

# A review of the 22<sup>nd</sup> Annual Congress of the European Association of Urology, 21-24 March 2007, Berlin, Germany



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*Although late March, the weather was nevertheless wintry with sleet and snow falling as delegates descended on Berlin for the 22<sup>nd</sup> Annual congress of the European Association of Urology.*

*Held at the Berlin Messe, it was attended by a record number of 12,500 delegates from 113 countries around the world, making this a leading global urology congress.*

## **IPBF booth**

Although there have been IC information booths at the EAU congress since 2000, there are nevertheless many doctors and nurses every year still seeking practical and up-to-date information for themselves or for their patients that they are apparently not receiving adequately elsewhere in their professional training, update courses or local conferences. Furthermore, for most clinicians IC takes second or third place to other more common urologic conditions such as prostate cancer, and the focus this year at the EAU congress was very much on oncology. However, we see very clearly that doctors who have even just one single IC patient are today seeking the best possible solutions for that patient.



## **Great need for treatment information**

As expected, many people – doctors and pharmaceutical representatives – stopped by the booth to discuss the problem of terminology and definitions. While there was no enthusiasm for a change of name, the right definition was considered to be more important. But what the doctors wanted most of all was detailed information on treatment options. There is a lack of information for doctors on all treatment that could be used, the most likely reason for this being that much of the treatment used for IC patients consists of non-evidence-based, off-label use of drugs. There is continued frustration about the unavailability and/or unaffordability of treatments and about what they should do with patients who fail to respond to any of the available treatments. There is also increasing interest in and awareness of associated disorders, particularly IC and irritable bowel syndrome symptoms.



One problem in developing countries, and particularly in Eastern Europe, is that many doctors do not yet have either email or easy access to the internet. This makes it even more important for IC organizations to distribute documentation at urology congresses such as the EAU.

A need was expressed for support groups and/or websites for patients with information in their own language. The IPBF has been asked to lend a hand in several different countries.

Urology nurses are increasingly involved in the treatment and care of IC patients and are seeking information not only on the medical aspects of the disease but also on the impact of IC on the patient. As we saw from the ICS 2006 conference in New Zealand, physiotherapists are also increasingly involved with IC patients.

Regarding the name painful bladder syndrome, French doctors informed us that in France they are currently discussing a different translation (at present this is *syndrome douloureux de la vessie*) and looking for an alternative to “*douloureux*” which they do not feel provides an adequate description of the often severe pain in PBS/IC patients.

### **IPBF survey questionnaire study launched**

The IPBF launched its survey questionnaire for urologists and gynaecologists treating IC patients during EAU 2007 and has decided to extend the survey period to the end of the year so as to include other international conferences, since it is already clear that it will provide valuable insight into the situation per country if we can succeed in getting sufficient responses. While doctors are very fond of asking their patients to fill in complex voiding charts and lengthy questionnaires, they are not so keen on doing it themselves!

### **EAU scientific programme:**

The great advantage of modern technology is that much of the EAU scientific programme can now be enjoyed online at home:

#### **- Webcasts**

ESU courses held during EAU 2007 can be followed online at:

<http://webcasts.prous.com/EAU2007> along with many plenary sessions. Please note that these webcasts will be accessible all year long.

#### **- UroSource**

More information on the EAU congress including interviews can be found on the new independent website UroSource at [www.urosources.com](http://www.urosources.com). This is an online service especially created to facilitate the retrieval and distribution of specialized medical information, events and related activities relevant to urologists. UroSource is an extensive database filled with scientific articles, fact sheets, key article reports, meetings and congress reports, abstracts and related urological literature. Future medical training is expected to exploit the use of online or internet-based databases and urologists will be able to benefit from an electronic-based information retrieval system. The new UroSource website will also serve as a focal point where urologists can quickly exchange information.

### **PBS/IC Course**

**ESU Course 5: Chronic pelvic pain syndromes (CPPS) with special focus on chronic prostatitis (CP) and painful bladder syndrome/interstitial cystitis (PBS/IC), chaired by Professor J.-J. Wyndaele from Antwerp with speakers J.L. Ruiz-Cerda from Valencia and B. Lobel from Rennes.**

This course on several different chronic pelvic pain syndromes was an opportunity to see differences and similarities between the different disorders and learn about the

neuropsychological background to all these conditions.

