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Yeast Infections and Vulvar Vestibulitis Syndrome

An Interview with Paul Nyirjesy, M.D.

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What are the symptoms of Vulvar Vestibulitis Syndrome?
A typical patient with VVS will complain of a burning sensation at the beginning of sexual intercourse. She may also experience discomfort at other times when there is contact with the area at the opening to the vagina (the vestibule), such as with tampon insertion. In her day-to-day activities, a woman with VVS will have variable amounts of burning and irritation, with an intensity that can range from minimal to quite severe.

What is your initial treatment regimen for VVS? What percentage of patients respond to this regimen?
We have developed a stepwise approach to treating VVS. In those with concurrent infections, for example, a yeast infection, we don't even give the diagnosis of VVS until we've eradicated the yeast, documented it with a negative follow-up culture, and assessed that the patient still meets the criteria for VVS. Our initial therapy is to give patients a corticosteroid ointment, either triamcinolone ointment or desoximetasone, twice a day for about a month. In general these are well tolerated, although patients may develop irritation from the ointment, and need to

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NIH Awards First Vulvodynia Research Grants

This past October, the National Institute of Child Health and Human Development (NICHD) selected four vulvodynia research proposals to receive grants beginning in 2001. Three will be funded under last spring's Request For Applications (RFA) on vulvodynia and the fourth was submitted and funded under the NICHD's ongoing Vulvodynia Program Announcement. In response to the RFA, seventeen research proposals were submitted and reviewed. The total amount allocated in the RFA was $1 million a year for the next five years. The four research projects that were selected will examine multiple aspects of the disorder, ranging from prevalence and risk factors to possible causes and treatments. This article will summarize each of the four projects.

Bernard Harlow, Ph.D., associate professor of gynecology and reproductive epidemiology, Harvard Medical School, and Dr. Elizabeth Stewart, M.D., director of the Stewart-Forbes Specialty Clinic for Vulvovaginal Disorders, submitted a proposal entitled, "Prevalence and etiological predictors of vulvodynia." The broad goal of this 5-year research study is to estimate the prevalence of vulvodynia and identify risk factors associated with the condition. A key hypothesis addressed by Harlow and Stewart is that vulvodynia may be the consequence of exposure to a wide spectrum of trauma from physical

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be monitored to make sure that they don't develop thinning of the skin from the medication. In our experience, about 30 percent of patients improve with steroids.

For those who do not improve, what is the next line of treatment?
For those patients, we have used the antidepressant, amitriptyline (Elavil), and more recently, the anticonvulsant, gabapentin (Neurontin). With amitriptyline, about 60 percent of patients develop satisfactory improvement of their symptoms.

What dosage of amitriptyline or gabapentin do you prescribe?
We don't use a set dose for either of these medications. We start with a low dose, and then have patients work their way up until their symptoms are relieved, the side effects become difficult to tolerate, or a maximum daily dose (150 mg. amitriptyline or 3200 mg. gabapentin) is reached.

What differences have been found in the vulvar tissue of VVS patients as compared to normal vulvar tissue? What are the clinical implications of this research?
In general, biopsies of women with VVS demonstrate findings consistent with chronic inflammation. In their biopsies, Chaim and Sobel (1997) have also found a greater preponderance of mast cells, inflammatory cells that release histamine and are commonly found in association with allergic responses. However, they have not found other local changes that one would associate with allergy. The present clinical implications are not clear. However, these findings are consistent with an exaggerated immune response that might be the result of a past or current infectious process. Perhaps it is this infectious process which has helped to initiate, or continues to stimulate, the inflammation that we characteristically see with VVS.

How would you describe the typical onset of VVS? Is it usually preceded by chronic vaginal infections?
Typically, most women with VVS describe a sudden episode, often marked by intense itching and burning, which eventually goes away but leaves the patient with more chronic burning and pain than she has ever had before. By the time these women get to a referral center and are given a diagnosis of VVS, it is difficult to tell whether or not the VVS was preceded by a vaginal infection. Most women with VVS report having been in good health until this problem began. This history of an acute event is suggestive of some sort of infection at the beginning.

