

Vulvodynia: A Focus on Management Strategies

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Learning Objectives

At the end of this presentation, the participant will:

- Understand the new Classification System for Vulvar Pain Syndromes
- Integrate basic science into evolving therapies
- Understand current treatments used for chronic pain conditions
- Gain knowledge on new treatments for vulvodynia

Disclosures:

Dr. Haefner has lectured for Merck and Co., Inc.

Dr. Haefner has served as a consultant for DataMonitor, Inc.

Introduction

Vulvodynia is a condition that is challenging for patients and health care providers. The pain and discomfort of vulvodynia affects the quality of life of women with this condition. Pain can be continuous or intermittent, often aggravated by activities such as sitting at a desk, bicycle riding, and sexual intercourse.

Historical Information on Vulvar Pain Terminology

Vulvar pain discussion first appeared in the literature in the late 1800's. A quote from Dr. T.G. Thomas described "excessive sensibility of the nerves supplying the mucous membrane of some portion of the vulva..."¹. In 1889, A.J. C. Skene commented on a condition characterized by "a supersensitiveness of the vulva. When, however, the examining finger comes in contact with the hyperaesthetic part, the patient complains of pain, which is sometimes so great as to cause her to cry out...."². In the same year, Kellogg wrote about a patient with "sensitive points about the mouth of the vagina". The topic was not readdressed until 1928, when Howard Kelly mentioned "exquisitely sensitive deep red spots in the mucosa of the hymeneal ring are a fruitful source of dyspareunia"³. In 1983, Friedrich reported on 13 patients with "vestibular adenitis"⁴. Terminology continues to change throughout time. The International Society for the Study of Vulvovaginal Disease (ISSVD) popularized a definition of vulvar pain in the 1980's (essential or dysesthetic vulvodynia) describing patients with a chronic discomfort, burning, stinging, irritation, and rawness of the vulva. In 1987, Friedrich developed the term "vulvar vestibulitis syndrome"⁵. The terminology of pain localized to the vulvar vestibule continues to undergo change. The most recent terminology changes are described below.

Table 1
PREVIOUS ISSVD TERMINOLOGY AND CLASSIFICATION FOR VULVAR PAIN

| | |
|---|---|
| <p>VULVAR DYSESTHESIA (1999) Santa Fe, New Mexico ISSVD World Congress</p> | <p>VULVAR DYSESTHESIA (2001) Portugal ISSVD World Congress (Of note: this is a provisional terminology system)</p> |
| <p>Generalized Vulvar Dysesthesia</p> | <p>Provoked vulvar dysesthesia</p> <ul style="list-style-type: none"> • Generalized • Localized (vestibule, clitoris, other) |
| <p>Localized Vulvar Dysesthesia.</p> <ul style="list-style-type: none"> • Vestibulodynia (formerly vulvar vestibulitis) • Clitorodynia • Other localized forms of vulvar dysesthesia | <p>Spontaneous vulvar dysesthesia</p> <ul style="list-style-type: none"> • Generalized • Localized (vestibule, clitoris, other) |

Salvador, Brazil October 2003

THE CURRENT TERMINOLOGY The 2003 ISSVD Terminology and Classification

Many ISSVD members were displeased by both the 1999 and 2001 nomenclature and, prior to the 2003 World Congress, the ISSVD leadership requested that two members, Micheline Moyal-Barracco, M.D. and Peter Lynch, M.D. develop, with widespread input from the membership, a proposal for new nomenclature, which would then be voted on at the forthcoming Congress. This was accomplished, and at the 2003 meeting, the membership voted to accept a reversion to the use of the well-accepted term “vulvodynia” and accept a slightly modified definition of vulvodynia as “vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder.” A classification of vulvodynia based on the site of the pain was also adopted. This official new terminology and classification is diagramed below. It was recently published in the Journal of Reproductive Medicine (Lynch PJ, Boyal-Barracco M. 2003 ISSVD Terminology and Classification of Vulvodynia: A Historical Perspective, J Reprod Med 2004;49:772-777.)