Professor J.-J. Wyndaele gave a superlative general introduction on anatomy, pathophysiology, confusable diseases and chronicity with an emphasis on the neuropsychological aspects. Neuropsychology is a difficult and complex topic, but Professor Wyndaele has the gift of reducing this to simple terms and making it palatable and digestible. He explained that the pelvic organs come from the same embryologic structures, have a close anatomic position, share some striated muscles and partly use the same innervation. Since all nerves are closely located, they may interact. The filling grade of one organ influences sensation in another. For example, if the bowel is full, sensation in the bladder may be different, and vice versa.

Both pain and emotion are controlled in the limbic system and are closely interrelated. Pain and sensations travel up and down between the organs and the brain. However, Professor Wyndaele emphasized that if this pain process continues for more than six months, the innervation of the body may change. This is one important reason why pain should not be allowed to continue too long untreated. Furthermore, it appears that pain in one organ can build up and spread to neighbouring organs and tissues. Knowledge in this field is growing rapidly, is fascinating to follow, but also essential in order to understand the mechanism of treatment for pain.



#### *International Confusion continues in the IC world...*

In his presentation on PBS/IC, Professor Wyndaele explained that the IC world is still faced with International Confusion and that it may take some time to reach agreement! The International Continence Society's definition of Painful Bladder Syndrome is: "The complaint of suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and night-time frequency, in the absence of proven urinary infection or other obvious pathology". The definition of interstitial cystitis by the European Society for the Study of IC/PBS (ESSIC) in its consensus report of the ESSIC meeting in Baden 2005 was as follows: "Interstitial cystitis is a disease of unknown origin consisting of the complaint of suprapubic pain related to bladder filling, accompanied by other symptoms, such as increased daytime (>8x) and night-time (>1x) frequency, and with cystoscopic (glomerulations and/or Hunner's lesions) and/or histological features (mononuclear inflammatory cells including mast cell infiltration and granulation tissue) in the absence of infection or other pathology." Prevalence is between 60-400 per 100,000 population according to the literature, with IC probably being under-diagnosed in men, according to Professor Wyndaele. He emphasized that the quality of life of patients is greatly disturbed by this disorder. Diagnosis is a combination of symptoms, signs, cystoscopy and biopsy plus the exclusion of other pathology and confusable diseases. In his review of treatment (see webcast for details), he emphasized that IC patients need psychological support from the doctor treating them. Patient-patient counseling via the support groups can also play a valuable role. Selfcare consists of stress reduction, adaptation of food/drink and bladder re-education. He advised re-assessing patients after some years to check that no other condition has been missed. He concluded by saying that a lot of research is still needed. This presentation with its useful slides with the most up-to-date information can be followed, like the entire course, on the EAU2007 Berlin webcasts.

#### *Urethral pain syndrome*

This was followed by presentations on other pain syndrome locations with a special focus on scrotal pain syndrome and urethral pain syndrome given by Dr J.L. Ruiz-Cerda. Urethral (pain) syndrome



has tended to disappear from sight in recent years since these patients have often been added to the IC patient group, despite the fact that many never develop symptoms in the bladder. It is still beset with unknown factors and Dr Ruiz-Cerda explained that there is no uniform definition, no readily available diagnostic marker, no known etiology, uncertain pathophysiology, no standardized methodology and no uniformity in the size of populations studied and demographics. In the past these women were often “diagnosed” as hysterical and psychosomatic. With regard to etiology, there are infection theories, including Chlamydia, and a theory that it could be an early form of interstitial cystitis since it appears to have the same dysfunctional epithelium as IC. Diagnosis is based on symptoms and exclusion. The symptoms may or may not be intermittent, with urgency and frequency, persistent urethral and/or pelvic pain and 59% of patients have pain with sexual intercourse. Dr Ruiz-Cerda emphasized that while the etiology remains unclear, it may be neuropathic pain without a specific stimulus. Knowing functional neuroanatomy is very important. Treatment should primarily be conservative such as antidepressants and anticonvulsants, and surgery avoided if possible.

### **ESU Course 20 on Neurourology**

Course 20 on Neurourology chaired by Professor P van Kerrebroeck provided a valuable update on this subject. For more information, see also webcasts and [www.urosource.com](http://www.urosource.com). In his introduction summary, Professor van Kerrebroeck explains that control of the lower urinary tract processes of storage and voiding, several brain regions, various levels of the spinal cord, smooth musculature of the bladder, bladder neck and urethra as well as striated muscles of the external sphincter and the pelvic floor are involved. The neurological integration and coordination of all these events occur in the rostral pons in an area known as the pontine micturition centre. He adds that nearly every neurological disease can cause lower urinary tract dysfunction.

