International Painful Bladder Foundation

The IPBF is a voluntary non-profit organization focused on
interstitial cystitis/bladder pain syndrome/hypersensitive bladder/Hunner lesion
https://www.painful-bladder.org/

IPBF e-Newsletter
Issue 67, June 2024

An IPBF update for patient support groups, healthcare professionals and friends around the world in the field of interstitial cystitis, bladder pain syndrome, Hunner lesion, hypersensitive bladder, inflammatory bladder, chronic pelvic pain and associated disorders.

This issue of the IPBF e-Newsletter includes the following topics:

- Upcoming 5th ICICJ, Kyoto, Japan 21-23 August 2024
- Conference reviews: AUA 2024, EAU 2024
- Book Review ERN eUrogen *Rare and Complex Urology*
- Complementary & Alternative Medicine
- Super Strength Aloe Vera now available in Europe
- ERN eUrogen webinar ketamine-induced uropathy
- IC/BPS Patients resident in Australia invited to apply for participation in clinical study
- Upcoming events
- Donations & Sponsoring

UPCOMING 5TH ICICJ, KYOTO, JAPAN 21-23 AUGUST 2024

A top meeting this year for the IC/BPS world will be the conference devoted to IC/BPS to be held in Kyoto, Japan. This will be the 5th International Consultation on Interstitial Cystitis, Japan (ICICJ) and will be held jointly with the International Society for the Study of Bladder Pain Syndrome (ESSIC) 2024. It will take place from Wednesday 21 August to Friday 23 August 2024 in Kyoto.
Information in English about the upcoming conference can be obtained at:
https://icicj.jp/meeting/2024/index_en.html
This conference will be hybrid with both in-person and online attendance. Prior registration is essential. The registration form can be found at: https://icicj2024.secretari.jp/registration/

Venue:	Kyoto Hotel Okura. Oike, Kawara-machi, Nakagyo-ku, Kyoto-shi, Japan Direct connection by Subway Tozai Line "Kyoto Shiyakusho-mae" Station Phone: +81(75) 211-5111 (main) https://www.hotel.kyoto.e.adw.hp.transer.com/okura
Theme:	"Diagnosis and Treatment of Bladder-Centric IC Including Hunner lesion" "AINAFHIC-Based Cystoscopic Diagnosis and New ESSIC Guideline"
Organized by:	International Consultation on Interstitial Cystitis, Japan (ICICJ) International Society for the Study of Interstitial Cystitis (ESSIC) Society of Interstitial Cystitis of Japan (SICJ)
Sponsored by:	Japanese Urological Association (JUA)

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CONFERENCE REVIEWS

REVIEW OF THE AMERICAN UROLOGICAL ASSOCIATION (https://www.auanet.org/) ANNUAL SCIENTIFIC MEETING, 3-6 MAY 2024, SAN ANTONIO, USA

In these difficult times, many people around the world are unable to travel long distances to conferences. This year's AUA annual scientific meeting offered a welcome solution with their excellent on-demand selection for those unable to attend in person. The 2024 programme once again included a selection of sessions on IC/BPS and related topics.

In **PD25: Infections/Inflammation/Cystic Disease of the Genitourinary Tract: Interstitial Cystitis poster and abstract session**, Namugosa et al discussed small fibre polyneuropathy in IC/BPS as an important feature of the non-Hunner lesion phenotype. There were two presentations on oral Pentosan Polysulfate Sodium (PPS) and potential ocular adverse effects which led to a lively pro/con discussion! A paper from Southampton, United Kingdom presented a study on the use of manuka and medical honey extract intravesically as an anti-inflammatory agent while another group looked at betulinic acid as a potential anti-inflammatory/healing agent for IC/BPS patients. Raymond Xu and colleagues reported on two bladder-centric phenotypic subgroups within IC/BPS patients with low bladder capacity, noting that IC/BPS may represent multiple different conditions. These were just a few of the abstracts and we hope to see full publications before too long.

