National Vulvodynia Association

NVA News

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Vulvodynia Experts Present Latest Research

This is the first installment of a two-part article on the vulvodynia conference held in Atlanta in October 2004. Part one summarizes current research on the epidemiology and etiology of vulvodynia, and Part two (in the next issue of NVA News) *will report on clinical research.*

The NVA recently participated in an important research conference, entitled Vulvodynia and Sexual Pain Disorders, organized and co-chaired by NIH vulvodynia grant recipient, Gloria Bachmann, MD, professor of obstetrics and gynecology and associate dean for women's health, and Ray Rosen, MD, professor of psychiatry and medicine, of the Robert Wood Johnson Medical School. In attendance were 150 vulvodynia specialists, NIH-funded researchers and representatives of the pharmaceutical industry.

The purpose of the conference was to develop a consensus document on vulvodynia to be submitted for publication in a peer-reviewed medical journal. The document will summarize the current status of research and clinical care, and provide recommendations for future research direction, the training of medical providers and strategies to prevent vulvodynia.

Dr. Vivian Pinn, director of the Office of Research on Women's Health at NIH, and Dr. Wulf Utian, executive director of the North American Menopause Society, served as the scientific co-chairs for the meeting. For many years, Dr. Pinn has played a key role in gaining recognition for vulvodynia and encouraging research efforts. Dr. Utian, an internationally respected women's health advocate, co-founded the International Menopause Society in 1976 and has written more than 100 papers on the female reproductive system.

After welcoming remarks by Drs. Bachmann and Rosen, Christin Veasley, NVA's director of research and professional programs, represented the patient's voice at the workshop, summarizing quality of life issues that women with vulvodynia face. Speaking on the issue of health care provider edu-

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Preventive Therapy for Recurrent Yeast Infections

By Paul Nyirjesy, M.D.

Dr. Nyirjesy is a professor of obstetrics and gynecology at Drexel University College of Medicine and a vulvovaginal disease specialist practicing in Philadelphia, Pennsylvania. He is also a member of the NVA medical advisory board.

In many ways, vulvodynia and vulvovaginal candidiasis (vaginal yeast infection or VVC) are linked to each other. As discussed in previous issues of the *NVA News*, many women are misdiagnosed as having VVC until they eventually receive a diagnosis of vulvodynia. Some experts think that VVC is a trigger that initiates vulvodynia in some women and that many vulvodynia sufferers (perhaps as many as 40 to 50 percent) also have co-existing VVC. In women with both conditions, it is difficult to get the vulvodynia symptoms under control if the yeast infections are not addressed properly. Finding a way to prevent recurrent yeast infections is always a difficult challenge and two recently published studies have cast new light on the issue.

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cation, Veasley emphasized that the current level of knowledge in the field simply isn't adequate to improve the standard of clinical practice. "We need greater funding of research on causes and treatments to give health care providers the knowledge to treat patients successfully," Veasley said. She outlined necessary steps for stimulating vulvodynia research and described some positive initiatives that have been taking shape in recent months.

John Gibbons, MD, past president of the American College of Obstetricians and Gynecologists (ACOG), and professor of obstetrics and gynecology at the University of Connecticut School of Medicine, described the current situation that women with vulvodynia experience, i.e., spending months to years visiting multiple providers in search of diagnosis and treatment, having to deal with the frustration of being misdiagnosed, and coping with the psychological and sexual toll that accompanies the disorder. He explained that because of the current healthcare situation, in which providers operate with low reimbursement rates and high overhead, many clinicians choose not to treat chronic disorders such as vulvodynia. To make matters more difficult, several different names and classification schemes for vulvodynia have been proposed over the years, creating confusion for everyday practitioners. Gibbons also highlighted the scarcity of research on treatment outcomes. "With a myriad of treatments and almost no data on their efficacy, caring for vulvodynia patients can be time-consuming and frustrating for both the provider and the patient," he commented.

Gibbons suggested that vulvovaginal specialists with an interest in advancing vulvodynia practice should develop a simple classification scheme and enlist the aid of large medical professional organizations such as ACOG. Collaborating with ACOG would serve multiple purposes. First, it would raise awareness of vulvodynia in the medical community and increase the number of providers able to diagnose it; once diagnosed, providers could refer patients to an appropriate specialist or, in some cases, treat patients themselves. Second, he proposed that joining forces with ACOG would strengthen efforts to obtain federal research funds to conduct large, randomized multi-treatment clinical trials.

