National Vulvodynia Association

NVA News

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Vaginal Diazepam for Pelvic Floor Muscle Dysfunction

Questions and Answers with Donna J. Carrico, WHNP, MS

Ms. Carrico, a certified women's health nurse practitioner, is the clinical director of the Women's Urology Center at Beaumont Hospital in Royal Oak, Michigan.

NVA: Is pelvic floor muscle dysfunction common in your vulvodynia patients?

Ms. Carrico: We find that a significant number of our patients with urogenital pain, including vulvodynia, have concurrent pelvic floor muscle (PFM) dysfunction. In fact, in 2008, we published an article on the clinical correlation between urogenital pain and PFM dysfunction in the *International Urogynecology Journal*. The study group consisted of 70 women with diagnosed interstitial cystitis/painful bladder syndrome (IC). After administering a cotton-swab test of the vulva and vestibule to determine how many women also suffered from vulvodynia, we performed a pain assessment of the levator ani muscles. (To view a diagram of the levator ani muscles, please see http://learnpatient.nva.org/intro_vulvovaginal_health_1.php.) Compared to women with IC alone, we found that women suffering from both IC and vulvodynia reported more pain with the muscle assessment. PFM dysfunction is frequently seen in women with long-standing urogenital pain disorders, however, due to a lack of research, we don't know how common it is in women with new-onset pain symptoms. Additionally, we don't know which disorder typically presents first – the PFM dysfunction or pain syndrome – or if they present together in most women. We do know from years of clinical experience, however, that identifying and treating concomitant PFM dysfunction is an essential component of an effective treatment plan.

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International Conference Highlights Vulvodynia

By Jay R. Trabin, MD, FACOG

Dr. Trabin practices gynecology, with specialization in vulvology, in West Palm Beach, Florida, and is also a staff gynecologist, with a specialty practice in vulvovaginal disorders, at the Cleveland Clinic in Weston. He is assistant professor of obstetrics and gynecology at the University of Miami, chairs the Florida Section of the American College of Obstetricians and Gynecologists (ACOG) and is a contributing author on ACOG's Committee on Gynecologic Practice.

For those unfamiliar with the International Society for the Study of Vulvovaginal Disease (ISSVD), it may be regarded as a companion organization to the National Vulvodynia Association. Composed of medical professionals and scientists from around the world who are

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NVA: What kind of medication is diazepam? Do you prefer to prescribe it by mouth or as a vaginal suppository?
Ms. Carrico: Diazepam, also known as Valium, is a muscle-relaxing agent. Oral diazepam use may cause systemic side effects such as drowsiness, which can interfere with one's ability to perform daily activities. When possible, we prefer to utilize localized treatments that can be applied directly to the site of pain, and we are fortunate to have excellent compounding pharmacists in our area that we work with on a regular basis.

NVA: What is the typical dose of vaginal diazepam? How is it applied?
Ms. Carrico: We typically prescribe 5 to 10mg of diazepam up to three times a day as needed for symptom relief. If women report medication sensitivity, we prescribe a lower dose. Women can simply insert a whole diazepam tablet moistened with water into the vagina, or they can crush the tablet, mix it with a hypoallergenic lubricant or olive oil and insert the mixture into the vagina using their finger. Alternately, a health care provider can work with a specialized compounding pharmacy to prepare a hypoallergenic suppository or cream that a woman can insert into the vagina. Before the compounding pharmacist mixes the prescribed formulation, he/she can provide patients with a sample of the base product to test. We advise women to apply the base product to the inner thigh or just outside of the vulvar area to check for a reaction. When we prescribe a cream containing diazepam, we take a conservative approach and prefer not to mix it with other medications such as lidocaine or estrogen, because we don't have much information on the absorption characteristics or potential interactions. We've found that some women achieve better pain control by alternating the use of compounded formulations with different active ingredients throughout the day.

NVA: Why was it important to conduct a research study on vaginal diazepam?
Ms. Carrico: Specialists have been prescribing diazepam in this manner for many years with reported success in treating PFM dysfunction, but very few researchers have conducted studies to determine its efficacy. (Brookoff 2006, Butrick 2009, Rogalski 2010) Additionally, no one has researched the absorption characteristics of diazepam when administered vaginally. Our aim was to prospectively follow women from our center as they were treated to determine the effectiveness of vaginal diazepam, and to assess how much of the medication was absorbed into the bloodstream.

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NVA: Please describe your study population.
Ms. Carrico: Twenty-one women between the ages of 22 and 61 who sought care at our center for previously diagnosed IC, vulvodynia and/or pelvic pain, with concomitant PFM dysfunction, were included. All had tried numerous therapies, including opioids, topical formulations, "pain-blocking" medications (e.g., tricyclic antidepressants, anticonvulsants) and dietary and behavioral modifications, without achieving adequate pain relief.

NVA: How was the study conducted?
Ms. Carrico: After taking a complete history, women underwent a cotton-swab test of the vestibule and examination of the pelvis. Additionally, a clinician assessed the levator ani muscles for spasm/trigger points by applying pressure to the vaginal wall with the index finger, and the women rated their pain on a scale of zero to 10. We then prescribed up to 10mg of diazepam. The usual starting dose was 5mg up to three times daily for symptom relief, unless women reported medication sensitivity, in which case the starting dose was 2mg. Women had the option of inserting into the vagina: i) the whole diazepam tablet moistened with water, ii) a crushed tablet mixed with a hypoallergenic vaginal lubricant; or iii) a specially compounded vaginal diazepam cream. Women recorded their weekly diazepam dose, frequency of use, pain scores and adverse effects once a week (on the same day) for one month. Women then had blood drawn and the same clinician conducted a second genital and pelvic examination.

