W3: Creating a circle for IC/BPS: Combining animal models and clinical data and artificial intelligence to improve patient management

Workshop Chair: Francisco Miranda Rodrigues Cruz, Portugal
17 September 2025 09:00 - 10:30

Start	End	Topic	Speakers
09:00	09:05	Introduction	Francisco Miranda Rodrigues Cruz
09:05	09:20	Choosing the model to study IC/BPS	Ana Charrua
09:20	09:25	Discussion	Ana Charrua
09:25	09:40	How do biomarkers and pathways translate back to the clinic	Dick A.W. Janssen
09:40	09:45	Discussion	Dick A.W. Janssen
09:45	10:00	Current treatment options in IC/BPS	Naside Mangir
10:00	10:05	Discussion	Naside Mangir
10:05	10:20	How can we introduce artificial intelligence for IC/BPS	Guldal Inal Gultekin
10:20	10:25	Discussion	Guldal Inal Gultekin
10:25	10:30	General discussion and take-home message	Francisco Miranda Rodrigues Cruz Ana Charrua Dick A.W. Janssen Naside Mangir Guldal Inal Gultekin

Description

Chair Prof. Francisco CRUZ - Introduction:

IC/BPS is one of the few unmet needs in the area of lower urinary tract pathology. On one side, IC/BPS is a diagnosis of exclusion since no pathognomonic symptoms, signs, or biomarkers exist to swiftly establish a firm diagnosis. On the other side, IC/BPS has no cure yet. Most treatments that try to replenish the urothelial glycosaminoglycan layer or decrease bladder inflammation are far from showing generalized effectiveness, leaving most of the time clinicians with the necessity of combating pain and bothersome lower urinary tract symptoms. Although assumed as relevant, the identification of subgroups of patients that might respond better to a particular treatment has not been fully explored. Facing this scenario, it is clear that translational research, identifying key unmet needs, and making smart use of animal models to test relevant questions will play an important role. In addition, bioinformatics methods are ready to gather clinical and experimental information to be used in the future diagnosis and treatment of IC/BPS.

Speaker 1 – Ana Charrua, PhD

Choosing the model to study IC/BPS
The evolution of concepts around IC/BPS led to the use of a multiplicity of IC/BPS models. The IC/BPS models began to replicate bladder centric aspects of IC/BPS, to find new treatments and biomarkers. In addition, non bladder centric models are gaining importance due to the frequent systemic symptomatology referred to by patients.
Key learning point 1 - Choosing the model to study IC/BPS
The most commonly used bladder centric models are the animal models of cyclophosphamide- and lipopolysaccharide-induced cystitis, which are used to replicate macroscopic (such as bladder wall lesions) and/or microscopic (such as inflammatory cell infiltration) bladder changes and study their implications for the appearance of urinary bladder disruption. In vitro models, such as urothelial cell cultures, have also been used.
The most recently used complex animal models consider that IC/BPS symptoms surpass those exclusively related to the urinary bladder. The stress models have gained special attention as, besides pain, they replicate systemic changes observed in IC/BPS patients, such as alterations in the hypothalamic-pituitary-adrenal axis (as is the case with the maternal deprivation models - MDM) or changes in the autonomic nervous system (as is the case with the MDM and the water avoidance stress model).
The advantages of each model will be listed, taking particular interest in the characteristics that replicate the systemic changes, such as those observed in the central nervous system of IC/BPS patients. Also, some of the critical points in each model will be emphasized. Suggestions for the models' improvement/refinement will be presented, taking into consideration the recent advances in the field.
The advantages and disadvantages of the in vitro and in vivo models will be discussed with the attendees.
Key learning point 2 - Methodologies to assess pain and other behaviors in animal models
To study pain-like behaviour in animals, there are a set of induced and spontaneous tests available. However, most of these tests were developed to evaluate the effects of analgesic drugs on the pain-like behaviour of non-visceral/pelvic animal models. Which of those tests can be used to study IC/BPS? What are the possible refinements these tests need to be used in visceral/pelvic animal models? Is there room for international standard operating procedures? How can animal models be used

to study changes in social interaction shown by patients? A list of tests available to study them will be presented, going from simple observation to more complex cognitive tests. Factors that influence test replicability and reproducibility will be discussed with the attendees. Also, the advantages and disadvantages of performing automated home cage analysis will be addressed.

