National Vulvodynia Association

NVA News

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Developing a New Diagnostic Algorithm for Vulvodynia

By Andrew Goldstein, M.D.

Dr. Goldstein is the director of the Centers for Vulvovaginal Disorders, which provide medical care to thousands of women with vulvodynia and other vulvar disorders in Washington DC, Annapolis, Maryland and New York City. He is the immediate past President of the International Society for the Study of Women's Sexual Health.

If you were to ask a lepidopterist, "What is a butterfly?" and the answer he gave you was, "It flies, and has wings, but is not a bird," it is likely that you would be very disappointed with his technically correct, but non-specific answer. With this definition, he could just as easily be talking about a bat, or even an airplane. Clearly, his definition would be reasonable only if he had no information with which he, or you, could distinguish a bird from a butterfly. Doesn't he know that butterflies are insects that have scales instead of feathers? The current definition of provoked vestibulodynia (also known as vulvar vestibulitis) is similarly disappointing. Since first described in 1987 by Dr. Friedrich, vestibulodynia has been defined by tenderness at the vestibule (it has wings), pain upon penetration (it flies), but is not a skin disease. The name has changed, but the diagnostic criteria have not.

Should we assume, therefore, that if a woman has tenderness at her vestibule, has pain upon sexual penetration, and doesn't have a skin disease, that she has exactly the same disease as every other woman with the same three diagnostic criteria? It is likely that you would agree that just as there are many different types of animals (and machines) that have wings and fly but aren't birds, there are likely several

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NVA Career Award Recipients: Where Are They Now?

In 2006, the NVA established the Dr. Stanley C. Marinoff Vulvodynia Career Development Award to encourage medical junior faculty to pursue a clinical or academic interest in vulvodynia. Have we achieved our goal? NVA staff contacted past award recipients to find out if they maintained their interest in vulvodynia.

Catherine Leclair, M.D.

Dr. Leclair, an assistant professor of obstetrics and gynecology and clinician in the vulvar health program at Oregon Health & Science University (OHSU), was one of the first recipients of the Career Development Award. In collaboration with her OHSU colleague, Martha Goetsch, M.D., she used her award to investigate a possible hormonal influence in the etiology of provoked vestibulodynia (PVD). The study was designed to: (i) quantify

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different "diseases" that have the same three diagnostic criteria for what we currently refer to as vestibulodynia.

Well, for the past three decades, almost every author of review papers on vulvodynia has acknowledged that vulvodynia is not one, but likely several different – though frequently overlapping – disease states. But, despite this acknowledgement, few have attempted to take the next step—*to start to separate out the different diseases*. All young physicians, nurse practitioners, physician assistants, etc., are taught to identify a list of possible diseases for any given set of signs and symptoms. This list is called a "differential diagnosis" and can be narrowed down by using laboratory tests and fine-tuning a patient's physical examination.

So this begs the question. In 2015, do we have enough information by which we can start to identify a differential diagnosis for the signs or symptoms that currently define vulvodynia/vestibulodynia? At the Centers for Vulvovaginal Disorders, we would contend that there are enough data to start this process, though not nearly enough to be definitive about each specific disease state. We are adamant, however, that it is essential to start this process because it is unlikely that we will develop specific treatments until this is done. To this end, the Centers recently published a proposed vestibulodynia and vulvodynia diagnostic algorithm in the journal of *Current Sexual Health Reports.*[1] How did we develop this algorithm? We used the data we already had from published studies on vulvodynia (many of which have been sponsored by NVA grants); we used our knowledge of other disease processes; and we applied our knowledge of anatomy, embryology, endocrinology and neurology. We acknowledge that it is likely that some of our diagnoses will ultimately prove false, and we also realize that there is a great deal of overlap between the diagnoses, but the only way to test a hypothesis is to come up with one in the first place!

So let's start by listing some of the things we *know* about vulvodynia.

1. Several studies show increased inflammation in women with vestibulodynia while others have shown genetic changes that lead to increased inflammation (and decreased ability to fight infection).[2,3]
2. Several studies show increased nerve endings in women with vestibulodynia.[4,5]
3. Several studies show tight pelvic floor muscles in women with vestibulodynia.[6,7]
4. Several studies show that decreased hormones (sometimes caused by hormonal contraceptives) may cause vestibulodynia.[8]
5. A few studies suggest that some cases of vestibulodynia may be the result of a congenital defect.[9]
6. Injury to the pudendal nerve can cause vulvar pain (vulvodynia), but the pain cannot be just confined to the vestibule.
7. Women with chronic pain conditions, including vulvodynia, develop a "wind-up" in which the brain perceives pain more easily.

(*See ALGORITHM, page 3*)

NVA News

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The National Vulvodynia Association is a nonprofit organization that strives to improve women's quality of life through education, support, advocacy and research funding.

The NVA is not a medical authority and strongly recommends that you consult your own health care provider regarding any course of treatment or medication.

ALGORITHM

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With this information, we started to develop distinct diagnoses. We have put these diagnoses in quotation marks because our terminology has not been adopted in any formal way by medical societies.