In a study by Sarma and colleagues (1999), women with VVS were five times more likely to have had a physician-diagnosed yeast infection than women who did not have VVS. What we don't know is whether these women truly had an infection or whether they had VVS from the beginning and were simply treated for yeast with the hope that yeast was the cause of their symptoms.

Is there an association between human papillomavirus and VVS?
Early on, several investigators found the human papillomavirus (HPV) in tissue samples of women with VVS, and attributed VVS to HPV. However, as the tools to detect HPV have become more sophisticated and accurate, the picture is becoming murkier. We know that HPV is a very common virus, present in a large percentage of the general population. The question is not whether HPV is present in women with VVS, but whether it is found more often in women with VVS than in healthy women and whether there is a cause and effect. In some studies, HPV has been found in as few as 10 percent of women with VVS. Women with VVS who harbor HPV seem to be identical in their histories to women with VVS who do not harbor HPV. Some studies have found HPV to be present more often in women with VVS, but the comparison group may not be closely enough matched to the study group. For now, I feel that the nature of the association remains unanswered.

Do you think that candidiasis (yeast) plays a role in the development of VVS? If so, how might this occur?
A possible association between yeast infections and VVS has not been studied very much, although I think that there is a link between the two conditions. In 1989, Ashman and Ott proposed that VVS could be the result of candidiasis. They suggested that women who get a lot of yeast infections develop a cross-reactive

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immune response. This might occur if there are antigens on the yeast organism that resemble the patient's own antigens. As the patient tries to fight off the yeast infections, her body would develop an immune response to those of her own antigens which resemble those of the yeast organism. Despite the absence of a yeast infection, she then develops a constant inflammatory response, which is stimulated by the body's response to her own antigens.

Most investigators who have studied VVS have not done cultures for yeast, and a possible link between the two conditions has not been adequately explored. In our experience, about 50 percent of women with VVS will at some point during their care with us have a positive culture for yeast. This 50 percent is greater than the 15-20 percent culture positivity rate in the general population. As I mentioned earlier, Sarma's study found that women with VVS were more likely to have been treated for yeast infections than control women.

Why are some women susceptible to recurrent yeast infections?

As noted above, about 15-20 percent of all women harbor yeast in the vagina (usually *Candida albicans*). In most of these women, the yeast doesn't cause any problems, or may at most cause an intermittent infection here or there that responds quite nicely to antifungal therapy. However, a subgroup of women will suffer recurrent yeast infections, defined as four or more infections in a 12-month period.

Current studies suggest that in many women with recurrent yeast infections, local immune factors play a key role. In these women, there appears to be an abnormal local response to yeast, almost like an allergic response, which helps to lay the groundwork for the next yeast infection. These patients get into a pattern of recurrent yeast infections which they can't break out of. Some factors that lead to an increased propensity to yeast infections may be genetic in nature. For example, two studies have shown that women who get recurrent yeast infections are more likely to be negative for Lewis antigens a and b. These antigens are proteins expressed on red blood cells. They are also found in vaginal cells, where they may block the binding of Candida albicans to vaginal cells. Women who lack these proteins may therefore be more prone to having yeast. Most women with recurrent yeast infections seem to have a healthy immune system in other ways, and very few have predisposing factors such as diabetes or HIV infection. The role of behavioral factors in causing recurrent yeast infections remains relatively unstudied.

Do you recommend the use of over-the-counter antifungal medication in VVS or vulvodynia patients?

In general , I don't recommend over-the counter antifungal medications for VVS patients. First of all, I think that it's important to have an accurate diagnosis, which is impossible if the patient self-treats and never makes it into the office. Not all yeast infections are caused by *Candida albicans*, and having a positive culture makes it a lot easier to figure out how best to treat the infection. Furthermore, in women with

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Treatment of Clitoral Pain

By C. Paul Perry, M.D., FACOG

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Clitoral pain is a specific subset of vulvodynia produced by neuralgia of the anterior division of the pudendal nerve. It is manifested by pain localized to the clitoris with or without associated pain such as vulvar vestibulitis and pelvic floor myalgia.

Unlike classical pudendal neuralgia, i.e, dysesthetic vulvodynia, the pain is very localized and may have more of an aching quality than the more commonly reported burning sensation that characterizes classical pudendal neuralgia.