NVA: What was the typical diazepam dose and frequency of administration?
Ms. Carrico: The reported dose and frequency of use varied greatly among women. The majority of the study group used 5mg, a few women administered just 2mg, and only one woman needed the maximum dose of 10mg three times a day. Most of the women in the study group administered the medication two to three times daily. The remainder used the medication a few times each week.

NVA: Briefly describe the study's significant findings.
Ms. Carrico: Overall, the response was very positive. After one month of diazepam use, the average pain score associated with a cotton-swab test decreased from 5.9 to 2.2 (on a 10-point scale). Likewise, after one month of treatment, the average pain score reported with the levator ani muscle assessment decreased from 3.8 to 1.8. Sixty-two percent reported that they were moderately or markedly improved, one woman reported slight improvement and seven women reported no change. None felt that they were worse.

NVA: Did women experience any side effects?
Ms. Carrico: The only side effect, noted by 33 percent of women, was some drowsiness, which did not impair their functioning.

NVA: What were the results of the blood work?
Ms. Carrico: After one month of treatment, we collected blood samples from the 15 women who used the medication at least once daily, and found that their serum levels of diazepam were well within normal range (0.20 to 1.00 ug/ml), with an average level of 0.29 ug/ml. The highest serum level of 0.70 ug/ml was noted two hours after one patient's last 5mg dose, and the woman who administered the maximal dose of 10mg three times daily for one month had a serum level of 0.16 ug/ml.

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NVA: What conclusions can you draw from the results of this study?
Ms. Carrico: Due to the study's small sample size, we cannot draw any widespread conclusions, although, the results do suggest that vaginal diazepam could be a potentially useful off-label therapy for women with urogenital pain and concomitant PFM dysfunction, especially for those who are unable to tolerate a vaginal exam or vaginal physical therapy techniques due to pain and/or spasm. Larger placebo-controlled trials are warranted.

NVA: In the interim, what advice do you have for women with vulvodynia and PFM dysfunction who'd like to consider this treatment?
Ms. Carrico: Women who have not already done so should have a pelvic floor muscle examination, because the results are essential to developing an effective treatment plan. If a woman's health care provider is not familiar with this exam, referral to a clinician who is familiar and/or a specialized pelvic floor physical therapist is in order. These specially trained therapists are able to conduct a thorough pelvic floor muscle assessment and recommend an appropriate treatment plan. Women who are unable to tolerate a vaginal exam due to pain and/or spasm of the muscles surrounding the vaginal opening may want to consider the use of vaginal diazepam. We often use this treatment to help decrease muscle spasm so that an exam and internal physical therapy can be performed. Women can get started with external physical therapy techniques, use the vaginal diazepam concurrently and start internal physical therapy work when they are ready. Women who would like to discuss vaginal diazepam treatment with their clinicians should provide them with a copy of this newsletter article and/or any of the references listed on page 13.

No matter where women are in their quest for help and healing, they should remember that there is hope and that there are clinicians who can help them!

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Definition and Types of Vulvodynia
Many different terms have been used to describe vulvodynia. As a result, confusion among patients and medical professionals is common. To encourage consensus and clarify terms used in this newsletter, we have provided a brief summary of the most current definitions and classification. For more detailed information, please visit http://learnprovider.nva.org/historical_overview.htm and http://learnprovider.nva.org/terminology_classification.html.

Vulvodynia is *chronic (more than three to six months) vulvar pain without an identifiable cause*. The location, constancy and severity of the pain vary among women. The two main subtypes of vulvodynia, which sometimes co-exist, are:

Provoked Vestibulodynia (PVD)
(Previously: Vulvar Vestibulitis Syndrome)
Women with PVD have pain limited to the vestibule, the area surrounding the opening of the vagina, that occurs during/after touch or pressure, e.g., with intercourse, tampon insertion and/or prolonged sitting. PVD is further classified as *primary (pain since the first attempt at vaginal penetration)* or *secondary (pain that starts after a period of pain-free vaginal penetration*).

Generalized Unprovoked Vulvodynia (GV)
(Previously: Dysesthetic or Essential Vulvodynia)
Women with GV have spontaneous pain in multiple areas of the vulva. It is relatively constant, but there can be some periods of symptom relief. Activities that apply pressure to the vulva, such as prolonged sitting or simply wearing pants, typically exacerbate symptoms.

NVA Year in Review: 2011

Once again, we are pleased to provide a summary of our most significant achievements of the past year, none of which would be possible without the continued generosity of our donors.

NIH Doubles Research Support

For 15 years, NVA has worked tirelessly with the U.S. Congress and the National Institutes of Health (NIH) to encourage the expansion of vulvodynia research. We are very pleased that in FY2011, the NIH awarded $6 million in research grants, a 200 percent increase over the prior year. In addition, five *different* NIH Institutes and Offices provided funding for five new vulvodynia studies this year, totaling $3 million in new grant support. These studies are summarized below.

