National Vulvodynia Association

NVA News

Volume XIV, Issue II Spring 2009

Treating Vulvar Pain: A Neurologist's View

By Allan S. Gordon, MD, FRCP(C)

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Introduction

Vulvar pain is not normally considered to be in the scope of practice of neurologists, but it should be. The pelvis, vulva, and vagina have a rich innervation with many nerves, somatic and autonomic, converging on the spinal cord and integrating with the rest of the pain system. Basic training gives neurologists an understanding of these neural systems and their function, which is important in understanding how to diagnose and treat chronic pain. In addition, neurologists are trained to conduct a medical history and neurological examination, and to perform tests to answer two questions: *where* is the lesion and *what* is the lesion? Neurologists also determine whether the pain is nociceptive (tissue damage) or neuropathic (nerve damage) and which treatments are necessary. What some neurologists may lack, however, is the interest or ability to treat pain in a multidisciplinary manner.

The Wasser Pain Management Centre (WPMC) in Toronto was formed in 1999 to offer a multimodal approach to pain problems, with staff members in neurology, nursing, dentistry, anesthesiology, gynecology, psychiatry, sex therapy, behavioral therapy, and addiction medicine. Additionally, the center has links with associate programs in physical therapy, urology, acupuncture, urogynecology, dermatology, and yoga. Six intertwining "programs of care" have been established: Complex Pharmacotherapy (e.g.,

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Superficial Dyspareunia in Postmenopausal Women

By Alina Kao, BA, Melanie Morin, PhD, PT, Yitzchak M. Binik, PhD, and Samir Khalifé, MD

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Painful sexual intercourse, or dyspareunia, is one of the most frequently reported problems of postmenopausal women seeking treatment. Dyspareunia is typically categorized as superficial (pain is felt in the vulva, labia, or vaginal entrance) or deep (internal genital or pelvic pain). Our research and clinical experience have focused on superficial dyspareunia, therefore this article will discuss only this subtype.

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antidepressants, anticonvulsants, opioids, anti-inflammatories, cannabinoids); Pain, Addiction, and Chemical Dependency; Pelvic and Genital Pain; Neuropathic Pain; Headache and Facial Pain; and Arthritis and Soft-tissue Pain.

Patients referred to the WPMC fill out a detailed questionnaire including, if relevant, questions on pelvic pain. Based on the letter of referral and previous documents, the individual is referred to the most appropriate practitioner who takes a detailed history and performs the examination. Other team members may participate, if necessary. Accurate diagnosis is emphasized, and multiple diagnoses may be offered. Further investigation may be ordered and then a treatment plan is devised.

The female pelvic pain team may include the neurologist, gynecologist, nurse, physical therapist, anesthesiologist and sex therapist. Evaluation includes a general and neurological examination; abdominal, back and pelvic exam; vulvar examination (including the cotton-swab test), and pin-prick evaluation. A drug and alcohol history is also taken.

Because we emphasize dealing with all aspects of chronic pain, the patients may be evaluated differently than in gynecology-based clinics. The following examples illustrate the range of patients presenting at the WPMC:

(1) A 55-year-old woman was referred for chronic migraine, and only during the course of the evaluation did she describe a 25-year history of dyspareunia, specifically, superficial pain upon penetration.

(2) A 34-year old woman developed urgency, frequency and dysuria. Urine cultures were negative. Investigations showed typical changes compatible with interstitial cystitis, or painful bladder syndrome. Three months later, she developed vulvar pain both at rest and with intercourse. She was started on 75 mg of pregabalin twice a day, and increased to 150 mg twice a day. Her urinary symptoms improved, as did her vulvar pain and dyspareunia.

(3) A 43-year old woman was referred with total-body pain. Her vulva showed multiple cotton swab sensitivity areas, pin-prick hyperalgesia (hypersensitivity to a painful stimulus) and an exquisitely sensitive clitoris. The vulvar pain in this case was so overshadowed by her widespread muscle pain that she did not complain of it.

(4) A 45-year old woman complained of abdominal pain that started after a total abdominal hysterectomy for fibroids. Initially, the pain was restricted to the transverse lower abdominal scar on the right; over time, the pain spread down to the vulva on the right side and up to the right rib cage margin. After numerous tests, no explanation was found for this

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NVA News
National Vulvodynia Association
P.O. Box 4491, Silver Spring, Md. 20914-4491
(301) 299-0775; FAX: (301) 299-3999
www.nva.org

NVA News is published three times per year.

Editor:
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Layout: Andrea Hall

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neuropathic pain other than the possible result of central sensitization (changes in the brain due to repeated nerve stimulation) from a lower abdominal segmental nerve injury. In this case, the vulvar pain was part of a larger neuropathic pain abnormality.

In addition, women presenting with provoked vestibulodynia (PVD, also known as vulvar vestibulitis), and/or generalized vulvodynia (GVD), or vulvar pain as part of a major genital or pelvic pain syndrome, are commonly seen in our center. Many of our patients do not fit into the strict classification of vulvar pain offered by the International Society for the Study of Vulvovaginal Disease (ISSVD). There can be many sacral nerve functions affected and a variety of pain syndromes involved, in addition to overlap among syndromes. Therefore, treatment of vulvar pain depends on the clinical context. As such, we have developed a classification of vulvar pain based on patients presenting to the center. (See Table 1)

An Approach to Vulvar Pain Management

Our approach incorporates some broad principles of pain management that are as applicable to the vulva as they are to other chronic pain syndromes. We refer to them as the 'five pillars' of pain management. (See Table 2, next page)

