

# A review of the **INTERNATIONAL MEETING ON UROGENITAL PAIN**

## **Update on Urogenital Pain: Current Issues and Controversies**

**15-16 August 2008, Glasgow, Scotland.**

A 2-day satellite symposium was held 15-16 August 2008 at the Glasgow Marriott Hotel, Scotland, organised by the PUGO (Pain of Urological Origin), one of the special interest groups (SIGs) of the International Association for the Study of Pain ([www.iasp-pain.org](http://www.iasp-pain.org)), prior to the start of the 12<sup>th</sup> World Congress on Pain.

Attended by a broad spectrum of specialists from the pain world (neurologists, pain consultants, anaesthesiologists, neurosurgeons, urologists, gynaecologists, internists, physiotherapists and psychologists) and also by patient representatives including IPBF chair Jane Meijlink, the purpose of this most interesting meeting was to consider the past, present and future of urogenital pain, to outline current practice and to take a look at what the future may hold. Much attention was paid here to interstitial cystitis, chronic prostatitis, endometriosis, pudendal neuralgia and other associated pelvic pain disorders. This proved to be a unique opportunity to view pelvic pain from all possible angles.

Each session was followed by interesting, fruitful and certainly very lively interactive discussions, with the patient representatives actively participating. The following review looks at a few highlights of this unique meeting with speakers from North America and Europe.

Following an introduction by organizers Andrew Baranowski, MD and John Hughes, MD, the meeting began with a session on Past, Present and Future with **Curtis Nickel**, MD, urologist from Canada, kicking off with a lively presentation on “Urologic Chronic Pelvic Pain Syndromes (UCPPS): Great hypotheses ruined by good science,” in which he reviewed the history of treatment hypotheses in recent years for both interstitial cystitis (IC) and chronic prostatitis (CP). Many of the treatments for IC initially looked very promising, even spectacular, but later proved to be effective in only a few patients. Several hundred million dollars were spent on scientific research, but failed to produce good results for treatment. In order to overcome this problem, in the immediate future diagnosis and treatment will depend on phenotyping. He emphasized that these conditions do not have a homogenous etiology and that some treatments work well for some patients and not at all for others. “We need to phenotypically categorize our patients with UCPPS and use phenotypically directed therapy”, he said. In the future, clinical trials will appropriately select patient phenotypes with the greatest chance of therapeutic success. The new strategy he put forward was to try to identify “initiators”, ameliorate the pain, deal with the pelvic consequences and work on cognitive modulators so as to deal with the patient’s depression and sense of helplessness and frustration. His suggestion was that progress in the patient from acute event to a chronic condition was based on an

initiator leading to inflammation with/without tissue damage. This may then lead in some patients to a urologic chronic pelvic pain syndrome which may develop into a regional pain syndrome and/or a systemic (pain) syndrome.

**Fred Howard**, MD, gynaecologist from the University of Rochester, USA, then reviewed the disorders most commonly associated with chronic pelvic pain:

*Gastrointestinal tract diagnoses*

- *irritable bowel syndrome*

*Urinary tract diagnoses*

- *interstitial cystitis*

*Reproductive tract diagnoses*

- *endometriosis*
- *pelvic congestion syndrome*
- *pelvic inflammatory disease*

*Musculoskeletal tract diagnoses*

- *myofascial pain syndrome*

*Uncertain origin*

- *chronic pelvic pain syndrome*

For the sake of clarity, Dr Howard provided definitions of the term syndrome versus disease:

1. *A set of symptoms that occur together; the sum of signs of any morbid state; a symptom complex;*

2. *A set of signs and symptoms that occur together characteristically in a particular medical situation for which the cause is not known.*

*- When a cause is discovered, the syndrome becomes a disease.*

*(source: Dorland's and Stedman's)*

His presentation focused on endometriosis, emphasizing that not all endometriosis is painful but that nobody knows what percentage of the patients have chronic pelvic pain. The three basic symptoms are: dysmenorrhoea (painful menstrual periods), dyspareunia (pain with intercourse) and chronic pelvic pain. Endometriosis is not a syndrome as such, he explained, since it is diagnosed on the basis of histologic findings from tissue samples. It is still a mystery, he said, why the pain can continue even when the lesions have been surgically removed.

