Vulvodynia: A Common and Under-Recognized Pain Disorder in Women and Female Adolescents

Integrating Current Knowledge Into Clinical Practice

Learning Objectives

At the end of this session, learners will be able to:

Recognize vulvodynia as a prevalent, misdiagnosed, and under-researched chronic pain disorder affecting millions of women and adolescent girls

Define vulvodynia and its subtypes

Summarize what is known about the pathophysiology of vulvodynia

Identify the infectious, inflammatory, neoplastic and neurologic disorders that need to be ruled out in order to make a diagnosis of vulvodynia

Perform a comprehensive exam to diagnose the condition

Implement an individualized, multidisciplinary treatment regimen

Historical Perspective

Early Descriptions • Current Definition

EARLY DESCRIPTIONS OF VULVODYNIA

1888 | 1928 | 1929-1974 | 1975

1880

"Hyperaesthesia of the Vulva"

Thomas described as "excessive sensibility of the nerves supplying the mucous membrane of some portion of the vulva, sometimes... confined to the vestibule... other times to one labium minus."

Thomas 1880

EARLY DESCRIPTIONS OF VULVODYNIA

1880 | 1928 | 1929-1974 | 1975

1888

"Supersensitiveness of the Vulva"

Skene: "This disease...is characterized by the supersensitiveness of the vulva...No redness or other external manifestation of the disease is visible...When 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. Sexual intercourse is equally painful and becomes, in aggravated cases, impossible."

Skene 1888

EARLY DESCRIPTIONS OF VULVODYNIA

1880 1888 1929-1974 1975

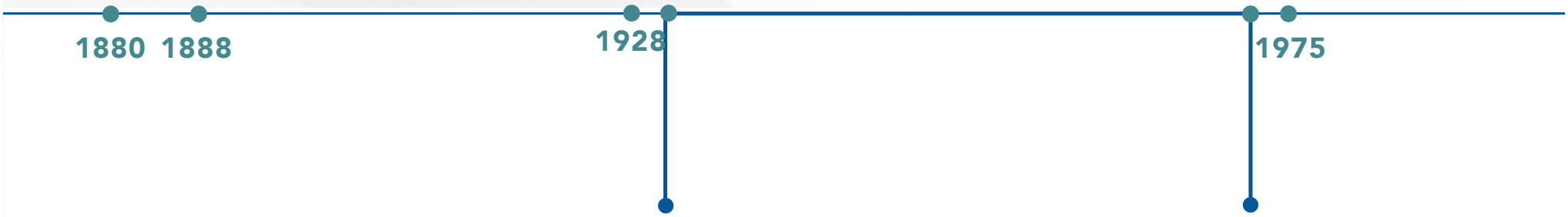
1928

"Sensitive Deep Red Spots"

Kelly described "exquisitely sensitive deep-red spots in the mucosa of the hymenal ring as a fruitful source of dyspareunia."

Kelly 1928

EARLY DESCRIPTIONS OF VULVODYNIA



1929-1974

No mention of the condition in medical texts for 5 decades.

EARLY DESCRIPTIONS OF VULVODYNIA

1975

"Burning Vulva Syndrome"

Vulvodynia is defined as *burning vulva syndrome* by the International Society for the Study of Vulvovaginal Disease (ISSVD) at 1975 World Congress.

McKay 1984, Moyal-Barracco 2004, Haefner 2007

CURRENT DEFINITION

The current ISSVD definition of vulvodynia is:

- *Vulvar pain of at least 3 months duration, without a clear identifiable cause, which may have potential associated factors.*
- *Diagnosis of exclusion*
- *Idiopathic pain disorder*

Bornstein 2016

Magnitude of the Problem

Prevalence • Incidence • Remission

Misdiagnosis • Economic impact • Quality of life

PREVALENCE & INCIDENCE

Prevalence

Four independent NIH-funded population-based studies, three of which included a clinical confirmation component, demonstrate a point prevalence of 3-7% in reproductive-aged women (Harlow 2003, Arnold 2007, Reed 2004, Reed 2006). Approximately 7% of American women will have symptoms consistent with vulvodynia by age 40, which significantly differ by ethnicity (Harlow 2014).

Vulvodynia has been documented in preadolescent girls (Reed 2008). A study of adolescent girls aged 12-19 suggests that the condition is quite prevalent among young women (Landry 2009).

Incidence

Annual incidence is 3.1% in one study (Reed 2012). More recently, the incidence was 4.2 cases per 100 woman-years and differed by age, ethnicity and marital status (Reed 2014).

REMISSION RATES

Remission

History of any remission ranges from 26 to 38%, depending on duration of pain (Nguyen 2015). In other population-based studies, remission ranged from 17-25%, with a rate of remission incidence of 22% over two years (Reed/Haefner 2008, Reed 2012).