"Inflammatory Vestibulodynia"

Background: Dr. David Foster and colleagues showed increased tumor necrosis factor-alpha and interleukin -1 beta (inflammatory proteins) in women with vestibulodynia.[2] Dr. Steven Witkin's laboratory at Cornell identified several genetic defects that cause increased inflammation and increased susceptibility to vaginal infections.[3] Additionally, Dr. Jacob Bornstein showed increased mast cells (inflammatory white blood cells) in the vestibular tissue of women with vulvodynia.[4] The results of these studies suggest that one type of vestibulodynia is an "inflammatory vestibulodynia."

Clinical history: Women with "inflammatory vestibulodynia" typically exhibit sensitive skin, chronic yeast infections and/or an allergic reaction to soap and medications that have been applied to the vulva. These women should be evaluated for chronic yeast infection with serial vaginal cultures to rule out chronic or recurrent candidiasis. In addition, women with a history of copious yellowish vaginal discharge should be evaluated for an inflammatory vaginal condition known as *desquamative inflammatory vaginitis*.

Clinical findings: Tenderness throughout the entire vestibule, as well as increased erythema (redness). In women with desquamative inflammatory vaginitis, a vaginal wet mount reveals an elevated pH, increased white blood cells and parabasal cells.

Treatments for "inflammatory vestibulodynia" include montelukast and steroid or interferon injections into the vestibule. Treatment for recurrent candidiasis includes weekly fluconazole.

"Hormonally Mediated Vestibulodynia"

Background: As discussed in our article in the Summer 2014 edition of the *NVA News*, decreased hormones, both estrogen and testosterone, can cause vestibulodynia.[10] Genetic changes in the androgen receptor gene increase the risk of this type of vestibulodynia.[8]

Clinical history: Pain beginning during use of hormonal contraceptives. Additional medications that may cause hormonally mediated vestibulodynia include Tamoxifen, spironolactone (used for acne, male pattern hair loss, or unwanted facial hair), aromatase inhibitors (used for breast cancer) and Lupron Depot (used for endometriosis). Additional causes include surgical removal of ovaries, perimenopause and menopause.

Clinical findings: Tenderness and erythema of the entire vestibule - especially at the Bartholin's and Skene's glands' ostia (openings), and atrophy of the vestibular mucosa, labia minora and clitoris. Symptoms of decreased lubrication, decreased libido and burning after intercourse often begin before the onset of vestibulodynia. Even if the pain does not resolve after eliminating the offending medication, one should still consider this diagnosis if the hormone levels are still low. (See Treatment below.)

Laboratory findings: Decreased estradiol, decreased total testosterone, increased Sex-hormone Binding Globulin and calculated free testosterone less than 0.4ng/dl (use the free testosterone calculator at http://www.issam.ch/freetesto.htm).

Treatment: Stop the offending medication and use a topical estrogen and testosterone cream. (Please note that this is an off label use of testosterone, which can only be obtained from a compounding pharmacy.)

Neuroproliferative Vestibulodynia

Background: In 1998, Nina Bohm-Starke, M.D., and Lars Westrom, M.D., Danderyd University Hospital in Sweden, discovered too many nerve endings in the removed vestibular mucosa of women who had undergone vulvar vestibulectomy.[5,11] Subsequent studies have shown that women with vestibulodynia can have up to 10 times the normal number of nerve endings. This type of nerve ending has been identified as a "c-afferent nociceptor," which is responsible for the sensations of burning, rawness and cutting.[12] Research has suggested two possible mechanisms by which women develop this neural proliferation.

