

REVIEW OF THE UROGENITAL PAIN MEETING HELD AT THE ROYAL SOCIETY OF MEDICINE, LONDON FRIDAY 18 JANUARY 2013

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Those who managed to get to the Urogenital Pain meeting at the Royal Society of Medicine in London, struggling through snow, ice and freezing fog deserved a medal! And we won't go into the details of the even greater problems of getting back home again afterwards, with roads, rail and airports affected by snowstorms! The purpose of this meeting, organised by urogynaecologist and uro-neurologist Sohier Elneil, MD, was to provide an overview of urogenital pain and how to manage this highly complex group of patients. It was aimed at doctors of different disciplines, nurses, physiotherapists, psychologists and patient liaison groups. Two patient advocates attended, Judy Birch from the Pelvic Pain Support Network in the UK and myself from the International Painful Bladder Foundation.

The day was divided into three sections: chronic pelvic pain syndrome, urogenital pain conditions and therapeutic approaches. Panel discussions were included and plenty of time was allowed for questions and discussions following presentations. This made it a lively, interactive and thought-provoking meeting.

Looking first at definitions and epidemiology/prevalence, Dr John Hughes presented the definition of chronic pelvic pain as defined by the EAU 2012 and IASP 2012:

"Chronic pelvic pain is chronic or persistent pain perceived in structures related to the pelvis of either men or women. It is often associated with negative cognitive, behavioural, sexual and emotional consequences as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor or gynaecological dysfunction."*

[Note: *"*Perceived indicates that the patient and clinician, to the best of their ability from the history, examination and investigations (where appropriate) have localised the pain as being perceived in the specified anatomical area."*] (See: EAU 2012 guidelines. Page 19 of the CPP section under 2.5.3.1.

http://www.uroweb.org/fileadmin/guidelines/2012_Guidelines_large_text_print_total_file.pdf)

Chronic Pelvic Pain Syndrome is defined as:

"Chronic pelvic pain when there is no proven infection or other obvious local pathology that may account for the pain."

Referring to the CMO report 2008/2009 from the UK Department of Health on "Pain: Breaking through the Barrier", Dr Hughes reported that it has been estimated that 7.8 million people in the United Kingdom now suffer with moderate to severe pain that has lasted over six months. Over a third of households have someone in pain at any given time. The numbers are rising. Repeated surveys show that chronic pain is two to three times more common now than it was 40 years ago. It is believed that 1 million women in the UK suffer from chronic pelvic pain. The CMO reports goes on to say that chronic pain has a major impact on people's lives, causing sleeplessness and depression and interfering with normal physical and social functioning and that early intervention may stop pain becoming persistent. The very fact that this was the first time that chronic pain has been included in the CMO report does seem to indicate that there is at last more political awareness of the problems of chronic pain, its significant impact on quality of life and last but by no means least the cost to society.

If you are interested in reading this report in full, it can be accessed via this link: http://www.pelvicpain.org.uk/uploads/documents/Pain%20call%20for%20network%20of%20clinics-%20DH_096233.pdf

Dr Hughes explained that it is difficult to gain a clear picture of the size of the problem and that prevalence studies may possibly not be producing reliable statistics, since many are conducted via telephone surveys and people may be unwilling to discuss embarrassing and socially taboo problems on the phone. Different

definitions and terminology including different names have caused a real hurdle in the past. For IC/BPS, different definitions have been shown to produce a different prevalence (*Clemens 2007*). However, there is today a more workable set of definitions, he noted. More than 1 million women in the UK are thought to suffer from chronic pelvic pain. In men, it is even harder to gain a clear picture, although some data is now being produced.

He noted that CPP is not a single condition, but a group of often poorly understood conditions for which there is now an agreed classification. Furthermore, the overlap of symptoms or patients fulfilling multiple condition criteria (with multiple associated conditions) is fairly common in the chronic pelvic pain/painful bladder group. However, the question is: what does this mean? Do the different chronic pelvic pain conditions have an underlying common theme or commonality, or are they separate entities?