Applying the Five Pillars to Vulvar Pain

Pillar One: Conduct a Risk Assessment

As a first step in treating anyone with pain or any other condition, the treating practitioner should establish treatment goals with the patient. In doing so, a risk assessment is needed. What are the risks of treating versus not treating the patient? At the WPMC, we treat vulvar pain patients within a multidisciplinary framework, using the universal precautions approach to pain management (a standardized

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Table 1: Vulvar Pain Classification

I Vulvodynia
- a. vestibulodynia (provoked)/aka vulvar vestibulitis or PVD
- b. generalized vulvodynia (unprovoked)/aka dysesthetic vulvodynia or GVD
- c. mixed provoked and unprovoked vulvodynia

II Vulvar pain associated with other genital syndromes
- a. clitoral pain
- b. urethral pain and interstitial cystitis
- c. anal pain

III Vulvar pain associated with comorbidities
- a. fibromyalgia
- b. temporomandibular syndrome
- c. migraine
- d. irritable bowel syndrome
- e. pain and dependency issues

IV Vulvar pain as part of a larger neuropathic pain syndrome
- a. peripheral, such as painful diabetic neuropathy
- b. central, such as multiple sclerosis
- c. part of a lumbosacral radiculopathy

V Vulvar pain stemming from a pelvic region neuropathic pain injury

VI Vulvar pain as part of pudendal neuralgia or pudendal nerve entrapment

VII Vulvar pain as part of a pelvic pain condition: endometriosis, pelvic congestion syndrome, fibroids or adenomyosis

VIII Vulvar pain as part of another entity
- a. yeast
- b. lichen sclerosus

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approach in the assessment and management of chronic pain patients). As part of this approach, we inquire about a history of alcohol and drug abuse in the patient and family, history of smoking or gambling addiction, history of sexual abuse and dysfunction, prior pain and its treatment, other pain issues, anxiety and depression, and any legal and litigation issues. Between 3 and 13 percent of the general population may have an addiction. The more 'red flags' an individual reveals, the riskier and more difficult the treatment. Based on this assessment, patients are divided into three groups:
Group I, low risk: little evidence to suggest addiction or psychiatric problems;
Group II, moderate risk: no active addiction but the presence of psychiatric problems; and
Group III, high risk: serious active addiction and psychiatric issues.

Typically, low-risk individuals can be easily, if not always successfully, treated by most knowledgeable practitioners. The treatment of moderate-risk patients may benefit from input from mental health and addiction specialists; at the very least, specific attention should be paid to these issues. To manage high-risk patients—the most challenging group to

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Table 2: The Five Pillars of Pain Management

Pillar One
Risk assessment. What is the risk of treating the individual, risk to the patient and risk to the practitioner? We apply the principles of universal precautions first enunciated by our colleague Doug Gourlay.

Pillar Two
Identify the underlying disease and treat it. This assumes that there are specific diseases causing pain and that treatment of the underlying condition will relieve the pain.

Pillar Three
Determine whether the pain is neuropathic or nociceptive (or both) and follow the evidence-based path of treatment for neuropathic and nociceptive pain. This applies more to pharmacotherapy than to nonpharmacological therapies.

Pillar Four
Treat psychosocial and comorbid conditions, such as anxiety, mood and depression, addiction, sexual dysfunction, and sleep.

Pillar Five
Establish a good therapeutic alliance with the patient. Encourage and teach self-management techniques to allow the individual to take charge and share responsibility for her condition.

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treat—direct input and care from experts in addiction and mental health is needed. Also, this pillar involves setting appropriate boundaries with patients, i.e., what the treatment will entail, what kind and how much medication or other treatment will be offered, and what will happen if those boundaries are broken.

Pillar Two: Identify the Underlying Disease Process and Treat It

The neurologist's aim is to identify whether a neurological lesion is present. If so, its location and potential cause(s) should be determined. This process involves conducting a neurological and general medical history, a physical exam, and confirmatory tests, such as a neurophysiology assessment, to find the anatomical and pathological cause of the symptoms. After this has been completed, treatment options can be considered.

Pillar Three: Diagnosing and Treating the Pain

Pain is typically classified as nociceptive or neuropathic. Nociceptive pain reflects stimulation of normal nerve endings by inflammatory substances and may be somatic (e.g., musculoskeletal) or visceral (originating from an internal organ). Neuropathic pain indicates damage to either the peripheral or central nervous system. Symptoms suggestive of neuropathic pain include burning, shooting, or knife-like sensations, pain upon contact, pain produced by a typically nonpainful stimulus (allodynia), and hypersensitivity to a painful stimulus (hyperalgesia). Most investigators feel that idiopathic vulvar pain (pain without a known cause) is neuropathic. However, it is important to keep in mind that many different pain mechanisms may be operating in this condition.

Another way of classifying pain conditions reflects the axes of pain management. Pain may be acute or chronic; mild, moderate, or severe; cancer- or noncancer- related; and nociceptive or neuropathic. A complete pain assessment collects all this information, which then helps to guide treatment.

For pharmacological treatment of neuropathic pain, the Canadian Neuropathic Pain Guidelines (CNPG) present a four-stage process. It is important to note that these medications have been studied extensively for neuropathic pain, but little empirical evidence exists on their effectiveness in treating vulvodynia. A survey of clinicians indicated that oral medications were more likely to be used for the treatment of GVD versus PVD. Since randomized, controlled treatment outcome studies are currently lacking in this area, firm conclusions cannot yet be drawn regarding the effectiveness of all oral medications in the treatment of vulvodynia. This pillar also includes nerve blocks, nerve stimulation techniques, and the use of botulinum toxin; however, formal trials on the efficacy of these techniques are lacking.

