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VISION

THE INTERNATIONAL PELVIC PAIN SOCIETY

Professionals engaged in pain management for women.

Vulvodynia Update: New Information from the NIH Symposium on Vulvodynia

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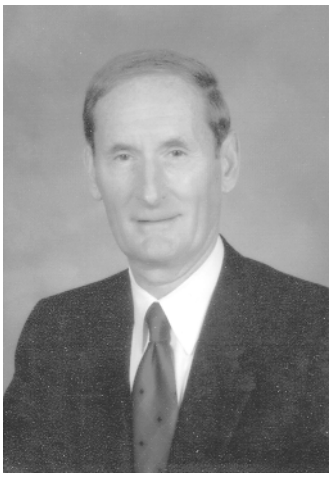
A recent symposium was conducted at the National Institutes of Health in Bethesda, Maryland bringing together many of the world's experts on Vulvodynia. It consisted of a comprehensive review of what is currently known and several presentations on new data which has yet to be published.

Dr. Bernard Harlow of Harvard University presented data on a new study regarding the epidemiology of vulvodynia. A study is in progress in the Boston metropolitan area to determine some of the population characteristics of vulvodynia. In their community study of 16,000 women, using both self-administered and telephone-administered questionnaires, they have estimated the prevalence of four types of unexplained lower genital tract discomfort that persisted for three months or longer; itching, burning, periodic knife-like or sharp pain, or excessive pain on contact to the genital area. A case control study was then performed using respondents who were likely to meet the ISSVD diagnostic criteria for generalized or localized vulvar dysesthesia, comparing them to controls with no pain matched for age and residential area. In the cross-sectional analysis, 8725 women were screened, of which 7178 could participate and 4841 responded to the questionnaires. They found that 12.4% of women had, at some time, experienced pain on contact for >3 months, while 3.3% had a history of chronic burning or knifelike pain. Also of interest, 40% of those women never sought treatment. At the time of the survey, 7% of respondents were experiencing pain on contact, or chronic burning, or knifelike pain. They found that the prevalence was similar in Caucasians and African American women, while Hispanic women were 70% more likely to experience chronic vulvar pain than Caucasian or African American Women. As this was a community questionnaire based study, patients were not examined, and therefore could not truly be diagnosed with vulvar vestibulitis or vulvodynia.

In the case-control analysis, a very interesting finding emerged: about 50% of all women with histories of chronic vulvar pain reported difficulty and great pain with their first use of a tampon, prior to any sexual activity. They found a highly significant association with premenarchial childhood victimization. Women who had been victimized, especially by physical abuse of a primary family member, had a 10 fold increased risk of a vulvar pain disorder. Major depression led to a 2 fold increase of risk, but only in women who had not suffered from abuse. These data suggest that some women may already have evidence of a vulvar pain disorder prior to menarche, sexual activity, or an infectious process. It suggests several possible etiologic events or conditions. In my practice I have found a significant prevalence of childhood straddle injuries, possibly leading to long term but generally undiagnosed pelvic floor dysfunction. Many of these women also have a history of urologic or pelvic floor complaints such as recurrent urinary tract infections, prolonged toilet training, the need for urethral dilitations, or chronic constipation. It also suggests the possibility of a genetic predisposition to the development of vulvar pain. The final analysis of this dataset should give us further insight to this complex disorder.

There were several presentations regarding basic science aspects of the neurophysiologic mechanisms of vulvar pain. There's a clear distinction between normal nociceptive pain and neuropathic pain. In normal nociceptive pain, a pain detection system is intact, working normally and providing a report to the central nervous system of the state of the innervated tissue. In the case of vulvar vestibulitis this may be a hyper excitable state due to chronic inflammation. In neuropathic pain the pain detection system itself is damaged or malfunctioning, therefore the pain experienced is unrelated to the state of innervated tissue. In this situation the problem is not in the vulvar mucosa but generally more central. Marshall Devor discussed a neuropathic model for vulvar hypersensitivity. He discussed the Chung model of Neuropathic pain after severing the spinal nerve root at L 5 in the rat, which innervates the foot. In this model after injury the nerve cell body changes its protein production

The President's Perspective



Jerome M. Weiss, M.D. • President

Since the successful treatment of most pelvic pain complaints requires a multidisciplinary approach, the IPPS Board has developed conferences that address a wide variety of issues that we believe will be of value to our diverse membership.

