

Vaginal Pain and Itching with No Known Cause?

Contributed by Andrew Goldstein, MD
 Tuesday, 24 July 2007
 Last Updated Friday, 13 November 2009

Your visit to the gynecologist has ended with you thinking that you're crazy. You've got vaginal burning, pain, and rawness that won't go away. Your genital area may be red and irritated looking. Your doctor has said that there is no infection, nor any other disease that is causing the problem. You've tried creams, over-the-counter yeast infection treatments, and every other itching treatment available. It's not in your head; you are not losing your mind. It could be vulvodynia.

The International Society for the Study of Vulvovaginal Disease (ISSVD) defines Vulvodynia as chronic vulvar discomfort or pain, characterized by burning, stinging, irritation or rawness of the female genitalia in cases in which there is no infection or skin disease of the vulva or vagina causing these symptoms. Burning sensations are the most common, but the type and severity of symptoms are highly individualized. Pain may be constant or intermittent, localized or diffuse.

Vulvodynia has been classified into the following subtypes: Dysesthetic vulvodynia, Vulvar Vestibulitis Syndrome, and Vulvar Dermatoses. In addition, vulvar skin disorders known collectively as "Vulvar Dermatoses" can also cause vulvar pain. This article describes in detail dysesthetic vulvodynia, vulvar vestibulitis, and the vulvar dermatoses in detail so that you can have the knowledge to speak with your doctor about your particular symptoms.

Dysesthetic Vulvodynia: Dysesthetic vulvodynia is defined as vulvar burning, rawness, and irritation without know cause. The pain is generally non-provoked- there is pain without any contact. It is usually generalized to the entire vulva, but sometimes can be located in one area (e.g. pain of the clitoris only called clitorodinia). The cause of this disorder is unknown. Most experts believe that the pain of dysesthetic vulvodynia is caused by a combination of nerve damage (with central sensitization) and pelvic floor muscle dysfunction. What does this all mean?

Nerve damage: The sensation of burning is almost always neuropathic pain (nerve pain.) How can you get nerve damage? Many ways. Back problems, allergic reactions, trauma, stretching the nerve, persistent infections (however, infection is almost always overemphasized as a cause of nerve damage).

Central sensitization: There are pain nerve centers in the pelvis, spine, lower parts of the brain, and the cortex (higher parts) of the brain. When these pain centers get persistent signals, they get more sensitive, so almost all sensations are then perceived as pain. This does NOT mean "it's in you head" or "you're crazy." This is a physiologic process and can be seen on brain scans called PET scans. Women with central sensitization experience pain more easily. Lastly, this is why stress and anxiety increase pain. The chemicals (called neurotransmitters) that activate these pain centers are the same neurotransmitters that are increased during stress/anxiety.

Pelvic muscle dysfunction: The muscles of the pelvic floor become dysfunctional- too tight and weak. When there is an increase in muscle tone then the blood flow through the muscles decreases. A 10% increase in muscle tone decreases blood flow by 50%. When there is decreased blood flow there is decreased oxygen, decreased glucose, decreased nutrients not just to the muscles, but to the rest of the tissue of the vulva. Lactic acid builds up and the muscles become tight and weak and they hurt. It is as if they are running a six-month marathon.

Treatments for Dysesthetic Vulvodynia

We must address all of the components above to treat DV. If you ignore one of these you are much more likely to remain in pain. The concept of treating neuropathic pain is very simple: "Numb the nerves." If you limit electrical signals going through the nerves, then the nerves can start to heal. Healing only begins when you are out of pain. Secondly, nerves heal very slowly over months not days/weeks.

So which medicines numb nerves?

Tricyclic antidepressants - amitriptyline, nortriptyline, desipramine do this (probably the best), but they have side effects: sleepiness, dry mouth, constipation, palpitation. Just because you may have a side effect (even palpitations) does not mean that the medication is dangerous. I do not have a "favorite" in this group. If one is not tolerated, then I

try the next.

Neurontin (gabapentin) an anti-seizure medication, also "numbs nerves." I find that it works best for focal pain such as clitorodynia. There is a HUGE range of doses that can work – from 100-4500mg. It is a relatively safe medication. In my experience it sometimes works very well, other times not at all. If I suspect that the pain may be from herpes (herpetic neuralgia) then I will start with Neurontin first.

For most diseases the general rule is to try to treat with one medication only. This is NOT true of DV. Usually, I use at least two (sometimes three or four medications). For example I often combine Effexor with Neurontin + an anti-inflammatory + topical lidocaine. This has proven to be an excellent combination.

It is ESSENTIAL that the pelvic floor dysfunction is also addressed. A combination of biofeedback and physical therapy often work the best. The concept behind both biofeedback and physical therapy is that the muscles of the pelvis become very tight and tender when a woman is in chronic pain. When the muscles are tight, they constrict the blood vessels and nerves that run through the muscles. This leads to decreased oxygen and nutrients going to the pelvis and can help perpetuate vulvodynia. In biofeedback a machine with vaginal sensors measures the activity of the muscles of the pelvis (a.k.a. the "pelvic floor" muscles). By using the biofeedback machine a woman is able to train the muscles of the pelvic floor to relax. Normally the muscles of the pelvic floor are not under voluntary control; however, the machine "teaches" you how to control these muscles. There are several different types of physical therapy including reflexology, cranio-sacral therapy and myofascial release, and trigger point muscle massage. All of these modalities are used to relax overly tight and tender muscles of the pelvic floor.