Possible causes

The etiology may be metabolic, traumatic, or idiopathic (unknown). The determinative factor is that the signaling mechanism of clitoral sensation becomes abnormal. Trauma from violent stimulation, tight clothing, or straddle injuries may produce these neuropathic changes. Other possible causes include vulvar laser vaporization or chemical ablation for human papilloma viral lesions (venereal warts). Metabolic disorders such as diabetes can produce clitoral pain. The majority of cases, however, will have no discernible cause.

Diagnosis

The diagnosis is made after careful history taking and physical examination. The key to a diagnostic history is the localization of the pain to the clitoral and periclitoral area. Patients may have a difficult time describing the location of their pain, but often report pain with intercourse, tight clothing, and exercise. It has been noted that stress usually aggravates the pain. Sometimes simply sitting increases the pain, for example, riding in a car for extended periods. Constant "aching" and "soreness" are the most commonly used adjectives to describe the pain. Occasionally, patients describe the pain as shooting or burning.

Sexual stimulation is painful because clitoral engorgement aggravates the pain, making intercourse impossible in many cases. Patients often suffer without seeking medical care because of embarrassment. In some cases, marriages may be threatened because of misunderstanding or lack of communication between spouses.

On physical exam, the absence of diffuse involvement of the entire vulvar and perineal area distinguishes it from the more common dysesthetic neuralgia. The tissues appear healthy with no evidence of inflammation or distortion. The Q-tip test of the minor vestibular glands, which is so characteristically positive in vulvar vestibulitis, is negative in pure neuropathic clitoral pain. However, light touch of the clitoris will reproduce the pain.

Treatment

The treatment regimen for clitoral neuralgia includes both medications known to benefit neuropathic pain and therapeutic desensitizing blocks of the dorsal nerve to the clitoris with local anesthetics. Drugs that may be beneficial include: amitriptyline, gabapentin, diphenylhydantoin, divalproex sodium, trazodone, doxepin hydrochloride, and lamotrigine. In cases of severe unresponsive pain, chronic time contingent opioid therapy may be necessary. Antidepressants should be used frequently since most patients with this chronic pain have some degree of serotonin deficiency from this stressful condition. Psychosocial counseling may be beneficial for many marriages.

The dorsal nerve to the clitoris is a division of the pudendal nerve. It divides from the posterior branch after leaving Alcock's canal and travels anteriorly in the labiacrural fold toward the pubis. At the mons, it takes an almost 180 degree turn to innervate the clitoral corpus. The nerve can be easily blocked on each side by injecting 5mls. of 0.5% bupivacaine about 2 cm. lateral and 1cm. anterior to

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the root of the clitoral corpus. The frequency of these blocks depends on the patient's response and can vary from weekly to once every few months.

Patients with chronic pelvic pain from clitoral neuralgia have found that loose clothing, nontraumatic exercises, and either cold or warm compresses will decrease the pain. Some patients have noted improvement after modifying their diet (avoiding spicy foods, increasing fiber and water intake to prevent constipation). Stress reduction, meditation, and compassionate counseling may help these patients to cope with their pain and changing lifestyle. Increasing social contacts and distraction with career and recreational activities may also be beneficial.

Conclusion

With proper diagnosis and treatment, this condition can be helped. As with any neuropathic pain, the longer the pain is present and the more intense the discomfort, the less likely treatment outcomes will be successful.

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If It's Not Vulvar Vestibulitis, What Is It?

By Richard Marvel, M.D.

Dr. Marvel is an Assistant Professor in the Department of Obstetrics, Gynecology and Reproductive Sciences at the University of Maryland in Baltimore.

Vulvar vestibulitis syndrome (VVS), a subset of vulvodynia, is a chronic vulvar pain condition associated with dyspareunia (painful sexual intercourse). This syndrome has been described for more than 100 years, beginning with a publication by Skene (1889) entitled, "Treatise on the Diseases of Women." The first modern U.S. publication on VVS by Woodruff and Parmley (1983) referred to the condition as "infection of the minor vestibular glands." The term vulvar vestibulitis was coined by Friedrich (1987) who established three criteria based on his observations of 87 patients. According to this definition, women should be diagnosed with VVS when they present with: 1) severe pain on vestibular touch or attempted vaginal entry; 2) tenderness to pressure localized within the vulvar vestibule and 3) physical findings confined to vestibular erythema (redness) of varying degrees.