Epidemiology and Risk Factors

Epidemiologist Bernard Harlow, PhD, of Harvard's School of Public Health, began the morning session by presenting data from his NIH-funded study on prevalence and risk factors. Harlow's study began in 2000 and aimed to survey 16,000 women aged 18 to 64 years from seven ethnically and socio-economically diverse Boston-area communities. He published his preliminary epidemiological data last year in the *Journal of the American Medical Women's Association*. Data on approximately four thousand respondents showed that almost 16 percent of women reported histories of chronic burning, knife-like vulvar pain, or pain on contact that lasted at least three months or longer; nearly seven percent were experiencing chronic vulvar pain at

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the time of the survey. In addition, almost 60 percent of respondents who sought care for their symptoms reported visiting three or more health care providers to obtain a diagnosis—and an astounding 40 percent remained undiagnosed. As the study continues, Harlow will focus on identifying risk factors associated with the development of vulvodynia, which will hopefully lead to strategies to prevent its onset. In particular, he is currently investigating oral contraceptive use and childhood victimization as possible precursors to the development of vulvodynia.

Gloria Bachmann, MD, of the Women's Health Institute at Robert Wood Johnson Medical School, presented prevalence data from her multi-faceted NIH-funded study. Using a mail-based survey, her group obtained information on the prevalence of gynecologic and vulvar pain symptoms, and their impact on quality of life. Questionnaires were sent to 5,600 patients that had visited a multidisciplinary practice in New Jersey and nearly 37 percent responded. The vast majority of respondents were Caucasian with a mean age of 50 years. Four percent of respondents reported chronic vulvar pain and 17 percent reported other types of gynecologic pain that were not located in the vulva. Women reporting either vulvar or non-vulvar pain were twice as likely as asymptomatic women to report a history of depression and vaginal infections, poorer quality of life and greater stress.

In the second arm of the investigation, Bachmann sought to determine potential risk factors for vulvodynia in a case-control study. Trained telephone interviewers identified 425 women from a national sample; 100 of the selected women reported vulvodynia symptoms and the other 325 served as asymptomatic matched controls. The preliminary results indicate that women with vulvodynia report more depression, autoimmune disorders, irregular menstrual history, and chronic yeast and urinary tract infections.

Etiology: Immunologic and Genetic Factors

The session on the etiology of vulvodynia began with a presentation by NVA grant recipient Steven Witkin, PhD, of Cornell University. Previous research had shown that vulvar vestibulitis syndrome (VVS) may be caused by a variety of triggers, that racial/ethnic differences in incidence may exist and that women with VVS report an increased sensitivity to pain at other body sites. Witkin hypothesized that all of these findings point toward the existence of a genetic component that influences susceptibility to VVS. He presented data from multiple studies that have screened women with VVS and controls for polymorphisms in three genes regulating immune response to inflammation: interleukin-1 receptor antagonist gene (IL-1ra), interleukin-1beta (IL-1b) and mannose-binding lectin (MBL). Genetic polymorphisms are small variations in the DNA sequence of a gene that present in at least one to two percent of the population. They result in individual differences in the quantity, stability or activity of a specific gene's protein product.

Witkin found that a subset of women with VVS, compared to pain-free controls, had a greater number of certain polymorphisms in IL-1ra and IL-1b genes, both of which are associated with elevated and prolonged pro-inflammatory responses. In addition, he found that some women with VVS were more likely to exhibit a variant of the MBL gene than controls. This polymorphism is associated with an increased rate of vulvovaginal Candida infections and with a reduced capacity to inhibit the proliferation of Candida, as well as other bacteria and viruses. All these findings considered suggest that a subset of women with VVS are genetically more susceptible to vulvovaginal infection and respond to such infections with an exaggerated inflammatory reaction. Further research is required to identify other genetic variations that influence susceptibility to the disorder and to more clearly understand how these differences lead to VVS. With this knowledge, scientifically-based clinical trials of new, specific therapies may be initiated.

David Foster, MD, of the University of Rochester, whose recent research has also focused on genetic factors in VVS, presented data from his NIH- and

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NVA-supported studies examining the variation in certain genes that act on the cellular level as "braking" mechanisms for inflammation and pain: nuclear factor kappa B (NF_KB), IL-1ra and melanocortin-1 receptor (MC1r). Certain polymorphisms of the MC1r gene are responsible for decreased activity of melanocyte stimulating hormone (MSH), a hormone secreted by the pituitary gland that regulates skin color. Foster hypothesizes that reduced MC1r activity or presence of the IL-1ra polymorphism increases the risk of developing VVS and that their combined presence results in additive risk. He presented data from 36 VVS patients and 69 pain-free controls, revealing that the combined presence of a certain polymorphism of the IL-1ra gene and at least one of six MC1r polymorphisms, resulted in an eight-fold additive risk for developing VVS.