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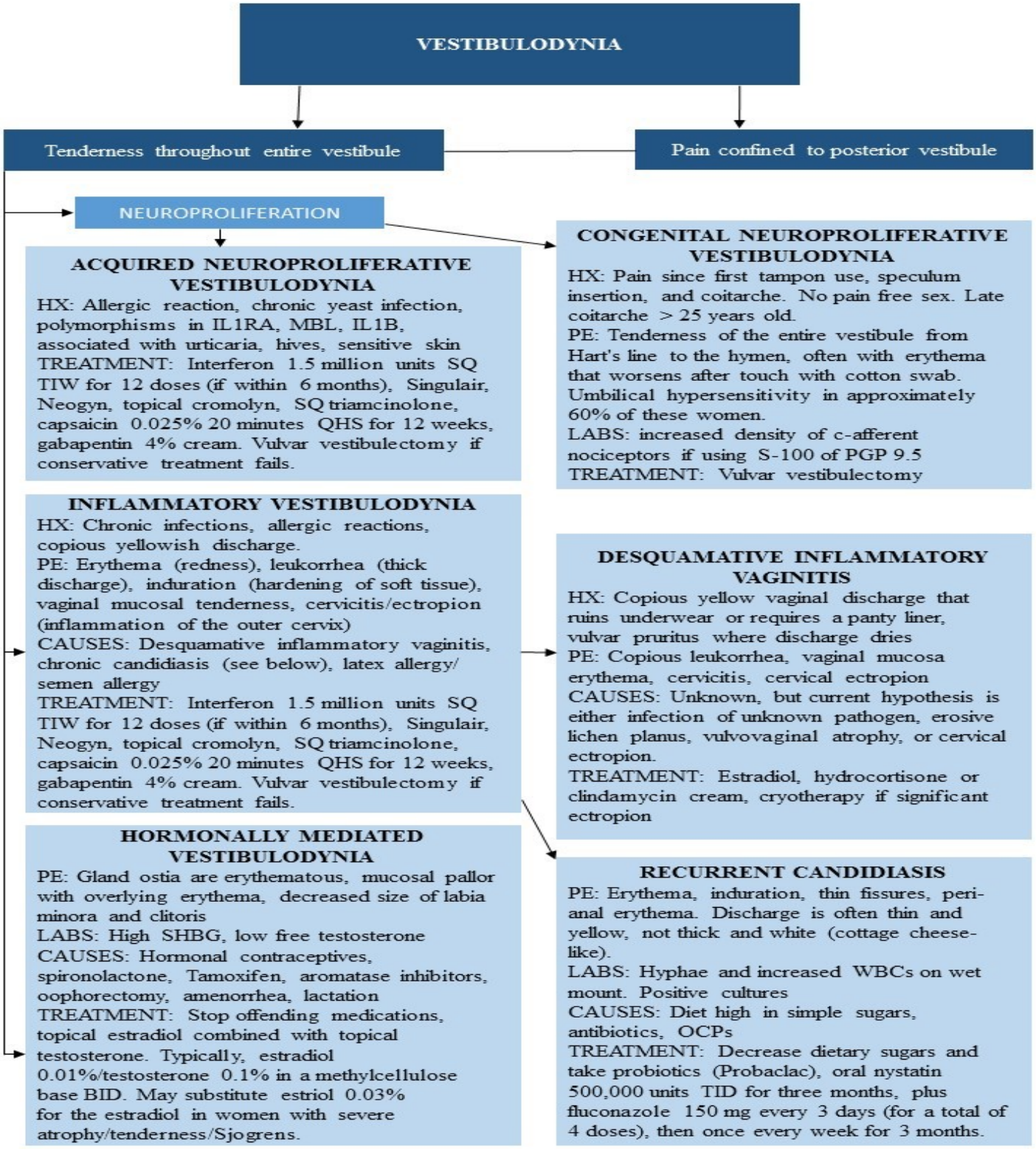
Introital Dyspareunia and Vulvar Pain: A Diagnostic and Treatment Algorithm

Andrew Goldstein M.D., FACOG, IF · Obstetrics@yahoo.com · www.CVVD.org

A proposed diagnostic and treatment algorithm for vulvodynia, vulvar pain, and dyspareunia. Comments and criticisms are welcome. It is essential that clinicians and researchers differentiate causes of vulvar pain to improve treatment and research. (See Key, page 5.)



Introital Dyspareunia and Vulvar Pain: A Diagnostic and Treatment Algorithm (cont.)

PAIN EXTENDS OUTSIDE VESTIBULE (SUBJECTIVE)

PUDENDAL NEURALGIA

Pudendal Nerve (PN) tender at ischial spine, unilateral or significantly greater on one side, history of coccyx trauma, history of hip pain or labral tear, better with lying prone or standing, worse with sitting, pain improves temporarily with PN block

Treatment: Serial PN blocks, gabapentin, Lyrica, PN neuromodulation

PERSISTENT GENITAL AROUSAL DISORDER

Causes: Pudendal Neuralgia, Tarlov cyst, pelvic varicosities, mass along dorsal nerve of clitoris, change in psychotropic medicine, Ehlers-Danlos Syndrome
DX: Tenderness at ischial spine, MRI, pudendal nerve block, dorsal clitoral nerve block

HYPERTONIC PELVIC FLOOR MUSCLE DYSFUNCTION

Pain at 4, 8 o'clock if hypertonus of pubococcygeus muscle
Pain at 6 o'clock if hypertonus of puborectalis muscle
Urinary symptoms (frequency, sensation of incomplete emptying, hesitancy) if it involves coccygeus muscle
Constipation, rectal fissures, hemorrhoids if it involves puborectalis
Associated with anxiety, low back pain, scoliosis, hip pain, "holding urine," excessive core strengthening exercises

TREATMENT: Pelvic floor physical therapy, diazepam suppositories, vaginal dilators, home pelvic floor exercises, Botox injection

LICHENIFICATION, ULCERATION, RESORPTION OF THE LABIA MINORA, CLITORAL PHIMOSIS, NARROWING OF THE INTROITUS WITH EVIDENCE OF FISSURING

LICHEN SCLEROSUS

Anogenital in a "figure 8" distribution but does not go inside the vagina.

Affects 1:60 women, 3-5% malignant transformation (vulvoscopy necessary), biopsy before treatment

Treatment: Clobetasol ointment, SQ triamcinolone. Surgery for phimosis or recurrent tearing (vulvar granuloma fissuratum)

Can co-exist

LICHEN PLANUS

Affects the squamous epithelium of the vulva and causes ulceration in the vestibule (Wickham's stria).
Affects mucous membrane of the mouth and vagina.
Can cause synechiae/scarring of the vagina.