The evaluation of patients with vulvar pain and dyspareunia requires a careful investigation to rule out other causes for the pain, localized tenderness and erythema. If additional physical findings or treatable conditions exist, this precludes a diagnosis of VVS. The differential diagnosis is extensive and requires taking a thorough history as well as performing a physical examination and laboratory tests.

Vulvovaginal disorders that produce similar symptoms to those associated with VVS can be divided into several categories including infection, dermatoses, dermatitis, iatrogenic (treatment-induced) conditions, atrophy, and dysesthetic vulvodynia.

Infection

One of the most common vulvovaginal disorders is yeast infection, characterized by itching, burning, and a thick white discharge. Recurrent yeast infection, which may be an initiating factor for VVS, should be ruled out by careful wet mount evaluation (KOH preparation), as well as culture. A culture is important for several reasons: 1) the sensitivity of a wet mount, i.e., the likelihood of seeing yeast organisms when present, is only 70 percent; 2) non-candidal albican yeasts are difficult to identify microscopically; and 3) non-candidal yeasts are less likely to respond to common yeast treatments. If identified, recurrent yeast infections usually respond to appropriate anti-fungal treatment, although a prolonged course of therapy may be required. A regimen that I have found successful in about 50 percent of women with recurrent yeast infection is Diflucan 100-200 mg weekly for 3-4 months.

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Cyclic vulvovaginitis, a similar, possibly identical syndrome to recurrent yeast infection, has been described by Dr. Marilynne McKay. Patients experience entry dyspareunia, vestibular burning, itching, irritation and aching after intercourse. The symptoms are usually cyclic, i.e., they wax and wane. Cyclic vulvovaginitis is believed to be due to subclinical candidal infection and, likewise, responds to 100-200 mg of Diflucan weekly for 4-6 months. I usually treat patients for 4 months and then wean the dosage to once a month as a prophylactic regimen to prevent recurrence of symptoms.

A bacterial infection that may be confused with VVS is cytolytic vaginosis. In this condition there is an overgrowth of the normal lactobacilli of the vagina. This leads to an overproduction of hydrogen peroxide resulting in a burning discomfort and pain with intercourse. History reveals a cyclic pattern–symptoms are usually most significant in the luteal phase of the menstrual cycle and relieved by menses. A wet mount reveals no pathogenic organisms, an increase in the normal bacteria, cellular debris, and naked nuclei from epithelial cells. The symptoms can be easily controlled with one or two douches in the second half of the menstrual cycle using 1 teaspoon of baking soda dissolved in one quart of water.

Cytolytic vaginosis, cyclic vulvovaginitis and recurrent yeast infection must be ruled out before a patient is diagnosed with VVS. Other common vaginal infections should be excluded as well, but they are generally acute conditions and tend not to be confused with VVS.

Dermatoses

There are several dermatologic conditions that can cause symptoms similar to those of VVS. Lichen sclerosus is a common skin disease that can affect the vulva and produce symptoms of itching and burning. The disorder causes visible skin changes with thickening or sometimes thinning of the skin of the vestibule, vulva, perineum and perianal skin. Lichen sclerosus usually presents as thin, white parchment-like skin with wrinkling. It is diagnosed by vulvar biopsy and generally responds to treatment with a potent topical corticosteroid for several weeks.

Lichen planus is a generalized skin disease that sometimes affects only the vulva. Patients present with burning, irritation, soreness and dyspareunia. In some cases of lichen planus, the vestibule has ulcerations and the entire mucosa is eroded. Patients with this disorder may also present with sores in the oral cavity: oral examinations frequently reveal a reticulated, gray, lacy pattern of whitened mucosa in the mouth. Diagnosis is confirmed by vulvar biopsy. Treatment consists of local or systemic steroids; one-half of a 25 mg hydrocortisone suppository can be inserted intravaginally twice a day for two months. Once improvement is noted, the medication may then be used once or twice a week for maintenance.