Foster concluded that the results of his study support a genetic contribution to VVS and suggest an increased risk of developing VVS for women with fair skin, since fair skin is associated with increasing numbers of the MC1r polymorphisms. This finding may lead to new treatments and primary prevention options such as administration of a melanocortin analogue (a substance that produces a reaction similar to that of the actual hormone).

Barbara Reed, MD, of the University of Michigan, presented data from her NIH-funded research study on immunologic alterations in women with vulvodynia. To determine if pro-inflammatory cytokine alterations occur in women with vulvodynia, Reed compared blood samples stimulated with Candida and Lipopolysaccharide (a fatty substance found in many bacteria) in 52 women with generalized vulvodynia or VVS and 54 matched controls. Cytokines are small proteins that regulate the body's immune response and are secreted by different types of cells in the body. Reed's preliminary data analysis did not find a difference in the production of multiple cytokines among women with or without vulvodynia, but instead found that women with vulvodynia have higher levels of nerve growth factor (NGF), a protein that promotes nerve cell growth. When she compared samples from women with generalized vulvodynia to those from women with VVS, she found that both groups had similar increases in NGF. This finding of increased NGF production may explain the increased branching of distal nerve fibers that has been previously demonstrated in women with vulvodynia.

Sensory Abnormalities in Women with VVS

In his second presentation, Dr. Foster provided evidence that central sensitization plays a role in VVS. Central sensitization is an increase in the excitability of neurons within the central nervous system, such that normal input produces an abnormal response. For example, someone burns her arm, and then after it heals, touches the area that was burned and experiences pain instead of touch. She may also feel pain when the undamaged area surrounding the burn is touched. In this example, central sensitization occurs because cellular changes have taken place in the central nervous system, leading to increased sensitivity of the skin to both normal touch and painful stimuli.

The skin's response to capsaicin (a derivative of red pepper) has been proposed as an assessment tool for central sensitization. In Foster's study, 10 women with VVS and an equal number of matched controls underwent two randomized, cross-over trials with an intra-dermal injection of capsaicin or a saline placebo in the forearm and foot on opposite sides of the body. He measured the subjects' post-injection spontaneous pain in both areas, as well as their responses to non-painful stimuli such as touch. Compared to control subjects, women with VVS experienced greater spontaneous pain and allodynia (pain upon touch). The area of pain extended far beyond the anatomic location of the injection site, suggesting that central sensitization is present in women with VVS. This research evidence indicates it is important to include systemic, centrally acting medications in the treatment of VVS patients.

Denniz Zolnoun, MD, of the University of North Carolina, presented a study that investigated responses of women with VVS to ischemic pain (caused by a decrease in blood flow) and thermal pain (induced by extreme hot and cold temperatures). Seventeen women with VVS and 14 pain-free controls underwent procedures that induced

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ischemic or thermal pain, such as placing a hand in extremely cold water or wearing an expanding blood pressure cuff. Subjects were asked to report when they first experienced pain sensations and when the pain became intolerable; in addition, they were asked to rate pain intensity on a visual analogue scale. Zolnoun found that even though women with VVS tolerated equivalent amounts of pain, they had a significantly greater perception of pain, indicating that VVS may be a somatosensory disorder similar in nature to fibromyalgia. She speculated that either central nervous system dysregulation may be a risk factor for development of the disorder, or alternately, that the chronic, pain state itself lowers sensory thresholds. Her research group is pursuing this investigation.

Kimberley Payne, PhD candidate at McGill University, presented an abstract on sexual arousal and pain perception in women with VVS. Payne commented that most researchers in the field assume that lack of sexual arousal results in painful intercourse, and conversely, that sexual arousal reduces pain perception and facilitates pain-free intercourse. Her research assessed the relationship between sexual arousal and sensory functioning in women with VVS compared to pain-free controls. Nine women with VVS and twelve controls underwent baseline sensory testing of touch and pain thresholds in the vulva and other body sites, including the vestibule, labium minus and forearm; subsequently they underwent sensory testing during exposure to both visually erotic and nature-oriented control films. Based on preliminary analyses of 50 percent of subjects, Payne found that all women, not just women with VVS, were more sensitive to pain in the vestibule during sexual arousal, but that women with VVS also exhibited central sensitization, i.e., they were more sensitive at all body sites, not simply in the vulva.