AFFECTED POPULATIONS

Affected Populations

All ages affected, although the incidence of symptom onset appears highest between ages 18 to 25 (Harlow 2003, Reed 2012, Harlow 2014)

All ethnicities affected, although Hispanic women have an increased risk (Harlow 2003, Reed 2012, Harlow 2014, Reed 2014) and different subtypes (Nguyen 2015).

MISDIAGNOSIS & ECONOMIC IMPACT

Misdiagnosis is Common

2003: First NIH-funded population-based study (Harlow 2003)

- 60% of women consulted at least 3 doctors in seeking a diagnosis; 40% of them remained undiagnosed after 3 medical consultations.

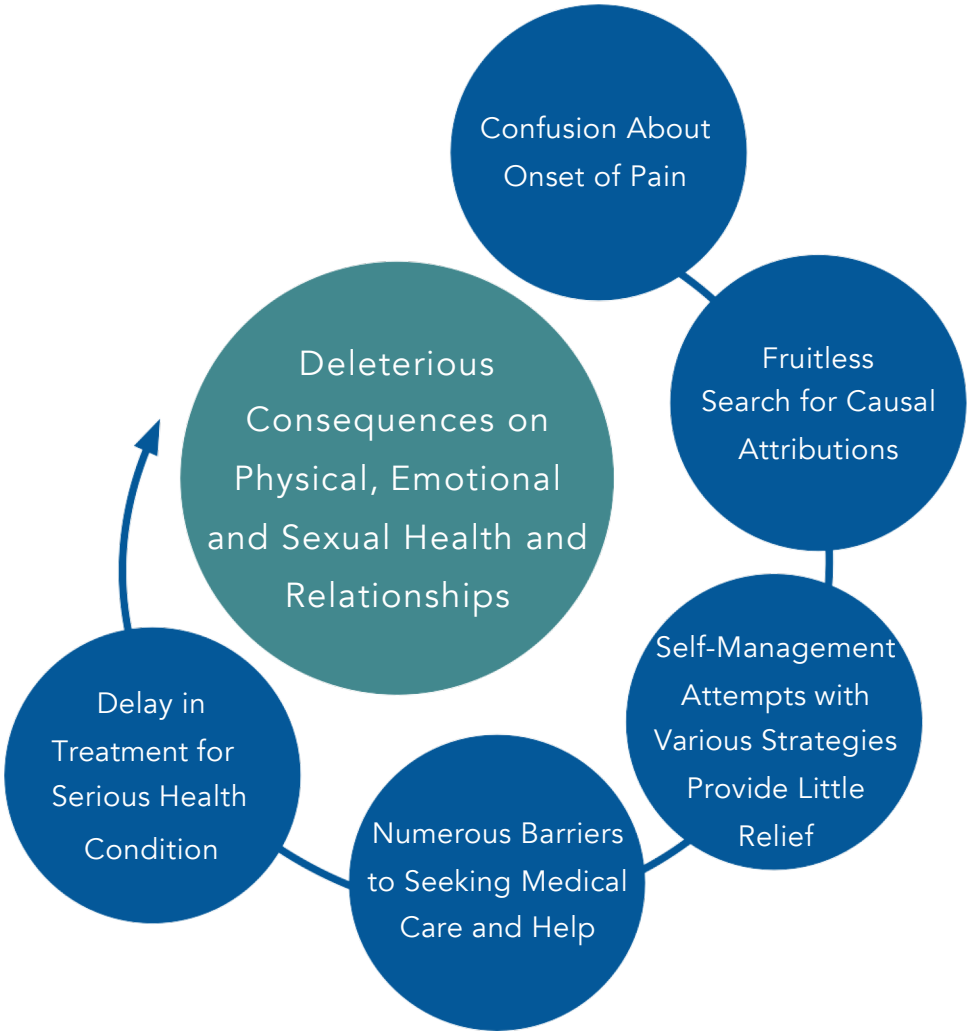
2012: Recent NIH-funded population-based study (Reed 2012)

- Only 1.4% of women seeking medical care were accurately diagnosed.

Significant Economic Impact

US direct/indirect cost is $31-$72 billion (Xie 2012).

QUALITY OF LIFE



This graphic summarizes common themes experienced by women with vulvodynia and their interrelation (Donaldson 2010). Living with vulvodynia often limits certain activities of daily living, such as sitting for extended periods, and engaging in sexual intercourse and physical exercise. In severe cases, women have to resign from their jobs and apply for disability.

Several studies summarize the negative biopsychosocial outcomes, personal distress and sexual dysfunction reported by vulvodynia sufferers.