Randomized Controlled Trial of Gabapentin

Candace Brown, PharmD, MSN, professor in the departments of obstetrics and gynecology, pharmacy and psychiatry at the University of Tennessee Health Sciences Center, longtime NVA Medical-Scientific Advisory Board member David Foster, MD, MPH, professor of obstetrics and gynecology at the University of Rochester Medical Center, and Gloria Bachmann, MD, interim chair and professor of obstetrics and gynecology at the University of Medicine and Dentistry of New Jersey, received grant support from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, vulvodynia's primary funding agency at the NIH, as well as the Office of Research on Women's Health, to conduct a randomized controlled trial of gabapentin. The multisite 16-week study will investigate the effectiveness of this anti-seizure medication, which is used to treat chronic pain, in reducing the painful symptoms of Provoked Vestibulodynia (PVD). The study also aims to identify predictors of treatment success and differentiate PVD subtypes caused or maintained by different underlying mechanisms. The group's long-term goal is to determine the underlying pathophysiologic mechanisms of PVD, to use this knowledge to develop evidence-based differential diagnoses of PVD subtypes and then individualize treatment for each subtype. For additional information on this trial, or to participate, please visit www.clinicatrials.gov and enter ID Number "NCT01301001" in the search field.

Complex Persistent Pain Conditions

The National Institute of Neurological Disorders and Stroke (NINDS) awarded a significant grant to William Maixner, PhD, DDS, director of the Center for Neurosensory Disorders at the University of North Carolina in Chapel Hill, to conduct the first multidisciplinary project of its kind to address vulvodynia and four common co-existing conditions: temporomandibular joint and muscle disorders, fibromyalgia, migraine headache and irritable bowel syndrome. The five-year study, *Complex Persistent Pain Conditions: Common and Unique Pathways of Vulnerability,* brings together, for the first time, a multidisciplinary group of accomplished clinicians and scientists in the fields of molecular and cellular genetics, gynecology, neurophysiology, epidemiology, biostatistics and psychophysiology. The primary aim of the study is to identify risk factors, patient clusters, and associated genetic variations that influence the development/maintenance of these disorders, as well as determine the biological pathways through which these genetic variations causally influence them.

The National Center for Research Resources awarded a grant, *Impact of Early Experience on Vulvovaginal Sensitivity in Adult Mice*, to Julie Carlsten Christianson, PhD, assistant professor in the department of anatomy and cell biology at the University of Kansas Medical Center. In addition

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to determining how neonatal stress and irritation affects the nerves supplying sensation to the vulvovaginal region, Dr. Christianson aims to develop an animal model of vulvodynia. As a preclinical test for treating vulvodynia in women, Dr. Christianson will also develop and test a nerve ablation technique that removes painful sensation from the vulvar sensory nerves in this animal model.

Relationship Among Urogenital, Gastrointestinal and Widespread Body Pain

The National Institute of Diabetes and Digestive and Kidney Diseases, with supplemental funding from the NIH Office of the Director, recently supported two studies with direct relevance to vulvodynia. J. Quentin Clemens, MD, associate professor of urology, along with co-investigators Barbara Reed, MD, professor of family medicine, and Daniel Clauw, MD, professor of medicine in the division of rheumatology, all of the University of Michigan Health System, will investigate the relationship among interstitial cystitis/painful bladder syndrome, vulvodynia and widespread body pain in women from the general population in their new study, *Sensory Sensitivity and Urinary Symptoms in the Female Population*. Because bladder symptoms (e.g., pain, urgency, frequency) and vulvar pain are common in the general population, and current treatments are non-specific with poor effectiveness, it is important to understand whether global pain hypersensitivity exists in these patient populations, and if so, to conduct additional studies to examine its pathophysiology, as well as design novel treatments aimed at centrally mediated, rather than peripheral, mechanisms.

In the newest phase of his longstanding study, *Function of the Enteric Nervous System,* Jackie Wood, PhD, professor of physiology and cell biology at Ohio State University College of Medicine, will investigate the relationship among gastrointestinal hypersensitivity and pelvic/urogenital pain syndromes, such as vulvodynia and interstitial cystitis/painful bladder syndrome, by studying signaling mechanisms among the enteric nervous system (i.e., the part of the nervous system that controls the gastrointestinal system), spinal sensory nerves and enteric immune cells (e.g., mast cells) in the small intestine of the guinea pig.

To read summaries of all NIH-funded studies pertaining to vulvodynia, please visit www.nva.org/nih_funding.html.

NVA Helps UNC Scientist Secure NIH Funding

In addition to publishing preliminary findings from his NVA grant in the *Clinical Journal of Pain*, Mark Tommerdahl, PhD, associate professor in the department of biomedical engineering at the University of North Carolina in Chapel Hill, is the most recent investigator to secure funding from the National Institutes of Health (NIH) by including data collected with NVA funding in his NIH application. Dr. Tommerdahl and his colleagues have created a new device, originally used in autism research, that measures the brain's response to sensory stimuli, similar to, but more sensitive than an MRI. In brief, his study demonstrates that a subgroup of women with vulvodynia exhibit an abnormal brain response to everyday sensory stimulation (e.g., light vibration applied to the finger), suggesting a central nervous system processing abnormality. According to Dr. Tommerdahl, there is a significant gap between neuroscience research findings and the translation of that research into everyday practice for many neurological disorders, including chronic pain and specifically vulvodynia. In his new two-year grant from the NINDS, *Sensory Based CNS Diagnostics for the Clinic*, Dr. Tommerdahl will test whether this new sensory device, which can

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be utilized in an office setting in less than five minutes, can reliably distinguish similarities and differences among patients suffering from five chronic pain disorders: vulvodynia, fibromyalgia, irritable bowel syndrome, migraine headache and temporomandibular joint and muscle disorders. In addition to adding to our understanding of the abnormal centrally mediated mechanisms present in some women with vulvodynia, this proposal works towards the goal of providing an inexpensive, efficient and reliable office-based test for clinicians to improve diagnostic performance and assess treatment efficacy. Dr. Tommerdahl has already included data from both grants in a second NIH application to secure an additional $1 million in research support.

