optimize this model.

Abstract # 1677
INTRA-TRIGONAL INJECTION OF BOTULINUM TOXIN A IN PATIENTS WITH REFRACTORY BLADDER PAIN SYNDROME DECREASES URINARY NEUROTROPHINS AND IMPROVES LOWER URINARY TRACT SYMPTOMS
Rui Almeida Pinto, Barbara Frias, Tiago Lopes, Andre Silva, Joao Alturas Silva, Carlos Santos Silva, Paulo Dinis, Celia Cruz, Francisco Cruz
The purpose of this study from Portugal was to evaluate the efficacy and tolerability of repeated intra-trigonal injection of Botulinum toxin A (BoNT-A) in patients with BPS/IC who failed to respond to first line treatment and to look at urinary levels of neurotrophins, nerve growth factor (NGF) and brain derived growth factor (BDNF) before and after treatment. It was concluded that intra-trigonal injection of 100 U of BoNT-A is a safe, effective and reproducible treatment for BPS/IC patients who have failed to respond to other treatment. BoNT-A promotes a temporary decrease in urinary levels of NGF and BDNF, which might indicate a decreased stimulation of nociceptive bladder afferents.

Abstract # 1678
PAIN AND PH: ACID-SENSING CHANNELS (ASICs) MAY PLAY A ROLE IN BLADDER PAIN SYNDROME (BPS)
Verónica Sánchez-Freire, Maxime Blanchard, Fiona C. Burkhard, Thomas M. Kessler, Annette Kuhn, Stephan Kellenberger, Katia Monastyriskaya
In this study from different centres in Switzerland, the goal was to determine whether acid sensing channels (ASICS) and transient receptor potential vanilloid 1 (TRPV1) play a role in BPS. The study demonstrated that TRPV1 and different types of ASICs are expressed in human bladder and the cultured human urothelial cell line TEU-2. The strong up-regulation of ASIC1b, 2a, 2b and 3 in BPS patients suggests a role in the increased chemonociception and pain in these patients.

Abstract # 1687
THE EFFECTS OF ACUTE AND CHRONIC STRESS ON BLADDER STRUCTURE AND FUNCTION
Ariana Smith, Joanne Leung, SunyKun, Rong Zhang, Shlomo Raz, Emeran Mayer, Iordanes Karagiannides, Charalabos Pothoulakis, Sylvie Bradesi, Larissa Rodriguez
It is noted that stress appears to play a role in the exacerbation of urinary tract disorders including painful bladder syndrome (PBS) and overactive bladder (OAB). This study was aimed at gaining a better understanding of the mechanism underlying this relationship, by characterizing changes in voiding, anxiety behaviour and bladder pathology in rats exposed to water avoidance stress (WAS), a potent psychological stressor. The rats exposed to WAS developed a significant increase in voiding frequency and a decrease in latency to void and volume voided when compared to sham and to baseline. It was concluding from the findings that psychological stress results in a strong, repeated, and lasting alteration in voiding.

SOCIETY FOR INFECTION AND INFLAMMATION IN UROLOGY (SIIU)

A number of interesting posters were presented at this society meeting:

CHILDHOOD AND RECENT TRAUMA IN WOMEN WITH INTERSTITIAL CYSTITIS / PAINFUL BLADDER SYNDROME: (IC/PBS): A CASE CONTROL COHORT STUDY
Curtis Nickel, Tripp Dean, Michel Pontari, Robert Moldwin, Robert Mayer, Lesley Carr, Ragi Doggweiler, Claire Yang, Nagendra Mishra, Jorgen Nordling
In recent years, there has been a lot of controversy in this field, with many patients who have not been abused or traumatized feeling stigmatized and upset by the claims in the literature. The purpose of this study was to determine and compare the prevalence and impact of childhood and recent traumatic events on patient quality of life and other biopsychosocial parameters. Questionnaires were completed by 207 IC/PBS patients and compared with 117 controls. The results show that childhood and recent traumatic events are commonly reported in both IC/PBS patients and control subjects and the impact of childhood sexual abuse is the same in both groups.

INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME PAIN AND QUALITY OF LIFE IS MODERATED BY SPOUSAL RESPONSES TO PATIENT PAIN IN WOMEN
Jess Ginting, Dean A. Tripp, J. Curtis Nickel, Robert Mayer, Mary P. FitzGerald
The purpose of this study was to examine the influence of spousal responses to pain behaviour on the association between pain and patient quality of life, depressive symptoms and disability. Three types of spouse responses were examined: solicitous (doing more for spouse with pain), distracting (shifting attention away from pain) and negative (ignoring spouse with pain). This study is the first to show the important role that distracting spouse responses may have in the psychological adjustment of women with IC/PBS. The results suggest that distracting spouse responses are associated with improved mental quality of life in women with IC/PBS.

PREVALENCE AND IMPACT OF BACTERIURIA AND/OR URINARY TRACT INFECTION (UTI) IN INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS)
J. Curtis Nickel, Karen Irvine-Bird, Daniel A Shoskes
This team found that bacteriuria is observed in an IC/PBS population of women whose urine is frequently and rigorously cultured, that patients with documented bacteriuria do not differ from those without evidence of bacteriuria, that bacteriuria episodes do not appear to be associated with
significant symptom flares and that antibiotic treatment of documented bacteriuria is not associated with significant IC/PBS related symptom improvement.

PELVIC FLOOR DYSFUNCTION IN THE INTERSTITIAL CYSTITIS POPULATION
David M. Faleck, Edan Y. Shapiro, Jane S. Cho, Jonathan D. Kaye, Arun K. Srinivasan, Robert M. Moldwin
This study demonstrated a pelvic floor dysfunction prevalence of 81% in IC patients, as shown by levator ani tenderness, together with co-existing constipation, decreased stream, hesitancy, straining with urination, low back pain and painful sex. This highlights the importance of defining clearer clinical criteria and of broader recognition of the need to evaluate for the presence of pelvic floor dysfunction complaints, providing them with multimodal therapy targeting areas beyond the bladder alone.

NEUROPATHIC PAIN IN THE CHRONIC PELVIC PAIN POPULATION
Mostafa Sadek, Arvin K. George, Sandeep S. Saluja, Jennifer Y. Fariello, Kristene Whitmore, Salim Wehbe, Robert M. Moldwin
Chronic pelvic pain (CPP) represents a wide range of conditions such as IC, CP/CPPS, myofascial dysfunction of the pelvic floor (PFD) and vulvodynia. Although pain may be perceived as ‘end organ’, according to the authors recent evidence suggests that pain may be derived from central and/or peripheral neuropathic mechanisms. It was concluded that CPP patients have a high prevalence of coexisting conditions when compared with the general population. Screening the CPP patient for other coexisting conditions may yield other pain generators. Identifying CPP patients with neuropathic pain may ultimately increase treatment strategies, additionally targeting factors beyond end organ pain.

AUA 2010 webcasts home page: