

## **REVIEW OF THE ESSIC ANNUAL MEETING 2014** **13-15 June, Geary Hall, Hahnemann Hospital, Drexel University,** **Philadelphia, USA**

*“The better you describe a disease, the better you understand it.” (Magnus Fall, MD)*

*“One of the problems of diagnosis is that we may not all be talking about the same people.” (Kristene Whitmore, MD)*

*“Identification of a Hunner lesion is clinically important because effective treatment is available for the patient.” (Kristene Whitmore, MD)*

*Jane Meijlink*

The 2014 ESSIC annual meeting was a unique occasion because it was the first ESSIC (International Society for the Study of Bladder Pain Syndrome) annual meeting to be held in the United States.

Hosts Philip Hanno, MD, Kristene Whitmore, MD, and Jørgen Nordling, MD emphasised that the focus of the meeting would be on the differences between patients with and without Hunner lesion, with the aim of making it an interactive meeting with maximum discussion. Attendees from around the world included patient advocates Lee Claassen (ICA Executive Director, USA), Rhonda Garrett (ICA, USA), Vicki Ratner, MD (Founder and President Emeritus ICA, USA), Loredana Nasta (President AICI, Italy) and Jane Meijlink (Chair IPBF, Netherlands), all of whom played an active role in this meeting. The working groups on the second day included a patient advocates working group.

### **USA Multidisciplinary Approach to the study of chronic Pelvic Pain (MAPP) Update**

First on the agenda was a much awaited update on the NIH/NIDDK MAPP project (Multidisciplinary Approach to the study of chronic Pelvic Pain) presented by Chris Mullins, PhD, from the NIDDK, followed by J. Quentin Clemens, MD (from University of Michigan Medical Center) who is chair of the MAPP Network.

Chris Mullins, addressing the organisational aspects, pointed out that the NIDDK in the USA has long had a special interest in urologic chronic pelvic pain syndromes (UCPPS), covering interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome, with numerous clinical trials and basic science projects over more than 15 years. However, in previous NIDDK-funded projects no statistically significant effective treatment options were identified, nor were any significant insights obtained into etiology or pathophysiology. What was noted, however, was that a) many current therapies are ineffective in randomized trials and that b) UCPPS have associated comorbidities, suggesting that these may be systemic disorders requiring a multi-system, multi-disciplinary approach. Why has progress been slow, he asked? This may have been due to overemphasis on the bladder and prostate without consideration of more systemic contributions. It now seems clear that patient populations potentially comprise many different phenotypic sub-types based on different underlying contributors. There may have been too few innovative scientific approaches and insufficient interaction between clinical and basic research expertise, as well as inadequate involvement of expertise from disciplines beyond urology. And last but not least, there may have been insufficient emphasis on patient-centred issues and outcomes.

It was therefore clear that a new approach was needed. The first phase of the MAPP project started in September 2008. The main objectives of the MAPP were: to develop a multidisciplinary, highly collaborative, integrated approach to study UCPPS as a systemic disorder, including associations between urologic and non-urologic pain conditions (such as chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, vulvodynia, etc); to address underlying disease pathophysiology and natural history; and to provide a translational

foundation for improved clinical trials/management (e.g. patient phenotypes, sub-groups, drug targets, diagnostic features, improved outcomes, etc).

A great deal of data was collected during the first phase, much of which still remains to be analysed. However, it was now considered regrettable that no split was made between Hunner lesion and non-lesion patients in the first phase. This would be changed in phase 2.

Phase 2 of the MAPP project runs from July 2014 to June 2019. The primary objectives here are: to continue analysis of clinical data and biological samples collected in the first project period; to develop and implement a second phase of collaborative protocols that build upon insights from the first phase and further address the central goals of the network; and to expand the expertise and scientific scope through the integration of new discovery sites.

#### Future MAPP directions

The emphasis will be placed on UCPPS symptom patterns (for example getting worse or better) and corresponding underlying biological changes. The project will further define the (treated) natural history of UCPPS through longer follow-up. It will correlate treatment changes and response with patient phenotype. An emphasis will be placed on identifying clinically relevant UCPPS patient sub-groups and corresponding unique phenotypic profiles; in addition, identifying new therapeutic targets through integrated basic science and in vivo studies of models validated for UCPPS phenotypes. All studies build on observations from first phase efforts and will be designed to address clinically important questions and with the central goal of informing clinical management of UCPPS. Engagement of advocacy groups is also of great importance.

In question time, the IPBF chair asked if more information about the MAPP project and its results could be placed on the MAPP website since many patients as well as professionals are continually asking what is happening, but are unable to find any information. Chris Mullins pointed out that the website was indeed several years out of date but that they would endeavour to place more updates on the website.

J. Quentin Clemens, MD, from the Michigan University Medical Center, who chairs the MAPP Network, then looked at the more medical aspects, noting that patients with urinary tract dysfunction come along to the doctor with symptoms and these may have sensory, motor or structural causes, as follows:

- Sensory (afferent) abnormalities: IC/BPS, CP/CPPS, OAB dry (urgency), orchalgia, chronic epididymitis, vulvodynia.
- Motor (efferent) abnormalities: detrusor failure, urge incontinence/detrusor overactivity, detrusor sphincter dyssynergia.
- Structural abnormalities: stress incontinence, pelvic prolapse, diminished bladder compliance, bladder outlet obstruction.

One of the difficulties is that patients may have multiple different combinations of these problems. Patients present with a spectrum of conditions and rarely correspond exactly to our labels/categories and this should be kept in mind as we study these conditions. The speaker expressed the hope that the MAPP would help to better understand sensory abnormalities by identifying useful, objective clinical tests.

Looking at terminology used in the MAPP, the term Urologic Chronic Pelvic Pain Syndromes (UCPPS) was used in the project to describe idiopathic chronic pelvic pain of urologic origin. In the MAPP Network Studies, this includes:

- Interstitial cystitis/bladder pain syndrome (men or women)
- Chronic prostatitis/chronic pelvic pain syndrome (men)

The term Non-Urologic Associated Syndromes (NUAS) was coined for other conditions that are often associated with UCPPS and the MAPP Network particularly focuses on fibromyalgia, chronic fatigue syndrome and irritable bowel syndrome.

The MAPP Research Network Studies include:

- Trans-MAPP Epidemiology-Phenotyping Protocol

- Additional, integrated Trans-MAPP Studies (e.g. Biomarker Protocol, Neurobiology/Neuroimaging Protocol, Infectious Etiology Protocol)
- UCPPS Animal Models/Translational Science Studies
- Discovery Site-Specific Studies

The inclusion criteria are very broad, quite different from a clinical trial, and these are:

- Diagnosis of IC/BPS or CP/CPPS
- Age 18+
- Standard exclusions

Target was 50% with symptoms less than 2 years.

A unique feature of the MAPP is that there are two control groups: one is completely asymptomatic while the other group (known as positive controls) may have diagnosed fibromyalgia, irritable bowel syndrome or chronic fatigue syndrome.

They found that psychosocial symptoms were similar in UCPPS patients and the “positive” controls with fibromyalgia, IBS and chronic fatigue syndrome.

Non-urollogic associated syndromes were present in 43% of the female patients with UCPPS and 30% of the males. These patients tended to have more severe urologic symptoms, poorer quality of life and more psychosocial symptoms.

Part of the study concerned looking at flares and what might be causing flares. There were more flares in women than in men and flares were associated with more severe UCPPS symptoms.

The MAPP [neuroimaging workgroup](#) has successfully collected multimodal brain imaging data from 293 MAPP Network participants. This had never been done before in the field of chronic pain. Initial analyses of data have yielded novel brain findings which distinguish UCPPS patients from controls and correlate with subjective symptoms. These findings are consistent with alterations in somatosensory, viscerosensory and affective brain regions.

So, to summarise their initial observations, J. Quentin Clemens reported that experimental pain testing and neuroimaging studies have identified objective and reproducible characteristics which distinguish UCPPS patients from individuals without pain. He noted that there is evidence of two significant clinical phenotypes which also correlate with symptom patterns over time: centralized (systemic) and bladder-specific. Focus groups and longitudinal data have provided an improved understanding of characteristics and patterns of symptom flares. And he also reported that the MAPP biomarker studies have identified 15 promising candidate markers for further focused investigation.

The second phase of the MAPP Research Network is hoped to include assessment of symptom patterns and corresponding biologic changes through longer follow-up, evaluation of promising candidate biomarkers, longitudinal neuroimaging and quantitative pain testing, in-depth assessment of treatment response, identification of clinically relevant UCPPS patient sub-groups.

*Note: Since the meeting, two articles on the MAPP project have been published on-line with free access:*

[The MAPP research network: design, patient characterization and operations.](#)

Landis JR, Williams DA, Lucia MS, Clauw DJ, Naliboff BD, Robinson NA, van Bokhoven A, Sutcliffe S, Schaeffer AJ, Rodriguez LV, Mayer EA, Lai HH, Krieger JN, Kreder KJ, Afari N, Andriole GL, Bradley CS, Griffith JW, Klumpp DJ, Hong BA, Lutgendorf SK, Buchwald D, Yang CC, Mackey S, Pontari MA, Hanno P, Kusek JW, Mullins C, Clemens JQ. *BMC Urol.* 2014 Aug 1;14(1):58. [Epub ahead of print]. PMID: 25085119. **Free access:** [click here for provisional text](#)

[The MAPP research network: a novel study of urologic chronic pelvic pain syndromes.](#)

Clemens JQ, Mullins C, Kusek JW, Kirkali Z, Mayer EA, Rodríguez LV, Klumpp DJ, Schaeffer AJ, Kreder KJ, Buchwald D, Andriole GL, Lucia MS, Landis JR, Clauw DJ. *BMC Urol.* 2014 Aug 1;14(1):57. [Epub ahead of print] PMID: 25085007. Free access: [click here for provisional text.](#)

Further information from the MAPP home page: <http://www.mappnetwork.org/> which will hopefully soon be updated.

It may be useful to know that more information can be found on the progress of the MAPP research network in reviews on the website of the AUA 2014 Daily News:

AUA Sunday: [http://www.nxtbook.com/tristar/aua/day2\\_2014/index.php#/0](http://www.nxtbook.com/tristar/aua/day2_2014/index.php#/0)

AUA Monday: [http://www.nxtbook.com/tristar/aua/day3\\_2014/index.php#/0](http://www.nxtbook.com/tristar/aua/day3_2014/index.php#/0)

## **SESSION: HUNNER LESIONS**

This was followed by the start of a session devoted to Hunner Lesions, chaired by Magnus Fall and Jørgen Nordling

Jørgen Nordling introduced this session by describing a patient case which illustrated how vital it is to diagnose and treat Hunner lesions. Unlike many patients without lesions, lesion patients can usually be very successfully treated. Nordling therefore suggested that lesions could be split off from non-lesion disease, even made a confusable disease. He also emphasized that it is essential for the “experts” to pass on their knowledge and teach other urologists how to recognize lesions.

### **ESSIC survey**

Jørgen Nordling then presented results and implications of the ESSIC survey in the form of a questionnaire on Hunner lesions. One aim was to try to discover whether anyone could provide evidence of a non-lesion patient developing lesions at a later stage. Since very little attention has been paid to the lesion patients in the past decades or to drawing a real distinction between the two, we know very little about the disease. This gave rise to a very interactive discussion among attendees and it was clear that a great deal of focused research is urgently needed.

### **Hunner and his ulcers: an historical setting**

*Jane Meijlink, IPBF*

This was the title of an historical presentation, looking at the influences on Guy Hunner, both in America and from Europe, and the background to his work. It is now virtually 100 years since Guy Hunner presented his first paper on a rare type of bladder ulcer in women at a meeting held in Boston on 30 November 1914, and subsequently published it in May 1915 in the Boston Medical and Surgical Journal.

### **Symptom differences between BPS type 3C (Hunner lesion) and non-type BPS 3C**

*Jörgen Quaghebeur, Osteopath DO, Jean-Jacques Wyndaele, MD, Belgium*

This talk presented by Jörgen Quaghebeur was based on non-invasive methods, for example questionnaires. A problem in their literature search was that so many different terms and classifications were used in the different articles that much of the material was unusable. They found that IC and BPS represent a heterogeneous population that presents with a wide variety of symptoms, but seem to have the same cluster of symptoms (Bogart et al 2007), while according to Peeker & Fall 2000, the lesion type appears to differ from non-lesion with regards to symptomatic, endoscopic and histological findings and the response to various forms of treatment. The authors concluded that their literature study did not show symptom differences between lesion and non-lesion IC/BPS, while specific questionnaires indicating subgroup diagnosis were not found and questionnaires did not seem to differentiate subtypes. It was concluded that a great deal of work remains to be done.

### **Physical examination and laboratory tests, markers.**

Jukka Sairanen, MD stressed that a thorough physical examination is an essential tool to exclude any confusable disease. At the present time, cystoscopy is needed to identify the Hunner lesion group. It is not

possible to identify this group purely by physical examination or laboratory tests. Anamnesis is more important than physical findings in his view.

Yr Logadottir, MD then continued on the topic of biomarkers, noting that finding the ideal biomarker requires detailed knowledge of the disease. She discussed nitric oxide as a successful marker for diagnosing Hunner lesion and for evaluating treatment. The problem is that the equipment needed – which is not in itself really so expensive as equipment goes - is not usually available in a urology department. More studies are needed. Interesting for the future in her view: the urothelium and lamina propria; and the connection with autoimmune diseases which could open up new treatment.

### **Endoscopy/cystoscopy.**

Magnus Fall, MD, indubitably the world's most experienced and knowledgeable person in the field of Hunner lesions, addressed this topic, noting that endoscopy/cystoscopy is still the method of choice for diagnosing Hunner lesion. There is enormous variability in reported cases. Some urologists do not see lesions at all, others consider it very rare, while some more experienced urologists have seen it in over 50% of their patients!

Cystoscopy with local anaesthesia can be useful to detect inflammatory changes in the bladder or urethra and any signs of confusable diseases. It is also an opportunity to examine for local tenderness of the vulva, bladder, urethra, prostate and components of the pelvic floor. Can Hunner lesions be detected at plain cystoscopy, he asks? The answer is yes, and pain when touching a lesion can support the diagnosis. However, he emphasizes that cystoscopy and distension are advisable if you are not to miss less distinctive changes. The method of doing this is using general or spinal anaesthesia, with superimposed pressure of 80 cm H<sub>2</sub>O, digital obstruction of leakage, stop filling when no fluid enters (dripping chamber), rinse the bladder and re-examine. He stressed that the rigid cystoscope is still the most useful for this purpose in his opinion. Magnus Fall showed examples of lesions and the many different features that may be encountered in a lesion bladder. However, he emphasized that cystoscopy is often not enough and bladder biopsies should be obtained to confirm the diagnosis of Hunner lesion (ESSIC 3C), but you needed to have a specially trained pathologist.

“The better you describe a disease, the better you understand it”, according to Magnus Fall. Everyone in the audience agreed with this and felt that clear pictures (with explanations) should be recorded in an atlas to help the urologist – and particularly the general urologist – to understand what he/she is looking for.

Tomohiro Ueda, MD from Kyoto, Japan, then explained about the narrow band imaging (NBI) system (already used to diagnose many other disorders) for diagnosis of Hunner lesions which can easily be recognized with NBI. For further information on NBI, see IJU supplement: *Mitsuru Kajiwara, Shougo Inoue, Kanao Kobayashi, Shinya Ohara, Jun Teishima and Akio Matsubara. Therapeutic efficacy of narrow band imaging-assisted transurethral electrocoagulation for ulcer-type interstitial cystitis/painful bladder syndrome. International Journal of Urology (2014) 21 (Suppl 1), 57–60 doi: 10.1111/iju.12350*  
<http://onlinelibrary.wiley.com/doi/10.1111/iju.12350/pdf>.

This was followed by a brief review of the multi-pathology of Hunner lesion and tools for diagnosis, before moving on to the next speaker.

### **Pathology**

Christina Kåbjörn Gustafsson, a pathologist from Gothenburg, Sweden, emphasised that good communication between the urologist and pathologist is essential in this field and that the pathologist can work more successfully if adequate clinical information is provided by the urologist.

Biopsies, she stressed, must be deep, and not superficial, in order to make a successful diagnosis of inflammatory diseases. This is sometimes difficult because the bladder wall may be thin. There are a number of confusable diseases which may resemble each other in the bladder, but which can easily be distinguished by the pathologist. The pathologist can histologically diagnose Hunner lesion and separate this diagnosis from other forms of cystitis with similar clinical symptoms. These may include for example carcinoma in situ, eosinophilic cystitis, tuberculous cystitis, chronic follicular cystitis, cystitis glandularis, squamous cell metaplasia and nephrogenic metaplasia.

In the ensuing discussion, it was evident that even in this expert company there was confusion about lesions and ulcers and that there are many pathologists without the requisite expertise in this field. No other pathologists were present at the meeting.

### **Diagnosis.**

*Chaired by Kristene Whitmore, MD and Andrey Zaitcev, MD*

The first presentation in this session on diagnosis of lesions was a video presentation from Philadelphia, including a demonstration of narrow band imaging (NBI), first under white light and then under NBI light to look for any bladder structural pathology. Typical Hunner lesions are easily seen on NBI. NBI also enhances the contrast between cracks and the normal mucosa and makes identification easier.

According to Kristene Whitmore, MD, one of the problems of diagnosis is that we may not all be talking about the same people. An area of confusion is the differences between standard NIH definitions and ESSIC definitions [and of course East Asian definitions]. We need to understand that there are syndromes and diseases, she said. A syndrome is a complex of concurrent symptoms and signs that is collectively indicative of a disease, dysfunction or disorder. There are several types of pain: nociceptive, somatic, visceral, neuropathic, centrally generated and peripherally generated. There are 9 domains in chronic pelvic pain, so this concerns more than just the lower urinary tract. These include lower urinary tract pain, male genital pain, female genital pain, gastrointestinal pain, musculoskeletal pain, neuropathic pain, a psychological overlay, sexual pain and extra-pelvic comorbidities. She stressed that it is the patient's perception of their pain that plays an important role, affecting how they answer questionnaires and how they respond to therapy.

An in-depth history is essential to see what precipitating or trigger event may have occurred together with a thorough physical examination looking for suprapubic tenderness, tenderness of the bladder, tenderness of the urethra, pelvic floor muscle tenderness and identification of trigger points.

Identification of a Hunner lesion is clinically important because effective treatment is available for the patient. Some urologists have detected it in up to 50% of their IC/BPS patients. Others say that have never seen a lesion.

Cystoscopy with hydrodistension allows for identification and treatment of all potential lesions and is required for definitive diagnosis. Clinical evaluation alone is not reliable in distinguishing between lesion and non-lesion types of IC/BPS.

It was noted that a rigid cystoscope is preferred for adequate biopsies.

Future directions include:

- global definition of IC/BPS to ensure a standardized patient population for universal interpretation of results.
- define phenotypes to aid in the design of study protocols
- prospective studies utilizing validated questionnaires that can capture IC/BPS patient phenotypes
- global definitions of the patient's perception of pain/pressure/discomfort and the potential effect on clinical studies
- increased funding for basic science research to classify organ versus the central nervous system regarding IC/BPS

Andrey Zaitcev, MD from Moscow then described the Hunner lesion and looked at the role of standard cystoscopy without hydrodistension and whether it is possible to detect Hunner lesions during a standard cystoscopy without hydrodistension.

Quoting Magnus Fall, MD: **"The Hunner lesion typically presents as a circumscribed, reddened mucosal area with small vessels radiating towards a central scar, with a fibrin deposit or coagulum attached to this area.** This site ruptures with increasing bladder distension, with petechial oozing of blood from the lesion and the mucosal margins in a waterfall manner. A rather typical, slightly bullous edema develops post-distension with varying peripheral extension." (*Van de Merwe JP, Nordling J, Bouchelouche P, et al. Diagnostic criteria, classification,*

*and nomenclature for painful bladder syndrome/interstitial cystitis: an ESSIC proposal. Eur Urol 2008 Jan;53(1):60-7.)*

The first sentence of this description shows what you can see on office cystoscopy. The speaker emphasized that in office cystoscopy fast inflow and a large volume of irrigation fluid is NOT recommended. In his Moscow practice, they use local anaesthesia, analgesics or NSAIDs. With the cystoscope inserted in the bladder, slow separate inflow of irrigation fluid is performed. At the same time, you start visual inspection in order to detect changes in the bladder surface. There is free inflow of irrigation fluid until the first pain sensation (usually around 100-150cc). When the inflow has stopped, the aspect of the bladder surface is carefully inspected again.

Office cystoscopy with local anaesthesia without hydrodistension can play a supplementary role in the diagnosis and treatment of BPS. Cystoscopy can detect primary objective changes in the bladder and help to define future initial treatment (e.g. conservative therapy or fulguration or triamcinolone injection into the lesions or transurethral resection of the bladder). Symptoms may improve in many patients with HL if the lesions are treated with electrocoagulation/resection, laser coagulation or steroid injection (triamcinolone). Endoscopic electrocoagulation can be greatly assisted by narrow band imaging. Cystoscopy under local anaesthesia can be repeated during treatment to evaluate progress.

*Note: A further detailed description of Hunner lesions can be found on the ESSIC website:*

[http://www.essic.eu/Hunner\\_lesion.html](http://www.essic.eu/Hunner_lesion.html)

Also in the book: *Bladder Pain Syndrome, A Guide for Clinicians*". Edited by J. Nordling, J.J. Wyndaele, J.P. van de Merwe, P. Bouchelouche, M. Cervigni, M. Fall. Published 2013.

### **Treatment and Outcomes.**

*Chaired by Mauro Cervigni, MD and Hikaru Tomoe, MD*

Hikaru Tomoe, MD from Japan provided an overview of treatment for IC/BPS, with lesions and without lesions, including pentosan polysulfate sodium (not used in Japan), amitriptyline, hydroxyzine, cimetidine, suptast tosilate, gabapentin, pregabalin, cyclosporine A, intravesical therapies including DMSO, heparin + lidocaine, lidocaine, heparin, steroid cocktails. Reviewing hyaluronic acid (HA) and alkalized lidocaine (AL), the speaker concluded that intravesical instillation of HA+AL and HA provides both immediate and sustained relief of symptoms in severe IC/BPS (*Lv YS, Zhou HL, Mao HP, Gao R, Wang YD, Xue XY. Intravesical hyaluronic acid and alkalized lidocaine for the treatment of severe painful bladder syndrome/interstitial cystitis. Int Urogynecol J. 2012 Dec;23(12):1715-20. doi: 10.1007/s00192-012-1802-3012-1802-3. Epub 2012 May 11. PMID: 22576327*). She then looked at nerve stimulation, concluding that PTNS improves pain, urinary and QoL scores, although a large multi-centre clinical trial is recommended. However, she noted that there are no data for sacral nerve stimulation.

Mauro Cervigni, MD from Rome then spoke about treatment and outcomes, focusing specifically on Hunner lesion. Looking at PubMed, he said that it was regrettable that most articles on treatment of Hunner ulcers date from around 50 years ago while the term Hunner lesion also produces very little. This means that there is an urgent need to focus on this specific task.

Reviewing the few recent papers, he mentioned for example:

- Logadottir Y, Delbro D, Lindholm C, Fall M, Peeker R. [Inflammation characteristics in bladder pain syndrome ESSIC type 3C/classic interstitial cystitis](#). Int J Urol. 2014 Apr;21 Suppl 1:75-8. doi: 10.1111/iju.12370.
- Rössberger J, Fall M, Gustafsson CK, Peeker R. [Does mast cell density predict the outcome after transurethral resection of Hunner's lesions in patients with type 3C bladder pain syndrome/interstitial cystitis?](#) Scand J Urol Nephrol. 2010 Dec;44(6):433-7. doi: 10.3109/00365599.2010.515613. Epub 2010 Sep 13.
- Quillin R, Erickson DR. [Management of interstitial cystitis/bladder pain syndrome: a urology perspective](#). Urol Clin North Am. 2012 Aug;39(3):389-96. doi: 10.1016/j.ucl.2012.05.007. Epub 2012 Jul 3. Review.
- Soucy F, Grégoire M. [Efficacy of prednisone for severe refractory ulcerative interstitial cystitis](#). J Urol. 2005 Mar;173(3):841-3; discussion 843.

- Cox M, Klutke JJ, Klutke CG. [Assessment of patient outcomes following submucosal injection of triamcinolone for treatment of Hunner's ulcer subtype interstitial cystitis](#). Can J Urol. 2009 Apr;16(2):4536-40.

Also:

- Whitmore et al, presentation at ICICJ/ESSIC joint meeting on Kenalog injections

The AUA Guideline recommends fulguration (laser or electrocautery) or triamcinolone injection into the lesion as 3<sup>rd</sup> line treatment and cyclosporine A (oral), intradetrusor botulinum toxin A and 5<sup>th</sup> line treatments.

Local treatment:

- Hillelsohn JH, Rais-Bahrami S, Friedlander JI, Okhunov Z, Kashan M, Rosen L, Moldwin RM. [Fulguration for Hunner ulcers: long-term clinical outcomes](#). J Urol. 2012 Dec;188(6):2238-41. doi: 10.1016/j.juro.2012.08.013. Epub 2012 Oct 22.

- Peeker R, Aldenborg F, Fall M. [Complete transurethral resection of ulcers in classic interstitial cystitis](#). Int Urogynecol J Pelvic Floor Dysfunct. 2000;11(5):290-5.

- Payne RA, O'Connor RC, Kressin M, Guralnick ML. [Endoscopic ablation of Hunner's lesions in interstitial cystitis patients](#).

Can Urol Assoc J. 2009 Dec;3(6):473-7. [Free PMC Article](#)

- Shanberg AM, Baghdassarian R, Tansey LA. [Treatment of interstitial cystitis with the neodymium-YAG laser](#). J Urol. 1985 Nov;134(5):885-8.

- Kajiwara M, Inoue S, Kobayashi K, Ohara S, Teishima J, Matsubara A. [Therapeutic efficacy of narrow band imaging-assisted transurethral electrocoagulation for ulcer-type interstitial cystitis/painful bladder syndrome](#). Int J Urol. 2014 Apr;21 Suppl 1:57-60. doi: 10.1111/iju.12350.

Surgery

- Rössberger J, Fall M, Jonsson O, Peeker R. [Long-term results of reconstructive surgery in patients with bladder pain syndrome/interstitial cystitis: subtyping is imperative](#). Urology. 2007 Oct;70(4):638-42.

- Peters KM, Jaeger C, Killinger KA, Rosenberg B, Boura JA. [Cystectomy for ulcerative interstitial cystitis: sequelae and patients' perceptions of improvement](#). Urology. 2013 Oct;82(4):829-33. doi: 10.1016/j.urology.2013.06.043.

- Kim HJ, Lee JS, Cho WJ, Lee HS, Lee HN, You HW, Jung W, Lee KS. [Efficacy and safety of augmentation ileocystoplasty combined with supratrigonal cystectomy for the treatment of refractory bladder pain syndrome/interstitial cystitis with Hunner's lesion](#). Int J Urol. 2014 Apr;21 Suppl 1:69-73. doi: 10.1111/iju.12320.

He concluded by mentioning the novel device (LiRIS) shaped like a pretzel which provides continual release of lidocaine intravesically, currently being trialled, and which seems to have promising potential.

### **Epidemiology and natural history of IC/BPS.**

*Chaired by Robert Moldwin, MD*

On the value of epidemiology, the speaker noted that it can provide more evidence for phenotyping and even some insights into pathophysiology. Finding more patients with chronic pelvic pain and bladder pain can lead to more awareness in the community, more political activity, more involvement of the patient organisations, hoping all ultimately leading to more governmental funding and private donations, increased interest and involvement by private industry and venture capitalists, resulting in new devices and pharmaceuticals.

Limitations include retrospective studies, non-population based, non-cohort, non-longitudinal and with a huge amount of selection bias. Part of this is the definition issue, what is IC, what is Hunner lesion etc. There is a very big link between prevalence data and diagnostic criteria, ultimately affecting whether the data has any value at all. In addition, there is a problem with data acquisition, are patients actually filling in their office questionnaires, or are we collecting incorrect data? How is data being retrieved? Is the coding correct? It could be a question of garbage in, garbage out.



A trend today is looking at comorbid or unexplained conditions overlapping in these bladder patients and the whole group of chronic pelvic pain. And while IC/BPS is more common in women, it is apparent today that the prevalence in men is on the increase.

Looking at prevalence studies over the past 50 years, it is clear that they were all carried out on a different basis. A turning point came with the paper:

Hanno PM, Landis JR, Matthews-Cook Y, Kusek J, Nyberg L Jr. [The diagnosis of interstitial cystitis revisited: lessons learned from the National Institutes of Health Interstitial Cystitis Database study.](#) *J Urol.* 1999 Feb;161(2):553-7.

This paper concluded that the NIDDK criteria are too restrictive to be used by clinicians as the diagnostic definition of interstitial cystitis.

It is interesting to note, he said, that most recent studies today are coming from Taiwan.

The speaker also looked at bacterial infection, bacteriuria, which forms a significant problem in clinical practice. He stressed that we need to know how common bacteriuria is in the IC/BPS patient, do bacteria cause symptoms, will eradication of bacteriuria (when present) improve symptoms and could bacteriuria be a “prodromal” phase in the case of some patients?

What do we know (or at least think we know) about the natural history of IC/BPS? In many patients bladder symptoms began in childhood (10-28%). Most patients appear to have a subacute onset of symptoms, often escalating, starting off with one symptoms and progress to many. Comorbid diseases may occur before or after IC/BPS symptoms commence or are diagnosed. There is a high prevalence of antecedent urinary tract infection (18-36%). Symptom flares are common and have a profound impact on the patient’s quality of life.

Where the natural history of Hunner lesions is concerned: we really don’t know very much about this! A lot more population-based, longitudinal studies are urgently needed. For this we need to clearly define a Hunner lesion and standardize diagnostic techniques. Hopefully we will see more about biomarkers for this group. And then there is the big question regarding whether IC/BPS progresses and if so, in whom? There is still lots to learn about the epidemiology and natural history of IC/BPS. This is an evolving field, concluded Robert Moldwin.

## **OPEN PRESENTATIONS AND DISCUSSION OF SUBMITTED ABSTRACTS**

### **A brief review**

#### **Clinical scoring system for bladder pain syndrome - five years’ experience**

*Taneja R, New Delhi, India*

Rajesh Taneja, MD from New Delhi presented a five-year study with 110 patients on a clinically useful scoring system and scale developed for grading and treating Bladder Pain Syndrome. He pointed out that there are flaws in the existing 4-domain scoring system and that bladder pain syndrome is a heterogeneous conglomeration of clinical entities. This presentation described the clinical methodology followed and the clinical outcomes as observed by Taneja.

#### **Mast cell activation syndrome (MCAS): a possible cause of interstitial cystitis**

*Ratner V, Founder and President Emeritus, ICA*

An hypothesis-based presentation on a new role for the mast cell, predominantly based on the hematology and mast cell literature. The author suggests that mast cell degranulation syndrome may play a role in the etiology of BPS/IC.

#### **Possible role of *Corynebacterium* sp. in causing Hunner lesion subtype of bladder pain syndrome/interstitial cystitis (BPS/IC) and results of comprehensive treatment.**

*Loran OB, Sinyakova LA, Kaprelyanc AS, Vinarova NA, Moscow, Russia*

A particularly interesting presentation from Russia concerning a study aimed at elucidating the frequency of the presence of infection in the urine of BPS/IC patients using a new culture and PCR methods. *Corynebacterium* is a genus of gram-positive rod-shaped bacteria. The authors believe that their results raise the possibility of biofilm-forming *Corynebacterium* sp. Involvement in the pathogenesis of BPS/IC and specifically in the Hunner lesion subtype. Further trials are essential.

**The concept of and first experiences with a new, non-invasive tool for diagnosis and follow up of IC/BPS patients**

*Lovasz S, Budapest, Hungary*

The concept of the new diagnostic tool is based on the hypotheses that concentrated urine has an irritative effect on bladder wall, resulting in more frequent urination corresponding with patients' observations. This team in Hungary is seeking partners for a prospective, multicentre clinical trial.

**The role of glomerulations in the diagnostics of BPS/IC**

*Wennevik GE, Meijlink J, Hanno P, Nordling J, Denmark, Netherlands, USA*

From the reviewed literature, the authors found no convincing data material that indicates that glomerulations should be included in diagnostics of BPS/IC, as they did not find that it correlated to symptoms, while glomerulations are frequently seen in patients not suspected of having BPS/IC.

**Intravesical tacrolimus in treatment of interstitial cystitis/painful bladder syndrome: a pilot study**

*Mishra N, Ahmedabad, Gujarat, India*

Immunosuppressants such as cyclosporine have been tried with success, but a limiting factor is side effects. Tacrolimus is similar to cyclosporine in action and also effective in diseases such as rheumatoid arthritis and atopic dermatitis. In this pilot study, tacrolimus has been used intravesically for the first time in patients with severe IC. Larger studies are needed before any conclusions can be drawn.

**Management and follow up of IC/PBS patients from 2001 to 2014**

*Mishra N, Ahmedabad, Gujarat, India*

This Indian study in 239 patients was undertaken to evaluate long-term results in the patients with IC/PBS irrespective of the therapy given.

**Impact of surgical treatment of pelvic organ prolapse on the clinical symptoms of bladder pain syndrome**

*Zaitcev A, Kasyan G, Tupikina N, Ibragimov R, Pushkar D, Moscow, Russia*

Simultaneous surgical correction of POP and BPS might lead to increase of pain and voiding disorders in patients with BPS, especially for mesh-surgery. Further comparative studies with large sample of patients are needed.