VULVAR VESTIBULITIS SYNDROME

Women with VVS have pain only in the vestibule, and only during or after touch or pressure is applied (see illustration above). Burning sensations are the most common symptom and may be experienced with some or all of the following: sexual intercourse, tampon insertion, gynecologic examination, bicycle riding, and wearing tight pants. Traditionally, VVS is diagnosed using three criteria established by Freidrich. These are: severe pain during attempted vaginal entry, tenderness to pressure localized to the vulvar vestibule, and erythema of the vulvar vestibule. In the last few years, increased awareness of vulvar vestibulitis syndrome (VVS) has led to exciting new research. This research focuses on many different aspects of VVS including possible genetic, infectious or allergic etiologies, and on multiple treatment regimens. Even basic assumptions of early researchers have been questioned, leading to a greater understanding of VVS.

Two studies question our assumptions that VVS has an infectious etiology. Until recently, many physicians believed that VVS is a consequence of human papillomavirus (HPV) infection. Using polymerase chain reaction (PCR) amplification to detect HPV DNA, Morin and co-workers [3] showed, however, that HPV is not more common in women with VVS. Another study, by Bornstein et al. [4], questions the assumption that women with VVS have chronic candidal infections. They showed that prolonged treatment with the oral antifungal, fluconazole, was ineffective treatment for VVS. While both of these studies do not eliminate the possibility that VVS is caused by an initial infection, it appears that VVS is not a consequence of chronic infections of HPV or Candida.

Recent studies from Sweden and Israel have independently shown abnormalities in the vestibular mucosa of women with VSS. Their conclusions showed that some women have ten times the area of nerve fibers within their vestibular mucosa. These nerve fibers are called nociceptors, which are "the pain" sensing endings. Therefore, even very light touch is extremely painful. Other studies have shown a possible genetic link that causes an exaggerated inflammatory or immune response. Data also indicates that some women have increased pain perception not limited to the vulvar area (such as fibromyalgia). [See Appendix A for detailed information on these particular studies.]

Treatments for Vulvar Vestibulitis Syndrome

Over the past few years many studies have examined treatment options for VVS. Several different treatment modalities have proven to be very successful in treating VVS. To date at least 10 papers were published examining the treatment of VVS with vestibulectomy (surgical removal of the mucosa of the vestibule). Bornstein et al. [11] performed a meta-analysis of all the published literature regarding vestibulectomy between 1981 and 1998 and concluded that 89% of women who had a vestibulectomy experienced a significant reduction in pain, and 72% of women had a complete resolution of their symptoms. Schneider and co-workers [12] report similar success and also present data showing that 83% of women who underwent vestibulectomy would recommend it to others.

Several papers have examined electromyographic (EMG) biofeedback for the treatment of VVS. McKay and colleagues [13] report that 52% of women demonstrated markedly decreased vestibular pain after EMG and 69% of the women resumed sexual activity. Sarig et al. [14] reported that 43% of women could have intercourse without pain after an average of 6 months of EMG treatment. Lastly, Bergeron et al. [15] performed the first randomized trial to compare EMG, group cognitive-behavior therapy, and vestibulectomy. They reported that all three treatment modalities offered significant improvement in the symptoms of VVS, but that women had a better outcome after vestibulectomy than with either EMG or cognitive-behavioral therapy.

Several studies have also examined interferon injections for the treatment of VVS. While this treatment strategy was initially started to treat HPV infection (which we now believe is not the cause of VVS), new data by Scherthaner et al. [16] show that interferon inhibits mast cells. If our new hypothesis about the cause of VVS is correct, this may explain why interferon has been successful. Further evidence to support this theory is provided by Gerber and team [17], who show that women with VVS are less likely to produce interferon-beta when they were exposed to a lipopolysaccharide stimulus than a control group of women. Marinoff et al. [18] report that 49% of women experienced reduction in their pain after a course of interferon injections.

Vulvar Vestibulitis

Notice the redness of the vestibule

There are many other treatments for VVS that have not well studied, but are being used at various medical center throughout the country. As there have been no randomized studies on any these medications, there usefulness cannot be accurately discussed. A list of these experimental treatments would include: Estrace cream, atropine cream, nitroglycerine cream, capsaicin cream, lidocaine, desipramine and other tricyclic antidepressant medications, antihistamines, and steroids.

VULVAR DERMATOSES

There are many dermatologic conditions that may cause pain in the vulva. The most common include: lichen simplex chronicus, lichen sclerosis, and lichen planus. These conditions may cause symptoms of itching and burning. Scratching the vulva and overusing topical medications may inflame the tissue, causing swelling and additional pain.