PREMALIGNANT TREATMENT:
Clobetasol, Elidel, Protopic
Need to treat vagina - use meds on vaginal dilators
Systemic steroids or other immuno-suppressants may be needed.

KEY

BID:	Twice a day
DX:	Diagnosis
HX:	History
MRI:	Magnetic resonance imaging
OCP:	Oral contraceptive pill
PE:	Physical examination
QHS:	Every night at bedtime
SHBG:	Sex hormone binding globulin
SQ:	Subcutaneous
TIW:	Three times a week
WBC:	White blood cells

ALGORITHM

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Dr. Jacob Bornstein has shown that persistently activated mast cells release a protein called *nerve growth factor* that causes new endings to grow. In addition, these activated mast cells release another protein called *heparinase* that allows the newly sprouted nerve endings to invade the superficial mucosa of the vestibule.[13] In this way, persistent "inflammatory vestibulodynia" may evolve into an "acquired neuroproliferative vestibulodynia." Alternatively, our group has published evidence that women with primary vestibulodynia (pain since the first attempt at intercourse or tampon use) may be born with too many nerve endings in the vestibule, a "congenital neuroproliferative vestibulodynia."[14]

Clinical history: Women with "acquired neuroproliferative vestibulodynia" have a history similar to women with "inflammatory vestibulodynia" in that they may have a history of sensitive skin, chronic yeast infections and/or an allergic reaction to soap and medications that have been applied to the vulva. Typically they have symptoms that have persisted for at least six months. Women with "congenital neuroproliferative vestibulodynia" have had pain since the first attempt at intercourse, tampon use or speculum examination. In addition, many show hypersensitivity of the umbilicus (belly-button). Women with either acquired or congenital neuroproliferative vestibulodynia experience pain throughout the entire vestibule.

Treatments: Medication used to numb nerves are the mainstay of treatment for neuroproliferative vestibulodynia. These include oral medications such as tricyclic anti-depressants (amitriptyline, nortriptyline, desipramine), SNRI anti-depressants (duloxetine, venlafaxine, desvenlafaxine) and anti-seizure medications (gabapentin, pregabalin). Topical medications that can be used are lidocaine, capsaicin and creams containing gabapentin, amitriptyline or ketamine, which are mixed by compounding pharmacists. If conservative treatments for neuroproliferative vestibulodynia fail, these women are candidates for vulvar vestibulectomy with vaginal advancement, surgical excision of the tissue that contains too many nerve endings.

Vestibulodynia Secondary to Hypertonic Pelvic Floor Muscles

Background: It has been long-acknowledged that tight pelvic floor muscles can cause pain at the vestibule. In the past, this was called *vaginismus* and it was thought that women who had been abused or were anxious involuntarily contracted the muscles surrounding the vagina. More recently, however, the term *vaginismus* has been discarded, because it has been shown that the pelvic floor muscles are not tight because of abuse. In addition, the muscles are tight all of the time, not just "when there is a threat of penetration." In this condition, the muscles that comprise the "floor of the pelvis" (levator ani muscles) and which come together in the back part of the vestibule (the pubococcygeus, puborectalis and transverse perineal muscles) become tight and tender. The tight levator ani muscles cause a constriction of the arterioles (small arteries) and this causes a decrease in blood flow to the muscles and the mucosa of the vestibule. This decrease in blood flow causes a decrease in oxygen going to these tissues and also leads to an increase in lactic acid. This build-up of lactic acid causes the sensations of burning, rawness, throbbing, aching and soreness. In addition, the capillaries in the vestibule dilate to try to bring more blood to the area and this causes the erythema of the vestibular mucosa.

Clinical history: Women with hypertonic pelvic floor dysfunction typically feel burning, rawness and soreness. These symptoms may occur only with penetration or may be constant (non-provoked). In addition, there may be a sensation of ripping, tearing or "hitting a wall" upon penetration. *It is very important to understand that vestibulodynia caused by tight pelvic floor muscles only affects the posterior (back) part of the vestibule at 4, 6, and 8 o'clock where the muscles attach directly under the vestibular mucosa.* As there are no robust muscles in the vestibule around the urethra, tight pelvic floor muscles do not cause pain around the top part of the vestibule. *Therefore, this distinction is extremely important in our diagnostic*

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algorithm and it should again be emphasized; in women who only have pain localized to the posterior vestibule, hypertonic pelvic floor muscles are almost always the cause of their pain. Women with hypertonic pelvic floor dysfunction often have urinary symptoms such as frequency, urgency and the sensation of incomplete emptying of the bladder. For this reason, these women are frequently misdiagnosed with a urinary tract infection or interstitial cystitis. In addition, constipation, hemorrhoids and rectal fissures (tears in the anal area) are common. Women with hypertonic pelvic floor muscle dysfunction frequently have low back pain and/or hip pain. In our experience, women with tight pelvic floor muscles frequently complain of tension headaches and grind their teeth at night; approximately 40 percent of these women meet the diagnostic criteria for an anxiety disorder. Additional behaviors that can cause hypertonic pelvic floor muscles include "holding urine" and overzealous core strengthening exercises.