The **Instructional course (049IC) on Emerging Concepts in Interstitial Cystitis/Bladder Pain Syndrome** was led by USA IC/BPS experts Quentin Clemens, Henry Lai and Leonore Ackerman who reviewed the recent updates to the AUA Guidelines and their impact on patient management, looked at the NIDDK MAPP research findings, discussed the importance of identifying patients with Hunner lesions and how the treatment approach differs for these patients, summarized the ocular complications that have been associated with pentosan polysulfate sodium and the Food and Drug Administration (FDA) recommendations for this issue, and discussed emerging data about the microbiome and other molecular diagnostic techniques in identifying potential infectious etiologies for IC/BPS.

On the difficult topic of nomenclature which nobody seems to be able to agree on, it was noted that IC is the term in the USA that is recognised for disability benefits, medical insurance etc in healthcare/electronic systems and it would cause big problems for patients if this term were lost. So it has been decided to use IC/BPS (with "IC" at the front) in the USA. The lack of consensus regarding terminology is a worldwide problem for patients, clinicians and researchers.

While cystoscopy is not mandatory in the USA, it was emphasized that it is important to ensure Hunner lesions are diagnosed because they need a different treatment approach to the non-lesion disease. The current USA approach, where cystoscopy is not mandatory, differs from other parts of the world where a cystoscopy may be either "mandatory" or "strongly recommended" for all patients suspected of having IC/BPS.

It is critical to rule out other conditions which may have similar symptoms, the so-called confusable diseases and disorders. Furthermore, if treatments fail to bring about any improvement, the diagnosis should be reconsidered and new checks carried out for a potential confusable disorder, including urological, gynaecological, gastro-intestinal, pelvic floor, infection etc.

A change in the AUA IC/BPS guideline means that the former tiered approach to treatment has gone. Bearing in mind that every patient is different and that there is no "one size fits all" treatment for IC/BPS, initial treatment depends on the symptoms and severity of the individual patient and also on clinical phenotyping/subtyping.

Shared-decision-making plays an important role in the choice of treatment today. The risks and benefits of a specific treatment, and what alternatives there are, should be discussed, focusing on outcomes that are important to the patient. The aim of treatment should be to improve the patient's daily functioning and quality of life.

Clinicians should counsel patients who are considering oral PPS on the potential risk for macular damage and vision-related injuries (new guideline statement). Symptoms of retinal pigmentary maculopathy that may be associated with oral PPS use in some patients include difficulty reading, slow adjustment to low or reduced light environments and blurred vision. While the prevalence is unknown, it varies widely in oral PPS users but appears to be related to the cumulative PPS exposure. The visual changes may be irreversible even after discontinuation of PPS.

This was followed by a presentation about the urinary microbiome by L. Ackermann emphasizing that fungi should not be forgotten when talking about infection and that little is still known about this.

REVIEW OF THE EUROPEAN ASSOCIATION OF UROLOGY (https://uroweb.org/) ANNUAL CONGRESS, 5-8 APRIL 2024, PARIS, FRANCE

While the EAU annual congress scientific programme tends to have a large focus on oncology, IC/BPS was not forgotten. IC/BPS expert Robert Moldwin, MD, from the USA gave the SUFU (Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction) lecture at the meeting of the EAU Section of Functional Urology (ESFU) with a presentation entitled **"Therapeutic Approaches to IC/BPS"**. He noted that following guideline algorithms does not always get the results you were hoping for in your individual patients. This is the big conundrum we have been faced with in the past few years, he explained. We need better phenotyping, to identify the most bothersome complaint, to take a look at urinary symptoms versus pain. Listen to the patients and what they are actually complaining of. Above all, don't forget that IC/BPS comprises pain plus urinary symptoms. While one patient may find the pain the worst symptom, another may find that the urgency/frequency and lack of sleep has by far the worst impact on their quality of life. Identify and treat co-existing pain generators. Consider adverse effects of medication (cognitive, ophthalmic). Involve ophthalmic specialists when treating with oral PPS. He too stressed that the former tiered approach to treatment – starting with conservative therapy – should be discarded. If a patient comes with incapacitating symptoms, you may need to start with more advanced, aggressive levels of therapy. Treatment should be individualised and based on symptom severity. Looking at the pain aspect, he discussed bladder-centric pain versus non-bladder centric/widespread pain. Management of IC/BPS patients should be multimodal and multidisciplinary.