NVA Helps to Establish Vulvar Pain Clinics

With a generous donation from Dr. Stanley C. Marinoff, NVA has helped establish vulvar pain clinics in Michigan, Wisconsin, New Jersey and Tennessee. This summer we awarded funding to three more medical professionals to support clinics in Texas, Connecticut and Ecuador. Anuja Vyas, MD, assistant professor of obstetrics and gynecology at Baylor College of Medicine in Houston, is using her NVA award, plus matching institutional funds, to establish multidisciplinary vulvar pain clinics within her hospital and outpatient center. By focusing on medical student and resident training, she aims to expand the number of providers who are trained in the medical management of vulvodynia. Elizabeth Jensen, DNP, CNM, APN, is using her NVA grant and matching funds from S.H.E. Medical Associates in Hartford, Connecticut, to establish a vulvar pain clinic in Hartford, and will eventually expand services to S.H.E. offices in Avon, Enfield, South Windsor and Marlborough. Using results from her national survey of advanced practice nurses, Dr. Jensen will develop educational programs for this subspecialty in an effort to significantly increase access to care for women with vulvodynia. With his NVA award and matching funds from the Runajambi Institute, Mario Maldonado, MD, will establish the first vulvar pain clinic in the Andes. *Clinica del Dolor Femenino* (Clinic for Vulvar Pain) will provide interdisciplinary and culturally adapted care to ethnically and culturally diverse underserved women in the Ecuador highlands, many of whom live on less than two dollars per day.

To obtain contact information for any of these clinics, please contact NVA's administrator Gigi Brecheen (gigi@nva.org, 301-949-5114). Medical professionals who are interested in developing vulvar pain clinics may submit an application in response to our next Request for Applications for the Career Development Award, to be circulated in early 2012. For more information on this funding mechanism, or to request an application, please visit www.nva.org/career_development_award.html or contact Christin Veasley by e-mail (chris@nva.org).

NVA Funds Six New Research Studies

Since the creation of NVA's Medical Research Fund in 1997, we have awarded nearly $1 million in grants for over 40 studies. Thanks to the generosity of our donors, half of our annual budget is spent on medical research and we solicit research proposals twice a year. In 2011, NVA's Executive Board approved funding for the six projects summarized below, four of which include women with Generalized Vulvodynia, a longtime neglected and understudied vulvodynia subtype.

Pregnancy and Childbirth Experiences

Lori Brotto, PhD, associate professor of obstetrics and gynecology at the University of British Columbia in Vancouver, Canada, will conduct the

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second NVA-funded study examining pregnancy and childbirth in women with all vulvodynia subtypes. In the first phase of the study, Dr. Brotto will compare self-reported data on vulvodynia patients' past pregnancy, childbirth and vulvar pain experiences to that of healthy controls. In the second phase, she will prospectively follow women with vulvodynia throughout their pregnancies and into the postpartum period to determine how pregnancy and childbirth affect the severity and constancy of vulvar pain symptoms (and vice versa). In the final phase, her research group will query local doctors and midwives who care for pregnant women to determine how frequently they encounter women with vulvodynia. Additionally, they will collect information on the strategies clinicians use to examine this patient population, as well as delineate the clinicians' pain management, childbirth and postpartum recommendations for vulvodynia patients. Due to the paucity of information available on this topic and in an effort to improve clinical care provided to pregnant women with vulvodynia, upon conclusion of the study, Dr. Brotto's research team will develop a document summarizing the study's significant findings and disseminate it to local health care providers who care for pregnant women.

Using Advanced Statistics To Identify Subgroups
Eric Bair, PhD, assistant research professor of biostatistics at the University of North Carolina in Chapel Hill, will use his NVA research grant to run cluster analyses and advanced statistical methods on one of the largest patient datasets in the country to identify vulvodynia subgroups that differ in their underlying pathophysiology. Differential contribution of central and peripheral factors may partially explain the large variation in clinical course and treatment response among women with similar vulvar pain symptoms. For example, peripheral factors (e.g., vulvar inflammation) may be the primary generator of pain in some women, whereas in others, vulvar pain may result from a heightened state of pain sensitivity in the central nervous system. The same treatment is therefore unlikely to be equally effective in both groups. The ultimate goal of this research team is to use the results of these advanced analyses to develop clinical criteria for classifying patients into appropriate mechanism-based subgroups, enabling the selection of appropriate effective treatment for each.

Using Ultrasound to Treat Muscle Dysfunction
Building on the findings of her previous NVA research grant (see Spring 2010 issue of *NVA News*), and with matching funds from her institution, Linda McLean, PhD, associate professor in the School of Rehabilitation Therapy at Queen's University in Ontario, Canada, aims to determine the nature of pelvic floor muscle (PFM) involvement in women with vulvodynia, and to use this information to enhance physical therapy approaches to treatment. In addition to being one of the first research studies to examine PFM dysfunction in women with Generalized Vulvodynia, Dr. McLean will examine the validity and utility of three-dimensional ultrasound imaging (USI) in assessing PFM dysfunction before, during and after physical therapy treatment aimed at relaxing the pelvic floor. The results of this study may demonstrate a novel, non-invasive approach to assess PFM involvement in women with all vulvodynia subtypes, as well as provide evidence of the benefits of visual biofeedback training using USI, rather than a vaginal probe, to promote relaxation of the pelvic floor muscles.