Presenting results from a study on vulvar and peripheral pressure sensitivity, Dr. Reed also furnished evidence substantiating a central sensitization component in vulvodynia. In the study, 13 women with vulvodynia and 20 pain-free controls underwent sensory assessment at two sites on the body, the vulva and the thumbnail, twice over a 4 to 8 day period. The order of pressure testing (vulva first vs. thumbnail first) was randomly assigned and then reversed at the second visit. Reed found that pressure pain sensitivity in the vulva was greater in vulvodynia patients and that the values did not differ significantly depending on the order of testing. Similar findings were observed for thumbnail pressure pain sensitivity. The results corroborate Reed's prior research finding that vulvodynia patients report lower pain thresholds at peripheral body sites, as well as in the vulva.

Primary vs. Secondary VVS

Sawsan As-Sanie, MD, MPH, University of North Carolina School of Medicine, and her colleagues hypothesized that women with primary VVS, who experience pain in the vestibule from the very first time of attempted insertion or intercourse, exhibit psychological and sensory differences compared to women with secondary VVS, those without pain initially who develop symptoms later. To assess symptoms, intercourse-related pain, depression and anxiety, As-Sanie administered five questionnaires to 16 women with VVS, eight with primary and eight with secondary VVS. The research team found that despite reporting a similar intensity of intercourse-related pain, the group with primary VVS 1) described the pain as more distressing, characterizing the pain as "very distressing" versus "very annoying;" 2) reported a significantly lower intercourse frequency; 3) had experienced pain for a longer average duration (6.4 years versus 3.4 years); and 4) reported suffering from other pain syndromes such as TMJ, PMS and dysmenorrhea more frequently. From the results of this study, As-Sanie proposed that primary VVS patients exhibit more abnormalities in sensory processing than secondary VVS patients.

Andrew Goldstein, MD, director of the Center for Vulvovaginal Disorders, presented data indicating that some cases of primary VVS may result from a congenital anomaly, i.e., a generalized disorder of the urogenital sinus-derived epithelium. He decided to test the hypothesis by comparing umbilical sensitivity in VVS patients and controls, because both the umbilicus and vestibule originate from the urogenital sinus. Based on VVS patients

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who presented to his clinic over a six-month period, he compared umbilical sensitivity in 12 women with primary VVS and 20 women with secondary VVS. As part of their evaluation, a q-tip test was performed at the umbilicus (belly button) and patients were asked if they experienced pain or hypersensitivity. Forty-two percent of patients with primary VVS reported hypersensitivity and exhibited allodynia (pain in response to a non-painful stimulus), whereas none of the 20 patients with secondary VVS did.

Goldstein also noted that investigators have observed that VVS and interstitial cystitis, a pain syndrome of the bladder, co-exist in some patients. He contends that this may be interpreted as further evidence that both conditions represent a generalized disorder of the urogenital sinus-derived epithelium, since both the bladder and vestibular epithelium are derived from the urogenital sinus during the 5th to 6th week of fetal development. An association between the two disorders has been found in patients as young as four years old, also lending support to the view that there may be a congenital defect in the tissue.

Hormonal Influence

Irwin Goldstein, MD, of Boston University, gave a presentation on the role that hormonal status may play in the pathogenesis of vestibular adenitis, or inflammation of the vestibular glands. Goldstein excised tissue samples from the vestibular glands of 22 women suffering from vulvar adenitis and compared them to those taken from a control group of five women who underwent vestibulectomy for removal of cancerous tissue. Compared to controls, women with adenitis demonstrated significantly more inflammation, abnormal tissue transformation, and decreased androgen and progesterone receptor expression, but exhibited no difference in estrogen receptor expression.

Based on these findings and his observation that, in some adenitis patients, pain is markedly reduced with androgen therapy, Goldstein proposed that androgen insufficiency may lead to diminished structure and function of the vestibular glands, resulting in increased inflammation and pain. The next step will be to compare tissue samples from women with vulvar adenitis to those of pain-free controls in a larger cohort of women.