ISSVD Terminology and Classification of Vulvar Pain (2003)

A) Vulvar Pain Related to a Specific Disorder

- 1) **Infectious** (e.g. candidiasis, herpes, etc.)
- 2) **Inflammatory** (e.g. lichen planus, immunobullous disorders, etc.)
- 3) **Neoplastic** (e.g. Paget's disease, squamous cell carcinoma, etc.)
- 4) **Neurologic** (e.g. herpes neuralgia, spinal nerve compression, etc.)

B) Vulvodynia

- 1) **Generalized**
 - a) **Provoked** (sexual, nonsexual, or both)
 - b) **Unprovoked**
 - c) **Mixed** (provoked and unprovoked)
- 2) **Localized** (vestibulodynia, clitorodynia, hemivulvodynia, etc.)
 - a) **Provoked** (sexual, nonsexual, or both)
 - b) **Unprovoked**
 - c) **Mixed** (provoked and unprovoked)

Patients with pain localized to the vestibule have a normal appearing vulva, other than erythema at times. The erythema tends to be most prominent at the duct openings (Bartholin's, Skene's and vestibular ducts). There are two major forms of vulvar pain, hyperalgesia (low pain thresholds) and allodynia (pain to light touch).

There are many diseases that can cause vulvar pain (Table 2). Since these diseases are associated with an abnormal appearance of the vulva, they do not qualify for the condition known as vulvodynia.

Table 2 Diseases that may be associated with vulvar pain, not qualifying for the diagnosis of vulvodynia

| | | |
|-----------------------------|--------------------|----------------------------------|
| Podophyllin overdose | Pemphigus | Crohn's disease |
| Condylox overdose | Pemphigoid | Bartholin's abscess |
| Behcet's disease | Atrophy | Trauma |
| Apthous ulcers | Lichen sclerosus | Prolapsed urethra |
| Herpes (simplex and zoster) | Lichen planus | Vulvar intraepithelial neoplasia |
| Candidiasis | Sjorgen's disease | Carcinoma |
| Trichomonas | Contact dermatitis | |
| Chancroid | Endometriosis | |

Etiologic theories on vulvodynia

The exact etiology of vulvodynia is unknown. There most likely is not one single etiology. Etiologic theories proposed include abnormalities of embryologic development, infection, inflammation, genetic/immune factors, and nerve pathways.

| Theory | Descriptions |
|--------------------------------|--|
| Embryologic development | It has been noted that tissues from these two distinct anatomic sites have a common embryologic origin, and therefore are predisposed to similar pathologic responses when challenged ^{6,7} . |
| Infection | Candida infections in patients with vestibular pain have been studied ^{8,9} . The exact association is difficult to determine since many patients report candida infections without verified testing for yeast. Bazin et al. found little association of infection and pain on the vestibule ¹⁰ . |
| Inflammation | “-itis” (as in vestibulitis) has been excluded from the recent ISSVD terminology since studies found a lack of association between excised tissue and inflammation. Bohm-Starke et al. found a low expression of the inflammatory markers cyclo oxygenase 2 and inducible nitric oxide synthase in the vestibular mucosa of women localized vestibular pain as well as in healthy control subjects ¹¹ . |
| Genetic/Immune Factors | Goetsch was one of the first researchers to question a genetic association of localized vulvar pain ¹² . Fifteen percent of patients questioned over a 6 month period were found to have localized vestibular pain. Thirty-two percent had a female relative with dyspareunia or tampon intolerance, raising the issue of a genetic predisposition. Another genetic connection was found in a study evaluating gene coding for interleukin 1 receptor antagonist ^{13,14,15} . |
| Neuropathways | Kermit Krantz examined the nerve characteristics of the vulva and vagina ¹⁶ . The region of the hymeneal ring was richly supplied with free nerve endings. No corpuscular endings of any form were observed. Only free nerve endings were observed in the fossa navicularis. A sparsity of nerve endings were noted in the vagina as compared to the region of the fourchette, fossa navicularis and hymeneal ring. More recent studies have analyzed the nerve factors, thermoreceptors and nociceptors in women with vulvar pain ^{17,18} . |

Foster DC, Hasday JD. Elevated tissue levels of interleukin-1 beta and tumor necrosis factor-alpha in vulvar vestibulitis. *Obstet Gynecol* 1997;89(2):291-6.