The Science of Pain was the topic of the next speaker, Dr Sohier Elneil, taking bladder pain as an example and explaining that normal bladder function depends on integrity of the macroscopic and microscopic anatomy of the bladder, the central nervous system and the peripheral nervous system.

For many years the sensory nerves were thought to stop at the basement membrane, but it is now known that they go all the way up to the apical urothelial cells. So the epithelial surface is actually as neurologically responsive as the rest of the bladder.

Dr Elneil said that while the known urothelial functions are:

- Protective barrier against urinary toxins, bacteria, trauma
- Prevents the urine from equilibrating with the blood
- Keeps noxious substances from reaching underlying bladder muscle and nerves,

the urothelium is also a sensory body participating in the afferent pathway sensing bladder fullness, urgency, pain and other changes in sensation.

Dr Elneil also mentioned that while for many years the immunity component of the bladder had tended to be overlooked, people are now increasingly starting to recognise its role, when looking at bladder responsiveness and function. If the urothelium becomes leaky, toxic substances can breach the surface, possibly triggering off autoimmune responses. You then see hyperexcitability of the afferent nerves with resultant inflammation, leading to pain, she explained. With regard to mast cells that were once considered diagnostically important, Dr Elneil stressed that the exact role and significance of mast cells and mast cell activation are not fully understood within the context of IC/BPS.

Where are we now with pain, asked Dr Elneil? At the present time, chronic diseases are episodically diagnosed and intermittently treated, consuming enormous resources driven by exacerbations, clinical decompensations, and complications. The future aim is for chronic diseases to be met with continuous care, improving outcomes and lowering costs by prediction and prevention of acute presentations. On the topic of futuristic technology, she mentioned skin-surface or implanted sensor technology, providing actionable diagnostic information, linked to learning systems and titratable therapies, enabling continuously-tailored (feedback controlled) treatment.

Dr Elneil explained that chronic pain is now starting to be treated as a disease rather than a collection of symptoms. Pain as a chronic disease has an impact on the individual's quality of life, family life, social life and ability to work. It also has a gigantic impact on national healthcare systems, with the WHO estimating that by 2020 it will become the most expensive problem for healthcare systems if not successfully managed. It is interesting to note that the WHO is now paying attention to pain not only in the developed world, but also for the first time in the developing world. Dr Elneil pointed out that it is particularly important to have this support from international organisations such as the WHO, because this can make it a little easier to obtain funding and grants for research.

Treatment for the bladder, said Dr Elneil, is currently aimed at enhancing the mucosal barrier, suppressing the immune system, suppressing inflammation, reducing mast cell activation, suppressing sensory mechanisms or

blocking histamine receptors. The fact that there are so many different treatments is an indication of how little we know of this bladder pain disorder. What is needed, however, is a pain approach targeted on all the different types of pain that may be involved, looking locally at the bladder and centrally at the brain and spinal cord.

Dr Andrew Baranowski, consultant in pain medicine, looked at pelvic pain mechanisms, clinical paradigms. He emphasised that somatic pain is different to visceral pain and that pain may be due to: ongoing pathology, nerve damage or chronic pain mechanisms. Causes may be surgery, trauma or infection, but in many cases the cause cannot be identified.

He explained that abnormal central afferent signalling can lead to sensory urge, urgency and pain while abnormal central efferent signalling can lead for example to neurogenic oedema, muscle spasm and organ dysfunction.

Dr Alex Digesu spoke on classification of chronic pelvic pain (CPP), noting that pain perceived within the pelvic may arise from a range of different mechanisms, many of which remain poorly understood. It may be described as a constellation of syndromes with a complex natural history, unclear etiology and poor response to therapy. Basic investigations must therefore be undertaken to rule out 'well-defined' pathologies. There is evidence to show, he said, that central changes can produce states of visceral and/or muscle hypersensitivity with long-term pain, sensory dysaesthesia, functional abnormalities, cognitive, behavioural, emotional and sexual dysfunction. The assessment and management of these patients therefore requires a multidisciplinary approach, requiring good integration and knowledge of multiple organ systems.