Relationship to Other Syndromes

Ursula Wesselmann, MD, PhD, of Johns Hopkins University, presented data from her NIH-funded research examining the pathophysiological mechanisms of vulvodynia. Wesselmann noted that some patients with vulvodynia report additional symptoms, such as gastrointestinal and pelvic pain, indicating that women with vulvodynia may exhibit alterations in the body's mechanism of pain modulation. She presented data from her basic science studies on rodents that measured the response of certain nerve cells in the spinal cord to inflammation of the uterus. Once the uterine inflammation subsided, she measured the response of spinal nerve cells to inflammation of the vagina. In rodents that had previously experienced uterine inflammation, subsequent vaginal inflammation produced a marked increase in both the number of nerve-related cells in the spinal cord and the number of levels of the spinal cord producing these cells. This effect did not occur in rodents without a history of uterine inflammation. In translating these results from the laboratory to the patient, Wesselmann proposed that previous pelvic inflammatory issues may sensitize some women to develop vulvodynia at a later point in time.

The next phase of her study assessed whether women with IC report a higher frequency of vulvar

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NVA Awards Vulvodynia Research Grants

Following the success of our June 2004 fundraising effort, NVA issued a request for research proposals on vulvodynia and received 27 excellent submissions. The proposals were read and scored by a review committee of vulvodynia experts who then gave their recommendations to the NVA executive board. This past November, the board awarded a $25,000 grant to Steven Witkin, PhD, and William Ledger, MD, Department of Obstetrics and Gynecology, Weill Medical College of Cornell University, to continue their investigation into the causes of vulvar vestibulitis (VVS). Witkin and Ledger received their first NVA research grant in 2000. Their long-term objective has been to determine the underlying mechanisms that predispose some women to develop (VVS) and to use that knowledge to devise preventive methods.

Since 2000, Witkin and Ledger have published seven studies reporting their consistent findings of polymorphisms (small changes) in genes associated with 1) a reduced capacity to terminate inflammation (IL-1ra gene), 2) an increased capacity to initiate inflammatory responses (IL-1beta gene), and 3) a reduced capacity to combat *Candida albicans* infections (MBL gene). They have also found alterations in the levels of certain substances in the bloodstream of VVS patients, including 1) decreased circulating levels of the antimicrobial compound, interferon-alpha, 2) increased ex vivo induction of a pro-inflammatory cytokine and 3) decreased production of an anti-inflammatory mediator.

Witkin and Ledger have attempted to differentiate VVS patients on the basis of time of symptom onset, factors associated with onset, history of recurrent yeast infections, degree of vestibular pain and allergic response to seminal fluid. Their research verifies that more than one biological process is responsible for the initiation of VVS. The consistent finding that many VVS patients have a relative inability to mount an effective antimicrobial immune response, coupled with a low capacity to terminate pro-inflammatory immune responses, is the basis of the study that will be funded by the NVA. Witkin and Ledger will test the hypothesis that a subset of VVS patients with constant or intermittent vestibular pain, whose pain is too severe to engage in sexual intercourse, has a diminished capacity to mount an innate immune response to microorganisms. They hypothesize that a relative inability to prevent the colonization and/or proliferation of microorganisms in the vagina may lead to a persistent induction of pro-inflammatory mediators and a continual stimulation of nerve fibers in the vestibular region, resulting in greatly enhanced sensitivity to touch or pain stimuli.

In early 2004, Andrew Goldstein, MD, director of the Center for Vulvovaginal Disorders in Washington, DC, was awarded an NVA grant to test the efficacy of a novel medication in the treatment of dysesthetic or generalized vulvodynia. The selection of the medication for this study was based on the widely held assumption that nerve damage, or dysfunction in the peripheral or central nervous system, is one of the components of generalized vulvodynia. Although other medications, such as tricyclic antidepressants, are typically used to treat generalized vulvodynia, their efficacy has not been proven and they often cause unacceptable side effects that limit their use. The present study, developed in cooperation with Justin Wasserman, MD, a specialist in the treatment of chronic pain and NVA medical advisory board member, is one of the first double-blind, placebo-controlled trials of any medication for generalized vulvodynia.

To be eligible to participate, you must have a current diagnosis of dysesthetic vulvodynia and be between 20 and 65 years of age. You must not currently be taking a tricyclic antidepressant, SSRI or anticonvulsant medication, or have diabetes, heart disease or bipolar disorder. The study requires five visits to the Center for Vulvovaginal Disorders in Washington, D.C. For more information, contact Dr. Andrew Goldstein at 202-887-0568. ■

Thank You!