Jeremias J, Ledger WJ, Witkin SS. Interleukin 1 receptor antagonist gene polymorphism in women with vulvar vestibulitis. *American Journal of Obstetrics & Gynecology* 2000;182(2):283-5.

Vaginismus

It is important to evaluate for vaginismus in the patients with vulvodynia, particularly localized vulvodynia¹⁹. It is an involuntary spasm of the pelvic floor muscles affecting the vaginal entranceway. It can make penetration painful or even impossible. One of the main causes is fear or anticipation of pain. When painful penetration has been experienced, this pain may be expected in further sexual intercourse attempts. The degree of vaginismus may then increase the amount of pain, and a vicious circle is established.

Treatment of localized vulvar pain (vestibulodynia)

Many treatment regimens exist for localized vulvodynia. Patients often combine a variety of the following regimens:

Vulvar care measures

Cotton underwear is recommended. No underwear should be worn at night. If the patient is sweating with exercise, Wicking underwear has been used by some patients. Vulvar irritants and douching should be avoided. The patient should use mild soaps for bathing and not apply soaps to the vulva. If menstrual pads are irritating, 100% cotton pads may be helpful. Adequate lubrication for intercourse is recommended (Olive oil, Replens, Astroglide, KY Liquid, Probe, Pjur women, Slippery stuff, uncooked egg whites, vegetable oil, Vitamin E oil, Surgilube, Sylk (Kiwi fruit vine), Moist Again Natural Feeling, Lubrin, Femigel Natural product from tea trees (<http://www.med.umich.edu/socialwork/shcs/resource.htm#lub>))

Other lubricant information

www.drugstore.com Search lubricants

Cool gel packs are helpful in some patients.

Topical medications

The use of lubricants should be discussed with the patient. For minor degrees of vulvar pain, consider 5% lidocaine ointment. Lidocaine/prilocaine (EMLA -eutectic mixture of local anesthesia) or ELA-MAX may be used, but any of these agents can be irritating. Doxepin 5 % cream can be applied to skin daily with gradual increase not to exceed four times daily. Topical amitriptyline 2% with Baclofen 2% in a water washable base (WWB) (squirt ½ cc from syringe onto finger and apply to affected area daily to three times a day) has also been used for point tenderness. Topical estrogens have been used by some for treatment of vulvar pain. Estrogen is applied to the vulva twice daily, with a gradual decrease to daily use, then every other day use.

Tricyclic antidepressants

A common treatment for vulvar pain is the use of a tricyclic antidepressant. This group of drugs (e.g., amitriptyline (Elavil®), nortriptyline (Pamelor®), desipramine (Norpramin®) has been used to treat many chronic pain conditions where a cause cannot be found. Published and presented reports indicate about a 60% response rate for various pain conditions. Currently, a NIH trial is analyzing antidepressants in patients with vulvar pain. While traditionally this treatment has been used for generalized vulvodynia, recent reports have found it to be helpful in the treatment of vestibular pain also. The mechanism of action is believed to be associated with blockage of re-uptake of transmitters; specifically, norepinephrine and serotonin. Yet, the mechanism may actually be from the anti-cholinergic effects. They affect the sodium channels and have effects on the N-methyl-d-aspartate (NMDA) receptor. If you choose to use a tricyclic antidepressant, to aid in patient compliance you might consider emphasizing its effect in altering the sensation of pain rather than its effect on depression. Patients should not be pregnant or intend to become pregnant or breast feed while using tricyclic antidepressants. These medicines will add to the effects of alcohol and other CNS depressants.