**Thibault Riant**, MD, from the University Hospital of Nantes in France, well-known worldwide for its unique work in the field of pudendal nerve entrapment (PNE), spoke on models of delivering care for UGP – Pudendal Neuralgia. The Nantes team (JJ Labat, M Bensignor, R Robert and M Guerineau) began working in the field of pudendal neuralgia 25 years ago. Dr Riant joined the multidisciplinary team 4 years ago.

In 2007, the Nantes team published the so-called Nantes Criteria, clinical criteria for the diagnosis of pudendal neuralgia caused by pudendal nerve entrapment. (JJ Labat, Riant T, Robert R, Amerenco G, Lefaucheur JP, Rigaud J. *Diagnostic criteria for pudendal neuralgia by pudendal nerve entrapment (Nantes criteria)*. *Neurourol Urodyn*. 2008;27(4):306-10).

The essential criteria were summarized by Dr Riant as follows:

- Pain in the anatomical sensory area that is supplied by the pudendal nerve (from the anus to the penis or clitoris);
- Pain never causes patients to wake in the night;
- Pain worsens when patient is sitting;
- No objective sensory loss is found on clinical examination;
- An immediate decrease in pain is required following a pudendal nerve anaesthetic block.

The absence of one of these criteria excludes the diagnosis of PNE. Their presence leads to a reasonable hope of a positive prognosis: it has been demonstrated by a retrospective study with a surgical cohort of patients under 70 years old that 70% of them presenting with all the main criteria improved after surgical treatment. However, only 30% improved if one of these criteria was missing. Age is also an important prognostic factor and the success rate decreases after the age of 70.

Dr Riant noted that complementary criteria can provide additional arguments in favour of a diagnosis of pudendal neuralgia and that these include:

- Pain spreading from the pudendal sensory area (burning, stabbing, electric shock type pain, also paresthesia)
- Pain following defecation or ejaculation
- Painful bladder
- Fibromyalgia
- Irritable bowel Syndrome
- Pelvic myofascial syndrome
- Truncated sciatica
- Obturator or cluneal neuralgias
- Thoraco-lumbar spinal disorders leading to inguino-scrotal or labial pain.

Common points in these patients according to Dr Riant are: a burning sensation, increased sensitivity using the KCI test, mast cell activation, urethral hypertonia, tension of the pelvic floor muscles.

The diagnosis of pudendal nerve entrapment is essentially clinical. There are no specific signs for this condition. If the pudendal nerve does not appear to be entrapped, other possibilities are the cluneal or obturator nerves.

Exclusion criteria include pain that is exclusively coccygeal, gluteal, pubic or hypogastric, also pruritus which causes not only tingling/ burning but also itching with a need to scratch. Pudendal neuralgia does not cause a need to scratch.

Management: A multi-disciplinary team is needed for the assessment and treatment of perineal neuralgia. The aim is to increase the patient's quality of life. Anaesthetic nerve blocks are used for both diagnosis and therapy. Medical treatment involves the use of neuropathic pain drugs, other treatment may involve neurostimulation including S2 Transcutaneous electrical nerve stimulations (TENS), physical therapy, psycho-social approach, hypnosis, surgery. A new experimental form of treatment for refractory patients is modulation in the brain consisting of radicular, medullary and cortical stimulation. Dr Riant emphasized that above all patients need support and should not be considered psychiatric patients: their pain stems from the perineal area and is not psychosomatic.

**Maria Adele Giamberardino**, MD, from the department of Medicine and Science of Aging, University of Chieti, Italy, discussed “Chronic pain syndromes in the pelvic area: the role of viscerovisceral hyperalgesia (VVH)” which occurs between different internal organs sharing part of the sensory innervation, with specific reference to urinary calculosis, dysmenorrhoea/endometriosis and irritable bowel syndrome and their inter-relationships. Dr Giamberardino also described the effects of treatment of one painful condition on typical symptoms of the other as shown in studies. She explained that when a patient complains of pain coming from one visceral organ in the pelvic area, the physician should always take into account the possibility that the symptoms reported are augmented/modulated by a condition affecting another organ.

