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The High Prevalence of Interstitial Cystitis in Gynecologic Pelvic Pain Patients: How to Diagnose and Treat

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One of the difficulties of the pelvic pain paradigm for gynecologic patients is the fact that interstitial cystitis, while included in it, is practically speaking never diagnosed. It has been our suspicion for a number of years that many patients seen by gynecologists have pelvic pain of bladder origin or interstitial cystitis. Much of the confusion is in the overlap of symptoms of interstitial cystitis and gynecologic pain. While it has been known for almost 60 years that interstitial cystitis patients flare the week before their menstrual cycle and have significant flares associated with sex¹ and dyspareunia as well as voiding frequency, the urologic symptoms are usually not recognized by the physician because the patient's pain will dominate their complaints. Since the pain symptoms essentially suggest a gynecologic etiology, one would suppose that most patients self-refer to their gynecologist where they are assumed to have a gynecologic origin of the pelvic pain and receive diagnoses such as endometriosis, yeast vaginitis, vulvar vestibulitis, vulvodynia or just pelvic pain²⁵. Since the patient isn't complaining specifically of urologic symptoms that have often come on insidiously, it is frequently not known that they void 10-14 times per day⁶. Once the patient is labeled with a gynecologic diagnosis, all diagnostic maneuvers then direct the patient toward a specific gynecological diagnosis not recognizing that the pain may be of bladder origin.

This discussion will focus on three primary issues. First, to alert the gynecologist to current thinking on the pathogenesis of interstitial cystitis. Second, to focus on a new and accurate method to diagnose interstitial cystitis in order to recognize the presence of interstitial cystitis in gynecologic patients. Third, new and successful methods (80%) to treat the disease.

Pathogenesis of Interstitial Cystitis

Substantial progress has been made in understanding some key elements in the causes of interstitial cystitis. It is a disease that is in a continuum. Patients start with mild and intermittent symptoms that, as the disease becomes more progressive, will cause the patient to seek a physician.

Fortunately, only a few reach end-stage. Whatever position an individual patient takes in this continuum, whether it be early or moderate phase, determines whether or not they have significant symptoms or pathologic findings. The majority of patients spend their life in the mid-phase where they void anywhere from 10-15 times per day, generally have dyspareunia and symptom flares after sex^{1,7,8}, and have chronic pelvic pain. Many may not even seek physicians since they have always had these symptoms and in a sense feel it is "normal" for them. Of course the disease is all about neurological activation. The sensory nerves of the bladder for urgency and pain upregulate and activate. The pain can travel to the spinal cord and then refer to any place in the pelvis, the labia, the urethra, the vagina, the lower abdomen, lower back, and even the medial thighs in more advanced cases¹. Pain can be in any one spot or multiple areas. In 10% of people, the only symptom may be pain. The urgency is so insidiously progressive, the patient may not notice it since pain is the usual dominating symptom.

The reason there are so many people with pelvic pain originating in the bladder is primarily related to how urinary potassium is metabolized. Potassium levels in the urine approach up to 140 mEq/L, levels way in excess of what is required to injure tissue, or to depolarize nerves and muscle⁶. Mother nature has provided a protective barrier on the bladder surface to make the epithelium relatively impermeable and that is its mucus⁹. When the mucus functions normally, potassium is confined to the urine until the next void cycle. When it is dysfunctional, potassium leaks downstream into the bladder wall and provokes a cascade of nerve stimulation and tissue injury^{6,10-15}. Also in that milieu are the mast cells, when active release histamine and other neurotransmitters that activate symptoms, cause even more of an epithelial leak and the cascade is promoted¹⁶⁻¹⁸. Hence, allergies play a substantial role in this disease process.

At our center, we have designed a new diagnostic tool called intravesical potassium sensitivity testing^{5,10,11,19}. It was

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The President's Perspective



John C. Slocumb, M.D., FACOG • President

These are exciting times with the growing national interest in chronic pain. JAHCO's regulations in prevention of acute pain, and awareness and medication of pain will help to stimulate further understanding and education in pain management.

With this interest has been the development of special interest groups (SIG's) as a part of the International Association for the Study of Pain (IASP) and our affiliate, The American Pain Society (APS). The sex and gender group is made up of researchers looking at differences of Urogynecological Origin (PUGO) is made up of mostly urologists and pain anesthesiologists, and meet in association with the IASP meetings in Spring 2002. While the IPPS is dominated by gynecologists, it appears to be more multidisciplinary with nurses, urologists, physical therapists, etc. Efforts are being made to combine PUGO meeting with the IPPS in 2002 by finding common educational objectives and agendas.

With multiple groups dividing the attention, if not finances and educational time of those interested in pelvic pain, our challenge to attract new members and attendees at meetings becomes increasingly important. Much of our meetings has been dedicated to the clinical practice of pelvic pain evaluation and management. Hopefully, this content will stimulate an improved clinical expertise, as well as new ideas in clinical research.

Lastly, I find it important to remind the reader of the dedication and support in time and finances that Dr. Paul Perry has made to the IPPS. With Linda Harman's management of administrative issues and Paul's insights into getting support, we continue to be blessed with their commitment.

I hope to see you, if not your financial support, in Phoenix in April.