He explained that there have been different classifications of chronic pelvic pain with many international working groups working on chronic pelvic pain, including: ESSIC, ICS, AUA, EAU, IASP, IPPS, drawing up their own classifications, terminology and taxonomy. In order to elucidate this situation, he looked at the specific case of interstitial cystitis/bladder pain syndrome and what changes have taken place in classification and nomenclature.

The second session of the day dealt with urogenital pain conditions and opened with Dr Heidi Tempist from Oxford looking at urological pain syndromes: BPS/IC, prostatic pain and urethral pain in men and women, with an overview of incidence, presentation and etiology and the range of treatments for the conditions while emphasising the importance of excluding other possible causes of symptoms. She emphasised that cystoscopy should always be done under anaesthesia as it is otherwise an excruciatingly painful procedure for the patient. Biopsy, she felt, is more controversial but should certainly be done if there is any suspicion of cancer. She recommended fulgurating any lesions found. Symptom scores should not be used for diagnosis, but may be useful for following progression. She too underlined that a multidisciplinary approach is the right approach. While joint clinics are ideal, it is very difficult to get funding to achieve this. Bearing in mind that these patients often have many other complaints, a holistic approach is also essential. Treatment is a problem since more than a hundred treatments have been described for IC/BPS, she said, and this is a clear indication of how little we understand about this condition. It also makes treatment a real challenge.

With regard to conservative treatment, and bearing in mind that this is likely to be a lifelong condition, she noted that self-management and empowerment are particularly important. She also felt that empathy on the part of the clinician plays an important role in treatment of the patient, including acknowledgement of the impact of the condition on the patient's quality of life. Patients need emotional support. Patient support groups can play an important role here too.

Pain medication can be difficult since many of these patients do not respond too well to the normal run-of-the-mill analgesics. If the patient has a big problem with frequency and urgency, it is worthwhile trying anticholinergics, she suggested.

In the UK there is currently considerable interest in the possibility of undiagnosed, occult infection in some patients diagnosed with IC/BPS for whom a number of clinicians are now recommending a minimum of 4-6 weeks of doxycycline, including a course of 2 weeks for the partner.

For intravesical treatment, she noted good temporary effects with alkalinised lidocaine while hyaluronic acid and chondroitin sulphate or a combination of the two, all aimed at temporary repair of the GAG layer, have all been shown to have good effects. DMSO is still sometimes being used, she noted, but has really gone out of fashion now and is felt by many to be too aggressive to be used as a bladder treatment. PPS is not licensed in the United Kingdom.

She also touched on urethral pain syndrome, which is occurrence of chronic or recurrent episodic pain perceived in the urethra, which she considered to be part of the IC/BPS spectrum. In men it leads to pain on ejaculation. She recommended lidocaine gel.

Dr Tempest emphasised how debilitating this condition can be and how desperate the patients can become, even suicidal. She concluded by saying that this spectrum of disorders is very difficult to treat, but the multidisciplinary approach is key. In the United Kingdom there is also increase pressure on the funding of treatment which can restrict the treatment generally available.

Dr Katy Vincent, also from Oxford, then discussed gynaecological pain syndromes, looking particularly at primary dysmenorrhea, endometriosis-associated pain, vulval pain syndromes and dyspareunia. On the topic of dysmenorrhoea (pain with menstruation), she first looked at primary dysmenorrhoea which is pain not associated with any pathology. Secondary dysmenorrhoea is associated with pathology but also usually associated with other symptoms. Approximately up to 90% of adolescents complain of period pain, but a more serious level of pain is found in around 20% and it is a major cause of school and work absenteeism in adolescents and young women. It is often considered “normal” with a common preconception that you grow out of period pain and therefore nothing needs to be done about it. It is also not covered by the Royal College of Obstetricians and Gynaecologists’ definition of chronic pelvic pain. Dr Vincent also looked at mechanisms by which endometriosis may generate pain, emphasising that there is a poor correlation between symptom severity and disease severity (similar to IC/BPS). Studies have shown that endometriosis may be associated with other chronic conditions, with one study showing that around 20% of the women with endometriosis have associated disorders including fibromyalgia, SLE, chronic fatigue syndrome, endocrine diseases and arthritis rather than pain condition. Studies have also shown that alterations in brain volume occur in patients with endometriosis compared to controls. However, women with CPP but without endometriosis also show similar alterations. Research is needed to understand some women with endometriosis develop pain and others not. Regarding treatment, it is preferable to aim treatment at the pain rather than undertaking drastic surgical procedures.