<u>Level 1 Medications</u>

Tricyclic antidepressants (TCAs) are the mainstay of pharmacotherapy for relieving neuropathic pain, because of the research evidence supporting their use. These medications also have gained some support for treating vulvodynia. McKay conducted a retrospective chart review of 20 women with GVD who were taking amitriptyline. The study showed that the average dose required for symptom resolution was 60 mg, with an average treatment period of seven months. Munday followed 32 GVD patients on TCAs for six months (11 of whom also reported PVD symptoms) and demonstrated that complete pain relief was found in 15 (47%). Only four patients obtained less than a 50 percent improvement in their symptoms. However, patients in this study received the TCAs as part of a comprehensive treatment program; thus, the effects cannot be solely

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attributed to the medication. At follow-up, Reed showed that women with GVD or PVD who were prescribed a TCA were more likely to have pain improvement than those not taking the medication. In fact, 49 women (out of 83) who were still taking a TCA at the first follow-up had improved by more than 50 percent.

Most practitioners begin with either amitriptyline or nortriptyline 10–25mg at bedtime. The dose can be slowly increased either weekly or biweekly, aiming for a dose that provides pain relief. A TCA will also improve sleep, and depending upon how high the dose, possibly mood. Generally, the maintenance dose is 50–75 mg per day, although antidepressant dose levels of 150 mg can be used. It must be emphasized to patients that any improvement will come slowly and that not all patients will respond. Side effects can include weight gain, mouth dryness, sleepiness, palpitations and other cardiovascular issues, dizziness, and precipitation of glaucoma. As many women with vulvar pain also have urinary symptoms, the practitioner should ask about symptoms of urinary retention and consider another medication if that is a problem.

In general, gabapentin and pregabalin also have been found useful for neuropathic pain; however, their expense could make these two anticonvulsant agents a second choice to the TCAs. The effectiveness of gabapentin for vulvodynia has been evaluated by three groups. Bates and Timmins reported improvement in two patients with GVD, and Ben-David and Bruce reported that 14 of 17 patients (82%) with vulvodynia had either partial or complete relief with gabapentin therapy. Of these patients, seven experienced complete pain relief and another seven had significant pain relief, which was typically seen between two and four weeks after treatment onset. Treatment failed in the remaining three patients. Further, a chart review indicated that 98 of 152 women with GVD had resolution of at least 80 percent of their symptoms, whereas 49 did not have adequate resolution. Women with longer histories of GVD were less likely to benefit from this treatment.

Gabapentin is usually started at 300 mg at bedtime, increasing by 300 mg every few days, with a target dose of 300 mg three times per day. If there is no effect, it can be increased slowly to 600 mg three times per day and even higher. The author does not usually increase past 1800 mg daily unless some positive effect is noted. It may take up to several weeks to notice any improvement and side effects include weight gain, edema, dizziness and cognitive changes. Gabapentin has few, if any, drug interactions.

Pregabalin has undergone extensive testing for both central and peripheral neuropathic pain. Additionally, it is of benefit for anxiety, sleep (pillar four effects; see Table 2 on p. 6), central pain, and fibromyalgia. As such, it should be a good choice for vulvar pain patients, particularly those with significant comorbidities. Although no specific studies of pregabalin for vulvodynia have yet been conducted, one case report indicated that it is successful in managing the pain of GVD.

The recommended starting dose is 75 mg twice per day. However, in our experience, many vulvar pain patients are quite sensitive to medications, and we often start with 25 or 50 mg twice per day, increasing once each week. An initial target dose would be 150–300 mg daily. Increases to 450 mg or even 600 mg per day are sometimes necessary, but note that adverse side effects will also increase. Many women complain of edema and/or weight gain, dizziness, cognitive changes, lowering of mood or libido, and muscle pain. Similar to gabapentin, it has few drug interactions.

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NVA Funds Five New Research Studies

The continued generosity of our donors has allowed NVA to award five new research grants and fund the creation of a vulvar pain clinic. NVA grants are an essential source of funding for clinicians and scientists, many of whom ultimately use their pilot data to secure large-scale grants from institutions such as the National Institutes of Health. Following are summaries of several recently funded studies.

NVA-Funded Research

In January, NVA awarded a research grant to Maureen Basha, PhD, assistant professor in the department of physiology and pharmacology at Drexel University College of Medicine, Philadelphia. In collaboration with Susan Kellogg-Spadt, CRNP, PhD, director of vulvar and sexual medicine at the Pelvic and Sexual Institute, Graduate Hospital, Philadelphia, and Kristene Whitmore, MD, medical director of the Pelvic and Sexual Institute and chair of urology at Drexel University School of Medicine, Dr. Basha will study the influence of the ovarian hormones, estrogen and progesterone, as well as testosterone, on vulvar sensory processing in women with and without vulvar vestibulitis syndrome, i.e., provoked vestibulodynia. There is a growing body of research evidence indicating that ovarian hormones play a role in pain modulation. The goals of this project are to determine: (i) changes in vulvar and non-vulvar sensory processing across the menstrual cycle; (ii) the impact of oral contraceptives on vulvar and non-vulvar sensory processing; and (iii) how ovarian hormone levels contribute to altered vulvar pain thresholds in women with vulvodynia. The results of this study will provide further insight into the role of ovarian hormones in causing and/or maintaining vulvodynia.

Nina Bohm-Starke, PhD, obstetrician/gynecologist and senior consultant of the vulvar open care unit at Danderyd Hospital in Sweden, also received an NVA grant, matched by her institution. She will investigate whether certain genetic variations are associated with general pain hypersensitivity in women with vulvar vestibulitis syndrome (VVS). Recent studies have found that women with VVS also have lower pain thresholds than controls in non-vulvar body sites (e.g., arm, leg), suggesting altered pain processing in the central nervous system. Furthermore, some studies show a significant percentage of women with VVS suffer from more than one pain condition, i.e., they also have fibromyalgia, interstitial cystitis, temporomandibular joint/muscle disorders, and/or irritable bowel syndrome. This has led researchers to propose that some women with VVS may be genetically predisposed to develop pain conditions. In VVS patients and controls, Dr. Bohm-Starke will investigate alterations in several genes that are involved in pain modulation and inflammation. This study aims to (i) increase our knowledge of the underlying mechanisms in VVS, and (ii) identify a subgroup of women with VVS at risk of developing other pain conditions.