Women with other types of vestibulodynia (inflammatory, hormonally mediated, neuroproliferative) often develop hypertonic pelvic floor dysfunction. In addition, women with *generalized vulvodynia* almost always have some degree of tightness in pelvic floor muscles.

Clinical findings: Women with hypertonic pelvic floor muscles will frequently have a "retracted" perineum upon inspection. In addition, they will have tight and tender muscles during a vaginal examination. It should be noted that an evaluation of the pelvic floor muscles is not a component of a typical gynecologic examination and, therefore, hypertonic pelvic floor muscles are frequently overlooked when a women complains of vulvar pain or pain with intercourse. An evaluation by a trained women's health physical therapist is very important in diagnosing this dysfunction.

Treatments: The goal of treatment of hypertonic pelvic floor dysfunction is to relax and lengthen the pelvic floor muscles. As such, the mainstay of treatment is trans-vaginal pelvic floor physical therapy by a skilled women's health pelvic floor physical therapist. This type of therapy can be augmented with biofeedback, vaginal dilators, pelvic floor relaxation exercises at home, rectal or vaginal diazepam suppositories, oral muscle relaxants (cyclobenzaprine, baclofen, carisoprodol), trigger point injections and Botox® injections. Pelvic floor physical therapists can be located using the following websites: http://www.isswsh.org; http://www.womenshealthapta.org/pt-locator/ and http://hermanwallace.com/practitioner-directory.

Pudendal Neuralgia

Background: The pudendal nerves are the major nerves that provide sensory innervation of the vulva and vagina. These nerves come out of the sacrum at the S2, S3, S4 spinal levels and follow a rather tortuous (and variable) course through the pelvic floor muscles and between the sacrospinous and sacrotuberous ligaments in *Alcock's canal*. Eventually the pudendal nerves split into three branches: the perineal branch, which goes to the perineum; the inferior rectal branch, which goes to the anus; and the dorsal clitoral branch, which goes to the clitoris. The nerves typically branch after exiting Alcock's canal, but may branch before or in the canal. Because of this, the entire pudendal nerve can be injured or just one or two branches can be injured depending on the cause and location of the injury. Even seemingly innocuous events such as sitting on a hard chair for several hours or riding a bicycle can cause injury to the pudendal nerves depending on the location of the trauma or the nerve. The pudendal nerve can be damaged in four main ways:

1) *Stretch injury* may occur when you push too hard during bowel movements, following the strain of vaginal childbirth (especially if the legs are pushed back) or by over-exercising, e.g., performing deep-knee squats while holding weights.
2) *Compression injury* may occur when the pudendal nerve is crushed or the blood flow to the nerve is reduced. Most commonly, it happens while sitting on hard surfaces. Compression injury is a particular risk during vigorous seated activities, such as bicycle or horseback riding.

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3) *Traumatic injury* usually happens during an acute trauma. For instance, falling and landing hard on your tailbone (coccyx or sacrum), a crush injury of the pelvis from a car accident, injury to the sacroiliac joint, or a labral tear (a tear in the cartilage of the hip).
4) *Surgical injury* may occur during pelvic or vulvar surgeries including hysterectomy; laparoscopic surgery for endometriosis, bladder slings, and repair of pelvic organ prolapse (especially if mesh is used); episiotomy or laceration during childbirth; Bartholin's gland surgery; and hemorrhoidectomy.

Clinical history: Women with Pudendal Neuralgia may experience any of the following sensations: burning, numbness, increased sensitivity, "electric shock sensation," tingling, stabbing pain, knife-like or aching pain, pulling or pinching sensations, abnormal temperature sensations, "hot poker" sensation, constipation, feeling of a foreign body in the vagina, rectum pain, straining or burning when urinating or defecating, painful intercourse, loss of clitoral sensation, and/or persistent genital arousal (sensations of genital arousal or orgasm without desire).

Clinical findings: Pain or hypersensitivity of the labia, perineum and clitoris typically is greater on one side. The pelvic floor muscles are almost always hypertonic and tender, especially the obturator internus muscle. The pudendal nerve is very tender when pressed at the ischial spine during vaginal examination.

Clinical tests: The following tests can be used to confirm Pudendal Neuralgia:

Quantitative sensory test - This non-invasive procedure uses temperature variations and vibrations to identify changes to the pudendal nerve structure or nerve fiber damage.

Pudendal nerve motor latency test - This test must be conducted in a neurologist's office by a trained technician. During the examination, the technician inserts a gloved finger into the rectum or vagina. The glove has electrodes on the tip, which stimulate the nerve. The speed at which the nerve conducts the stimulus is recorded by a small needle inserted in the perineum. If the nerve responds slower than normal, it means it could be entrapped or damaged.