Vulvar Pain in the Brain
Irv Binik, PhD, professor of psychology at McGill

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University in Montréal, Québec, was awarded an NVA grant to investigate brain activity and anatomy in women with primary and secondary Provoked Vestibulodynia (PVD). According to Dr. Binik, the study of PVD has focused on peripheral mechanisms underlying chronic vulvar pain (e.g., dysfunction of peripheral vulvar nerves, tissue inflammation), with little attention paid to abnormal pain processing in the spinal cord and brain. Using functional magnetic resonance imaging (fMRI), Dr. Binik will compare brain activity during the application of vestibular stimuli (both painful and non-painful) in women with PVD and pain-free controls. In addition to adding to our understanding of pathological pain processing in PVD, Dr. Binik proposes that a detailed analysis of brain activity and anatomy will aid in the identification of imaging biomarkers, which could be used to identify PVD subtypes, as well as novel therapeutic targets based on specific structural and anatomical abnormalities.

First Proteomics Study of Vulvodynia
Joanna Floros, PhD, professor of obstetrics and gynecology and pediatrics, and co-investigator Colin MacNeill, MD, assistant professor of obstetrics and gynecology, both of the Pennsylvania State University College of Medicine in Hershey, are using their NVA grant, along with matching institutional funds, to conduct the first proteomics study of vulvodynia. The study goals are twofold. First, the doctors are comparing vestibular fluid samples from healthy control women and women with both Generalized Vulvodynia and PVD to identify protein types and concentrations that may be abnormal in affected women. Next, they will use this information to identify the underlying pathways and mechanisms that may be involved in the pathogenesis of vulvodynia. Data derived from this study will help to identify women who may be at risk of developing the condition, as well as new therapeutic targets and biomarkers that could be useful in the diagnosis and/or subtyping of women with vulvodynia.

New Animal Model of Vulvar Pain
Devavani Chatterjea, PhD, assistant professor of biology at Macalester College in St. Paul, Minnesota, was awarded a grant to develop an animal model of chronic vulvar pain. Prior studies demonstrate that mast cells, which play a critical role in the body's immunological response, may contribute to the initiation and/or maintenance of vulvodynia in a subgroup of women. To determine the role of mast cells in the disorder's pathophysiology, Dr. Chatterjea and her group will establish a mast cell-specific mouse model of inflammatory pain. This model will add to our understanding of specific mast cell-related mechanisms responsible for triggering/maintaining vulvar pain, and also aid in the discovery of novel treatments.

NVA will next solicit research proposals in early 2012. To obtain an application, please contact Christin Veasley by e-mail (chris@nva.org). For additional information on the Medical Research Fund and/or to read summaries of other NVA-funded studies, please visit www.nva.org/research_fund.html.

NVA Expands Treatment Registry
The generous five-year pledge of a longtime NVA donor, plus two complementary grants from The Patty Brisben Foundation for Women's Sexual Health and in-kind support from Florida Hospital in Orlando, have enabled NVA to launch the first national multi-center Vulvodynia Treatment Outcomes Registry, and expand it to include postmenopausal women and the collection of DNA samples at eight patient enrollment sites in the

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U.S. Current Registry sites are located in Florida, Arkansas, California, Colorado, Ohio, Maryland and Washington DC, and the Registry's director, Georgine Lamvu, MD, director of the gynecology unit at Florida Hospital, is working to add three additional sites in Fort Lauderdale, Pittsburgh and New York City in early 2012.

NVA is now in the process of expanding the scope of the Registry project to include the investigation of pathophysiological mechanisms of all vulvodynia subtypes. In brief, Registry investigators will collect both vaginal and vulvar swabs that will be tested in the laboratory of Steven Witkin, PhD, professor of immunology in obstetrics and gynecology at Weill Cornell Medical College, for the presence and/or concentration of compounds in the lower genital tract that have the potential to trigger and/or maintain vulvar pain symptoms. These include asymptomatic infection by members of the herpesvirus family and bacterial infection, as well as the presence and concentration of novel mediators or biomarkers of chronic inflammation, anti-viral immunity and allergic response. In addition to DNA samples, these new factors will be correlated to treatment response, vulvar/vestibular skin and pelvic floor muscle pain sensitivity and the numerous other biological measures being collected throughout the Registry project. NVA anticipates that this data will aid in the identification of: i) novel biomarkers, ii) effective treatments for different vulvodynia subtypes, iii) potential genetic treatment targets, and iv) women who may be at risk of developing the disorder.

For more information about the Registry project, or to participate, please visit www.nva.org/treatmentregistry.html or contact the Registry's Research Coordinator Katy Capote (katerina.capote@flhosp.org, 407-303-2721).

NVA Participates in Third NICHD Conference

In July, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), with support from the Office of Research on Women's Health, convened its third vulvodynia workshop, *Vulvodynia: A Chronic Pain Condition – Setting a Research Agenda*. Building on their 2003 conference, the meeting advanced understanding of vulvodynia as a chronic pain syndrome, rather than a gynecological disorder, by bringing together a wide array of scientists and clinicians in the neuroscience field and exploring the underlying mechanisms of chronic pain. In addition to stimulating new ideas that will enhance ongoing vulvodynia research, NICHD aimed to encourage investigators working in the general area of chronic pain, as well as those currently involved in the study of other chronic pain disorders, to expand their focus and include vulvodynia in their studies. NVA's Christin Veasley and longtime Medical-Scientific Advisory Board member Ursula Wesselmann, MD, PhD, served on the planning committee, and Ms. Veasley also led one of the five breakout sessions.