Desquamative vaginitis is a dermatological condition with purulent discharge, severe erythema, and erosions of the vaginal and vestibular mucosa. Some experts believe that desquamative vaginitis is a severe form of lichen planus. When this disease affects the vagina and/or the vulva, it is treated with the same regimen as lichen planus, i.e., intravaginal suppositories of hydrocortisone, alternating with 2% clindamycin cream for two weeks, then completing the course of vaginal hydrocortisone.

Dermatitis

Over time, exposure to local vaginal/vulvar irritants can lead to contact dermatitis, producing burning, itching, and painful intercourse. There are a multitude of vulvar irritants that can cause contact dermatitis. Some common offenders are scented or deodorant soaps, douches, perfumes, feminine sprays and dyes in toilet tissues. Because these irritants may cause symptoms similar to those of a yeast infection, many patients who have contact dermatitis are treated with an anti-fungal cream. Instead of finding relief, some of these patients have a negative reaction to the medication's carrier molecules (e.g., propylene glycol), as discussed by Dr. Ledger in a recent NVA newsletter. (*See* Spring 2000 issue.) This can create a vicious cycle, resulting in a prolonged exacerbation of symptoms.

The best treatment approach for contact dermatitis is to eliminate all irritants to the vulva and provide symptomatic relief through warm soaks with Tannic acid (tea) or

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Domborrow's solution (a soothing astringent). Other helpful measures include wearing loose clothing and white cotton undergarments to provide adequate ventilation and keep the vulva dry. After bathing, using a hair dryer to dry the vulva is recommended. In some cases, a low potency corticosteroid cream may be prescribed. For many patients, symptoms tend to resolve with this approach, but in severe cases systemic corticosteroids may be required.

If vulvar itching is the predominant symptom, or there is a history of adverse reaction to a treatment, allergic contact dermatitis should be suspected. Many agents included in topical preparations, e.g., preservatives, cause allergic reactions which can be diagnosed by patch testing. Some common substances that can result in allergic reactions are local anesthetics (e.g., Benzocaine), perfumes, clotrimazole, butalbital, thiabendazole, benzol peroxide, and even topical corticosteroids themselves. A repeated open application test (ROAT) for allergens can be performed by applying the suspected product three times a day to a 5 x 5 cm area on the forearm and then checking for a reaction. If specific allergens are identified in any of the products or treatment agents the patient is using, they should be discontinued immediately.

The local application of potent or super potent steroid creams for more than three to four weeks can also cause dermatitis. After prolonged use of these creams, the vulvar skin can become irritated and patients report poor tolerance of local medications and post-coital irritation or swelling. Examination reveals erythema, telangiectasia (abnormal blood vessels) and a papular rash. This condition, steroid rebound dermatitis, is treated by tapering the potent steroid cream over several weeks. A low potency steroid, such as 1% hydrocortisone, can then be used for maintenance and relief without the risk of rebound dermatitis. Potent steroids should be reserved exclusively for biopsy proven dermatoses such as lichen sclerosus.

Atrophy

In postmenopausal women, a lack of estrogen can lead to severe atrophic vaginitis which may cause burning, irritation and pain with intercourse. On exam, the vagina is pale, there is thinning of the vaginal mucosa, and a yellow vaginal discharge may be present. This condition responds well to treatment with a vaginal estrogen cream which often resolves the symptoms.

Dysesthetic Vulvodynia

Dysesthetic vulvodynia is a neuropathic pain condition characterized by constant vulvar burning. It is not limited to focal areas of tenderness and is not necessarily

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If you have any questions about these programs, please contact Christin Veasley at chris@nva.org.

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exacerbated by touch or pressure. This disorder is more common in postmenopausal women or younger women with a history of back injury. Treatment usually involves the use of tricyclic antidepressants such as amitriptyline or anticonvulsants such as Neurontin. Surgical resection is not recommended for dysesthetic vulvodynia as the failure rate is significant.