Andrea Nackley, PhD, assistant professor of pharmacology, and Denniz Zolnoun, MD, associate professor of obstetrics and gynecology and director of the Vulvar Pain Clinic, both of the University of North Carolina – Chapel Hill, were awarded an NVA grant to investigate possible common mechanisms in vulvodynia and temporomandibular joint/muscle disorders (TMD). In their proposal, Drs. Nackley and Zolnoun note that little is known about the cause(s) and factors that maintain these disorders and conventional treatments provide limited pain relief. Recent studies have demonstrated that persistent pain conditions occurring in isolation may result from *local* increases in peripheral nerve activity and proinflammatory cytokines (substances that trigger inflammation). Alternately, pain conditions occurring in concert may result from changes in both the central nervous system's processing of pain and *circulating* proinflammatory cytokines. Drs.

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Nackley and Zolnoun hypothesize that vulvodynia and TMD share common central pathophysiology and will compare pain sensitivity and circulating cytokines in four groups: women with vulvodynia, women with TMD, women with concurrent vulvodynia/TMD and healthy controls. This study aims to provide: (i) a better understanding of the key mechanisms that drive vulvodynia and TMD, (ii) more accurate differentiation of distinct subgroups of vulvodynia and TMD patients, and (iii) the development of new therapeutic strategies tailored to these subgroups. Their ultimate goal is to uncover the underlying mechanisms and perpetuating factors for each subgroup and utilize treatments that target those factors.

In March, Theodore Fellenbaum, MD, director of the Mid-Michigan Vulvar Care & Colposcopy Center in Flint, was awarded a grant that was matched by Genesys Medical Regional Center, Grand Blanc, Michigan. The goal of this study is to test the effectiveness of a potential new treatment for VVS. Dr. Fellenbaum will clinically test the proposed link between mast cells, which play a key role in the inflammatory process, and the development of VVS. When triggered, mast cells degranulate, releasing toxic substances, such as histamine and cytokines, into the surrounding tissue. Mast cell degranulation may lead to an increase in nerve growth factor (a molecule that stimulates the growth of certain sensory nerves) and excessive hypersensitivity of the nerve fibers in the vestibule. This hypersensitivity may account for the pain of vulvar vestibulitis. In this study, Dr. Fellenbaum is investigating the action of an oral medication that reduces mast cell degranulation to see whether it alleviates VVS pain. He will compare the degree of pain relief reported by women taking this oral medication to that of two other groups of women being treated with topical medications.

Robert Moldwin, MD, director of the Pelvic Pain Center at the Smith Institute of Urology, Long Island Jewish Medical Center, New York, and medical student Amin Herati, were awarded a grant to investigate myofascial trigger points in women with vulvodynia. Women suffering from myofascial dysfunction have multiple trigger points, or hyperirritable spots of taut skeletal muscle, throughout their bodies. When active, trigger points cause pain and other symptoms. Although patients with chronic pelvic and urogenital pain can have trigger points in their pelvic floor muscles, very little is known about their prevalence and distribution. The goal of this study is to determine whether the locations or pattern of pelvic trigger points differ among three pelvic pain disorders – vulvodynia, interstitial cystitis (painful bladder syndrome) and chronic prostatitis. If distinct trigger point patterns can be identified for vulvodynia and interstitial cystitis, clinicians could add trigger point evaluation to the diagnostic workup of women presenting with pelvic pain and be better-equipped to differentiate vulvodynia from interstitial cystitis.

Dr. Stanley C. Marinoff Vulvodynia Career Development Award

E. Cristian Campian, MD, a urogynecology and pelvic reconstructive surgery fellow at Saint Thomas Health Services in Nashville, Tennessee and Yaniv Farajun, MD, a third-year medical resident at Western Galilee Hospital in Israel, are the 2009 recipients of the *Dr. Stanley C. Marinoff Vulvodynia Career Development Award*. Dr. Campian will use his NVA award, matched by Baptist Hospital in Nashville, to establish a multidisciplinary vulvar pain clinic at Saint Thomas Health Services Center for Pelvic Health, the largest pelvic pain clinic in the area. In addition to improving women's access to specialized clinicians in the region, Dr. Campian's long-term goal is to collaborate with other vulvar pain centers in applying for research funding from the National

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Gabapentin and pregabalin have a similar mechanism of action, but their therapeutic effects are not identical. The highest dose for pregabalin is typically 600 mg per day, whereas gabapentin doses can reach 3600 mg, or even higher, per day. If one medication does not work, the practitioner can switch to the other and either one may be combined with a TCA.

Level 2 Medications

Serotonin norepinephrine reuptake inhibitors (SNRIs) have also proven effective in treating neuropathic pain, but have not been well studied in treating vulvar pain. Venlafaxine, an SNRI, not only helps alleviate neuropathic pain, it also has anxiety-relieving and antidepressant effects. It is available in immediate release and extended-release formulations. The initial dosing is 37.5–75 mg once daily, increasing up to 150–225 mg. Side effects may include nausea, dizziness, insomnia, changes in blood pressure, vasodilatation, cardiac arrhythmia, gastrointestinal symptoms, and sexual dysfunction. Headache is common and there is increasing concern about the potential for suicide. The author's impression is that it is only of modest help in treating vulvar pain.