Speaker 2 – Dick Jansen, MD PhD

UPDATE ON IC/BPS BIOMARKERS:
How do biomarkers and pathways translate back to the clinic
Discussion on what is currently known on the pathophysiology of IC/BPS from a fundamental and clinical science perspective. The aim is to develop a better understanding of the underlying molecular mechanisms of IC/BPS by discussing molecular pathways.
IC/BPS is a clinical diagnosis and currently consists of a heterogenous group of patients with different pathophysiological profiles. This is reflected in differences in responses to treatment amongst IC/BPS patients and the lack of molecular biomarker tests available for clinical diagnosis. This diversity has to be taken into account when using preclinical models for research. The stratification of IC/BPS subgroups has been improved with the ESSIC criteria, but this is mainly done by cystoscopy and pathological evaluation of biopsy specimens. There are currently two types with bladder wall centric inflammatory characteristics, as well as one non-inflammatory type with normal bladder wall characteristics on cystoscopy. A more refined stratification using biomarker profiling is needed to improve targeted therapy and, therefore, treatment success rates. The diagnosis of Hunner´s lesion and non-Hunner´s lesion subtypes is improving. Using RNA sequencing, microbiome sequencing, and protein identification techniques, we are increasingly capable of detecting the pathways affecting different IC/BPS patients. However, challenges remain. Finding the correct in vivo model representing the specific clinical IC/BPS features and pathophysiology is key. As far as is currently known, only cats show a similar Hunner´s lesion type disease comparable to human IC/BPS and using cats for experimental research is problematic. Therefore, the current strategy relies on models that focus on bladder centric problems representing epithelial dysfunction and inflammation and other models with a focus on more systemic problems relating to neuroinflammation and peripheral and central pain pathways.
Key learning point 1 - Genes and proteins that are known for IC/BPS and how they are representative of the molecular pathways that lead to pathology.
For the most appropriate translational model, we can and have learned from pathway analyses from genetic fishing and other experiments on human samples, and these can be translated into biomarkers such as nitric oxide pathways, anti-proliferative factor, cytokines, substance P pathways, neurotrophins, and urothelial barrier molecules. These are our quality controls to show we can mimic these pathways in our preclinically applied in vitro and in vivo models to investigate novel treatments, but these biomarkers should also translate back and lead to improvements in clinical diagnosis and treatment outcomes.
This part of the workshop will focus on the IC/BPS associated pathways and biomarkers derived from preclinical studies and how they translate to clinical IC/BPS characteristics.
Key learning point 2 - Learning about strategies to implement biomarkers into clinical practice to improve stratification and healthcare in IC/BPS?
The main goal of this section is to give a current overview of where we stand regarding biomarkers and pathways and the research strategies to actually translate these into clinical practice.

Speaker 3 – Naşide MANGIR, MD, PhD

Current treatment options for IC/BPS: Management and Treatment Guidelines
Treatment is highly individualized, recognizing that no single therapy is universally effective. Approaches are categorized into non-pharmacologic, pharmacologic, procedural, and surgical options. Shared decision-making between clinicians and patients is emphasized, especially in balancing symptom management with treatment risks.
1. Behavioral and Non-Pharmacologic Approaches
- Education: Patients should be informed about bladder function, the variability of treatment effectiveness, and the need for multiple therapeutic trials. Managing expectations is crucial, as symptom flares are common even with treatment.
- Lifestyle Modifications: Dietary changes (e.g., avoiding bladder irritants like caffeine or acidic foods) and maintaining adequate hydration can help reduce symptoms.
- Stress Management: Stress is a known trigger for symptom exacerbation. Techniques like mindfulness, relaxation training, and coping strategies are encouraged.
- Physical Therapy: For patients with pelvic floor tenderness, manual physical therapy can alleviate symptoms by targeting muscle contractures or trigger points. Pelvic floor strengthening exercises (e.g., Kegels) should be avoided as they can worsen symptoms.
2. Pharmacologic Therapies
- Pain Management: Analgesics, including acetaminophen, NSAIDs, and, in some cases, opioids, may be prescribed for pain relief. These should follow principles used for chronic pain management.
- Oral Medications: Medications like amitriptyline, cimetidine, hydroxyzine, and pentosan polysulfate (PPS) are options, though their efficacy varies. Patients considering PPS should be warned about the risk of macular damage. Cyclosporine A may be used for patients with Hunner lesions unresponsive to other treatments.