Genital fissures

Patients who have chronic, non-healing posterior fissures (small tears in genital skin) also present with vulvar pain, burning and entry dyspareunia. Many complain of a "tearing" sensation with intercourse as well as post-coital spotting. On exam, these patients have an area of scarring, usually at the most posterior portions of the fourchette ,which can easily tear upon even gentle separation of the labia. A modified posterior vestibulectomy with vaginal advancement is the most successful treatment for this condition. In this surgery, skin of the perineum and posterior vestibule is removed and vaginal tissue is brought down and sutured to the surrounding skin.

Summary

Although the foregoing is by no means a comprehensive list of vulvovaginal disorders, I have reviewed the conditions that are most likely to be confused with VVS. As is the case with all medicine, a thorough evaluation and careful diagnosis is the key to successful treatment.

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Clitoral Pain Study

Investigators in Toronto are seeking information on women with clitoral and/or nipple pain. The researchers would like to create a database and a protocol for evaluating and treating women with these problems.

You do not have to live in Canada to participate in this project. If you experience clitoral and/or nipple pain, or nipple pain and vestibular pain, and would like more information, please contact Dr. Allan Gordon, Wasser Pain Management Centre, Mount Sinai Hospital, at 416-586-5181 or agordon@mtsinai.on.ca.

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VVS who already have inflamed skin, creams or suppositories to treat yeast infections often worsen their irritation and burning. This irritation is noticeable enough in patient histories that Marinoff and Turner have studied whether topical antifungals could be the cause of VVS. Finally, in those women who do have a yeast infection and VVS, a week of antifungal cream isn't really an adequate therapy.

As a rule, how often should VVS patients be cultured for candidiasis?
Since many investigators who treat VVS don't agree with me that yeast contributes to VVS, I don't think I should be suggesting any general rules! With the patients that we see, we practice the philosophy of "culture everyone for yeast and culture often." I am constantly struck by the number of patients that we see who have initial negative cultures, then get a positive one, and finally see all of their symptoms improve once they get started on antifungal therapy. We may be overtreating some patients where the yeast is an innocent bystander, but I prefer that to ignoring a potential cause of symptoms. However, except for rare occasions, we will not treat someone for yeast unless we have culture corroboration. I should emphasize that I believe that these principles apply mainly to a patient population with chronic vulvovaginal problems.

If a VVS patient tests positively for candidiasis, what regimen of antifungal therapy do you prescribe?
Most of our VVS patients test positive for *Candida albicans* so we

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give them six months of fluconazole (Diflucan). For most patients, 100 or 200 mg once or twice a week will keep them culture negative. This prolonged therapy helps to keep the yeast infections out of the picture while we focus on other symptoms (and often the other symptoms disappear before we have a chance to treat them). Six months of daily ketoconazole (100 mg daily) has been shown to decrease the chance that the yeast infections will recur after therapy. Our experience with fluconazole suggests that it has a similar protective effect.

In your clinical experience, are there any other measures (diet, acidophilus, etc.) that can help to minimize the recurrence of yeast infections?

In general, I think that dietary measures can be very difficult to follow, and that they have an uncertain benefit. For every patient I see who has tried the "yeast-free" diet and swears by it, I have 7 or 8 who stuck to the restrictive diet and found that it made their lives miserable and didn't help their yeast infections. Acidophilus pills, taken either by mouth or vaginally, are used by many women with vaginal problems. However, current studies suggest that a lack of lactobacilli is not the cause of recurrent yeast infections. Furthermore, acidophilus preparations do not contain the right types of lactobacilli (those that produce hydrogen peroxide), and many contain viruses that may have activity against a woman's own lactobacilli. For these reasons, I discourage use of acidophilus preparations to reduce the recurrence of yeast infections.

By the time they get to me, most women are following all the standard recommendations about white cotton underwear, avoiding wet bathing suits, etc. Although I agree with those recommendations, I think that they're not enough to prevent recurrent yeast infections in susceptible women.

What hypothesis led you to try cromolyn cream in the treatment of VVS? Have you had any positive results using cromolyn cream in these patients?