The **ESU course on chronic pelvic pain practical guidelines for diagnosis and treatment** was divided into separate sections for men and women. Pedro Abreu-Mendes, MD, from Portugal discussed the EAU guideline on chronic pelvic pain in men & women, looking at pain versus nociception, primary versus secondary syndromes and pain chronification.

He took a look at ICD-11 (World Health Organization International Classification of Diseases 11th Revision) in which chronic pain is now an entity or disease in itself. Chronic secondary pain is pain as a result of a well-known disease. Chronic primary pain is pain as a disease in its own right, such as chronic primary bladder pain syndrome or chronic primary pelvic pain syndrome. The EAU now uses the term Primary Bladder Pain Syndrome/Interstitial Cystitis. Pain is the key symptom in the EAU guideline. This pain syndrome concept (originating from the International Association for the Study of Pain (IASP)) considers these diseases to be pain-predominant syndromes with the urinary symptoms in IC/BPS sadly sidelined. However, patients who are constantly looking for toilets and out of bed multiple times

in the night due to urinary symptoms are not likely to be too happy about this approach, since pain treatment does not automatically relieve these urinary symptoms.
Quoting the ESSIC Hunner lesion paper of 2020 (Fall M. et al), the speaker noted that some experts are now of the opinion that Hunner lesion disease and non-lesion IC/BPS are likely to be two different diseases.

In the **ERN eUrogen Patient Advocacy Group (EPAG) session**, IC/BPS patient advocate Anna De Santis from Italy spoke on "When Pain Invades the Mind" in which she emphasized that IC/BPS patients' symptoms may consist of pelvic pain plus a need to urinate up to 60 times per day (day and night) with painful urgency. There is a lack of options for pain management for these patients, leading to an overwhelming sense of helplessness and desperation. Despite the significant impact of IC/BPS on patients' lives, research in this field has always received limited attention and funds. This has resulted in a shortage of innovative treatments and options.

Patient Day: Roundtable #3: Inflammatory Bladder Disorders

This session chaired by Dick A. W. Janssen, MD, from the Netherlands covered three inflammatory bladder topics: IC/BPS, radiation cystitis and ketamine cystitis. Both included either presentations or recorded interviews with patients. There are many of these inflammatory bladder conditions. They are sufficiently common for every urologist to see one from time to time, but not sufficiently common to attract any real attention in the urology world. Other than for IC/BPS, there have so far been no global guidelines for the inflammatory bladder disorders category (NB a guideline is currently under development within ERN eUrogen) and this means that diagnosis and treatment tends to be unstructured, resulting in a lack of clarity.

IC/BPS:

The **IC/BPS patient perspective** was presented by Anna de Santis, a member of the Italian AICI patient support group, who spoke about a patient's care pathway experience from diagnosis to deciding on treatment. The key symptoms are: pain (pelvic, suprapubic, perineal, urethral, vulvar, anal, scrotal, muscles and nerves), urgency & frequency and dyspareunia. These symptoms can be extremely debilitating and can make patients suicidal. It is often misdiagnosed. In Italy IC has been recognised as a rare disease, providing patients with free medical care. Prevalence in Italy is around 1.9 per 100,000 inhabitants. Many doctors do not know about it or do not believe it even exists. Patient support groups play an invaluable role.