The NVA is grateful to the **Enterprise Rent-A-Car Foundation** for its continued support and generous unrestricted grant. This year's Enterprise grant will support the publication of two new resources for women with vulvodynia.

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pain than women who do not have IC. The findings corroborated the animal research in that women with IC were more sensitive to touch in the vulva, but not in other areas of their bodies. Wesselmann is continuing her research to determine whether it is possible to predict vulvodynia risk and develop strategies for early intervention.

Bruce Kahn, MD, of Scripps Clinic in San Diego, presented data from a research project examining the incidence of bladder symptoms and IC in women with vulvodynia. More than one hundred women with generalized vulvodynia underwent screening for IC using a Pain-Urgency-Frequency (PUF) questionnaire and a potassium sensitivity test (PST). The PUF questionnaire is used as a screening tool to identify women who may have IC and the PST is a simple office procedure that confirms the diagnosis. During the PST, a very small catheter is placed into the bladder and two different solutions – first sterile water and then a solution containing potassium – are administered. After insertion of each solution, patients are asked to rate both discomfort and the urge to urinate. If the potassium solution causes any symptoms compared to sterile water, a diagnosis of IC is confirmed. (The painful reaction to potassium is probably the result of a defect in the bladder lining.)

Kahn found that 84 percent of women with vulvodynia reported urinary symptoms and 87 percent had a positive PST. He noted that the potassium solution typically reproduced the vulvar pain for which patients were seeking care, thus demonstrating for patients the neural connection between the bladder and the vulva. Kahn speculated that symptoms of vulvodynia may be part of a more generalized "visceral pain syndrome" that manifests in multiple pelvic organs. Based on his research findings and clinical observation, he concluded that testing for IC deserves greater consideration in patients with vulvodynia.

Is VVS a Pain Disorder?

Yitzchak Binik, PhD, of McGill University, and Alessandra Graziottin, MD, of the Center of Gynecology and Medical Sexology in Milan, participated in a panel discussion on whether current evidence supports the conceptualization of VVS as a pain disorder rather than a sexual disorder. Graziottin summarized the similarities and differences between dyspareunia (painful sexual intercourse) and vulvodynia, and proposed that dyspareunia involves a nociceptive pain process, whereas vulvodynia involves a neuropathic pain process. (Nociceptive pain is due to tissue injury and neuropathic pain results from nerve damage or dysfunction of the nervous system.) Binik summarized research on women with VVS that shows evidence of altered sensory processing in the vestibule and other areas of the body, heightened innervation of nerve fibers, an increase in blood flow and erythema, and heightened activity in certain parts of the brain. After reviewing all the evidence, Binik and Graziottin concluded that VVS satisfies the criteria of a pain syndrome and should be conceptualized as a pain disorder rather than a sexual disorder.

Future Research Direction

In the afternoon, attendees broke into small groups to discuss gaps in research knowledge and prioritize future research goals. Groups focused on specific areas, such as 1) basic science research, 2) diagnosis and treatment, and 3) epidemiologic and clinical research. The groups' recommendations will be incorporated into the published consensus document.

The workshop closed with encouraging commentary by the scientific co-chairs, Drs. Vivian Pinn and Wulf Utian. Dr. Pinn was impressed by the significant advances in vulvodynia research over the last decade. "We are encouraged by the quality of the research presented today and the growing interest of young investigators who have focused their scientific careers on vulvodynia. There are still many areas that need further investigation, but after witnessing the commitment the medical community has shown here today, we are confident that research will continue to yield quality and purposeful scientific information that will ultimately help patients suffering from this condition." ■

Behind the Scenes at the NVA

By Phyllis Mate, NVA Executive Director

In September 2004, *Good Housekeeping* magazine published the personal story of Chris Veasley, NVA's director of professional programs and research. The magazine's editor subsequently told us that Chris' story produced more letters than any other article in recent history. Most letters were either from women seeking help or readers praising the magazine for tackling such an intimate subject. The article described her lengthy ordeal with vulvar vestibulitis, from not being able to have sexual intercourse at age 19 to eventually giving birth to her daughter Grace. Chris' willingness to discuss her personal experience is merely one of the reasons we're so proud of her.

Chris Veasley (left) and Phyllis Mate, of the NVA, at a Capitol Hill briefing on vulvodynia last year.