Chaim and Sobel's work in Detroit has shown that women with VVS have more mast cells in biopsy specimens than control women. We thought that if mast cells play a role in VVS, a medication that inhibits mast cell function might help women with VVS. Cromolyn, a commonly used allergy drug, prevents mast cells from releasing histamine. We developed a cream with cromolyn as an active ingredient. In an initial pilot study, 9 of 11 patients exhibited a dramatic response to this therapy. We then did a placebo-controlled, double-blind study (neither patients nor physicians knew which cream they were getting). Overall, 11 of 26 patients (42 percent) felt at least 50 percent better. Unfortunately, there was no difference between the placebo and cromolyn groups. Clinically, I have had patients who have done remarkably well with this treatment after having no success with other treatment approaches; they refuse to stop using it because they feel so much better. Our placebo-controlled study suggests that some other factors may be responsible for their improvement, but I continue to use cromolyn cream in selected cases.

Do many of your patients concurrently suffer from dysesthetic vulvodynia and VVS?

Although there is probably an overlap between VVS and dysesthetic vulvodynia patients, I consider these two entities as separate conditions. Women with VVS will have definable point tenderness on examination which reproduces their burning pain, whereas the dysesthetic patients will have an essentially normal examination and burn all the time.

How do your treatments of dysesthetic vulvodynia and VVS differ?

I don't try corticosteroids in dysesthetic vulvodynia patients, and tend to use amitriptyline right away. If dysesthetic vulvodynia patients also have low back problems, I'll refer them early on for pelvic floor and lower back muscle rehabilitation.

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Women's Health Research in the 21st Century

The National Institutes of Health (NIH) have developed an ambitious agenda for studying women's health in the 21st century, according to Dr. Vivian Pinn, director of the Office of Research on Women's Health (ORWH). In her opening remarks at an NIH lecture for the public, Dr. Pinn credited women's health advocacy groups for the important role they played in focusing attention on the need to include female subjects in clinical research. Beginning with the creation of the ORWH in 1990, the NIH has demonstrated a commitment to rectifying this situation. Previously, the term "women's health research" referred primarily to studies of the reproductive system during a woman's childbearing years. The revised NIH women's health research agenda encourages studies on every body system across a woman's entire lifespan, as well as an examination of sex and gender differences and similarities.

In addition to summarizing current research priorities, Dr. Pinn expressed concern regarding some widespread misconceptions about women's health. First and foremost, she contradicted the widely held belief that breast cancer is the leading cause of death among women in the United States. To the contrary, heart disease has been the number one killer of women for nearly a century, accounting for about 57 percent of deaths in women. Cardiovascular disease kills almost twice as many American women as all cancers combined! According to a 1995 Gallup poll, 32 percent of primary care physicians did not know that heart disease is the leading cause of death among women. The unfortunate result of this lack of awareness is that many physicians are not counseling their female patients about behavioral changes that could decrease their risk of heart disease.

In her discussion of women and cancer risk, Dr. Pinn asked the audience which cancer causes the most deaths in American women. At least half the audience responded "breast cancer," whereas the correct answer is lung cancer. Dr. Pinn also highlighted some recent advances in the study of cancer, such as the discovery of a genetic basis for some breast cancers and the link between HPV infection and cervical cancer. She also pointed out that research on cancer prevention is underway, citing studies on the use of tamoxifen in the prevention of breast cancer.

Among current women's health research priorities are the auto-immune diseases such as rheumatoid arthritis, lupus and multiple sclerosis. It has been known for some time that auto-immune diseases, in which the immune response is directed at the body's own tissues, disproportionately affect women. Rheumatoid arthritis is the most common chronic pain condition in women. Other chronic pain conditions on the women's health research agenda include pelvic pain and vulvodynia. Last month, the NIH announced that four vulvodynia studies will receive funding over the next five years (*See* NIH article on page 1).

In recent years, it has become increasingly accepted that a healthy lifestyle can help prevent the development of serious disorders such as osteoporosis and heart disease. As a result, the NIH is committed to supporting research on disease prevention as well as treatment. One of the NIH's most ambitious undertakings to date has been the Women's Health Initiative, one of the largest primary prevention studies in postmenopausal women in the US. This comprehensive longitudinal research is examining 1) the effect of a low-fat diet on the prevention of breast and colon cancer and coronary heart disease, 2) the effect of hormone replacement therapy on prevention of coronary heart disease and osteoporotic fractures, and 3) the effect of calcium and Vitamin D supplementation on prevention of osteoporotic fractures and colon cancer. This multi-center research project began in 1993, but the initial results will not be available until 2005.