Dosage for pain control varies dependant on the age of the patient and the agent used. Often amitriptyline is used as a first line agent. It is started at 10 to 25 mg nightly and increased by 10-25 mg weekly, not to exceed 150 mg qhs. A sample prescription follows:

Initial Amitriptyline prescription:

Amitriptyline HCL 25 mg

Sig: 1 po qhs x 1 week; If sx's persist, 2 po qhs x 1 wk, if sx's persist, 3 po qhs x 1 wk; if sx's persist, 4 po qhs. Maintain nightly dose that relieves symptoms (Not to exceed 4 po qhs) Do not stop suddenly (i.e. wean)

Start at 5-10 mg in patients age 60 or older and increase by 10 mg weekly

It is important to have patients avoid more than 1 drink of alcohol daily while on this medication. Contraception should be utilized in the reproductive age population. For the elderly patient, lower doses should be used.

Other antidepressants

Cymbalta

Start at 30 mg po qd for 1 week. If symptoms persist increase to a total of 60 mg po qd. (If there is no depression, use Cymbalta as 60 mg po q am. If there is depression, use Cymbalta as 30 mg po bid.)

Effexor XR is also utilized at times for pain control.

Anticonvulsants

Gabapentin (Neurontin®) and carbamazepine (Tegretol®) have been used to treat chronic pain conditions^{20,21}. Gabapentin comes in 100 mg, 300 mg, 400 mg, 600 mg and 800 mg tablet sizes. Generally it is started at 300 mg po qd x 3 days, then 300 mg po bid x 3 days, then 300 mg po tid. It can gradually be increased to 3600 mg po total daily (usually in a tid regimen). No more than 1200 mg should be given in a dose.

Neurontin side effects include: somnolence, mental change, dizziness, weight gain.

Carbamazepine is used rarely for resistant cases.

The newest anticonvulsant utilized for chronic pain is pregabalin (Lyrica®).

Lyrica

-50 mg po qd x 4 days, if sx's persist, 50 mg po bid x 4 days, if sx's persist, 50 mg po tid

-Can gradually increase up to 100 mg po tid; some reports using 300 mg po bid exist (maximum).

Biofeedback and physical therapy

Biofeedback and physical therapy are also currently used in the treatment of vulvar pain^{22,23,24,25,26,27}. These techniques are particularly helpful if there is concomitant vaginismus, not uncommon in this population. Biofeedback and physical therapy have been used successfully in the treatment of a number of disorders, including migraine and tension headaches, asthma, chronic pain and anxiety disorders. Biofeedback aids in developing self-regulation strategies for confronting and reducing pain. Patients with vestibular pain in general have an increased resting tone and a decreased contraction tone. With the aid of an electronic measurement and amplification system or biofeedback machine, an individual can view a display of numbers on a meter, or colored lights to assess nerve and muscle tension. In this way it is possible to develop voluntary control over those biological systems involved in pain, discomfort, and disease. The time required for biofeedback and the frequencies of visits will vary with each person. Success rates in the 60 to 80 percent range have been reported. Physical therapists with experience in vulvar pain can frequently be helpful.

Low oxalate diet with calcium citrate supplementation

It has been suggested that vulvar burning may be associated with elevated levels of oxalates in the urine^{28,29}. Oxalate is an irritating material. It is produced by several tissues in the human body during normal metabolism. It can enter the body through digestion of foods containing oxalate. The use of oral calcium citrate along with a low oxalate diet is controversial but may help some women. The "natural" and nutritional approach is certainly attractive to many people. The time for symptom relief varies. However, another study cast doubt on this theory³⁰.

Intralesional and trigger point injections:

Trigger point steroid and bupivacaine injections have been successful for some patients with localized vulvodynia³¹. It is recommended that not over 40 mg of triamcinolone be injected monthly. Draw up the triamcinolone prior to the bupivacaine to prevent contamination of the triamcinolone. Combine it with bupivacaine (large area use 0.25%; small area use 0.5%) Inject the combined drugs into specific area or use as a pudendal block³². This regimen can be repeated monthly. Generally patients do not tolerate more than three or four injections. Consider topical anesthetic use prior to the injection. Interferon has also been studied and utilized for vestibular pain^{33,34,35,36,37,38,39,40}. It has a varied response long term and is used less frequently today.