Duloxetine is another SNRI that is new to the market. Approved for major depression, it is also helpful in the neuropathic pain of diabetics. There are no studies of this medication in vulvodynia patients. Doses of 30–60 mg per day are used, with 60 mg as the recommended dose. Drowsiness, nausea, dizziness, constipation and dry mouth are common, and there is the possibility of serotonin syndrome (rapid heart rate, confusion) if mixed with a TCA.

The Canadian neuropathic pain guidelines do not include selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine, citralopam), because they are not particularly effective in the treatment of neuropathic pain, including vulvar pain. However, they may be helpful for concurrent anxiety and/or depression.

Topical lidocaine, particularly in gel form, can be effective in localized neuropathic pain conditions such as postherpetic neuralgia. It can also be helpful in treating PVD. Of particular interest to us, is the efficacy of daily application of topical capsaicin 0.0125% over topical anesthetic. Although an initial burning sensation is common, we have achieved some positive outcomes. Steinberg and colleagues report significantly reduced discomfort and an increase in sexual relations using 0.025% capsaicin for PVD. The author has not found topical amitriptyline or ketamine to be effective in these patients. There has, however, been a recent study on topical gabapentin that showed a positive effect.

Level 3 Medications

Tramadol, a weak tricyclic and μ-opioid receptor agonist (a drug that activates the opioid receptor), has become useful in the treatment of neuropathic pain. It is considered a third-line treatment approach by the CNPG and is often used to treat the comorbid conditions associated with vulvar pain, such as fibromyalgia. There are, however, no formal studies of its effectiveness for vulvar pain. Clearly, it is a more conservative approach than prescribing a full opioid. It may be combined with acetaminophen or used alone in an immediate release or sustained release formulation, with a maximum dose of up to 300–400 mg per day. Side effects include nausea, dizziness, headache and sleepiness. More serious, but rare, side effects include seizures, and one must be cautious using it with a TCA or SNRI, because of the risk of serotonin syndrome.

Opioids include slow release formulations of codeine, oxycodone, morphine or hydromorphone, as well as the fentanyl patch. Such medications are

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reserved for use in complex vulvar pain patients. The use of short-acting opioids, such as meperidine (Demerol), is discouraged. Because of addiction risk, an assessment is necessary to decide on dosing, dispensing and boundaries. An experienced addiction specialist should be consulted if there are concerns.

Level 4 Medications

Included in this category are the 'other' medications, such as carbamazepine, oxcarbazepine, lamotrigine and methadone. Although some of these medications have shown efficacy in treating some types of neuropathic pain, none of them have been studied in vulvar pain patients.

Nabilone (Cesamet ®) is a synthetic cannabinoid, i.e., a synthetic form of marijuana. Although its use has not been studied in vulvar pain, it has been found to be effective in pain management. The pill comes in 0.5 and 1.0 mg tablets and the target dose is 3–6 mg per day. Side effects of nabilone include drowsiness, dizziness, mood changes, dry mouth, unsteadiness, blurred vision, loss of appetite and headache. In one placebo-controlled, double-blinded pilot study of 30 patients with chronic pain, there was benefit with Cesamet®.

Sativex® is a cannabinoid-based medication (available in Canada) approved as an adjunct for neuropathic pain and multiple sclerosis. It appears to be effective for conditions that present with allodynia, suggesting that it may be effective for PVD or GVD. Although it has not yet been formally tested in vulvodynia patients, we have found that several (but not all) of our patients have experienced some benefit from taking it.

Pillar Four: Treating Psychosocial and Comorbid Symptoms

Patients with chronic pain often have other issues with which to contend, including anxiety, depression, sleep disturbances, sexual dysfunction, and addiction, as well as issues with work and finances. Attending to these problems is essential for a good quality of life and treatment outcome; pain medications generally do not work well when there are outstanding difficulties in these areas. The use of medications, such as the TCAs or SNRIs, can help with some of the psychosocial issues. Also, pregabalin is noted for its positive effect on anxiety, sleep and mood, in addition to relieving pain. However, it is important to note that many medications, such as the anticonvulsants and antidepressants, interfere with sexual function. Thus, the inclusion of psychiatrists, psychologists, behavioral therapists and sex therapists—as well as adjunct medications to offset side effects—can be helpful in pain management.

It is important to note that physical therapy could be included in pillars three, four, or even five.

Pillar Five: Establishing A Good Therapeutic Alliance and Self Management Techniques

Essential to a successful outcome is the inclusion of the patient as an active participant in her own management program. As such, a therapeutic alliance is necessary for success. This process begins with establishing agreed upon and realistic goals, and continues with the assessment and management of the patient's expectations throughout treatment. Also, it is important to emphasize that success depends on the patient, who has to learn techniques to reduce pain and improve function. Whether this is achieved through exercise, yoga, stretching, walking, or relaxation techniques, having the patient take some control and responsibility for the outcome is essential. If the practitioner is working harder than the patient, there is something wrong. In our unpublished vulvar pain survey, a significant

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number of women used self-management techniques. Unfortunately, programs in cognitive behavioral therapy or mindfulness may not be easily available or too expensive. Still, the patient must learn what she can do for herself and acquire her own set of self-management skills and tools.

Conclusion

Vulvar pain may be caused by a number of conditions. A comprehensive plan, such as the five pillar approach, is necessary if patients are to be successfully managed. Unfortunately, there is relatively little high-level research evidence on the efficacy of vulvar pain treatments.