- Intravesical Instillations: Bladder instillations of dimethyl sulfoxide (DMSO), heparin, or lidocaine are offered as localized treatments.

3. Procedural Options

- Cystoscopy with Hydrodistension: A diagnostic and therapeutic option, hydrodistension can help some patients by increasing bladder capacity and relieving symptoms.
- Treatment of Hunner Lesions: Patients with these lesions should receive targeted therapies, including fulguration (laser or electrocautery) and, or triamcinolone injections.
- Botulinum Toxin Injections: Intradetrusor injections of onabotulinumtoxin A may benefit patients who fail other treatments but come with risks such as requiring intermittent self-catheterization.
- Neuromodulation**: Nerve stimulation techniques, including implantable neurostimulation devices, are considered for refractory cases.

4. Surgical Interventions

Surgery is reserved for severe, refractory cases where all other treatments fail. Options include: substitution cystoplasty (bladder augmentation), urinary diversion with or without bladder removal (cystectomy). These procedures are invasive and carry significant risks but may be necessary for patients with end-stage bladder disease.

5. Treatments to Avoid

Long-term antibiotics, intravesical bacillus Calmette-Guérin (BCG), and systemic glucocorticoids lack efficacy and may cause harm. High-pressure, long-duration hydrodistension is also discouraged due to its adverse effects.

Key learning point 1 – Current treatment alternative and updates and discuss reasons for the lag of basic science translation into actual clinical usage.

Key learning point 2 – Treatment should be multimodal whenever necessary

Take home messages

The main goal of this section is to give a current overview of treatment options and where we stand regarding biomarkers and pathways usage in treatment of IC/BPS. The attendees will get an overview of on the difficulties of transferring basic science results into actual clinical usage.

Speaker 4 - Güldal Inal Gültekin, PhD

How can we introduce artificial intelligence for IC/BPS

A key area of collaborative work in IC/BPS research is in the field of computational biology. Studies producing massive amounts of publicly available OMICS data can be re-analyzed using various methods and statistical approaches. The addition of clinical data, such as imaging, pathology, laboratory results, pain levels, etc., will enable even more accurate estimations for disease predictions. Thus, computer-based tools can increase the chance of discovering putative biomarkers for IC/BPS. Once the disease can be 'accurately' diagnosed using artificial intelligence, specific biomarkers can be proposed as targets for treatment. The main purpose of this part of the workshop will be to propose and discuss the potential utility of and AI approaches to potentiate the discovery of novel biomarkers and therapy targets for IC/BPS. As well as discuss the limitations related to the availability (lack of patient registries) and use of clinical data under the current regulations.

Key learning point 1 – Assessing artificial intelligence for IC/BPS and evaluating data repositories

Artificial intelligence and machine learning are computer tools and software that learn from combined layers of high-throughput data. With the growing use of AI in medical research, it is possible to develop algorithms that address complex diseases such as IC/BPS at multiple levels instead of analysing pooled gene expression data.

AI models are trained on data, and these models require a large amount of high-quality data for better stratification of patient groups. The data sources include descriptive data, clinical and laboratory data, genetic data such as gene expressions, environmental data such as diet and lifestyle, and bladder and brain imaging data. With the proper grouping of the ‘features’ and repetitive simulations, AI tools can learn to ‘effectively and accurately’ predict disease status. The importance of the completeness of ‘IC/BPS data’ for AI analysis and the differences between bioinformatics and AI will be discussed. The overall consequence of effective biomarker acquisition through bioinformatics and AI research will pave the way for a successful diagnosis of disease by minimally invasive means. Following a brief introduction to the notions of bioinformatics and AI, this part of the workshop will discuss the benefits and expansions that computerised approaches will provide for IC/BPS research.