The Institute viewed this meeting as *one* important step in expanding NICHD-funded research on vulvodynia. In his opening remarks, NICHD Director Dr. Alan Guttmacher promised that the Institute directors and staff would listen very carefully to the presentations and general discussion, as well as the recommendations that stem from the meeting. In January, the NICHD posted on their web site the resultant white paper, which includes a strategic research plan, and accepted public comment for three weeks. The Institute will include a summary of these comments in the final version of the document. NVA will meet with NICHD staff in February to discuss research

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priorities for the upcoming year and coordinate efforts to advance the strategic research plan.

NVA Active in First Federal Pain Initiatives

IOM Publishes Landmark Pain Report

In June, after seven months of deliberation, the Institute of Medicine (IOM) released the *first* comprehensive report on chronic pain, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research*, alerting Congress and the American public to the enormity of this growing public health epidemic that affects one-third of the U.S. population at an annual cost of $635 billion. The report calls for a coordinated national effort to transform how our society understands and approaches pain management and includes a blueprint for implementing the committee's recommendations, assigning tasks to several federal health agencies, private and public organizations, health care providers, medical professional and patient advocacy organizations, private insurers and academic institutions. The NVA, along with hundreds of women with vulvodynia and health care providers who treat vulvar pain disorders, submitted written testimony that communicated the urgent need for *all* initiatives resulting from the IOM study to include long-overdue and appropriate focus on the condition, which resulted in vulvodynia's inclusion in multiple sections of the report.

In the weeks following the report's release, more than 1,500 media outlets featured stories on chronic pain, the IOM report and its major findings, helping to raise public awareness of the gravity of this issue. After months of working cooperatively with a number of medical professional and patient advocacy organizations to convince the U.S. Senate to convene a hearing on this issue, the Committee on Health, Education, Labor and Pensions announced that a hearing will be held in February 2012. The hearing will be the first of many steps necessary to implement the IOM's recommendations, building upon federal research efforts to significantly improve the quality of medical care provided to those affected by chronic pain. (To view or download the report, visit www.nap.edu/catalog.php?record_id=13172.)

NVA Serves on Federal Pain Committee

In addition to commissioning the Institute of Medicine study described above, Secretary of Health and Human Services Kathleen Sebelius mandated the development of the NIH Interagency Pain Research Coordinating Committee (IPRCC) and invited NVA's Christin Veasley to serve as a member. The committee will coordinate federal agency activities related to pain, develop a summary of advances in pain research supported or conducted by federal agencies, and identify critical gaps in basic and clinical research on the symptoms and causes of pain. It will also make recommendations to ensure that: i) the activities of the NIH and other federal agencies are free of unnecessary duplication of effort, ii) information on pain care is widely disseminated and available to those in need, and iii) potential partnerships between public and private entities to expand collaborative cross-cutting research are identified and utilized. The committee's first meeting will be held in March 2012.

NVA Collaborates to Advance Pain Therapies

The U.S. Food and Drug Administration recently selected the University of Rochester Medical Center to lead a new initiative – Analgesic Clinical Trial Translations, Innovations, Opportunities and Networks (ACTTION) – to accelerate the identification of improved pain treatments. Robert

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Dworkin, PhD, professor of anesthesiology, neurology, oncology and psychiatry at the University of Rochester, is the director of this public-private partnership in which professional societies, advocacy groups, industry and government will collaborate to accelerate the development of pain treatments with improved efficacy and safety. NVA was pleased to accept Dr. Dworkin's invitation to serve on ACTTION's Scientific and Professional Advisory and Recommendations Committee, which provides recommendations to the Executive Committee regarding ACTTION's objectives and scientific/professional activities, as well as feedback on its progress and accomplishments.

NVA Studies Presented at National Meetings

In June, Ruby Nguyen, PhD, assistant professor in the division of epidemiology and community health, and Ali Ecklund, MPH, both of the University of Minnesota School of Public Health, presented an abstract summarizing the results of the *first* survey study to examine the temporal relationship between vulvodynia and common coexisting pain disorders at The TMJ Association's biannual scientific meeting, *Comorbid Chronic Pain Conditions: Mechanisms, Diagnosis and Treatments*. While numerous studies have demonstrated that women with vulvodynia are more likely to suffer from other chronic pain disorders, none have examined whether vulvodynia typically precedes the development of these conditions, develops at the same time or presents at a later time. The abstract summarized the study's findings specific to temporomandibular joint and muscle disorders (TMD) from 1,500 women with vulvodynia who completed an anonymous web-based survey on NVA's web site. Twenty-two percent of women with vulvodynia reported a TMD diagnosis, 66 percent of whom developed TMD prior to vulvodynia, 28 percent at the same time and 6 percent after. Additionally, compared to women with vulvodynia alone, those with both disorders were significantly more likely to suffer from all eight comorbid disorders included in the survey. Dr. Nguyen is currently preparing a manuscript summarizing the full results of the survey, which she will submit for publication by spring 2012. We look forward to summarizing these results in a future newsletter issue.

In December, Lizheng Shi, PhD, professor in the department of health systems management of Tulane University School of Public Health and Tropical Medicine in New Orleans, Louisiana, and his research team presented the findings of the *first* economic impact study on vulvodynia at the 17th Annual Maternal and Child Health Epidemiology Conference of the Centers for Disease Control and Prevention. The abstract summarized cost data related to office visits, lab work, diagnostic tests, surgical procedures, hospitalizations, transportation expenses, lost wages and inability to perform household chores from 300 vulvodynia patients who completed a survey on NVA's web site. Based on the reported prevalence range for vulvodynia of 3 to 7 percent in the U.S., the data analysis yielded an annual national burden of $29 to $67 billion. Dr. Shi has since submitted the full manuscript to *Current Medical Research and Opinion*, and anticipates publication in spring 2012. ■

Thank You

The NVA would like to thank Purdue Pharma, L.P., for its generous grant support in 2011.