**A randomized, open-label, multicentre study of efficacy and safety of intravesical hyaluronic acid and chondroitin sulphate (HA 1.6% and CS 2%) vs dimethyl sulfoxide (DMSO 50%) in women with Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC)**

*Cervigni M, Sommariva M, Porru D, Ostardo E, Tenaglia R, Giammò A, Pappagallo G. Italy.*

Glycosaminoglycans (GAGs) instillation therapy is an important therapeutic approach to BPS/IC for ameliorating or delaying recurrence of symptoms, restoring GAGs concentration into the damaged bladder. The aim of this study was to evaluate the efficacy and safety of intravesical instillations with high concentration HA 1.6% and CS 2.0% (Ialuri<sup>®</sup>, IBSA) versus DMSO 50% (RIMSO-50<sup>®</sup>, Bioniche) in female patients with diagnosis of BPS/IC based on ESSIC criteria, experiencing pain (pelvic pressure or discomfort) and at least one other urinary symptom (i.e. urgency or frequency) for at least 6 months.

**Examining prolapsed repair on IC symptoms**

*Ginzburg N, Morrissey D, O'Hare P, Whitmore K. Philadelphia, USA*

The authors found that prolapse surgery is reasonable in patients with IC/BPS. Symptoms that are stabilized prior to surgery are not exacerbated by pelvic floor surgery with dermis graft, some symptoms may improve in some cases Warrants future study with a prospective, randomized, controlled trial

**Patients with bladder mucosal cracks: who are they and can they benefit from corticosteroid treatment?**

*Morrissey D, El-Khawand D, O'Hare P III, Ginzburg N, Whitmore K. Philadelphia, USA*

The purpose of this study was to define the patient with interstitial cystitis who has bladder mucosal cracks and to evaluate the effectiveness of treating bladder mucosal cracks with submucosal corticosteroid injections. The authors concluded that data for bladder mucosal cracks do not mirror data for Hunner's lesions and the phenotypic difference between these two lesions remains to be determined

### **Symptom differences between BPS type 3C and non-type 3C BPS**

*Quaghebeur J, Wyndaele JJ*

The diagnosis and prevalence of symptoms in patients with interstitial cystitis remains a challenge. Furthermore, the difference in symptoms between lesion disease (ESSIC type 3C) and bladder pain syndrome (BPS) is unclear. In this study, the literature did not indicate specific questionnaires able to show symptom differences between lesion and non-lesion IC/BPS. The authors suggest that the ESSIC guideline should be used to differentiate between lesions and non-lesions. Questionnaires do not seem to differentiate between subtypes.

### **Sunday 15 June**

#### **Patient Organizations Session**

The second day of the meeting opened with a session presented by patient organizations, chaired by Vicki Ratner, MD.

#### **Interstitial Cystitis Association: 30 years of action.**

*Vicki Ratner Founder and President Emeritus, ICA*

Over thirty years ago, IC was barely mentioned in the standard urologic textbooks. It was frequently reported as a psychosomatic condition in elderly women. We have come a long way as evidenced by many things, including this meeting. While many have contributed to the understanding and treatment of IC, the Interstitial Cystitis Association of America (ICA) has been a major contributor to the advancement and anchoring of this disease in the medical community and the public.

#### **A view from the USA.**

*Lee Bryan Claassen, ICA Executive Director*

The ICA provides advocacy, research funding and education to ensure early diagnosis and optimal care for those affected by IC. The ICA empowers patients with knowledge and hope, provides phone, email and online support. In the field of research, it provides novel research projects with initial grants to obtain preliminary data needed to pursue larger grants. Importantly, the ICA participates in steering committee meetings of the MAPP Research Network.

#### **A view from Europe.**

##### **Interstitial cystitis as a public health priority**

*Loredana Nasta, President AICI Italy and National Rare Diseases Federation Past President*

The aim of this questionnaire-based study was to evaluate the current situation in health care systems among different European countries in which a National IC/BPS Association is present. The European Commission policy is stressing that all EU Member States should ensure homogeneous health care, especially for less advantaged countries, promoting cross-border care, and identifying High Expertise Centres for different diseases. We believe that a strong network among: a) patient organizations representatives, b) ESSIC as an Expert organization and c) Eurordis which deals with governance at EU level, may respond to the needs of patients in terms of dissemination, awareness, information, research, diagnosis and access to all treatments available in Europe and in the world.

#### **Meeting of working groups**

Working groups on different themes related to Hunner lesion then met for discussion, led by subcommittee chairs. One of these working groups was patient organization led. This was followed by preliminary presentations by each working group. It is hoped that all working group findings will be included in an article for publication.

#### **Next year in Rome!**

At the end of the meeting, Jørgen Nordling announced that the 2015 annual meeting of ESSIC would be held in Rome in September.

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