Sincerely,

John C. Slocumb, M.D., FACOG
President, International Pelvic Pain Society

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developed by challenging both normal and interstitial cystitis bladders with a solution of potassium. Normals have been found not to react and we have evaluated and published results on close to 100 normals^{6,19}. About 80% of interstitial cystitis patients have significant reaction to urgency or pain and over 1000 tests have been reported in the literature^{6,10,13-15,19,21} from a variety of centers. This is probably the most useful diagnostic tool to utilize because one can take any pelvic pain patient and screen them with potassium sensitivity testing to determine if there is a substantial component of epithelial dysfunction and thereby determine the presence of interstitial cystitis. When positive, the bladder is abnormal.

Gynecological Presentation of Interstitial Cystitis

To test the hypothesis that a significant number of gynecologic pelvic pain patients had interstitial cystitis as a critical component of their symptoms, three gynecologists in the United States, serially evaluated their pelvic pain patients. After they were assigned an initial clinical diagnosis, the patients were screened for urologic symptoms and had a potassium sensitivity test performed²¹. The results showed that 75% of the patients had urologic symptoms when screened and 85% had positive potassium sensitivity testing. These data suggest that interstitial cystitis may not only be an important cause of pelvic pain, but also show that IC should be given much greater consideration in the diagnosis of pelvic pain patients seen by gynecologists.

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There were a variety of diagnoses given although the most common was pelvic pain, followed by dyspareunia, yeast vaginitis, urgency/frequency syndrome, and endometriosis. It did not make any difference what the clinical diagnosis was, the potassium positivity was the same for all diagnostic categories (79-91%).

These data are important because they indicate that the pelvic pain paradigms in gynecology may need to be revised substantially in that interstitial cystitis is not a rare cause of pelvic pain but the most common one. As a result, when the gynecologist evaluates pelvic pain, interstitial cystitis should be the first disease ruled out, especially if associated with dyspareunia and a premenstrual symptom flare. By considering IC as a common cause of pelvic pain, the gynecologist can redirect the ultimate therapeutic regimen to one that is aimed at improving the bladder symptomatology that actually underlies many cases of pelvic pain. To aid in the recognition of a primary urologic problem as the cause of pelvic pain, a routine urologic history should be obtained including a 2-day voiding logs done at home. The physician should learn to do potassium testing in the office. This test has good financial reimbursement and is easily performed by the nurse. Since gynecologists see such a large volume of patients with chronic pelvic pain, they should diagnose and treat their own patients with interstitial cystitis. Refer to a urologist when other procedures are needed such as a cystoscopy for hematuria.

Therapy

Perhaps the most important point of this discussion is to recognize that the patient has bladder origin pain and therapy can be very successful. Three principles have emerged to guide the physician in treating interstitial cystitis. First, the dysfunctional epithelium in the bladder needs to be corrected. A new drug on the market, pentosanpolysulfate (Elmiron), which we recommend in dosages of 200 mg twice a day for most females, is up to 70% effective when used for periods of 6-12 months^{22,26}. The disease will slowly and steadily improve with this medication, which, in effect, fixes the epithelial permeability problem in part by coating the bladder and acting similar to the native mucus that is present. Perhaps the most important point to be made is that these patients don't get a little bit better, the 70% that showed improvement got substantially better, losing almost if not all their symptoms and they stay better. The responses are durable but, for most of these patients who have chronic disease, they will require chronic therapy with this medication. If the patients do stop therapy when they are doing well, medication can be resumed if they relapse with equal efficacy.

Second, neuromodulation is important because the bladder sensory nerves are very activated. Drugs such as the tricyclics, particularly amitriptyline, are beneficial at helping inhibit the sensory nerve urgency and pain during the initial treatment phase while one is waiting for Elmiron activity to ultimately result in good symptom relief. The SSRI class of antidepressants can also be very valuable in this phase of therapy as well as drugs like Pyridium, Polycitra (Urocit-K (10 mEq b.i.d), or Polycitra-K crystals (one packet

b.i.d). Even traditional anticholinergic therapy such as Oxybutinin and Detrol can be of value.

Third, it is important to manage allergies. Mast cell activation during allergy seasons, particularly pollen and mold season can severely aggravate the patient's disease. Hydroxyzine is perhaps the best antihistamine to use¹⁶⁻¹⁸. A dose of 25 mg at bedtime can inhibit allergic reactions when used chronically as it will stabilize mast cells after 2-3 months and reduce allergic reactions by blocking histamine release. The dose can be increased during allergy seasons to 50 or 75 mg as necessary. We have found that up to 70% of patients may need this drug chronically.

With the above medications in combination, usually referred to as multi-modality therapy, one can expect close to 85-90% of chronic pelvic pain patients to get substantial and durable relief. The cornerstones of therapy will be pentosanpolysulfate combined with long-term management of the allergies utilizing hydroxyzine. Remember, continuing these medications for periods beyond 9-12 months improves efficacy rates. When asymptomatic, patients themselves should ultimately determine whether to stop therapy since it is their pain. Relapse rates for people with a long history of symptoms are high, perhaps 70% within a few months.

In summary, substantial progress has been made in identifying the etiology or source of chronic pelvic pain in the majority of females. It would appear that 80%+ have bladder origin of pelvic pain or interstitial cystitis caused by abnormalities in the urinary potassium cycle associated with an epithelial dysfunction. The principle symptoms of interstitial cystitis are dyspareunia, premenstrual symptom flares and urinary frequency. Interstitial cystitis can readily be identified by the potassium test as a diagnostic tool. The disease can be successfully treated with chronic medical therapy as described.

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