On the subject of vulval pain syndromes: there is a large number of conditions that can cause vulval pain such as infection (candida albicans, herpes simplex), inflammation (lichen sclerosus, eczema, contact dermatitis, psoriasis, Crohn’s disease), iatrogenic (postepisiotomy, postsurgical scar), hormonal (hypoestrogenism), trauma and a number of rarer conditions such as symptomatic dermographism, aphthous ulceration, sacral meningeal cysts and pudendal nerve entrapment. These possibilities naturally have to be eliminated. Patients with vulval pain syndromes have an increased risk of developing IC/BPS and chronic fatigue syndrome. Treatment is problematic since while a wide variety of treatments are prescribed, there is little supporting evidence. Treatment should be individualised and multidisciplinary. However, according to Dr Vincent, there is good evidence for use of lamotrigine (an anticonvulsant), physiotherapy, cognitive behavioural therapy, while patient support groups can play an invaluable role since this is a group of patients that can feel very isolated. While women with endometriosis are now beginning to be able to talk about their disease, this is not the case with women with vulval/vaginal pain which is still considered too embarrassing to discuss and a taboo subject.

On dyspareunia, she noted that health professionals are now moving away from old concepts and exploring the problem more seriously. It can have a major impact on quality of life, not just affecting sexual activity, but also such basic things as use of tampons, going for a smear test etc. Looking at the multiple causes, she added that while psychological causes do exist, doctors should beware of giving that label.

On hormonal factors, she noted that the menstrual cycle has an influence on many pain disorders, with pain being exacerbated during the menstrual cycle. Concerning whether sex hormones directly influence pain perception, she reported that unfortunately many studies in this field have been flawed. They have used very small numbers and have timed their investigations around cycle phase rather than hormonal state, and often

include women using exogenous hormones as part of their control group. So whether hormones have an influence on pain perception is still very unclear in healthy women. However, cyclical variation is consistently seen in women with CP, dysmenorrhoea, IBS, IC/BPS and TMJD. Hormonal factors appear to have a greater influence in patients with chronic pain conditions than in healthy controls. While hormone treatments can prove very useful, they are associated with altered psychological profiles and while some patients can feel much better, others may feel worse. Nevertheless, hormonal treatment need not be reserved for gynaecological disorders but can also be used for other pain conditions such as IBS and IC/BPS.

The morning ended with a most useful and very active panel discussion with many questions from the audience. A question on inflammation, what types of inflammation exist and how it should be defined led to a very lively discussion among not only panel members but also the audience. Everyone on the panel had a different view regarding a definition and nobody could provide a satisfactory answer, despite the fact that many speakers had referred to inflammation including neurogenic inflammation in their talks. There was much debate as to whether we were talking about mast cells or white cells, acute inflammation or chronic inflammation... It was clear that there is considerable confusion and looks as though we might need some new (updated) definitions of inflammation. Whatever the case, some light needs to be shed on inflammation in this context.

In the afternoon, we moved on to a multidisciplinary and interdisciplinary approach to urogenital pain management with a presentation by Dr Natasha Curran. Looking at their own urogenital, pelvic and visceral pain management team, she listed the team participants as follows: 2 consultants in urogenital pain medicine. 2 clinical nurse specialists, 3 physiotherapists, 4 psychologists, plus the rest of the pain department. It has taken ten years to develop this team method. They also work with urogynaecologists, gastroenterologists, gynaecologists, urologists and specialist endometriosis centres. They handle 10 new patients a week and have a long waiting list! An important aspect is getting all these people in one room on a regular basis to ensure that the professionals understand what each other is talking about and that the patient hears the same message. They hold weekly multidisciplinary team meetings with fortnightly management meeting. The configuration can change as required. The clinical nurse specialist plays a key role and is present at the first consultation, is the point of contact for the patient via telephone or email and is a key team member on pain management programmes.