QUALITY OF LIFE

Xie found that women with vulvodynia report lower quality of life scores than kidney transplant recipients and those with prior osteoporosis-related fractures (Xie 2012). Newly diagnosed women report substantial impact of vulvar pain on their lives, and little control over their symptoms (Piper 2012). Among women of reproductive age, Johnson found that barriers to consistent health carefrequently experienced in early adulthood contributed to not finding successful medical management (Johnson 2015). However, those who became pregnant reported finding a personally acceptable level of pain (Johnson 2015). Stigma and isolation are common. Only 1 in 4 women report feeling comfortable discussing the condition with women friends (Nguyen/ MacLehose 2012). They also report an increase in feelings of invalidation and isolation when they have co-existing pain disorders (Nguyen/Ecklund 2012).

Anatomy and Neurobiology of the Urogenital Tract

Vulva and Vulvar Vestibule • Innervation of the Vulva

Pelvic Floor Musculature

VULVA AND VULVAR VESTIBULE

Vulva

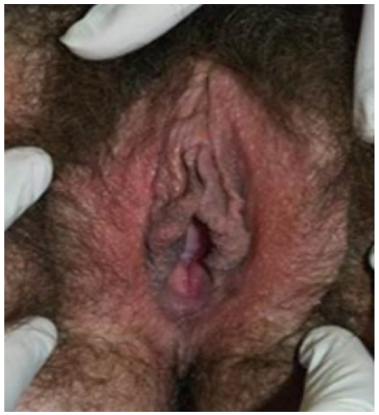
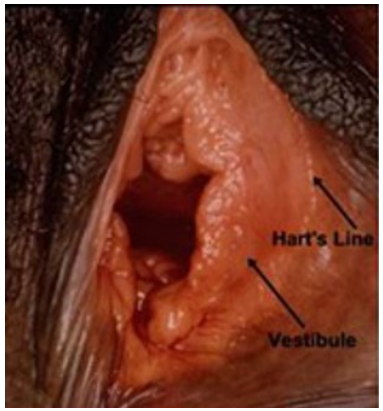


Image courtesy of Dr. Libby Edwards.

Vestibule



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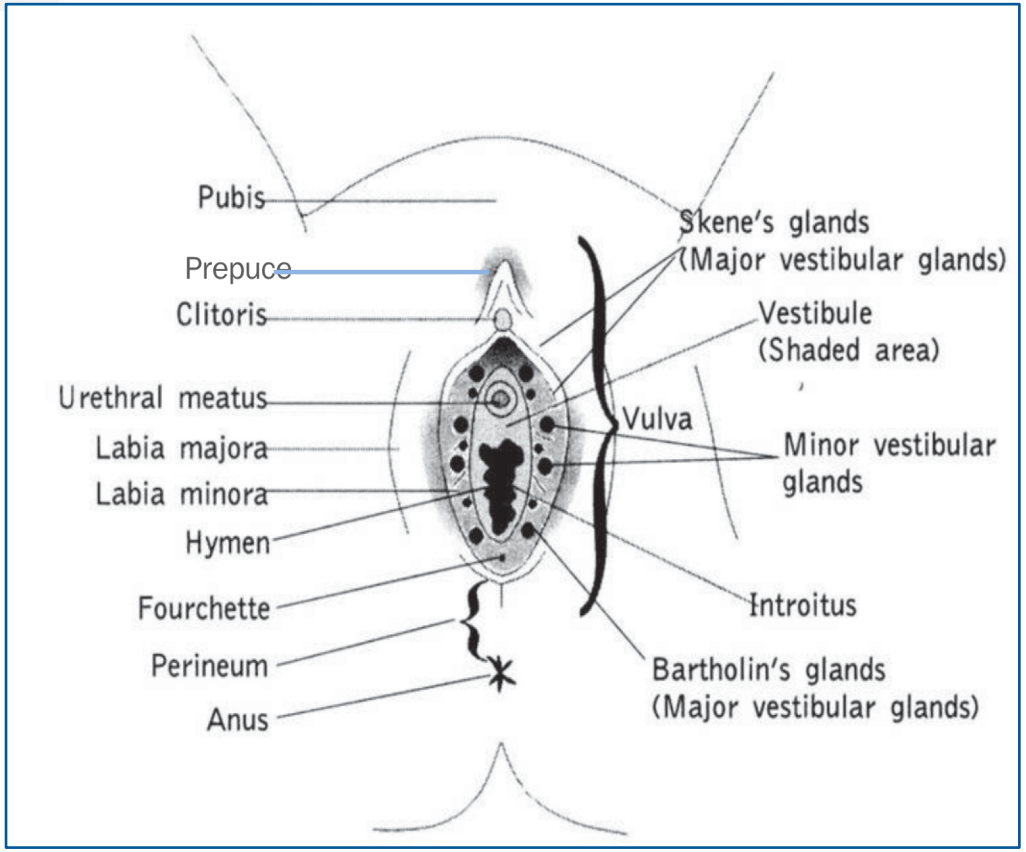
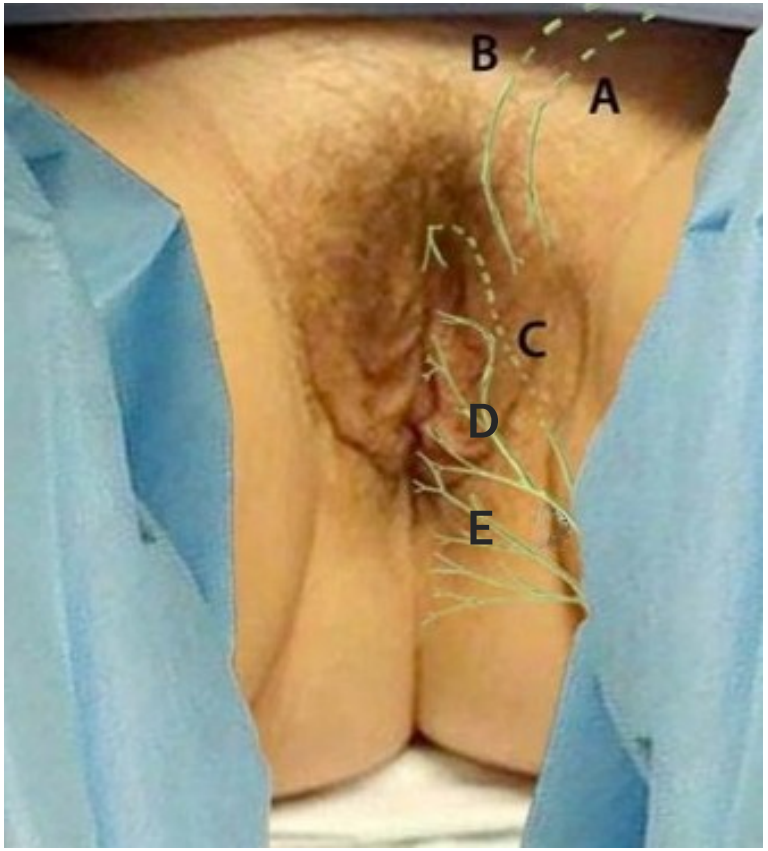