Dick Janssen, MD, focused on how to deal with different subtypes of IC/BPS, with/without Hunner lesion and with/without inflammation (ESSIC types 1 & 2). With regard to diagnosis, he noted that IC/BPS is still a symptom complex and all confusable diseases or disorders need to be thoroughly excluded. Cystoscopy is strongly recommended for all patients and, if indicated, biopsy. While there has been more focus in the past decade on stratification into subtypes, he stressed that many clinical trials may have failed because subtyping was not adequately addressed. In the past decade it has been claimed by many that IC/BPS without Hunner lesion disease is not inflammatory. The speaker emphasized that he does not agree with this. There is a poor correlation between what we see in cystoscopy and biopsy, he said. No apparent damage does not necessarily rule out a leaky urothelium. We may be missing this. Inflammatory infiltrates may nevertheless be found in the biopsy. He mentioned a very useful study in this field: *Geurts N, Van Dyck J, Wyndaele JJ. Bladder pain syndrome: do the different morphological and cystoscopic features correlate? Scand J Urol Nephrol. 2011 Feb;45(1):20-3. doi: 10.3109/00365599.2010.519346. Epub 2010 Sep 17. PMID: 20846081.*

He concluded that without biopsy, we are not fully able to:

- Determine who has local inflammatory disease
- Who has urothelial dysfunction/damage
- Who might benefit from local therapy (oral/intravesical GAG therapy, other than anti-inflammatory drugs).

Studies have shown that 93% of patients do have inflammatory infiltrate!

Finally, no Hunner lesion does not mean no inflammation!

Radiation-induced cystitis:

Marko Koivuneva, Board Member of Europa Uomo and chairman of the Prostate Cancer Foundation Board in Finland, shared his very moving experience as a patient who developed radiation cystitis following unsuccessful surgery for prostate cancer followed by external radiation therapy. This radiotherapy has caused regular bladder bleeding, which is sometimes so extensive as to require hospitalisation and blood transfusion. He knows that he may ultimately need cystectomy. One possible treatment is hyperbaric oxygen therapy but this is not yet available in Finland, other than in private clinics.

Lotta Renström Koskela, MD, from Sweden, explained that radiation cystitis is an inflammation of the urinary bladder that occurs after radiotherapy to the pelvic area. It causes a significant impact on quality of life and the evidence on how to treat radiation cystitis is low. It may occur during radiotherapy and last for several weeks, but can also occur later, even up to 20 years after radiotherapy. There are different grades of severity. In severe cases, the bladder may become fibrotic and contracted and in some cases cause obstruction of the upper urinary tract with hydronephrosis and renal failure. Ulcers and fistulas may develop. Symptoms include urgency, frequency, dysuria and haematuria. This is a patient group with great suffering. Treatment is based on symptoms and severity of symptoms. Intravesical treatment with hyaluronic acid and/or chondroitin sulfate can be used, also hyperbaric oxygen therapy. Cystectomy may be necessary for severe, intractable cases.

Ketamine-induced cystitis: Effects & Addiction. Wouter van der Sanden, MD, from the Netherlands explained that ketamine is a very strong painkiller and dissociative anaesthetic, first used in the Vietnam war. In the late 90s, medical use shifted to the party scene and then things started to go radically wrong. It is mainly used as a party drug for its hallucinogenic effects. It is cheap and – erroneously - believed to be safe. This talk included a video presentation by a patient Juul and her mother describing the terrible effect on her bladder after Juul became addicted to street ketamine. Although she is now “clean”, her bladder has been irreparably damaged. Patients can end up with cystectomy, kidney transplants and can even die from it. The so-called safe image of street ketamine is a complete fallacy. It is a growing problem in Europe. Abstinence is crucial but difficult since it is highly addictive.

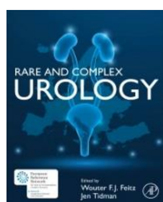
Further reading: The EAU patient information section has fact sheets for radiation cystitis and ketamine cystitis, with an overview of inflammatory bladder disorders in the pipeline.