Dr Amanda Williams spoke with great empathy and realism on the role of psychology in managing patients with chronic pelvic pain. The role of the psychologist is to explain what pain is, to foster self-management and facilitate psychological pain management. While many of the psychological problems associated with adjustment to persistent pain, and management of the pain, apply to chronic pelvic pain as well as to pain in other areas of the body, there are also practical and social problems which need to be understood. The various mechanisms of facilitation, amplification, and failure of inhibition found in chronic pain mean that there is no simple relationship between physical findings, psychological findings, psychological history, pain experienced and resulting distress and restriction of activities.

Women have been studied more than men. However, Dr Williams discussed a study done by *Showghi et al* with men attending a urogenital pain clinic who were interviewed at length about their understanding of pain before and after consultation. Men found it very important to have an explanation and expressed fewer fears than had been expected. Dr Williams explained that the men seemed to need to “own” the explanation, whether worked out on their own or adopted/adapted from consultations with others. They emphasised the logic of the explanation, and their very active efforts to make sense of it all. Unfortunately their ideas about how their bodies worked were not entirely accurate. Trust in the doctor was very important to them and could reduce anxiety. They also felt that it was the doctor’s role to explain pain. When there was no explanation, criticism was generally directed at doctors for making men feel that nobody was interested enough to work it out and perhaps that nobody had the courage to tell the patient bad news. They also felt that pain was not considered serious enough (unlike e.g. prostate cancer) and that the doctor was making them feel like a hypochondriac and wasting time. The men felt that explanations were helpful and that knowing the cause is helpful in itself since it reduces uncertainty, provides reassurance that the problem is not life-threatening. It makes sense of symptoms. Furthermore, they felt that if somebody could understand their pain, it implied a

clear possibility of specific treatment at some time in the future. It also gave them something definite to be able to tell others about their pain. The study also took a look at the internet to see what kind of information was available for men. They indeed found that the men with urogenital/pelvic pain were right when they asserted that there was little available for them on the web.

A study of women with pelvic pain showed that women had high levels of distress about what was wrong compared with women with no pain, but similar levels of distress to other women with chronic pain (*Savidge & Slade 1997*). A study of women with CPP interviewed before the initial gynaecological consultation (*Price et al 2006*) revealed that many were very preoccupied with explanations, some were worried about cancer, most simply wanted to understand about their pain. Few of them had explanations or the explanations were felt to be inadequate, or conflicting with previous ones. The patients were also seeking validation and recognition (*McGowan et al 2007*). A lack of abnormal findings made women feel that they were being seen as neurotic. Being told that nothing was wrong was interpreted as denying the pain existed and usually fractured the therapeutic relationship, unless someone explained that of course you can have pain even if the investigations come back negative.

Looking at healthy women's knowledge of their bodies, Dr Williams said that healthy women undergraduate students were asked to indicate the size and location of specific organs on an abdominal outline. Many of these intelligent students were incredibly inaccurate! This, said Dr Williams, means that doctors need to be cautious about assuming basic anatomical knowledge by patients. Furthermore, if you don't have a good knowledge of your body, it is easy to worry that there might be something seriously wrong. Good information is essential and patient support groups can also help out here.

The aims of (any) pain treatment, she explained, were to improve control of pain, help build a realistic model of the problem, reduce disabling effects of pain by working towards short and long-term goals by graded steps, reduce distress associated with pain and projected future, reduce effects of pain on family and friends, reduce unhelpful encounters with the health system. She emphasised that focus on the pain alone may leave the patient inactive and anxious, while focus on getting people active again without efforts to relieve the pain makes the patient feel disbelieved and uncared for.