**John Loeser**, MD, neurosurgeon and anaesthesiologist from Seattle, had the audience spellbound with his presentation on “Pains without Pathology”. He described how, as medical knowledge gradually increased in the past, there was always a group of diseases which defied explanation because the pathology for these disorders had not yet been discovered. However, when they couldn’t find an identifiable cause, doctors had the tendency to say it was “all in the mind”, and many of the terms they invented were distinctly pejorative. Indeed an entire field of medicine grew up to explain symptoms without cause, namely psychiatry and psychoanalysis. Unexplainable diseases in adulthood were ascribed to early childhood experiences. A whole range of conflicting explanations evolved for symptoms in many chronic pain patients: structural or physiological pathology, mental process beginning in infancy, or environmentally induced factors that occur in adult life.

Modern imaging of brain function has made it clear that the brain is the organ of behaviour and confirms the important principle when dealing with these patients: all pain is real. Dr Loeser emphasized that we should remain alert to the possibility that hidden pathology could explain a disease that has no apparent pathology. Think for example of gastric ulcer disease and the discovery of *heliobacter*. He suggested that functional alterations in peripheral nerves, innervated tissues and the central nervous system are most likely to be responsible for pains without pathology. Evidence is mounting, he said, for changes in the central nervous system as being important factors in the development and perpetuation of chronic pain.

He concluded by stressing that patients who have pain without pathology are just as deserving of care as those who have a fractured femur.

**Magnus Fall**, MD, urologist from Gothenburg, Sweden, explained that interstitial cystitis (IC/PBS/BPS) covers a heterogeneous spectrum of disorder, so far only fragmentarily explored and that IC has a different meaning for different physicians and stakeholders. Today’s trend is to base diagnosis on symptoms and exclusions.

His presentation covered the use of cystoscopy, hydrodistension and biopsy in IC, with different parts of the world using different approaches. He emphasized the differences between Hunner’s lesion IC (known as Classic IC) and non-ulcer IC, stressing that what has traditionally been known as a Hunner’s ulcer (now also known as Hunner’s lesion or patch) is not in fact an ulcer; this name is a misnomer and may be a reason for failure to diagnose classic IC since many doctors may have failed to identify Hunner’s lesion because they have been looking for “ulcers”. He stressed that the difference between the two forms of the disease is important because the treatment used for Classic IC is likely to be different.

**Richard Berger**, MD, urologist from the University of Washington, Seattle spoke on organ ablation in the treatment of interstitial cystitis and/or non-bacterial prostatitis. He said that these patients may be really desperate and look to physicians and surgeons to guide them in making irreversible surgical treatment decisions. Unfortunately, he added, we have little reliable evidence on the therapeutic efficacy of ablative therapy for either IC or CP/CPPS. The literature suggests that cystectomy is of therapeutic value in IC patients with severe intractable symptoms who have small contracted bladders. Sources of pain after cystectomy include phantom pain, muscle spasm, hypersensitivity/allodynia of neuroadjacent organs or failure to treat psychosocial aspects of pain. Possible problems following diversion or bladder reconstruction include incontinence, urinary infection, sexual dysfunction, urinary stones or recurrence in subtotal ablation. He concluded that ablation should be undertaken with extreme caution in patients with pelvic pain and careful studies should be carried out in the patient to determine the extent of hypersensitivity in the organs and tissues innervated by adjacent dermatomes. Careful long-term follow-up is essential and the findings should be reported in the literature.

Conclusions specifically for IC:

- Cystectomy and supratrigonal cystectomy may improve pain in some highly selected patients with IC.
- Evidence of severe local disease is a positive predictor of good ablation outcome.

**Dean Trip**, PhD, clinical psychologist from Ontario, Canada discussed the psychological consequences of chronic pelvic pain under the heading “The emerging biopsychosocial model of a male chronic pelvic pain syndrome”. Depression and anxiety lead to poor quality of life for these patients. He noted that the reality is that pain programmes or psychological issues are not highly prioritized in CP/CPPS management.