(*Editor's note: To receive a footnoted copy of this article with a complete set of references, please send an email to gigi@nva.org. This article was adapted from a chapter by Dr. Gordon in Female Sexual Pain Disorders, edited by Andrew Goldstein, MD, Caroline Pukall, PhD, and Irwin Goldstein, MD © 2009. Permission granted by Wiley-Blackwell. You can purchase the book, at a 10% discount, by calling toll-free 1-877-762-2974 and mentioning code GOLD9.)* ■

Dyspareunia

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Superficial dyspareunia can severely impact mood and sexual functioning, and cause relationship difficulties and reduced quality of life. Unfortunately, many postmenopausal women suffering from dyspareunia do not achieve resolution of their pain. For some, this might be due to shyness about discussing the topic with a health care professional; for others, the difficulty may stem from longstanding biases amongst health care providers about its causal mechanisms.

The traditional conceptualization of superficial dyspareunia identifies the cause as a decline in estrogen level and the ensuing vulvovaginal atrophy, or thinning of the tissue. However, this viewpoint may be overly simplistic because studies have shown inconsistent findings regarding the relationship between dyspareunia, declining estrogen and vulvovaginal atrophy. Furthermore, although painful intercourse associated with vulvovaginal atrophy is often effectively treated with local estrogen supplementation, a substantial proportion of dyspareunia sufferers do not gain significant pain relief with this treatment. This suggests that, similar to premenopausal women, superficial dyspareunia in postmenopausal women is a multifactorial condition with many potential mechanisms involved in pain onset and maintenance. For example, in premenopausal populations, it is recognized that the condition has many different causes and that provoked vestibulodynia (PVD), also known as vulvar vestibulitis syndrome, is the most common cause of painful intercourse. PVD is characterized by vestibular pain upon touch or pressure and is usually described as "sharp" or "burning" in quality. Our preliminary research has found that the majority of postmenopausal women suffering from painful intercourse experience similar symptoms. Additionally, estrogen replacement users and nonusers alike met diagnostic criteria for PVD within our sample. This indicates that, in all likelihood, PVD also occurs after menopause.

Additional causal mechanisms have been suggested for postmenopausal superficial dyspareunia, including effects of the aging process on the body, pelvic floor muscle dysfunction, a dampened physiological sexual response, and lack of lubrication during intercourse. Furthermore, psychological

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and interpersonal factors such as anxiety, fear, and levels of sexual desire and arousal, as well as relationship characteristics, are correlates of the disorder in premenopausal women. However, there is a lack of research into how these factors may be involved in the postmenopausal population. As a result of the widely held unidimensional perspective that postmenopausal superficial dyspareunia is caused by declining estrogen, other potential diagnoses and non-hormonal treatments are often not considered for this group of women, even when hormonal supplementation does not alleviate their pain. In light of this, we propose an individualized and pain-focused approach to treatment, which entails treating associated medical conditions and addressing the psychological, interpersonal and physiological consequences of the disorder. This multi-disciplinary assessment and intervention should include, in most cases, expertise from gynecologists, dermatologists, urologists, physical therapists and psychologists.

Medical Assessment and Treatment

Superficial dyspareunia can be an indicator of a variety of conditions and warrants a thorough medical assessment. In addition to a standard gynecological examination, a cotton swab test to locate painful areas, fluid or cell cultures, tissue biopsy, colposcopy and ultrasound may be necessary. Visual inspection may uncover mechanical causes such as scar tissue, active fissures (small cuts in the skin), fistula (opening in the vaginal wall that allows urine or stool to pass into the vagina), musculoskeletal problems, or a narrow or partially obstructed introitus (vaginal opening). Conditions that should be ruled out include inflammatory conditions (e.g., irritant vulvitis), bacterial and fungal infections, and dermatological disorders such as lichen sclerosus. Chronic pain or medical conditions, such as fibromyalgia and gastrointestinal problems, as well as cancer treatments, may also contribute to dyspareunic pain.

The menopausal reduction of estrogen levels and resulting vulvovaginal atrophy are likely contributors to superficial dyspareunia. In addition to decreased genital blood flow, lack of estrogen can lead to loss of elasticity, thinning, and increased fragility of the vulvovaginal tissue. Atrophy symptoms include vaginal dryness, burning or itching sensations, and thick, cloudy or foul-smelling discharge. The condition can also be a side effect of medications that diminish estrogen levels, such as tamoxifen, danazol and leuprolide. During intercourse, vulvovaginal atrophy may cause a lack of lubrication, increased susceptibility to genital fissures and bleeding, diminished physiological arousal, and pain.

Localized estrogen replacement, in the form of a conjugated estrogen cream, sustained-release intravaginal ring, or low-dose vaginal tablet, is recommended as the frontline treatment for postmenopausal dyspareunia due to vulvovaginal atrophy. Women with considerable atrophy should be prescribed this estrogen cream and instructed to apply it to the vulvar tissue and intravaginally. Estrogen replacement is contraindicated in some cases, however, e.g., for women undergoing cancer treatment, or with high-risk profiles for breast or uterine cancer. Current guidelines recommend that these women use Replens®, a non-hormonal moisturizer; however, evidence supporting its efficacy in alleviating pain is limited. Application of vitamin E oil directly to the external and internal genitalia can also be beneficial.

While hormonal supplementation can reverse the symptoms of vulvovaginal atrophy, clinical trials have demonstrated that it does not alleviate pain in 10 to 27 percent of dyspareunia sufferers with vulvovaginal atrophy. This finding suggests that, for some postmenopausal women with dyspareunia,

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other causal mechanisms are involved. For others, the pain may be initially caused by atrophy, but persists following hormonal treatment, suggesting that it is maintained by non-hormonal factors. As such, other potential biological or medical conditions and psychosexual factors should be investigated, particularly when an adequate trial of estrogen replacement therapy does not produce significant relief.