At the society's inception, gynecologists, who represented the largest percentage of specialists, were responsible for the contents of the teaching programs. As the organization has grown, we have come to recognize that a balance is necessary, not only to attract new members, but also to disseminate new concepts in non-gynecologic pelvic pain and to fulfill our educational goals. As both a urologist and a physician who treats a wide variety of myofascial pelvic pain complaints in both sexes, I hope to lessen the divide between male and female pelvic pain.

It is important to recognize that males lag far behind when it comes to diagnosing and treating pelvic pain. When women present with pelvic pain complaints, many diagnostic possibilities are entertained, whereas men are given only one diagnosis--prostatitis, whether or not it can be substantiated.

In order to open our minds to other possibilities, a postgraduate course on male pelvic pain will be offered at the 10th annual IPPS scientific meeting on chronic pelvic pain in Banff, Alberta, Canada, on August 14, 2003. This should be of interest not only to many of our non-gynecologic members, but because of similar underlying disease mechanisms in males and females, to gynecologists as well. The course will review male anatomy, physiology and a wide variety of pain conditions that have similarities in women. The underlying myofascial and nerve dysfunction can create scrotal and perineal pain in men and vulvar pain in women, or urinary urgency and frequency in both. The postgraduate course will be directed to showing these similarities and the rationale for the treatment of a variety of common male pelvic pain syndromes.

Our panel members, Drs. Rollin Bearss, Joel Teichman and I look forward to presenting our information and exchanging ideas with those who attend.

Sincerely,

Jerome M. Weiss, M.D.
President, International Pelvic Pain Society

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and is upregulated. A state of central sensitization at several levels ensues with the development of tactile allodynia. The area of injury leads to ectopic firing both in the injured area as well as in the dorsal root ganglion. This ectopic firing causes ongoing burning pain, central sensitization and tactile allodynia. There are also signs of neurogenic inflammation. In this state membrane stabilizers such as Neurontin and Amitryptiline are effective at decreasing this ectopic firing leading to pain reduction. The Chung neuroma model in the Rat leads to a highly variable pain behavior in the animal. There tended to be genetic selection for a high and low pain phenotype. With multiple generations of rats bred together in the high and low pain phenotypes an autosomal recessive inheritance pattern developed. It was believed to be due to an allele in chromosome 15 which probably controlled electrical excitability especially after nerve injury. In this model 50 - 65% of the difference of pain sensitivity seemed to be genetic in basis. This could, however, be different in different animal pain models. Several possible human pain susceptibilities genes have been described and may be related to differences in pain phenotypes in the human.

In the nociceptive model, the nerve functions normally but is in a hyperactive state due to up regulation, possibly from chronic low grade inflammation. Another component

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of this model is that there is visceral convergence of nociceptive information from multiple sites to the same neuron in the Dorsal Horn of the spinal cord. Inflammation at any of these sites, or a combination of sites, leads to a state of central sensitization. With central sensitization there is a decreased threshold for activation of the receptor, an increased magnitude of response of the cell and possibly an increase in spontaneous activity. Thus inflammation in pelvic viscera, such as the bladder with Interstitial Cystitis, can lead to tactile allodynia in the vulvar vestibule due to central hypersensitivity. With light touch, such as intercourse, the nociceptors of the C fibers are activated leading to a sensation of burning pain. Depolarization of the C-fibers leads to release of neuropeptides not only in the periphery, but along the entire nerve cell, including the dorsal root ganglion (DRG) and in the Dorsal Horn. The response to these neurotransmitters depends on the receptors or inflammatory cells that are present. In vulvar vestibulitis, Calcitonin Gene Related Peptide (CGRP) released from the C fiber leads to an increase in blood flow, vasodilatation, and erythema. Also, substance P can be released activating NK-1R receptors (usually on glandular cells, i.e. vestibular glands) releasing proinflammatory cytokines.