**Bert Messelink**, MD, urologist from Groningen University Hospital in the Netherlands, spoke on “Pelvic floor muscles and urogenital pain”, looking specifically at anatomy & physiology, pathology, psychology, pain, diagnosis and treatment. With regard to treatment options, he discussed pelvic floor muscle education, physical therapy, biofeedback, myofascial triggerpoint therapy and injection of botulinum toxin A into the muscles and experimentally into triggerpoints. He concluded that in patients with urogenital pain, the pelvic floor muscles should be taken into account when talking and thinking about causative factors and possible options for treatment. In the near future there will hopefully be more research done on the role of this complex organ system in relation to CPP.

“Opioids and guidelines for use in chronic pelvic pain” was the topic presented by **Eija Kalso**, MD from Helsinki University pain clinic and department of anaesthesiology. He explained that opioid treatment should be considered for both continuous neuropathic and nociceptive pain if other reasonable therapies fail to provide adequate pain relief within a reasonable period of time. He felt that strong opioids should not be used as monotherapy, but should form part of a multi-therapy approach. There is still very little known about the use of opioids in chronic pain syndrome/idiopathic pain. Their adverse effects include constipation, nausea, sedation, tolerance and hyperalgesia, hormonal, immunological and psychiatric effects. The management of chronic pain should be directed by the underlying cause

of pain. Whatever the cause, the primary goal of patient care should be symptom control. Use of opioids without a clear diagnosis of the cause of pain is appropriate if the pain is severe and continuous and is responsive to opioids. The aim of opioid treatment is to relieve pain and improve the patient's quality of life. Quality of life can be improved by a) relieving the pain and b) improving the patient's ability to function normally. Both of these aspects should be assessed during a trial period of 3-4 months. Opioid treatment is initiated at a low dose and this dose is gradually increased if the patient reports unsatisfactory pain relief with acceptable or no adverse effects.

Useful reference: Recommendations for the appropriate use of opioids for persistent non-cancer pain. A consensus statement by the UK Pain Society can be found at: [www.britishpainsociety.org](http://www.britishpainsociety.org). The picture was completed by a presentation by **Sam Chong**, MD from London on drugs and chronic pelvic pain.

The second day was opened by a presentation from veterinarian Tony Buffington, DVD, on "Multiple pathologies – What does it all mean?" He discussed co-morbidities – idiopathic pain syndromes – including interstitial cystitis, chronic pelvic pain syndrome, irritable bowel syndrome, fibromyalgia and chronic fatigue syndrome as well as affective disorders such as post-traumatic stress disorder (PTSD), panic disorder, anxiety and depression. He explained that the syndromes of IC, CPP, IBS, CFS and FM are examples of medically unexplained symptoms (MUS) and are commonly found together. He discussed the brain as the central organ of the stress response. The brain determines what is stressful and what the response is. He hypothesized that early life experiences can impact individuals both before and after birth, and may result in durable changes in brain, autonomic, endocrine and immune function. He also hypothesized that this sensitization makes a person more vulnerable to life stressors, putting them at greater risk of developing pain disorders.

**Karen Berkley** PhD, from Tallehasse, USA, spoke on "Chronic Pelvic Pain: lessons from translational studies of endometriosis". She began by showing her table with its growing list of therapies of every kind for chronic pain and asking: so why are so many people in pain? Could one contributing factor be how we use this table? And could the way in which we use this table be influenced by how we conceptualize mechanisms of pain. She focused on the example of endometriosis, a disorder whose signs are growth of endometrial tissue in abnormal locations and whose symptoms include: no symptoms, subfertility, severe dysmenorrhoea, dyspareunia (vaginal hyperalgesia), dyschezia, chronic pelvic visceral/muscle pain. It may co-occur with irritable bowel syndrome, IC, ureteral stones, temporomandibular disorder, migraine, fibromyalgia, vulvodynia, chronic fatigue syndrome and more. She presented her research with rats into mechanisms of pain in endometriosis. Dr Berkley discussed the implications for classification, diagnosis and treatment. For classification issues, she suggested that it is likely important to accept the possibility that all chronic pain conditions may include symptoms seemingly indicative of "multiple" sources and causes and to recognize the possibility that classifying the patient's disorder by his/her current most distressing bodily problem (e.g. bladder, uterus, prostate) could prove misleading or even detrimental.