Acupuncture

Very few studies have been done using acupuncture for vulvar pain. Three studies have evaluated acupuncture for vulvar pain therapy, with a variety of outcomes^{41,42,43}.

Hypnotherapy

A recent article by Kandyba and Binik describes the use of hypnotherapy as a treatment for pain localized to the vestibule⁴⁴. The patient received 8 sessions of hypnosis and is pain free at a 12- month follow-up.

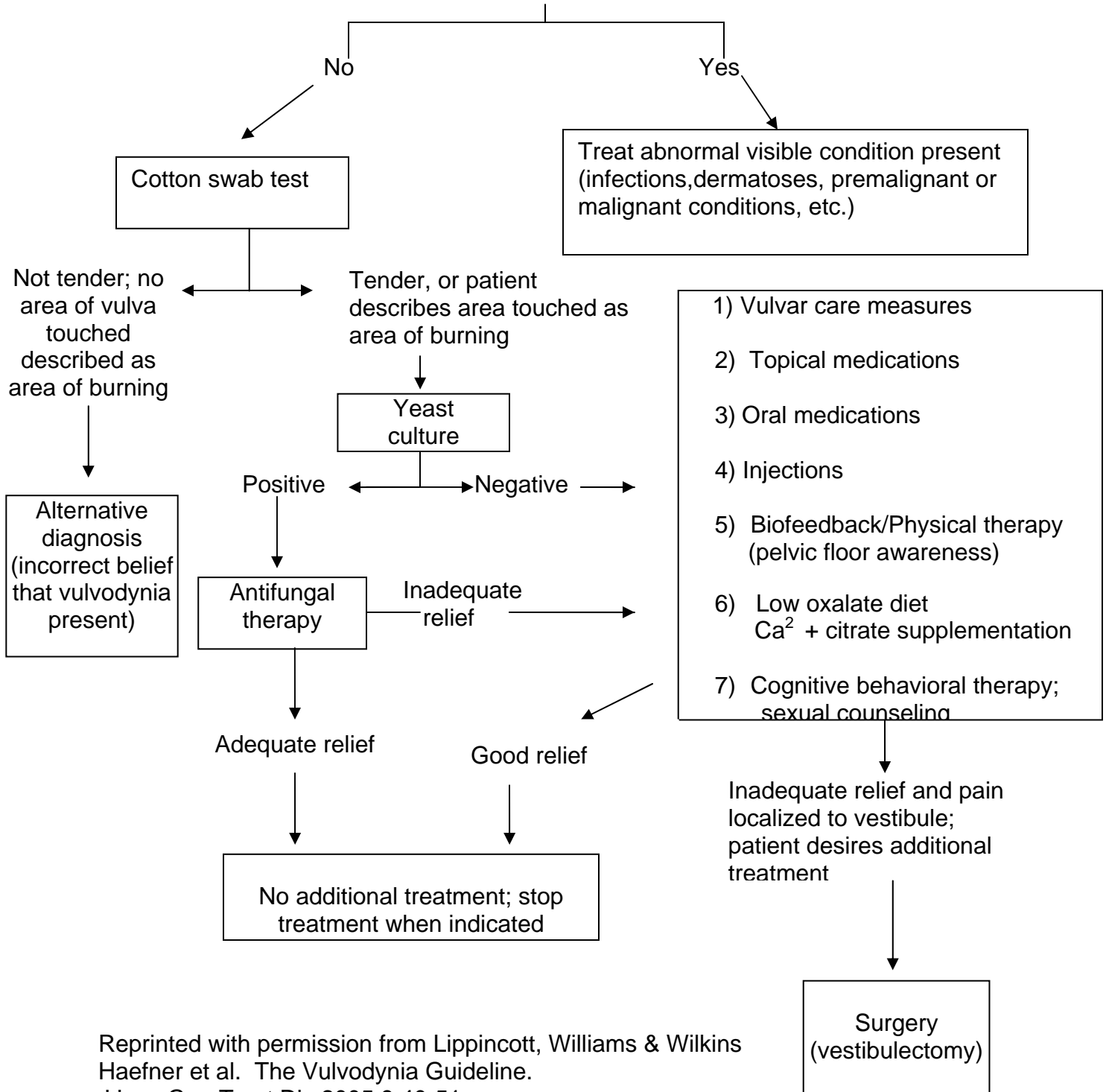
Vestibulectomy Surgical excision

Surgical excision of the vulvar vestibule has met with success in up to 80% of reported cases, but should be reserved for women with long standing and localized vestibular pain where other management has failed⁴⁵. The patient should undergo Q-tip testing to outline the areas of pain prior to anesthesia while in the operating room. Often the incision will need to extend to the opening of Skene's ducts onto the vestibule. It is carried down laterally along Hart's line to the perianal skin and the mucosa should be undermined above the hymeneal ring. The specimen should be excised superior to the hymeneal ring. The vaginal tissue is further undermined and brought down to close the defect. The defect should be closed in two layers using absorbable 3'0 and 4'0 sutures. A review of this technique with illustrations is described in a recent article⁴⁶.

Vulvodynia algorithm

Physical examination

Cutaneous or mucosal surface disease present



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Haefner et al. The Vulvodynia Guideline.
J Low Gen Tract Dis 2005;9:40-51.

New Research

Nitroglycerin – Topical nitroglycerin has been used for the treatment of localized vulvar pain⁴⁷. Unfortunately, a significant number of patients developed headaches with its use.

Botox- Botulinum toxin type A is used as a treatment for many chronic pain disorders^{48,49}. Recent research has been done on injectable Botox for vulvar pain⁵⁰. Further studies are being performed.