For those with an interest in ketamine uropathy, a useful open access paper has just been published: *Belal M, Downey A, Doherty R, Ali A, Hashim H, Kozan A, Kujawa M, Pakzad M, Rashid T, Osman N, Sahai A, Biers S; BAUS Section of Female, Neurological and Urodynamic Urology. British Association of Urological Surgeons Consensus statements on the management of ketamine uropathy. BJU Int. 2024 May 22. doi: 10.1111/bju.16404. Epub ahead of print. PMID: 38778743.*
https://bjui-journals.onlinelibrary.wiley.com/doi/full/10.1111/bju.16404?campaign=woleartyview

ERN eUROGEN WEBINAR – KETAMINE-INDUCED UROPATHY
Wednesday 12 June, 18:00 CEST

This webinar on uropathy with an inflammatory bladder induced by addiction to street ketamine will be presented by Michel Wyndaele, urologist at the University Medical Center Utrecht in the Netherlands, and Wouter van der Sanden, urologist at Jeroen Bosch Hospital in Den Bosch, the Netherlands, and a PhD candidate on Ketamine Induced Uropathy. As the recreational use and abuse of ketamine is increasing worldwide, the prevalence of ketamine induced uropathy is increasing rapidly as well.
Ketamine-induced uropathy is an inflammatory bladder disorder with specific characteristics among the challenging young addicted patient population, including the devastating reinforcing cycle of induced pain leading to increased ketamine use to suppress the pain, again inducing more damage to the urinary tract. Patients present with debilitating lower urinary tract symptoms and (upper and lower) urinary tract dysfunction, which may become irreversible and eventually lead to the necessity for urinary tract reconstruction, which has a lifelong impact.
In this webinar, the speakers will present an overview of the epidemiology, clinical presentation, pathophysiology, diagnostic assessment, and treatment of ketamine induced uropathy to raise awareness of this fast-growing health problem and provide insights specific to ketamine induced uropathy.
Registration link: click here.

BOOK REVIEW



Rare and Complex Urology has been produced by the European Reference Network (ERN) for rare urogenital diseases and complex conditions, ERN eUROGEN. This book combines information on network developments and clinical and surgical aspects, allowing for better diagnoses, treatments, and patient outcomes. Areas covered include interstitial cystitis/bladder pain syndrome.

Chapter 19 – Bladder pain syndrome/Interstitial cystitis (BPS/IC). Mariangela Mancini, Dick Janssen, Alessandro Morlacco, Enrico Ammirati, Alessandro Giammo. This chapter can be ordered separately.
Further information: https://eurogen-ern.eu/ern-eurogen-book-launched-on-rare-disease-day-2024/

COMPLEMENTARY & ALTERNATIVE MEDICINE (CAM)

Complementary & Alternative Medicine (CAM) represents a group of therapies not considered to be conventional medicine. If a non-conventional approach is used together with conventional medicine, it is described as "complementary." If a non-mainstream approach is used instead of conventional medicine, it is described as "alternative." When combined with conventional healthcare, the term integrative care is used. (See: NIH National Center for Complementary and Integrative Health https://www.nccih.nih.gov/health/complementary-alternative-or-integrative-health-whats-in-a-name)

SUPER STRENGTH ALOE VERA (DESERT HARVEST) NOW AVAILABLE IN EUROPE

An example of CAM is Super Strength Aloe Vera (SSAV). Aloe vera extract is a traditional herbal medicine, believed to have antimicrobial, anti-inflammatory and immunomodulating properties. The U.S. Food and Drug Administration has approved a study by Wake Forest University to explore the

efficacy of supplement manufacturer Desert Harvest's Super Strength Aloe Vera (SSAV) capsules in reducing symptoms associated with IC/BPS. This will be the first double-blind, placebo-controlled study that specifically addresses safety and efficacy as primary endpoints in patients with IC/BPS. Aloe vera has been shown in previous studies and a survey to have the potential to reduce bladder pain, urinary frequency and urinary urgency in IC/BPS.