I've been the volunteer executive director at NVA since 1996. In the early days, we couldn't afford to hire staff and I answered all NVA phone calls in my Maryland home. One day, 22 year old Chris from Wisconsin called, asking me for names of vulvodynia researchers. Her goal was to spend a year doing research and then attend medical school to become a vulvodynia specialist. I told Chris I wasn't optimistic, but I'd contact some researchers. The truth was that there were few people doing research on the condition in the mid-1990s. I didn't get back to Chris in the next few weeks, so she called again. She was disappointed that I hadn't heard of any opportunities. Another month passed and Chris inquired again. I was handling hundreds of calls a week and gave her short shrift, but I admired her persistence. I contacted Ursula Wesselmann, MD, at Johns Hopkins, because she had recently been awarded an NVA research grant, and coincidentally, she needed a research assistant. Chris and her boyfriend Melvin (now her husband of four years) packed up their things in Madison and moved east to Baltimore so she could work for Dr. Wesselmann.

About a year later, Chris started applying to medical schools. At that time, the NVA was growing rapidly and my workload had become overwhelming. I suggested to Chris that if she didn't go to medical school, I'd like her to work with me. She accepted the offer because she felt it was an opportunity to help other women and further research on vulvodynia. I didn't know it then, but that was one of the luckiest days of my life and a turning point for the NVA.

Chris started by juggling all sorts of tasks, including managing our rapidly growing database. As NVA grew and we could afford a full-time administrative assistant, she focused on developing educational tools for healthcare professionals as well as patients. For the past five years, she has been a driving force behind most of the NVA's accomplishments. Among her many innovations, Chris developed a teaching CD on vulvodynia, an online newsletter of vulvodynia research abstracts, a highly informative website and a self-help guide for patients. She organizes vulvodynia symposia and gives presentations at major medical conferences across the country. She also spends hundreds of hours discussing vulvodynia with researchers and pharmaceutical representatives, fostering their interest in developing treatments for vulvodynia.

Now, because budget constraints at the National Institutes of Health have negatively impacted funding of vulvodynia research, Chris has ventured into the political arena, developing relationships with representatives from the Society for Women's Health Research, and the American College of Obstetricians and Gynecologists. She hopes that by joining forces with other women's health advocates we can obtain greater federal research funding for vulvodynia and other neglected disorders that are prevalent in women.

Chris has come a long way from her early days as a support group leader in Madison. She's a shining example of someone who found strength in adversity and chose to dedicate her life to making a difference in the lives of others. Fortunately for all of us, she's made her home at the NVA. ■

Yeast

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One of the most commonly used methods to prevent yeast infections is taking lactobacillus preparations. (Lactobacilli are the "friendly" bacteria in yogurt.) In women, vaginal lactobacilli are important organisms that help to regulate and inhibit the growth of other vaginal organisms, possibly including yeast. For many years, it had been assumed that lactobacillus preparations, used either by mouth or vaginally, could prevent yeast infections. This type of therapy is frequently used by women with chronic vulvovaginal problems, although research has shown that available products contain the wrong types of lactobacilli and have other bacterial contaminants that may be detrimental to overall vaginal health. Furthermore, research by Jack Sobel, MD, professor of internal medicine and chief of infectious diseases at Wayne State University School of Medicine, has demonstrated that women with recurrent VVC have the same number and types of lactobacilli as asymptomatic women. This finding indicates that, at least in this patient population, episodes of VVC are not caused by a deficiency in lactobacilli.

A recent study by an Australian group, published in the *British Medical Journal Online*, investigated the role of lactobacillus therapy in preventing yeast infections in women using antibiotics. It has been hypothesized that antibiotic use is associated with yeast infections because antibiotics decrease lactobacilli. Even though taking antibiotics is one of the major risk factors that can lead to the development of VVC, no prior studies had evaluated methods to prevent antibiotic-associated VVC.

The research group took 278 women who had just started short-term oral antibiotic treatment and randomized them to oral and/or vaginal lactobacillus therapy with appropriate placebo arms. Thus, there were a total of four different treatment groups, including one group that received both vaginal and oral placebo. The researchers diagnosed VVC in women who had symptoms of a yeast infection, in conjunction with a culture swab that was positive for yeast. Overall, 23 percent developed post-antibiotic VVC. There were no differences in VVC infection rates between those taking oral, vaginal, oral plus vaginal, or placebo preparations. The study was terminated before completion because of the extremely low likelihood that it would show a benefit of lactobacillus therapy. As noted by the authors, the strengths of the study were recruitment from a broad community-based population, the study design, and the use of cultures based on self-collected swabs to corroborate the diagnosis of yeast infection. It was also one of the first studies to quantify the risk of getting VVC from antibiotic use. Although the study elegantly showed that a particular lactobacillus preparation did not prevent VVC, the question remains as to whether other preparations might be more effective. However, given Sobel's prior finding that has raised doubts about the role of lactobacilli in VVC, it seems unlikely that lactobacillus therapy will prove to be an effective way of preventing yeast infections. Since millions of women self-treat themselves with lactobacillus preparations, probably unnecessarily, the *British Medical Journal* deserves credit for recognizing the importance of these disappointing negative findings and publishing the results.