Although a thorough medical examination is essential, it may not identify any specific disease or abnormality. An absence of positive findings is also typical for a substantial number of premenopausal women suffering from PVD. Furthermore, similar to other chronic pain conditions, dyspareunia may persist even when the initial condition that caused it has been successfully treated. Even in the absence of medical findings, an important, under-diagnosed potential maintaining factor of postmenopausal superficial dyspareunia is pelvic floor dysfunction, which can develop in response to experiencing pain.

Pelvic Floor Dysfunction Assessment and Treatment

The pelvic floor muscles (PFMs) play a crucial role in sexual function. Findings from a study of premenopausal women suggest that PFM dysfunction may develop consequent to an initial pain episode triggered by a medical condition (e.g., bladder or vaginal infection). Excessive tension, or hypertonicity, of the PFMs may persist after the original cause of dyspareunia has been treated and become a maintaining factor of intercourse-related pain. This could explain why the pain does not resolve for many postmenopausal women, even after their vulvovaginal atrophy and dryness have been effectively treated with hormonal replacement therapy.

In addition to the changes associated with declining estrogen, postmenopausal women are at greater risk for experiencing other urogynecological conditions that can lead to dyspareunia. Our previous research demonstrated that aging is associated with a reduction in PFM hypotonicity, or a lack of muscle tone. Such hypotonicity is thought to cause dyspareunia due to instability of the pelvis. Moreover, the presence of pelvic organ prolapse (e.g., uterine, bladder or rectal descent) can contribute to painful intercourse. Surgical procedures for incontinence or prolapse may also be associated with dyspareunia, since they can lead to vaginal erosion or reduction in the length of the vagina.

Specialized physical therapists assess PFM dysfunction by taking a thorough medical history and conducting a physical examination to verify vaginal flexibility, tissue redness/dryness, and the presence of prolapse, atrophy and/or scars. The physical therapist will also examine PFM function, including muscle tone/tension, strength, endurance, rapidity of contraction, myofascial pain, and the ability to relax and control the PFMs. A musculoskeletal examination also is performed to verify if pelvis, back or hip problems are an underlying cause of pain. Finally, if necessary, an anorectal examination is conducted.

Physical therapy treatment of PFM dysfunction includes education, biofeedback, and manual and insertion techniques, as well as electro-therapeutic modalities. To date, no studies have assessed the effectiveness of these treatments in the postmenopausal population. Nonetheless, since treatment goals are similar in pre- and post-menopausal women, we can expect comparable effectiveness. In our clinical experience, physical therapy reduces pain and improves PFM function associated with vulvovaginal atrophy in postmenopausal women, whether or not they use supplemental estrogen.

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Education concerning genital hygiene habits, sexual function, behavior modification and stress reduction techniques is an integral part of the physical therapy treatment. For example, the physical therapist can suggest sexual positions for facilitating less painful vaginal penetration. Moreover, educating women in PFM anatomy, using both visual observation and vaginal palpation, plays a crucial role in pelvic floor muscle rehabilitation.

PFM exercises and biofeedback prescribed by the physical therapist are specifically adapted to address each woman's dysfunction. The main goals of exercise are to: (i) augment awareness and proprioception (sensory awareness of position and movement) of the pelvic floor musculature; (ii) improve ability to discriminate between and relax muscles; and (iii) normalize muscle tone. Furthermore, PFM exercise may increase blood flow, promoting healing processes within the genital area. Biofeedback consists of measuring and displaying a woman's level of PFM contraction or pressure on a screen, in real time, so she can see the changes. By providing a woman access to this physiological information, biofeedback allows her to gain control over her musculature. In an uncontrolled study, premenopausal women reported a mean decrease of 83 percent in their level of pain following biofeedback therapy.

Physical therapists employ several stretching and massage techniques to promote muscle relaxation, enhance blood circulation, and improve the mobility in the pelvis and genitals. Such interventions adjust postural imbalances, increase the size of the vaginal opening and desensitize the area. These techniques are used to release adhesions (internal scar tissue) related to previous surgery or episiotomy, or tearing during childbirth, all of which can contribute to painful intercourse. Dilators and insertion techniques are aimed at increasing elasticity of the tissue at the vaginal opening, desensitizing the painful area(s) and alleviating fear of vaginal penetration. Postmenopausal women who have a constricted vaginal opening, as a result of atrophy, would particularly benefit from these techniques.

In addition to exercises and stretching techniques, application of different types of electro-therapeutic interventions such as electrical stimulation, high voltage pulsed galvanic stimulation, and transcutaneous electrical nerve stimulation (i.e., TENS) can be used to increase control of the PFMs and reduce vulvovaginal pain.

Pain Assessment and Management

A comprehensive pain assessment is essential to guide differential diagnosis and treatment formulation. Furthermore, inquiring about dyspareunia in an understanding and candid manner can help to reduce awkwardness about this sensitive topic and validate the suffering it causes. The duration and onset of the pain problem (e.g., gradual vs. acute), and whether it coincided with any specific medical, reproductive, or psychosocial event, are clues to potential causal mechanisms involved. Critical variables to evaluate include pain location(s), sexual and non-sexual activities or situations that elicit and exacerbate pain (e.g., bicycling, wearing tight clothing, urinating, masturbation), and whether it is provoked or occurs spontaneously, or both. The sensory nature of pain may give clues to its origins; for example, neuropathic pain tends to be described as "burning" or "shooting" while muscular pains are generally perceived as "aching," "sore" and "diffuse." (See related article on vulvar pain, p. 1.)