**Andrew Baranowski**, MD, pain consultant from London, dealt with classification of urogenital pain – phenotype, terminology and taxonomy. Phenotyping (categorizing the patients into defined sub-types) was an important topic at this meeting. Dr

Baranowski explained that not all patients will fit a sub-type and some patients may change their phenotype. There are “aberrations” and “transitions” that need to be considered and we may have to accept “best fit”. A very lively interactive discussion produced multiple different points of view!

**Jose de Andres**, MD, anaesthesiologist from Valencia University Hospital, Spain, spoke in detail on the role of sacral nerve root stimulation (SNS) and spinal cord stimulation (SCS), including a percutaneous, “retrograde”, epidural approach. He concluded that consideration of the advances in understanding of the neurobiology of chronic pelvic pain syndromes compels us to consider novel treatment options. The role of central sensitization and viscerosomatic and somatovisceral reflexes in the maintenance of chronic pelvic pain needs to be recognized: treatments aimed primarily at central and peripheral nervous system neuromodulation are likely to play a larger role in the treatment of chronic pelvic pain in the future.

**Anna Mandeville**, MD, clinical psychologist from London, gave a particularly patient-oriented and patient-sympathetic presentation on the topic of: “The psychology of managing pain in the pelvis – do we need a specialist approach”. She emphasized the importance of the consultation. There may be confusion about what is causing the pain. The patient may be dissatisfied with the quality and quantity of information given. The patient may feel uncertain, anxious and have a sense of not being believed by the medical profession and have a need to be understood. The patient may be overwhelmed by a sense of helplessness. It was this term “helplessness” that cropped up time and time again in discussions about the IC patient who feels he/she has lost control of his/her life. It is important how much impact or “interference” the chronic pelvic pain disorder has on the quality of life of the patient and on valued activities, including sex and relationships, sitting tolerance (work and social activities), driving etc. The focus is different for every patient. She stressed that while the psychology of sexuality and relationships is important, it is not an issue for all patients. One problem is that even when the pain aspect has been reduced, many patients are unable to return fully to their pre-pain sex life and may find it impossible to restore their former relationship. Dr Mandeville felt that even though some women do have a history of traumatic sexual encounter, the role of distressing sexual experience may be being overestimated.

She described the cultural myths currently attached to Sex:

- Reserved for the ‘perfect’ or at least the healthy
- Must be ‘spontaneous’; planning ‘kills’ it
- Physical contact must always lead to intercourse
- Partners should instinctively know what the other wants (mind reading)!

Common difficulties in sex and relationships are:

- Sex may feel overwhelming and painful and may be cut out of the patient’s life completely
- There may be fears of losing the partner – this may lead to the patient denying his/her own comfort, going ahead with painful sex and consequently escalating the problem
- The patient may have difficulty in communicating needs to the partner
- There may be a lack of opportunities for support for the patient.

She recommended a very practical approach based on establishing what the patient is actually going through, what the patient wants to achieve and what the goals are

for improvement. She reviewed methods of teaching the patient muscle relaxation, including via hypnosis and then gradually reintroducing sexual activity See also: <http://www.drannamandeville.com/> where a lot of information about pain can be found.

The following speaker was **Melissa Farmer**, PhD, psychologist from McGill University Health Center, Canada, speaking on “Sexual Pain” who stressed that dyspareunia is not a sexual dysfunction, it is a pain syndrome. The definition of Dyspareunia (DSM-IV-TR, 1994) as “Recurrent or persistent genital pain associated with sexual intercourse in either a male or female” has its limitations since the pain also occurs in non-sexual situations, the pain may occur “pre-sexually”, it is unclear what constitutes “recurrent” or “persistent” and it is an “interference” with an activity (intercourse). Furthermore, medical causes of pain are difficult to rule out. Her conclusions were:

- Dyspareunia transcends sexual dysfunction
- Dyspareunia is a pain syndrome
- Assessment and treatment require concurrent, multidisciplinary action.