Another approach to preventing yeast infections in women prone to recurrences is to place them on chronic maintenance antifungal therapy. In a 1985 study, Sobel demonstrated that patients with recurrent VVC who took ketoconazole daily for six months had significantly fewer recurrences than a placebo group and that much of the protective effect persisted after terminating treatment. However, because ketoconazole can cause severe and unpredictable liver toxicity, it never achieved widespread use for this indication.

In a recent study published in the *New England Journal of Medicine*, Sobel and his colleagues evaluated the effectiveness of weekly fluconazole, 150 mg. once-a-week for six months, in preventing recurrent VVC. After initial treatment of an acute yeast infection with three doses of fluconazole given three days apart, 283 patients were randomized to weekly fluconazole vs. weekly placebo for six months. (It should be noted that 94 percent of the women in this study had an infection caused by *Candida albicans*, the most common cause of yeast infections.) At the end of treatment, 64 percent of the fluconazole patients vs. 9 percent of the placebo patients were disease-free. During the six month follow-up after terminating treatment, however, 57 percent of the

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Research Participants Needed

Vulvar Vestibulitis Study

Vulvar vestibulitis (VV), an inflammation of the tissues that surround the entrance to the vagina, is the most common cause of pain during intercourse in younger women. Dr. David C. Foster, an international authority on diagnosing and treating vulvar pain and disease is principal investigator for the first major trial of a medical treatment for VV. The study is funded by a $1.2 million grant from the National Institutes of Health.

The study will test two medications, used alone and together, to determine how effective they are at relieving the pain and possibly curing the inflammation. To be eligible for the study, you must be:
• a woman diagnosed with VV or who has experienced vaginal pain and suspect you may have it;
• between the ages of 18 and 50;
• available to participate in a 12-week medical trial in Rochester, New York, with six- and 12-month follow-up visits; and
• willing to undergo genetic and psychological testing, as well as close monitoring of your pain.

For more information, please call (585) 275-7919.

Vulvodynia in Post-Menopausal Women Study

Researchers at Johns Hopkins Hospital in Baltimore, Maryland, are looking for post-menopausal women to participate in a research study concerning the mechanisms of pain in vulvodynia, a chronic pain syndrome of the vulvar and vaginal area.

Women who have had a hysterectomy are ineligible for this study. You may be an appropriate candidate for this study if you:
• are 45 or older;
• have been diagnosed with vulvodynia for at least 6 months;
• have not had a menstrual period for at least 12 months; and
• have been on or off hormone replacement therapy (HRT) for at least 12 months.

You will receive a stipend for participation. For information call (410) 614-4517 or e-mail women @bme.jhu.edu. (*Support: National Institutes of Health, National Vulvodynia Association; Principal Investigator: Ursula Wesselmann MD, PhD, Dept. of Neurology, Johns Hopkins Hospital.*) ■

Yeast

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fluconazole-treated patients developed a recurrence. The most reliable predictor of relapse was having a positive culture for yeast during the treatment portion of the study.

As an investigator in the fluconazole study and as someone who has used maintenance antifungal therapy for women with recurrent VVC since 1991, I can attest to its effectiveness in patients with *Candida albicans*. The medication is well-tolerated by most women. Only one patient in the study developed a mild non-significant elevation in her liver function tests. Although side effects such as headache, GI upset and skin rashes can occur, no patient in the study dropped out because of any side effects. It should be noted that fluconazole is not approved for use during pregnancy and is considered much less effective for yeast infections caused by species other than *Candida albicans*.

In summary, one recent study has shown that lactobacillus therapy is ineffective in preventing vaginal yeast infections, at least after antibiotic use. Another recent study has demonstrated that yeast infections can be brought under control with aggressive long-term fluconazole therapy. However, the finding that relapses were common after termination of fluconazole therapy means that we still have a long way to go to provide the ideal long-term solution for women with recurrent VVC.

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