In order to have any understanding of the chronic pelvic pain syndromes and their treatment, it is now essential to keep up-to-date with this complex material and its continual developments.

### **Posters and abstracts**

The abstracts can all be read online via the UroSource website. Go to [www.UroSource.com](http://www.UroSource.com) and on the right-hand side of the screen select Databases: Abstracts. This produces a search engine to search according to various criteria.

### **Urothelium: more than a barrier**

Abstracts 56-70

The number of posters and abstracts in this section are an indication of the large amount of research being done into many different aspects of the urothelium including into bladder sensation. It is to be hoped that this will eventually shed more light on urgency and pain and lead to improved treatment. Abstracts 61, 62 and 63 looked into TRPV (transient receptor potential vanilloid) 1 and 4. TRPV1 was found to be upregulated following inflammation.

### **Botulinum toxin**

Botulinum toxin A is currently being trialed for use in many different bladder disorders where it can produce major beneficial effects and was a major topic at this EAU congress.

The large number of abstracts on studies with botulinum toxin included several on botox and PBS/IC patients. While nobody fully understands exactly how botox acts, botox could theoretically have antinociceptive effects when injected into the bladder wall, according to Professor Dirk De Ridder from Leuven, Belgium. However the role of botox in IC remains to be evaluated.

It is impossible to compare the different studies since the different groups of researchers were using different dilutions and different injection techniques, sometimes changing halfway through the same study. It was clear at the EAU congress that studies with botox are a learning curve, leading to continual changes in techniques. It was emphasized that botox for PBS/IC patients is still very experimental.

These abstracts and poster presentations triggered a discussion on botox causing retention in patients. According to a British study for overactive bladder (abstract 727), the frequency of incomplete bladder emptying and the need to perform intermittent self catheterization following treatment varies in the reported literature and can be as high as 45%. IPBF chairman Jane Meijlink said that since retention in a PBS/IC bladder is exceedingly painful and patients may develop retention when at home and a long way from medical facilities, they should be instructed on self-catheterisation before taking part in a study and given catheters to take home. The researchers for a British-based study said that this is already written into the British protocol, but it was apparent from discussions during the poster session that it is not included in all protocols in other countries and centres conducting botox trials with IC patients.

It was suggested by the researchers that injecting into the bladder neck and trigone only, avoiding the side walls, in IC patients would lead to lower risk of retention. When the whole bladder is injected, this can lead to major retention problems. Differences were also noted between injecting into the smooth muscle versus striated muscle. It was emphasized that the site and dosage are likely to be the key to success in IC.

Abstract 895

**Intravesical passive delivery of botulinum A toxin in patients affected by painful bladder syndrome: A pilot study.**

*A. Giannantoni, E. Costantini, S.M. Di Stasi, E. Mearini, F. Santaniello, A. Vianello, M. Porena.*

In this study, Botox A was administered intravesically as an instillation, not by injection. Unfortunately, due to the molecular weight, botox A could not penetrate intact epithelium to reach the sub-urothelial nerves involved in bladder pain transmission. It was thought that the lack of efficacy might have been due to an inadequate dose and/or no pre-instillation use of substances aimed at increasing permeability of the urothelium.

Abstract 901

**Treatment of interstitial cystitis with botulinum toxin type A.**

*Carl S, Grosse J, Laschke S.*

This was a two-centre pilot study to analyse the effectiveness of botox A in 29 IC patients diagnosed in accordance with NIDDK criteria. The results of this study suggested that botox A may have an antinociceptive effect on bladder afferent pathways in patients with IC and showed an improvement in symptoms in 83% (24 out of 29) of patients. They largely avoided retention by changing the dilution and only injecting submucosally into the bladder neck and trigone. Only one patient had urinary retention.

Abstract 902

**Intravesical botulinum toxin type A in interstitial cystitis.**

*Ramsay A, Small D, Conn G.*

These researchers from Glasgow suggest that there is increasing evidence to support the hypothesis of neurogenic inflammation. It is thought that this process activates bladder afferent nerves and provokes bladder pain and a hypersensitive bladder.

The 11 female patients in this study were diagnosed with IC according to NIDDK criteria. The patients in this study were kept in hospital overnight with an indwelling catheter and were only allowed to go home after voiding normally. However, some of these patients did subsequently suffer retention.