**Amanda C de C Williams**, Clinical Health Psychology, University College London, spoke on assessment of urogenital pain and felt that it is important to establish what the patient wants and which outcomes are important to the patient. This is not always an easy task since patients may hope for improvement across many areas of their life affected by pain. The main domains of outcome are: pain, physical function, emotional function, symptoms and adverse events, willingness to adhere to methods of treatments and satisfaction with treatment. The question is: how much improvement is enough?

Having often been left for long periods of time to manage their pain alone, patients may avoid painful activities (disability), lose valued social roles and productive pursuits (depression, identity), lose confidence in their capacity to manage their health and illness, and be afraid about the future. It is frightening and deeply depressing. They feel fear, hopelessness, pessimism, isolation and frustration.

Dr Williams felt it was time to drop the term “somatization”, feeling that it was conceptually problematic, culturally specific and incompatible with pain science.

**Jørgen Nordling**, MD , urologist from Denmark and chairman of the European Society for the Study of Interstitial Cystitis (ESSIC) reviewed routine investigations for the end organ specialist.

On the topic of interstitial cystitis, he said that no accepted definition of IC exists, and we have never even been close to reaching world consensus on criteria. Consequently everyone has his/her own perception and this differs enormously from person to person.

He presented the ESSIC standard procedures to evaluate patients presenting with pain in the bladder and lower urinary tract symptoms, covering history, physical examination, pain mapping, vagina, laboratory tests, symptom evaluation, urodynamics and cystoscopy. He added that the presence of other organ symptoms should be addressed, as well as cognitive, behavioural, emotional and sexual symptoms.

**Tim Ness**, MD, anaesthesiologist from the University of Alabama, then reviewed routine investigations for the pain specialist. He said that when the pelvic pain patient

first sees the pain specialist, they may be very distressed and have often been through extensive investigations. They are there because they want pain relief.

The types of therapeutic approaches employed by the pain specialists include interventional, medical, behavioural, physiotherapy, complementary/alternative medicine. He emphasized that treatment may need to be modified or even avoided based on co-morbidities.

He ended on a provocative thought that perhaps a taxonomy could be based on responsiveness to therapy, e.g. anti-inflammatory responsive, opioid responsive, gabapentinoid responsive, combination responsive, physiotherapy responsive, PPS responsive, behavioural modification responsive etc.

**Philip Hanno**, MD, urologist from the University of Pennsylvania, USA, took a look at practical considerations and management algorithms for pelvic pain, examining the different perceptions in different parts of the world as revealed in recent meetings this year. For example: pain is not a prerequisite criterion for diagnosing IC in Taiwan. The term hypersensitive bladder syndrome is the preferred umbrella term in the Asian countries.

On the principles of management:

- Expert opinion should be the basis since data does not permit firm conclusions
- Treatment decisions should be based on placebo-controlled random controlled trials as far as possible
- Treatment should be guided by patient-driven outcomes
- Begin with least invasive therapies
- Approach surgical treatment with caution.

He suggested that doctors should add or subtract treatments on the basis of results in the individual patient, consider more extensive evaluation and more invasive treatment in patients who have failed oral and intravesical treatment. Unproven (experimental) treatment should be given only in the framework of a clinical trial. Irreversible surgery should be the last resort, with rare exceptions.

He put forward the following definition for IC/PBS/BPD:

**“An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6 weeks duration, in the absence of infection or other identifiable disorders”.**

The meeting was rounded off with a discussion led by Dr Andrew Baranowski and Dr Curtis Nickel with Dr Nickel stressing that all patients are different and respond differently to treatment. Therapies that should theoretically benefit patients do indeed benefit some patients, but not all. The Urologic Chronic Pelvic Pain patients are not a homogenous group. Patients need to be phenotyped in a clinical meaningful way that can guide therapy for the individual patient. A phenotyping management strategy would lead to targeted therapy. They concluded that knowledge is evolving and felt that future benefits will come from a translational science approach.

The PUGO website can be found at: <http://www.indoorcat.org/pugo/>.

*Jane Meijlink*

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