Internet Addresses of Interest

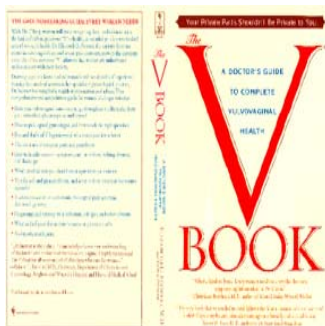
| | |
|---|---|
| <p>The Vulvodynia Awareness Campaign http://orwh.od.nih.gov/health/vulvodynia.html Order the Vulvodynia Awareness Campaign information packet by contacting the National Institute of Child Health and Human Development Information Resource Center at 1-800-370-2943 or visiting: http://orwh.od.nih.gov/health/vulvodynia.html</p> | <p>National Vulvodynia Association http://www.nva.org/</p> |
| <p>Biofeedback www.bcia.org</p> | <p>Physical Therapy http://www.apta.org/</p> |
| <p>The Vulvodynia Guideline www.jlgttd.com click on archive click on Volume 9 (2005) Jan 2005 (pp 1-63) Scroll down to The Vulvodynia Guideline Click on PDF (350 K)</p> <p>Pudendal Nerve Information http://www.pudendalnerve.com/</p> | <p>International Society for the Study of Vulvovaginal Disease www.issvd.org</p> <p>Libby Edwards, MD http://www.libbyedwardsmd.com/</p> <p>The University of Michigan Center for Vulvar Diseases http://www.med.umich.edu/obgyn/cvd/ref_phys.htm</p> |

Summary

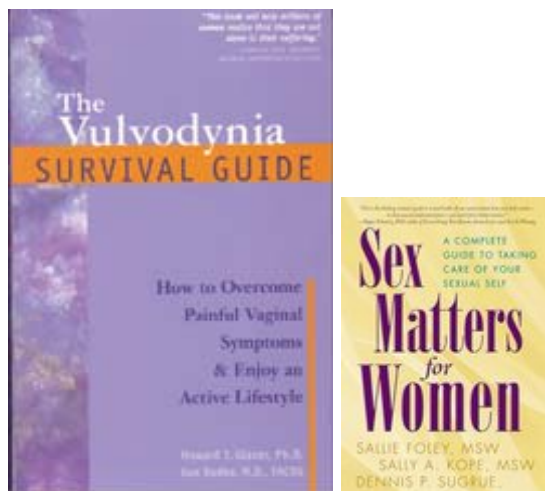
Vulvar pain is a complex disorder that is frequently frustrating to both practitioner and patient. It can be a difficult process to treat. Improvement may take weeks to months. Spontaneous remission of symptoms has occurred in some women, while with others, multiple attempts with medical management have proven unsuccessful in relieving 100% of the symptoms. The treatment of vulvar pain is confounded by the fact that the cause is unknown in a great majority of cases. It is important to recognize that rapid resolution of symptomatic vulvar pain is unusual even with appropriate therapy. Additionally, no single treatment program is successful in all women. Concurrent emotional and psychological support can be invaluable.