Lichen simplex chronicus: Lichen simplex chronicus (aka: neurodermatitis, pruritus vulvae, squamous hyperplasia, and hyperplastic dystrophy) is the end stage of an itch- scratch-itch cycle. The cause of the initiating itching that leads to lichen simplex chronicus includes atopic dermatitis, contact dermatitis, and eczema. Intense, chronic itching from these diseases results in repetitive rubbing and scratching. The skin responds by thickening, with increased skin markings called lichenification.

Lichen Simplex Chronicus

Lichen sclerosis: Lichen sclerosis is a chronic skin disorder with a predilection for the vulva. The typical lesions of lichen

sclerosis are white plaques, often with areas of bruising and ulceration. Often, there is destruction of vulvar architecture with scarring of the clitoral prepuce, resorption of the labia minora, and narrowing of the opening of the vagina. Symptoms of lichen sclerosis include: chronic itching and soreness of the vulvar area. There can be splitting of the vulvar skin, causing stinging, pain, inflammation and swelling. The skin becomes fragile and pale and white in appearance and these skin changes often cause difficulties with sexual intercourse. Historically, the treatment of lichen sclerosis until the early 1990s was topical testosterone. Well-designed randomized studies, however, demonstrated that clobetasol propionate, an ultra potent topical corticosteroid, was significantly more effective in the treatment of lichen sclerosis with fewer side effects. Lichen sclerosis must be followed closely as 3-6% of women with LS develop vulvar cancer.

Lichen Sclerosis

Lichen Planus: Lichen planus is a skin condition that can occur on the limbs, mouth, vulva and vagina. When it occurs on the mucous membranes of the mouth or vagina it causes erosions or ulceration. Lichen planus is an auto-immune disease- your own body starts to attack a component of the skin causing breakdown of the tissue. Lichen planus may be painful in the mouth and vagina and secondary infection may occur. If the areas touch one another, scarring may occur resulting in a narrowing of the vagina. Lichen planus is most often treated with topical steroid creams. If scarring has occurred, vaginal dilators may be used to help prevent further scar formation. Surgical separation of the vaginal scar tissue is sometimes necessary.

Lichen Planus

While the diagnosis and management of vulvodynia or the vulvar dermatoses is often difficult, once an accurate diagnosis is made there are very effective treatments. If one treatment does not work, do not hesitate to ask your doctor to try something else. Remember, these are conditions that may take months to relieve. Take heart that you are not alone. It's not in your head. Your determination to find relief can help the medical community continue to develop treatment for millions of women.

Appendix A

Although some of our previously held beliefs about VVS have not survived scientific scrutiny, several new ideas do have strong experimental backing. Bohm-Starke and colleagues [5] used PGP 9.5 immunohistochemistry to demonstrate that the number of intraepithelial nerve endings in the vestibular mucosa in women with VVS is significantly increased. In addition, they showed that calcitonin gene-related peptide, which is known to exist in nociceptive afferent nerves, was the only neuropeptide detected in the superficial nerves of the vestibular mucosa. Therefore, the increased free nerve endings within the vestibular mucosa of women with VVS are nociceptors. Bornstein et al. [6] confirmed these results and used computer-assisted histomorphometry to show that women with VVS have ten times the area of nerve fibers than women without VVS. Furthermore, they demonstrated the presence of increased mast cells in the mucosa of women with VVS [6]. If we examine these results along with data from Velangi [7] that shows that the skin of women with VVS is more sensitive to chemical irritants than asymptomatic women, we can formulate a new hypothesis about the cause of VVS. VVS may be initiated by an allergic reaction to a chemical irritant in the vulvar vestibule. This irritation – possibly to topical antifungal agents used to treat suspected candidiasis (yeast infection) – causes mast cells to migrate to the vestibule. If the irritation persists, activation of mast cells leads to an uncontrolled proliferation of nociceptors in the mucosa. This hypothesis explains why up to 80% of women with VVS complain of an acute onset of symptoms that includes burning and itching, which then progress to severe pain on touch. The pain on touch often then persists even after the initial symptoms of itching and burning disappear. Of course, further studies should be performed to assess the validity of this hypothesis.

Witkin and associates [8] are the first to examine a possible genetic link to VVS. They examined the relation between vulvar vestibulitis and polymorphisms in the gene coding for the interleukin-1 receptor antagonist, a naturally occurring down-regulator of pro-inflammatory immune responses. They demonstrated a unique distribution of interleukin-1 receptor antagonist alleles among women with vulvar vestibulitis. This suggests that polymorphism in this gene may lead to elevated levels of interleukin-1 (IL-1), thereby creating an exaggerated inflammatory or immune response. This

hypothesis is further supported by data from Foster and Hasday [9], who showed that tissue levels of IL-1 were 2.3-fold greater in women with VVS than in controls.

Several articles have suggested that women with vulvar vestibulitis have increased pain perception that is not limited to their genitalia. Pukall and colleagues [10] used modified von Frey stimuli to measure tactile and pain thresholds around the vulvar vestibule and in five non-vestibular areas. Their data show that women with VVS had significantly lower tactile and pain thresholds than controls in the vulvar vestibule in non-vestibular regions such as the deltoid. This may imply that VVS is part of a systemic pain syndrome (such as fibromyalgia) and not just a genital condition.

09/2003