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Pelvic Floor

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To obtain a list of vulvar pain specialists in your geographic area (including specialized physical therapists) please contact NVA's administrator Gigi Brecheen (gigi@nva.org, 301-949-5114). The International Pelvic Pain Society (www.pelvicpain.org) maintains a list of health care providers who treat pelvic pain disorders. The American Physical Therapy Association's Section on Women's Health also maintains a list of pelvic floor physical therapists (www.womenshealthapta.org). To find a local compounding pharmacist, check your local listings or visit www.project-aware.org/Resource/Pharmacy1.shtml.

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ISSVD

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involved in treatment and research of vulvovaginal disorders, it is oriented toward professionals more than patients. This past September, ISSVD President Micheline Moyal-Barracco, MD, vulvar dermatology specialist from the University Paris Descartes, hosted the 21st ISSVD World Congress and Postgraduate Course in Paris, France. Experts in vulvovaginal disease from around the world gathered to discuss clinical management, new research findings and even the politics and economics of this exciting field. Attendees included gynecologists, dermatologists, physician assistants, nurse practitioners, physical therapists and psychologists - a truly broad interdisciplinary representation.

World Congress

The majority of the presentations summarized new research findings from investigators interested in becoming ISSVD fellows. In addition, international faculty presented the most advanced and up-to-date information on vulvovaginal disorders. This article highlights the presentations on vulvodynia and related disorders.

The first day of the conference featured discussions of some of the less common vulvar conditions, including plasma cell vulvitis, Paget's disease and pediatric vulvovaginal disorders. A detailed discourse on desquamative inflammatory vaginitis (DIV) reminded the attendees that the severe dyspareunia (painful intercourse) associated

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with this disorder can be easily mistaken for other vulvovaginal conditions, even vulvodynia. The patchy redness and distinctive microscopic findings are usually adequate to make the correct diagnosis. Up to 8 percent of vaginitis cases may fall into this category, so clinicians should be familiar with DIV treatment, including the combination of clindamycin and hydrocortisone, used when each of these therapies alone has failed to provide relief.

An especially fascinating subject was that of vaginal moisturizers and lubricants. Although this issue comes up during many patient encounters, scientific scrutiny of available products is infrequent. In a comprehensive lecture, NVA Career Development Award recipient Ahinoam Lev-Sagie, MD, an obstetrician-gynecologist at Hadassah University Hospital in Israel, and Susan Kellogg-Spadt, CRNP, PhD, professor of obstetrics and gynecology at Drexel University College of Medicine, described the physical and chemical properties of moisturizing and lubricating products, as well as the clinical advantages and side effects of each. They also discussed sensitivity to preservatives, such as parabens, as well as the differential properties of water-, oil- and silicone-based agents. Although lubricants can reduce vulvar symptoms by reducing friction, irritation can occur. Organic lubricants are commercially available. Usually, vaginal dryness is associated with a lack of estrogen, but women are advised to consider whether medications, such as anticholinergics, antihistamines, decongestants and SSRI antidepressants, are to blame.

Of special interest to NVA constituents was the discussion led by Barbara Reed, MD, professor of family medicine at the University of Michigan Health System, and NVA Medical-Scientific Advisory Board member David Foster, MD, professor of obstetrics and gynecology at the University of Rochester Medical Center, on the genetic, immunological and neurological pathophysiologic mechanisms of vulvodynia. NVA Medical-Scientific Advisory Board member Libby Edwards, MD, clinical associate professor of dermatology at the University of North Carolina in Chapel Hill, presented an extensive overview of the infectious and non-infectious causes of *vaginitis*, in which there is an inflammatory component, and *vaginosis*, a disturbance not associated with the classic inflammatory response. Hope Haefner, MD, professor of obstetrics and gynecology at the University of Michigan Health System, and Lynette Margesson, MD, assistant professor of obstetrics and gynecology at Dartmouth Medical School, reviewed a number of disorders that cause vulvar pain, along with established and newer state-of-the-art treatments for lichen sclerosus, lichen planus, lichen simplex and contact dermatitis. New medications, such as biological agents and compounded preparations, which may not yet be FDA-approved and require off-label prescription, should only be used by vulvovaginal experts who are familiar with these drugs. The doctors reinforced the importance of consulting with a variety of medical specialists, including pain management clinicians, surgeons, allergists and immunologists, dermatologists, physical therapists and psychologists. Patient education and partner involvement is important, as is continuing emotional support.

Dr. Haefner began the thorough session on vulvodynia by reviewing the current ISSVD nomenclature, which defines vulvodynia as chronic vulvar discomfort characterized as stinging, burning or rawness in the absence of other diagnoses such as yeast infections, DIV, atrophic vaginitis and

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pudendal nerve entrapment. Additionally, subclassification is used to differentiate vulvodynia into generalized, localized, provoked and/or unprovoked types. An accurate diagnosis relies on a complete history and pain assessment with a cotton-swab test. The challenge of making an accurate diagnosis is only one of the obstacles to assessing treatment effectiveness, as are placebo effects and the absence of prospective double-blind, case-controlled studies.