Pudendal nerve blocks are used to treat Pudendal Neuralgia, but can also be used as a diagnostic tool. The doctor administers an anesthetic adjacent to the pudendal nerve. This can be done transvaginally or transgluteally (through the buttocks). If the pain disappears, even temporarily, then the diagnosis is confirmed. Steroids may be added to the injection to help reduce inflammation and treat the Pudendal Neuralgia.

Treatments: Recommended lifestyle changes include less sitting and more standing. Patients with Pudendal Neuralgia should also give up activities such as bicycling and horseback riding. Many women find that sitting on a donut-shaped cushion with an opening in the center (similar to those recommended for hemorrhoid sufferers) can ease the pain. Physical therapy can help with the accompanying hypertonic pelvic floor muscle dysfunction. (This is important because most women with Pudendal Neuralgia have a very tight, short pelvic floor.) Medical treatments include pudendal nerve blocks every three to four weeks, tricyclic anti-depressants (amitriptyline, nortriptyline, desipramine), SNRI anti-depressants (duloxetine, venlafaxine, desvenlafaxine) and/or anti-seizure medications (gabapentin, pregabalin). Surgical procedures include *neuromodulation or neurolysis of the pudendal nerve*. During pudendal neurolysis, a surgeon exposes the nerve and removes any scar tissue or ligaments that are compressing or restricting it. In pudendal neuromodulation, an electrical wire is placed next to the nerve to gently stimulate it, which causes a reduction in pain.

How to Use the Diagnostic Algorithm

Now that you are familiar with the diagnoses included in our algorithm, let's examine how you and your health care provider can use it to help make a diagnosis and choose diagnosis-directed treatments. Beginning with the top of the algorithm, your health care provider should examine you with a moist cotton swab to determine if the pain you are experiencing is localized to the vulvar vestibule or if it is more extensive. Please only pay attention to where it hurts when you are touched, not where you think the pain is located.

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(A recent study presented by our group showed that almost 90 percent of women with vulvar pain had pain localized to the vestibule even though many said that their whole vulva hurt.[15]) If the pain is confined to the vestibule (vestibulodynia), it is important to determine if the pain is confined only to the posterior part of the vestibule or if the anterior vestibule (mucosa near the urethra) is also tender. Very frequently the posterior vestibule is more tender, but it is essential to determine if there is any pain in the anterior vestibule. If the pain is confined only to the posterior vestibule, it is very likely that the sole diagnosis is *hypertonic pelvic floor muscles*. If there is pain in the anterior vestibule, then the diagnosis can be "hormonally mediated vestibulodynia," "inflammatory vestibulodynia," "acquired neuroproliferative vestibulodynia," or "congenital neuroproliferative vestibulodynia." If the pain is throughout the entire vestibule, but is much greater at 4, 6, and 8 o'clock, it is important to consider a dual diagnosis with hypertonic pelvic floor muscles. If the pain extends outside the vestibule on the cotton swab test, consider the diagnosis of Pudendal Neuralgia and/or hypertonic pelvic floor muscle dysfunction.

Conclusion

Most people agree that the best strategy to piece together a jigsaw puzzle is to start with the edges. While we clearly do not have all the pieces of the vulvodynia puzzle, it is time that we at least start to put the edges together. Hopefully, the diagnostic algorithm that we have outlined is a concrete step toward solving this puzzle. Lastly, the current terminology that we use to describe vulvar pain (vulvodynia, vestibulodynia) is woefully out of date. Therefore, we are very pleased to announce that a vulvar pain nomenclature conference will be held in April 2015 in Annapolis, Maryland. The International Society for the Study of Vulvovaginal Disorders, along with the International Society for the Study of Women's Sexual Health and the International Pelvic Pain Society will co-sponsor the conference, with NVA participation. The goal of this conference is to develop new terminology for different vulvar pain disorders that are currently lumped together under the term vulvodynia.

(Editor's note: *To obtain footnoted references, please contact our administrator, Tamara Matos, by email at admin@nva.org or phone at 301-299-0775.*)■

CAREER AWARD

(*from page 1*)

differences in estrogen and progesterone receptor density; (ii) assess accompanying nociceptors (nerve receptors that sense pain); and (iii) measure nerve fiber density in PVD patients. Drs. Leclair and Goetsch examined tissue samples from painful and non-tender sites of the vestibule and compared samples from patients with primary and secondary PVD to those of asymptomatic women. Results indicated that biopsies of tender sites from primary PVD patients showed increased nerve density compared with biopsies in the secondary and control groups. Biopsies of tender sites from secondary PVD patients had more lymphocytes than those of primary PVD patients and controls. In both PVD groups, mast cells were increased in tender sites compared to nontender and control sites. There was no difference among groups in estrogen and progesterone receptor expression.[1]

Dr. Leclair remains very active in the field of vulvovaginal health and her focus is to improve both the physical and psychosexual health of women. As a clinician and researcher, she provides care to this population, participates in local and national educational efforts, and performs clinical and basic science research. She is the current President of the North American Chapter of the International Society for the Study of Vulvar Disease, as well as director of the OHSU Program in Vulvar Health. This specialty consultative clinic is devoted to the evaluation and treatment of women with vulvovaginal disorders and sees over 400 new and 800 returning patients annually. The OHSU clinic is the only one of its kind on the west coast, providing care for women from Oregon, Washington, northern California and Idaho.