The results indicated that botox A appears to provide relief from symptoms in IC and is potentially a treatment option for patients who have failed to respond to conservative treatment. Further work is needed in a randomized controlled trial with more patients.

**EMDA and PBS/IC**

Abstract 726

**Our experience of endovesical electromotive drug administration in females with PBS/IC.**

*Pushkar D, Zaicev A, Korsunskaya I, Kosko JW.*

257 patients were included in this Russian study with endovesical electromotive drug administration using various preparations. Patients were divided into three groups according to bladder capacity measured as voiding volume. There was a significant reduction in symptoms. It was concluded that EMDA provides a rapid effect and is well tolerated. The treatment can be repeated to prolong the therapeutic effect. The authors feel that administration of the drug directly to the submucosal bladder layer in PBS/IC patients is an important part of the treatment.

**Prevalence**

Abstract 583

**The prevalence of symptoms related to interstitial cystitis in apparently healthy women.**

*Wehrberger C, Ponholzer A, Marzalak M, Berger I, Temml C, Madersbacher S.*

The aim of this study was to determine the prevalence of IC symptoms in an urban female population, to study their impact on quality of life and sexual function and to identify correlates for IC-symptoms using a validated questionnaire. 981 women participated in the study, aged 19 to 89 years. The authors concluded that the prevalence of IC-symptoms is higher than previously estimated and these symptoms substantially affect quality of life and sexuality. An article has already been published (March 2007 European Urology) on this study. PMID: 16979286.

**Nitric Oxide (NO)**

Abstract 584

**Nitric oxide synthase expression in patients with interstitial cystitis.**

*Renstrom Koskela L, Thiel T, Ehren I, De Verdier PJ, Wiklund NP.*

The purpose of this study was to analyse endogenous NO formation and NO-synthase (NOS) gene expression in the urinary bladder of 6 patients with interstitial cystitis and 8 control patients and to obtain further knowledge of the localisation of inducible NOS (iNOS) within the bladder mucosa. It was concluded that the increased levels of endogenously formed NO in IC patients corresponds to increased iNOS mRNA expression and protein levels in these

patients. iNOS was shown to be located both in the urothelium and in macrophages in IC patients.

### **Quality of life following treatment**

Abstract 585

#### **Quality of life in patients with interstitial cystitis/painful bladder syndrome after treatment with DMSO, BCG, Cyclosporine and Pentosan Polysulfate Sodium.**

*Sairanen J, Leppilahti M, Tammela T, Ruutu M, FinnIC Study Group.*

The aim of this study was to evaluate the quality of life in relation to responses to different types of treatment in two clinical trials using a 30-item questionnaire. 164 patients took part. It was concluded that this questionnaire can be used to evaluate quality of life in PBS/IC patients and that treatment had a clear effect on QoL. CyA therapy had more impact on QoL than DMSO, PPS or BCG therapy, correlating with the clinical results of these different treatments.

### **History of urology**

Abstract 145

#### **Urine, the liquid white gold.**

*Rao A, Omar A, Karim O, Motiwala H, Das S.*

If you enjoy historical texts, this is the one for you. The term “urology” literally means the study of urine. And urine has been used from prehistoric times to the present day for a variety of medical and other applications, sometimes quite bizarre. While Aztecs recommended the use of urine for stomach complaints, urine has recently been used to rehydrate US army food packets. Other uses of urine have included: to produce gunpowder, cure tobacco, dyeing, tanning, cheese making, tattooing, hair shampoo, skin conditioner, antiseptic, mouthwash, pain killer and many other weird and wonderful applications.

### **EAU guidelines 2007 edition**

The 2007 edition of the EAU Guidelines is now available and was distributed at the EAU conference. The guidelines include Chronic Pelvic Pain which can be found at

[http://www.uroweb.org/fileadmin/user\\_upload/Guidelines/22\\_Chronic\\_Pelvic\\_Pain\\_2007.pdf](http://www.uroweb.org/fileadmin/user_upload/Guidelines/22_Chronic_Pelvic_Pain_2007.pdf)

The terminology problems in the field of PBS/IC are evident here too with differing nomenclature being used in different parts of the text of the complete guidelines and different again in the useful pocket guidelines.

### **Grateful thanks to sponsors**

Since the International Painful Bladder Foundation is a voluntary, non-profit organization, it is most grateful to its sponsors for helping us to organize a booth at this important congress. Many thanks to the Medtronic Foundation and Bioniche Pharma for their continued financial support which enables us to continue our international work for the PBS/IC patients.

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