Dr Williams concluded by saying that helping patients understand pain is an investment in their health and in adherence to treatment and success of the treatment. It is common, particularly in women, for chronic pain to be associated with significant distress. Treating the pain usually reduces this distress. Psychological interventions drawn from the evidence base in other areas of chronic pain should be used in chronic pelvic pain, alone or in combination with medical and physical therapies.

Physiotherapist Katrine Petersen then talked about understanding how the cognitive behavioural approach can be used in pelvic pain management physiotherapy and why it differs from a traditional medical physiotherapy model.

On the impact of chronic pelvic pain on the patient, she noted that it may lead to:

- Reduced social contact
- Impaired functional activities – difficulties sitting, standing, walking
- Loss of hobbies, sports, exercise
- Reduced capacity to work
- Reduced confidence and mood
- Relationships issues, sexual activity and communication difficulties
- Problems with bowel and bladder function
- And more besides...

She described the main aims of pain management physiotherapy as follows:

- Moving towards a biopsychosocial model, focusing treatment on function rather than cure
- Acknowledging complexity of the condition and its effects on mood, expectations and future
- Providing information, knowledge and education
- Helping patients identify their baseline of fitness/activity and setting appropriate goals

- Empowering the patient with skills for them to build up and practice
- Show that exercise/sport is achievable
- Minimising the need for the patient to seek further referrals.
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30% of patients with chronic pelvic pain are particularly concerned about the cause of the pain. This is more troubling than the pain itself! (Grace & Zondervan 2007). Patients who are misinformed about pain have fewer coping strategies, lower adherence to treatment and higher intensity of pain (Jackson 2005).

She concluded by saying that giving information is not enough to change behaviour long-term. The key role of pelvic pain management physiotherapy involves providing information and explanations, but also supporting the implementation of pain management strategies and self-management to improve confidence and function. She also noted that there is strong evidence that addressing catastrophising and physical activity can mediate outcomes in pain management.

Dr Maya Nagaratnam from Malaysia gave an excellent presentation on pharmacotherapy in CPPS, explaining that there is little evidence for much of the treatment used for chronic pelvic pain and that medication optimisation is important. Many patients prefer to take one drug rather than a combination and in Malaysia they prefer pain-killing injections. While cure is not a realistic goal in these patients, treatment is aimed at symptom management in order to lessen the impact, improve the quality of life, but needs to be constantly reviewed for new pain types, adverse side effects, tolerance and management of acute flare-ups.

Paracetamol is not likely to help pain in chronic situations, while NSAIDs have been shown to be more effective than placebo or paracetamol in dysmenorrhoea and conditions with a clear inflammatory component, and additionally spare the use of opioids. COX2 inhibitors are therapeutically safer, but not more effective than NSAIDs. Opioid-like agents such as tramadol produce analgesia by two mechanisms: an opioid effect and an enhancement of serotonergic and adrenergic pathways. It has fewer of the typical opioid side effects, less constipation and less addiction potential, but 30% of patients are unable to tolerate the adrenergic side effects. Anti-depressants have an important role to play in the treatment of neuropathic pain but may give rise to significant side effects. She mentioned tapentadol, a new strong narcotic painkiller that acts differently to tramadol. However, the studies conducted have so far all been with patients suffering from osteoarthritis. If everything else has been tried, opioids can be considered. In functional abdominal pain and IBS, citalopram is emerging as a potential treatment. Dr Nagaratnam noted that in her experience prolonged release oxycodone/naloxone (Targinact) has revolutionised treatment of some of their visceral pain patients although more trials are needed.

Dr Andrew Baranowski rounded off the meeting by looking at other interventions for treatment of chronic pelvic pain, noting that interventions for functional reasons must be clearly delineated from those for pain. Evidence-based medicine supported by common sense is essential, such as seen in the British Pain Society Chronic Pelvic Pain Patient Pathway Maps, see http://www.britishpainsociety.org/members_articles_ppp.htm for further information.

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