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CAREER AWARD

(*from page 9*)

Beri Ridgeway, M.D.

Dr. Ridgeway is a fellow in female pelvic medicine and reconstructive surgery at Cleveland Clinic in Ohio. With her NVA Career Development Award, and matching funds from her institution, Dr. Ridgeway investigated the efficacy of the anti-convulsant pregabalin (Lyrica) in the treatment of vulvodynia. Pregabalin has been shown to be effective in the treatment of other chronic pain disorders, such as post-herpetic neuralgia, diabetic neuropathy and fibromyalgia. Her primary objective was to determine whether, and to what extent, pregabalin relieves vulvar pain in women suffering from either generalized vulvodynia or provoked vestibulodynia. In addition, she assessed whether the medication was well-tolerated and its effect on quality of life. Unfortunately, despite Dr. Ridgeway's best efforts for several years, she was unable to complete this study because of difficulty recruiting patients. In spite of this disappointment, Dr. Ridgeway decided to submit her data for publication to discuss the challenges she experienced and the critical need for multicenter trials.

Dr. Ridgeway continues to treat patients with chronic vulvar pain. She lectures locally, teaching vulvodynia treatment options to generalist ob-gyns. Cleveland Clinic has also established a multidisciplinary pelvic pain center in which Dr. Ridgeway will be involved.

Yaniv Farajun, M.D.

Dr. Farajun, Medical Director of Kiryat Tivon District in Israel, was awarded our 2009 Career Development Award. He used this award, which was matched by the Chief Scientist Fund of the Israeli Ministry of Health, to evaluate the effectiveness of an anticoagulant drug, enoxaparin, in treating women with localized provoked vestibulodynia. Enoxaparin, a form of the drug heparin, inhibits the action of the enzyme, heparanase, and also exerts an anti-inflammatory effect. The results were published in *Obstetrics & Gynecology* and indicated that enoxaparin reduced vestibular sensitivity, dyspareunia, and intraepithelial free nerve fibers in women with localized provoked vulvodynia.[2] Specifically, the enoxaparin-treated women showed a greater reduction in vestibular sensitivity at the end of the treatment period and three months later. Seventy-five percent of them reported more than a 20 percent reduction in pain whereas only 28 percent of the placebo group reported similar pain reduction. Pain relief was correlated with a decrease in the presence of intraepithelial-free nerve fibers in the enoxaparin group, but not in the placebo group. Seven enoxaparin-treated women, compared with three in the placebo group, experienced almost pain-free intercourse at the end of the study.

Dr. Farajun remains active in the care of women with vulvodynia. He is now a member of the International Society for the Study of Vulvovaginal Disorders and lectures on vulvodynia, explaining the importance of correctly diagnosing the condition and avoiding inappropriate treatments that delay recovery. Dr. Farajun also works at two clinics to provide specialized care for women with vulvovaginal conditions and cervical pathology. He is a dedicated ob-gyn who devotes extra time explaining treatment options to women affected by vulvodynia.

Ruby Nguyen, Ph.D.

Dr. Nguyen is an assistant professor in the division of epidemiology and community health at the University of Minnesota School of Public Health. She was the recipient of the 2010 Career Development Award and used it to conduct a prospective study of 160 pregnant women, half of whom suffered from vulvodynia. Very few researchers have investigated how pregnancy and childbirth affect the severity of vulvodynia, leaving obstetricians without guidelines for vulvodynia patients who are, or want to become, pregnant. At each trimester and two months postpartum, these women completed questionnaires on vulvar pain intensity and factors that can modify pain levels, such as vulvovaginal infection, dermatological conditions, vulvar varicosities, mode of childbirth delivery and episiotomy/tear with vaginal childbirth. Dr. Nguyen assessed whether pregnant women with vulvodynia experience a change in vulvar pain severity or remission of symptoms over the course of pregnancy and postpartum period, and/or have an increased risk of developing postpartum

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vulvovaginal pain. Results indicated that women with vulvodynia were more likely to deliver by Cesarean section than vaginally. In addition, 37 percent of women with vulvodynia who underwent a vaginal delivery, versus 11 percent of controls, reported pain at two months postpartum. As might be expected, women with vulvodynia who experienced intermittent pain (as opposed to constant pain) were more than twice as likely to become pregnant.[3]

Dr. Nguyen has published an astounding 12 papers on vulvodynia in peer-reviewed journals since receiving our Career Development Award. In the past year, she has presented three original articles (of which she is first author) at national scientific meetings; in addition, she was the senior author of two vulvodynia-related student presentations at national research conferences. The funding sources for Dr. Nguyen's vulvodynia research are a National Institutes of Health R01 grant, three foundation grants, and one sub-contract from the NVA's Treatment Registry, for which she is the Principal Investigator.