<u>Aims of Workshop</u>

This workshop aims:

- Discuss the in vitro and in vivo models used to study IC/BPS, and the limits of how they mimic the disease.
- To discuss how chronic pain and other symptoms may be evaluated in the IC/BPS animal models.
- To discuss current molecular pathways and biomarkers for IC/BPS subtypes.
- To discuss the current treatment options for IC/BPS
- To discuss the necessity bioinformatic tools and artificial intelligence to study IC/BPS
- To understand some basic notions of computational analysis

Educational Objectives

Since its first definition in the late 17th century, there have been no major advancements in the treatment of IC/BPS. This could be partly explained by the lack of an organized, multidisciplinary, and multinational effort to understand disease mechanisms and underlying pathophysiological pathways.
The science of bioinformatics and artificial intelligence can offer unique opportunities in processing clinical data that can facilitate understanding of underlying pathologies.
There have also been recent studies on developing improved experimental models that can replicate pathophysiological pathways in IC/BPS in humans.
This course will gather clinicians and scientists from different disciplines to take a snapshot of the current clinical status of IC/BPS treatment and define the available trends in artificial intelligence and translational medicine. The potential contribution of findings of computational science and bioinformatics will be explored by a multidisciplinary group of researchers. Developments in search for a more representative source of experimental models will be explored.

Learning Objectives

1. At the end of the workshop the attendees will know the available models of IC/BPS and choose among them those that mimic specific IC/BPS problems.
2. At the end of the workshop the attendees will understand where translational research is needed to fill unmet needs in the fields of diagnosis and treatment.
3. At the end of the workshop the attendees will acquire basic notions of computational analysis and will recognize the importance of bioinformatic tools in IC/BPS basic and clinical research.

Target Audience

Urology, Urogynaecology and Female & Functional Urology, Bowel Dysfunction, Pure and Applied Science

Advanced/Basic

Basic

Suggested Learning before Workshop Attendance

- Clemens JQ, Erickson DR, Varela NP, Lai HH. Diagnosis and treatment of interstitial cystitis/bladder pain syndrome. J Urol. 2022;208(1):34-42.
- Nunez-Badinez et al. Preclinical models of endometriosis and interstitial cystitis/bladder pain syndrome: an Innovative Medicines Initiative-PainCare initiative to improve their value for translational research in pelvic pain. Pain. 2021;162(9):2349-2365.
- Inal-Gultekin G, Gormez Z, Mangir N. Defining Molecular Treatment Targets for Bladder Pain Syndrome/Interstitial Cystitis: Uncovering Adhesion Molecules. Front Pharmacol. 2022;13:780855.
- Neuhaus J, Berndt-Paetz M, Gonsior A. Biomarkers in the Light of the Etiopathology of IC/BPS. Diagnostics (Basel). 2021;11(12):2231.
- Akiyama Y, Luo Y, Hanno PM, Maeda D, Homma Y. Interstitial cystitis/bladder pain syndrome: The evolving landscape, animal models and future perspectives. Int J Urol. 2020 Jun;27(6):491-503.
- Ueda T, Hanno PM, Saito R, Meijlink JM, Yoshimura N. Current Understanding and Future Perspectives of Interstitial Cystitis/Bladder Pain Syndrome. Int Neurourol J. 2021 Jun;25(2):99-110.
- Kalkan H, Akkaya UM, Inal-Gültekin G, Sanchez-Perez AM. Prediction of Alzheimer's Disease by a Novel Image-Based Representation of Gene Expression. Genes (Basel). 2022 Aug 8;13(8):1406.
- Inal-Gültekin G, Çetin Z, Mangir N. Exploring Drug Repurposing for Interstitial Cystitis/Bladder Pain Syndrome: Defining Novel Therapeutic Targets. Neurourol Urodyn. 2024 Dec 26. doi: 10.1002/nau.25651. Epub ahead of print. PMID: 39723619.