Dr. Pinn is confident that the implementation of the NIH's women's health research agenda for the 21st century will lead to many important research findings and clinical applications in the next few decades. The results of this research will ultimately lead to improved women's health care, as physicians and consumers become better-informed about the prevention and treatment of disorders that are prevalent in women. n

Research

(from page 1)

or sexual abuse, accidental or iatrogenic (treatment-induced) injury, or exposure to environmental irritants, abrasives, or topical treatments for vaginal disorders.

To assess the prevalence of vulvodynia and test the hypothesis described above, the investigators will first determine the current prevalence of chronic vulvar pain symptoms in a general population sample of 16,000 women between 20 and 59 years of age. Based upon a secondary screening assessment within the subset of all women reporting vulvar pain symptoms, they will utilize diagnostic criteria to estimate the age specific prevalence for current vestibulodynia (pain in vestibule only) or dysesthetic vulvodynia.

The second research project, "Vulvodynia prevalence and efficacy of four interventions," was submitted by Gloria Bachman, M.D., professor of obstetrics, gynecology and medicine at the University of Medicine and Dentistry of New Jersey. This proposal is divided into three sections: epidemiology, education, and intervention. The aim of the epidemiology section is to update prevalence data, determine which age groups are most affected by vulvodynia and assess whether any similarities/risk factors exist in the vulvodynia population. The educational portion of the project will disseminate information on vulvodynia to the medical community and women's health organizations. The third section is designed to compare the efficacy of different treatments for vulvodynia ; both traditional and new pharmacologic and dietary interventions will be evaluated.

Barbara Reed, M.D., associate professor of family medicine at the University of Michigan Medical School, will investigate potential causes of vulvodynia in a study titled, "Neuroimmunology and cytokine alterations in vulvodynia." The broad, long-term objectives of this proposal are to assess the differences in specific neuroimmunological characteristics between women with vulvodynia and asymptomatic controls. The specific aims include review of: 1) the individual cytokine/neurokine production response to stimulation of peripheral blood; 2) local changes in nerve fiber, mast cell, Substance P and serotonin density in vulvar tissue; and 3) the interactions of the systemic and local immunologic systems assessed in 1) and 2).

The final step will be a multivariable assessment of laboratory results with historical risk factors for vulvodynia, in an attempt to explore whether these pathophysiological mechanisms might account for the historical risk factors identified.

The research design involves a case-control review of 100 women with vulvodynia, 100 controls matched for ethnicity, and 100 African-American control women, using questionnaires, physical examinations and clinical laboratory data. Results from this study should lead to improved understanding of neuro-immunologic alterations in women with vulvodynia and the development of therapeutic strategies for this disorder.

The fourth proposal, "Cognitive behavior therapy for vulvodynia patients," was submitted by Robin Masheb, Ph.D., associate research scientist in the Department of Psychiatry of Yale University School of Medicine. The primary aim of this study is to evaluate the efficacy of cognitive-behavioral therapy as a complementary intervention for women with vulvodynia. Cognitive behavioral therapy is a well-established psychosocial intervention that has been shown to decrease pain severity, physical disability, and emotional distress for various chronic pain conditions.

This study is designed to compare the outcome of cognitive behavioral therapy vs. supportive psychotherapy. Since Vulvar Vestibulitis Syndrome (VVS) and Dysesthetic Vulvodynia are the most common and enigmatic vulvodynia subtypes, this study will enroll only women who have been diagnosed with one of these conditions. Over three years, 60 participants with VVS or dysesthetic vulvodynia will be randomly assigned to 10 weeks of either cognitive behavioral therapy or supportive psychotherapy.

Current applications

Until further notice, vulvodynia research proposals should be submitted under the NICHD's ongoing Program Announcement (PA-98-112). The Website address for this PA is http://www.nih.gov/grants/guide/pa-files/PA-98-112.html. n

National Vulvodynia Association
Membership/Donation Form

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