It has been shown that women with Vulvar Vestibulitis Syndrome (VVS) have an increased risk for homozygosity of the Interleukin 1 Receptor Antagonist gene (IL-1 RA allele 2). Studies by David Foster have shown an increase in cytokines, such as Interleukin 1 and 8, in the vestibular tissue of women with Vulvar Vestibulitis. They have also found that six MC1R single nucleotide polymorphisms (SNP's) have been found to exist at significantly higher proportions in VVS cases than controls. The MC1R gene has been associated with modulation of inflammation and pain via NFkB transduction. These polymorphisms have been shown to be more common in Caucasians and in redheads.

There were fewer presentations regarding treatments of vulvodynia, as there are few controlled trials. There were no new trials of medical therapy presented, although several medical approaches were discussed. The general theme suggested a centrally acting agent, such as Amitryptiline or Neurontin, should be combined with a locally acting agent such as Lidocaine. In regards to Amitryptiline, the point was made that metabolism of the drug can markedly differ between patients due to enzyme function. About 7% of the population has decreased metabolism leading to significantly greater effect at low doses while a similar percentage have increased metabolism necessitating higher doses. Some experts push the dose to as high as 200mg to achieve benefit in those patients. Dr. Jacob Borenstein presented his series on Vestibultectomy with vaginal advancement. He felt that to be successful a complete vestibulectomy excising from midway between the hymen and anus, along Hart's line up to and adjacent to the urethra with vaginal advancement was the preferred procedure. In his series of 646 cases, the largest reported to date, 57% of women were asymptomatic, 32% improved with 11% the same. His series included follow up from 0.2 - 10 years. Sophie Bergeron, Ph.D., presented findings on a Randomized Controlled trial of therapy for Vulvar Vestibulitis. Seventy-eight total patients were randomized to vestibulectomy, Group Cognitive Behavioral Therapy (GCBT) or Physical Therapy with biofeedback. Patients were assessed at pretreatment, post treatment, 6 months and 2.5 years after treatments with gynecological exams as well as validated pain questionnaires, sexual function instruments and the Brief Symptom inventory measuring psychological adjustment. Data were analyzed using an intent-to-treat strategy. All three groups significantly improved on measures of psychological adjustment and sexual function, however, frequency of intercourse remained markedly below community sample norms. Patients were also found to continue to improve and maintain benefit at the 2.5 year follow-up evaluation in all three groups. Findings of the long term follow-up continued to support the superiority of vestibulectomy, despite 7 patients randomized to the vestibulectomy group declining to have the surgery. Pre-treatment predictors of outcome at long term follow-up were also evaluated. Negative sexual attitudes were a strong predictor of poor surgical outcomes while higher pretreatment pain intensity and lower confidence in treatment predicted less benefit for biofeedback and GCBT.

In summary, the mechanism of pain generation in vulvodynia is not well delineated, nor is the best medical approach. There does appear to be a genetic predisposition to developing vulvodynia, with a significant proportion of patients having significant pain with initial use of tampons, well before sexual activity or recurrent infection. This leads to the hypothesis that vulvodynia and vulvar vestibulitis are multifactorial and may be caused by different factors or genetic alterations in different women.

With regrets, our previous newsletter contained a typo on a product we mentioned. Below is the correct spelling of Prelief encompassed within its original notation.

For patients who experience an increase in IC symptoms from eating food with a high acid content, calcium glycerophosphate (Prelief®) has demonstrated relief (Table 2). A prospective, nonrandomized study of 203 patients demonstrated that calcium glycerophosphate (Prelief®) helped reduce IC symptoms among patients who ingested foods that would regularly exacerbate their IC symptoms. Symptom exacerbaters were foods determined by a 4-week food diary. Patients were then instructed to take 0.66 gm of calcium glycerophosphate before ingestion of the symptom exacerbaters. Symptoms were recorded by voiding diaries, and Likert scales for urgency and pain. Seventy percent of the patients reported a reduction in pain, while 61% reported a reduction in urinary urgency.

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