Self-help books

- [The V Book: A Doctor's Guide to Complete Vulvovaginal Health](#)



- [The Vulvodynia Survival Guide: How to Overcome Painful Vaginal Symptoms & Enjoy an Active Lifestyle](#)



- [Sex Matters for Women](#)

Prescriptions for Vulvar Pain

Pain Medications

Xylocaine

5% Xylocaine ointment

sig: apply to vulva prn

Disp: 35 grams

Amitriptyline

Initial Amitriptyline prescription:

Amitriptyline HCL 25 mg

Sig: 1 po qhs x 1 week; If sx's persist, 2 po qhs x 1 wk, if sx's persist, 3 po qhs x 1 wk; if sx's persist, 4 po qhs. Maintain nightly dose that relieves symptoms (Generally not to exceed 4 po qhs) Do not stop suddenly

Start at 10 mg in patients age 60 or older; increase by 10 mg weekly

Future Amitriptyline prescriptions

Amitriptyline HCL ____mg

Sig: i po qhs (comes in 10 mg, 25 mg, 50 mg, 75 mg, 100 mg and 150 mg tablets)

(Other tricyclics, such as desipramine are dosed in a similar manner)

Cymbalta® (duloxetine)

Cymbalta 30 mg

Sig: 1 po q am x 1 week. If sx's persist, 2 po q am. (If the patient is depressed, it is better to increase after one week to a bid dose such as 30 mg po bid).

(also comes in 20 mg; can start at this dose if desired)

Neurontin

Neurontin® (gabapentin)

Sig: 300 mg po qd x 3 days; if sx's persist, 300 mg po bid x 3 days; if symptoms persist, 300 mg po tid. Stay on this dose for a month and increase gradually if needed.

It comes in 100, 300, 400, 600 and 800 mg doses

Do not exceed 2700 to 3600 mg total dose per day. Do not give more than 1200 mg in a single dose.

Gabapentin ointment 3% or 6%

Sig: apply to affected area bid-tid

Disp: 3 month supply

Lyrica

-50 mg po qd x 4 days, if sx's persist, 50 mg po bid x 4 days, if sx's persist, 50 mg po tid

-Can gradually increase up to 100 mg po tid (Some report utilizing up to a maximum of 300 mg po bid)

Blocks

Bupivacaine (0.25% or 0.5%) and Kenalog® (triamcinolone acetonide)
Draw up Kenalog® first (40 mg /cc) (can use up to 40 mg steroid in single dose per month. Must be a large area however, or tissue can erode). Combine with Bupivacaine (large area use 0.25%; small area use 0.5%) Inject into specific area or use as a pudendal block
Can be repeated monthly

Medications for localized pain or itching

Zonalon® (Doxepin) 5 % cream

Sig: apply to skin q d with gradual increase not to exceed qid Disp:30 gms

Topical amitriptyline 2% with baclofen 2% in WWB (water washable base)- squirt ½ cc from syringe onto finger and apply to affected area q d to tid Disp: 30 day supply

Vaginal Dilators

www.vaginismus.com

[w.milex.com](http://www.milex.com)

<http://www.myarkadia.com/ProductView.aspx?productid=10>

Syracuse Medical Devices, Inc. 315-449-0657

Orders taken from health care providers

Lubricant information

www.drugstore.com

<http://www.quickcondoms.com/phome.jsp?p=lubricant>

www.goodvibes.com

New Thoughts

Overview

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www.baylorcme.org 2006

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Vaginismus

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