The emotional, sexual, and relational aspects of superficial dyspareunia are often overlooked in the treatment of postmenopausal women. Various psychological factors, such as mood states and

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erroneous beliefs, can affect a woman's ability to cope, as well as the intensity and impact of pain she experiences. Similar to patients with other chronic pain conditions, dyspareunia sufferers experience heightened anxiety and depression compared to women not experiencing pain. When left unaddressed, these emotions can impede pain treatment. Thus, a mental health professional experienced in pain management, sex therapy and couple counseling is a critical member of the inter-disciplinary team conducting the assessment and formulating a treatment plan.

Specialized cognitive behavioral therapy, a type of psychotherapy that modifies thought patterns to change mood and behavior, is a useful pain management intervention for women with superficial dyspareunia. This type of therapy can be conducted in individual or group format. It is critical to educate women about the influence that thoughts, emotions and behaviors have on physical pain and the ways that they can modulate each of these factors to decrease their negative impact. Central to this approach is an explanation of how superficial dyspareunia is exacerbated by attentional focus on the pain, which increases anxiety and negative mood, and leads to increased muscle tension during intercourse, thereby creating a vicious cycle. The overarching goals of therapy are pain alleviation and improved emotional and behavioral coping in response to pain. Relaxation training is taught to assist women in controlling their stress response to pain. Dyspareunia-associated fear and maladaptive cognitive styles, such as catastrophization (excessive preoccupation with worst case scenarios), are also important issues to address in pain management therapy.

Psychosexual and Relationship Assessment

Women with postmenopausal dyspareunia may also suffer a sense of loss, particularly if they experienced a satisfying sex life prior to pain onset. Concerns associated with aging and the menopausal transition, such as loss of fertility or femininity, poor body image, and vulnerability to losing their partner are often exacerbated by the onset of pain during intercourse. Couple conflict may develop or intensify with sexual dysfunction and a decline in intimate contact. Moreover, psychosocial stressors, such as children leaving home and caretaking responsibilities for ill family members, are common for women at this stage of life. Related anxiety and distress can dampen libido and further impair sexual functioning. As such, reducing dyspareunic pain without addressing associated psychosexual and relationship issues may not restore sexual functioning.

An in-depth psychosexual assessment should include queries about previous and current sexual functioning, history of physical or sexual abuse, and the impact of pain on the different aspects of the sexual response cycle (i.e., sexual desire, components of sexual arousal such as lubrication or ability to achieve orgasm). Also, information should be obtained about relationship history, current relationship satisfaction and dynamics, the partner's sexual functioning, and how dyspareunia impacts the couple. Whenever appropriate, a woman's partner should be encouraged to take part in the assessment and treatment process. This will help to reframe dyspareunia as not just the woman's dysfunction, but as the couple's problem. In doing so, repercussions of the pain on both partners are validated and addressed, and the partner's empathy, cooperation and support during treatment are encouraged.

Sex and couple therapy for the dyspareunia sufferer and her partner are aimed at addressing the disruption in sexual intimacy and consequent relationship

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distress. Interventions should include sexual education and the promotion of non-painful sexual activities to reinstate sexual desire and arousal, thereby enhancing sexual functioning and decreasing anxiety and avoidance of intimate contact. Interpersonal factors such as partner solicitousness and hostility, as well as poor relationship adjustment, have been shown to be risk factors for increased pain. Thus, increasing relationship satisfaction through effective communication, conflict management and improved sexual functioning helps to diminish the negative impact of dyspareunia on the couple.

Although there is a current lack of research specifically examining the efficacy of psychosocial treatments for superficial dyspareunia sufferers in the later reproductive phases, a recent randomized trial comparing cognitive-behavioral therapy to traditional supportive psychotherapy for vulvodynia included postmenopausal women as one-third of their participant sample. This investigation found that cognitive-behavioral therapy produced significantly greater improvement in pain severity and sexual function from pre- to post-treatment and that treatment gains were maintained at one-year follow-up. In our team's clinical experience, interventions that have included components addressing pain management, reinstatement or improvement of sexual functioning and relationship distress have proven beneficial for both postmenopausal women with superficial dyspareunia and their partners.

Conclusion

Although estrogen replacement therapy is currently the frontline, and often exclusively offered, treatment for postmenopausal superficial dyspareunia, it often does not adequately address the pain or its associated problems. Lack of significant relief with estrogen supplementation is a good indicator that other, potentially non-hormonal, mechanisms are involved in pain onset or maintenance. It is crucial that medical providers bear in mind that superficial dyspareunia can dramatically impair sexual functioning. This has broad-reaching repercussions, extending well beyond physical discomfort for sufferers and their partners. As such, there is increasing recognition of the value of an interdisciplinary and individualized approach to assessing and treating both the causes and consequences of superficial dyspareunia in postmenopausal women. ■

Research

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Institutes of Health. In an effort to promote earlier diagnosis and timely treatment, he also intends to lecture on vulvar pain to primary care physicians. Women interested in making an appointment at this new vulvar pain clinic can call 615-284-4664 or visit: www.centerforpelvichealth.org.

Dr. Farajun will use his NVA award, matched by the Chief Scientist Fund of the Israeli Ministry of Health, to evaluate the effectiveness of an anticoagulant drug, enoxaparin, in treating vulvar vestibulitis syndrome (VVS). Enoxaparin, a form of the drug heparin, inhibits the action of the enzyme heparanase. In a prior study, Dr. Jacob Bornstein found that heparanase was present in the vestibular tissue of women with VVS, but not in the control group. Dr. Farajun proposes that heparanase, which is released by mast cells, may play a role in the etiology of the condition, degrading the vestibular tissue and allowing nerve fibers that sense pain to penetrate the skin's surface. In the current study, participants will self-administer daily injections of enoxaparin into the abdomen, which will inhibit heparanase action and also exert an anti-inflammatory effect. This study will add to our understanding of the etiology of VVS and test a potential new treatment for the condition. ■