Many suspect that a "feedback loop" involving neural stimulation, tissue vasodilatation and nerve proliferation, along with the presence of inflammatory tissue mediators, is involved in vulvodynia's pathogenesis. Because there are many points along this complex path to intervene, experts report using an array of treatments. Some of these include the off-label use of anti-seizure medications (gabapentin, pregabalin), muscle relaxants (baclofen, diazepam), tricyclic antidepressants (amitriptyline, nortriptyline, desipramine, doxepin) and SNRI antidepressants (duloxetine, venlafaxine), in highly variable doses. Although these medications are often used systemically, many vulvar specialists utilize compounding pharmacies to formulate topical creams and ointments containing these and other drugs. In addition, opioids can be used to treat pain, but the possibility of dependency and abuse limits their clinical use.

Attendees benefitted from a lecture on physical therapy by Dee Hartmann, DPT, director of Dee Hartmann Physical Therapy for Women in Chicago. Treating pelvic floor muscle dysfunction is a valuable adjunct treatment to first-line therapies, as it can ease spasm-induced pain, reduce anticipatory muscle contraction and improve blood flow to involved areas. Contraindications to physical therapy include active infections and unresolved skin conditions. Only those patients with pelvic floor muscle dysfunction should be referred for pelvic floor muscle therapy, and it is important to seek the expertise of a therapist specially trained in pelvic floor muscle dysfunction.

Wendy Likes, PhD, DNSc, associate professor in the department of obstetrics and gynecology at the University of Tennessee Health Science Center in Memphis, summarized the psychosexual impact of vulvodynia and highlighted the importance of desensitization techniques, improved partner communication, re-establishment of control and counseling for sexual techniques and expressions of intimacy.

Research Abstracts

NVA donors should be pleased with the presentations that summarized research studies funded by the Association. These vulvodynia-specific abstracts are valuable contributions to our continuing knowledge of the disorder and were published in the *Journal of Lower Genital Tract Disease*. NVA research grant recipient Nina Bohm-Starke, MD, obstetrician-gynecologist at Danderyd Hospital in Sweden, and her colleagues proposed that generalized pain hypersensitivity should be considered as a predictive factor of treatment effectiveness after finding that women in their study who had both PVD and at least one other pain disorder did not respond as well to treatment as did those with PVD alone. NVA Career Development Award recipient Yaniv Farajan, MD, obstetrician-gynecologist at Western Galilee Hospital in Israel, provided evidence that injections of enoxaparin, a heparin-like anticoagulant, reduced vestibular sensitivity by 33 percent, compared to only 10 percent with placebo. Colin MacNeill, MD, assistant professor of obstetrics and gynecology, and Joanna Floros, PhD, professor of obstetrics, gynecology and pe-

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diatrics, both of the Pennsylvania State University College of Medicine, summarized preliminary findings from their NVA-funded study (see *Year in Review: 2011* on page 9) demonstrating that vulvodynia patients exhibit a unique set of vestibular proteins. NVA research grant recipients Tzipora Falik, MD, and Jacob Bornstein, MD, of Western Galilee Hospital in Israel, demonstrated a genetic influence in the development of PVD, although the biological pathway(s) is as yet unexplained. Another 17 investigators from around the world presented vulvodynia-specific abstracts summarizing results of their recent research. (To view these abstracts, see www.nva.org/pdf/ResUpdate-Dec2011.pdf.)

Postgraduate Course

As Dr. Moyal-Barracco stated in her introduction to the postgraduate course, "*To generate interest and disseminate knowledge on vulvar conditions are two paramount missions of the ISSVD*." This course included information on vulvar disease valuable to both the novice and expert. Nearly 50 authorities from around the world gave presentations on topics ranging from vulvar anatomy and histology to the latest treatment strategies for vulvodynia.

Experts summarized a number of systemic disorders that can affect the vulva, such as Crohn's disease, Epstein-Barr virus, autoimmune diseases and hidradenitis suppurativa. Infections, such as herpes and candidiasis, can also cause vulvar symptoms. In her review, Dr. Margesson presented photographs of the many kinds of ulcers and excoriations that cause vulvar pain, and her colleagues reviewed vulvar Paget's disease, as well as malignant and pre-cancerous vulvar intraepithelial neoplasia. Additional lecture subjects included the psychosexual aspects of vulvar disease and pelvic floor neuromuscular disorders.

Dr. Gérard Amarenco, neurologist at Rothschild Hospital in Paris, described neurologic conditions such as sacral spinal cord injuries and tumors, viral myelitis and pudendal neuralgia. If the patient's pain worsens in the sitting position, tends to be unilateral, is confined to the area of distribution of the pudendal nerve, worsens after a bowel movement or toward the end of the day, is exacerbated by digital pressure on the ischial spine and is alleviated by a properly administered pudendal nerve block, pudendal neuralgia may indeed be the culprit of vulvar-perineal pain. The use of advanced testing such as electromyography was discussed, and although this methodology may assist diagnosis in certain cases, its limited availability and poor specificity restricts its clinical usefulness.

The course also featured a separate series for surgeons on the latest vulvar surgery techniques. This interactive, day-long session included both lectures and hands-on demonstrations of vulvar cancer surgery and methods for removing painful vulvar lesions, along with meticulous cosmetic repair following surgery. Instructors covered biopsies, flaps, grafts and node resections in detail, and participants were able to practice some of these methods under the watchful supervision of international experts.

In summary, this year's ISSVD World Congress and Postgraduate Course combined up-to-date vulvology clinical data and research information with the camaraderie of experts from around the world - all against the exquisite backdrop of Paris.

The next ISSVD Postgraduate Course will be held in October 2013 in Israel, followed by the World Congress, which will take place on a 7-day Royal Caribbean Mediterranean Cruise to Italy, Turkey and Greece. For additional information, please visit www.issvd.org. ■