Super Strength Aloe Vera is now available in Europe. Customers from the European Union should contact www.deserthavesteurope.com. Those in the United Kingdom should contact www.pelvicrelief.co.uk. For all other countries, contact www.deserthavest.com.

IC/BPS PATIENTS RESIDENT IN AUSTRALIA INVITED TO APPLY FOR PARTICIPATION IN CLINICAL STUDY

Glycologix, Inc. is currently conducting an **Australian only clinical research study** evaluating the effect of GLX-100 Bladder Instillate, a new and novel glycosaminoglycan (GAG) replenishment therapy designed to temporarily coat the inner lining of the bladder for the treatment of interstitial cystitis/bladder pain syndrome (IC/BPS). This is a phase 1b, open-label, single arm study being conducted at multiple centres in Australia. The study involves 12 clinic visits over approximately 18 weeks and will include standard catheterisations to administer GLX-100 Bladder Instillate. Investigator sites are located in **Sydney, Melbourne, Newcastle, and the Gold Coast.**

Eligibility criteria include:
Females aged > 18 diagnosed with IC/BPS with symptoms for the prior ≥ 6 months, with prior cystoscopy and no known Hunner's lesions; been on unchanged oral medication for IC/BPS for at least 3 months; had no more than 3 UTI's over the last 12 months; and not been treated with pentosan polysulfate, intravesical treatment or hydrodistension for IC/PBS within 1 month prior to treatment, or Botox injections for IC/PBS within 6 months prior to treatment.
For more information, please send an email inquiry to info@glycologix.com

UPCOMING EVENTS

EULAR EUROPEAN CONGRESS OF RHEUMATOLOGY

12-15 June 2024 at the Messe Wien Congress Center, Vienna, Austria.
EULAR provides excellent background information for the rheumatic comorbidities of IC/BPS.

IASP 2024 WORLD CONGRESS ON PAIN

This congress is organised by the International Association for the Study of Pain (IASP) during IASP's 50th Anniversary year.
5-9 August 2024, Amsterdam RAI, Amsterdam, Netherlands
https://www.iasp-pain.org

5TH ICICJ AND ESSIC 2024, KYOTO, JAPAN 21-23 AUGUST 2024

Kyoto, Japan. Wednesday 21 August to Friday 23 August 2024.
5TH International Consultation on Interstitial Cystitis,
held jointly with the Annual Meeting of the International Society for the Study of IC/BPS (ESSIC) 2024.
This will be a hybrid meeting.

GIBS 2024 - 9TH ANNUAL CONGRESS ON IC/BPS

24-25 August 2024, New Delhi
Theme: "Containing the Bladder Blaze"

ICS 2024 – 54th MEETING OF THE INTERNATIONAL CONTINENCE SOCIETY
23-25 October, IFEMA, Madrid, Spain

DONATIONS AND SPONSORING

The voluntary, non-profit IPBF is entirely dependent on sponsoring and donations to be able to continue to carry out its international advocacy, projects and newsletters. In these difficult economic times, it is not easy for us to keep going and ensure continuity. All donations to our international work, however small, will be most gratefully received. The IPBF has fiscal charity status in the Netherlands. If you are thinking of making a donation, please go to this link for bank details: https://painful-bladder.org/donations/

We would like to take this opportunity of thanking our donors for their greatly appreciated support in the past year for our foundation, projects, patient advocacy, website and newsletters.

THE BOARD - INTERNATIONAL PAINFUL BLADDER FOUNDATION (IPBF)

The International Painful Bladder Foundation does not engage in the practice of medicine. It is not a medical authority nor does it claim to have medical knowledge. Information provided in IPBF emails, newsletters, patient information and website is not medical advice. The IPBF recommends patients to consult their own physician before undergoing any course of treatment or medication. While the IPBF endeavours to ensure that all information it provides is correct and accurate, it does not accept any liability for errors or inaccuracies.

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