Several aspects of Dr. Nguyen's work have contributed to our understanding that the central nervous system (CNS) is a key contributor to the chronicity of pain in women with vulvodynia. First, she determined that a majority of women with vulvodynia also suffer from another pain condition. In addition, she found that the presence of other chronic pain significantly increased feelings of isolation and stigmatization by doctors and peers. From an NVA community-based survey, she determined that women with vulvodynia and a comorbid pain condition (particularly irritable bowel syndrome) were likely to report more extensive vulvar pain. In a separate feasibility study, in which she and her technology partner designed a Smartphone application to prospectively measure pain, Dr. Nguyen found that women with persistent pain elsewhere on their bodies experienced increased site-specific vulvar pain. This finding was further supported in an NIH-funded study using quantitative sensory testing of the vulva, which showed that women with vulvodynia and another pain condition had a lower pain threshold at all painful sites and were even more sensitive to skin pressure from a non-painful stimulus. Viewed as a whole, Dr. Nguyen's research thus far supports the theory that the CNS contributes to chronic pain in many, if not all, women with vulvodynia. This is an important finding because it suggests that treatments addressing the CNS may be more beneficial than site-specific treatment, leading the management of such patients to multiple specialists. She plans to continue investigating the complex interrelationship between vulvodynia and comorbid pain conditions in upcoming NIH grant proposals.

Dr. Nguyen has also contributed to critical biopsychosocial and methodological areas of vulvodynia research. Previous studies, including her own, have shown that half of women with symptoms consistent with vulvodynia do not seek health care for the pain. No studies, however, shed light on this phenomenon. Following her publication in *Pain Medicine*,[4] which reported high levels of perceived stigma among women with chronic vulvar pain, Dr. Nguyen secured an NVA research grant to identify attitudes and pain states associated with seeking health care for vulvar pain. Data collection is currently underway. Using NVA community-based data, Dr. Nguyen recently found that women who do not seek care tend to have milder and intermittent pain, are likely to be younger, and are less likely to be under the care of a gynecologist for any other gynecologic condition, including the prescription of hormonal contraceptives. She has also expanded this research to investigate whether hormonal contraceptives increase the risk of vulvodynia.

Stéphanie Thibault-Gagnon, P.T.

Ms. Thibault-Gagnon, a physical therapist and clinical researcher at Queen's University in Kingston, Canada, received the Career Award in 2011. Prior to a large controlled trial investigating the efficacy of physical therapy in women with PVD, Ms. Thibault-Gagnon used the award to test the validity and reliability of 3D transperineal ultrasound for measuring their muscle function. This imaging device is a non-invasive tool for evaluating women's pelvic floor muscles, and may be more reliable and comfortable than intravaginal palpation and probes, which are typically used to

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measure pelvic floor muscle tone and function. Recently, Ms. Thibault-Gagnon used 4D translabial ultrasound imaging, another promising tool for measuring impairment in pelvic floor musculature, to confirm that women with PVD tend to have higher pelvic floor muscle tone than controls. She is currently summarizing the results and will submit the article for publication.

Ms. Thibault-Gagnon's research and clinical work continues to focus on this field. After receiving the NVA award, she pursued research at the graduate level to advance knowledge of the nature of pelvic floor muscle impairment in women with vulvodynia. She is completing the final year of her PhD in the Rehabilitation Science program at Queen's University. Upon completion of her degree, Ms. Thibault-Gagnon intends to continue her career as a researcher and clinician, focusing on the pathophysiology and impact of vulvodynia, developing new methods of assessment and advancing quality of care.

Ahinoam Lev-Sagie, M.D.

Dr. Lev-Sagie is an ob-gyn at the Hadassah University Hospital, Jerusalem, Israel, and spent several years in the United States training in vulvovaginal disorders under specialists Drs. Paul Nyirjesy, Steven Witkin and Lynette Margesson. In 2011, she used her Career Development Award to conduct a randomized placebo-controlled trial investigating the efficacy of low-level laser therapy in the treatment of PVD. Low-level laser therapy is an emerging medical technique in which exposure to non-thermal laser irradiation relieves pain. Dr. Lev-Sagie recently submitted the results of this study for publication. Although its mechanism of action is not fully understood, low-level laser therapy has already shown promising results in soft-tissue inflammation, neck pain, tendinopathies, rheumatoid arthritis and osteoarthritis. Dr. Lev-Sagie currently directs a vulvar pain clinic at Hadassah Hospital and sees approximately 70 patients each week, about half of whom are new patients. She treats a wide spectrum of vulvar pain conditions, from infections and dermatologic disorders to generalized vulvodynia and PVD, and is frequently approached by ob-gyn residents interested in joining her clinic to specialize in vulvovaginal disorders. Dr. Lev-Sagie is a senior lecturer at the Hebrew University in Jerusalem, teaching medical students and other health professionals about vulvovaginal disorders and continuing to conduct research. In addition, she teaches about vulvovaginal health at public health events, including Jewish bride instructors' courses and women's health forums.

(Editor's note: *References are available upon request. Please contact our administrator, Tamara Matos, by email at admin@nva.org or phone at 301-299-0775.*)■

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