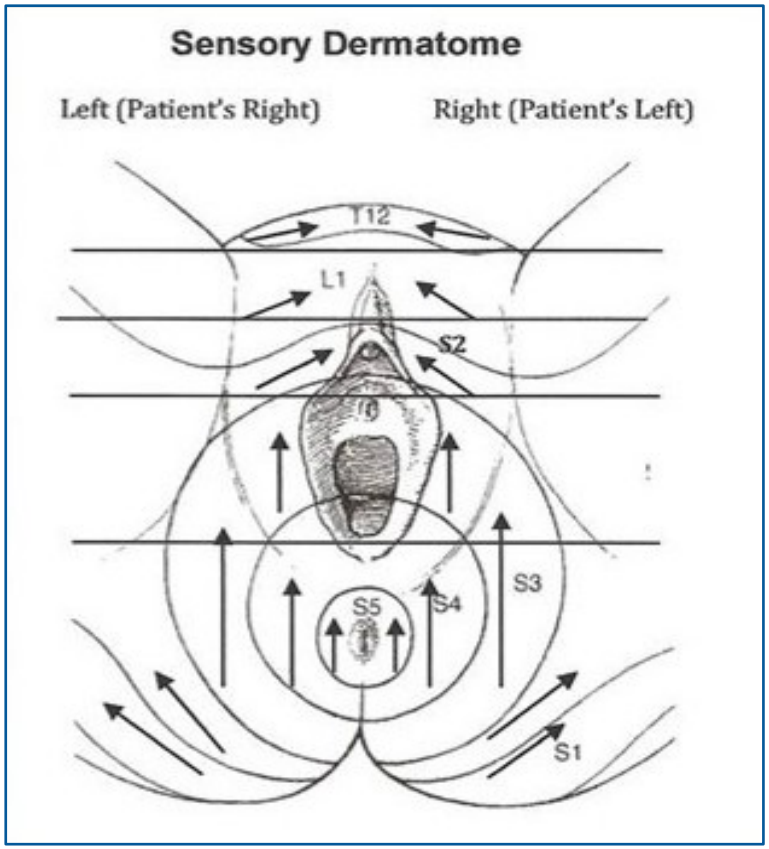
Reprinted with permission from Glazer HI and Rodke G, The Vulvodynia Survival Guide, New Harbinger Publications, 2002

For a thorough review on vulvar anatomy and physiology, see Farage 2006.

INNERVATION OF THE VULVA

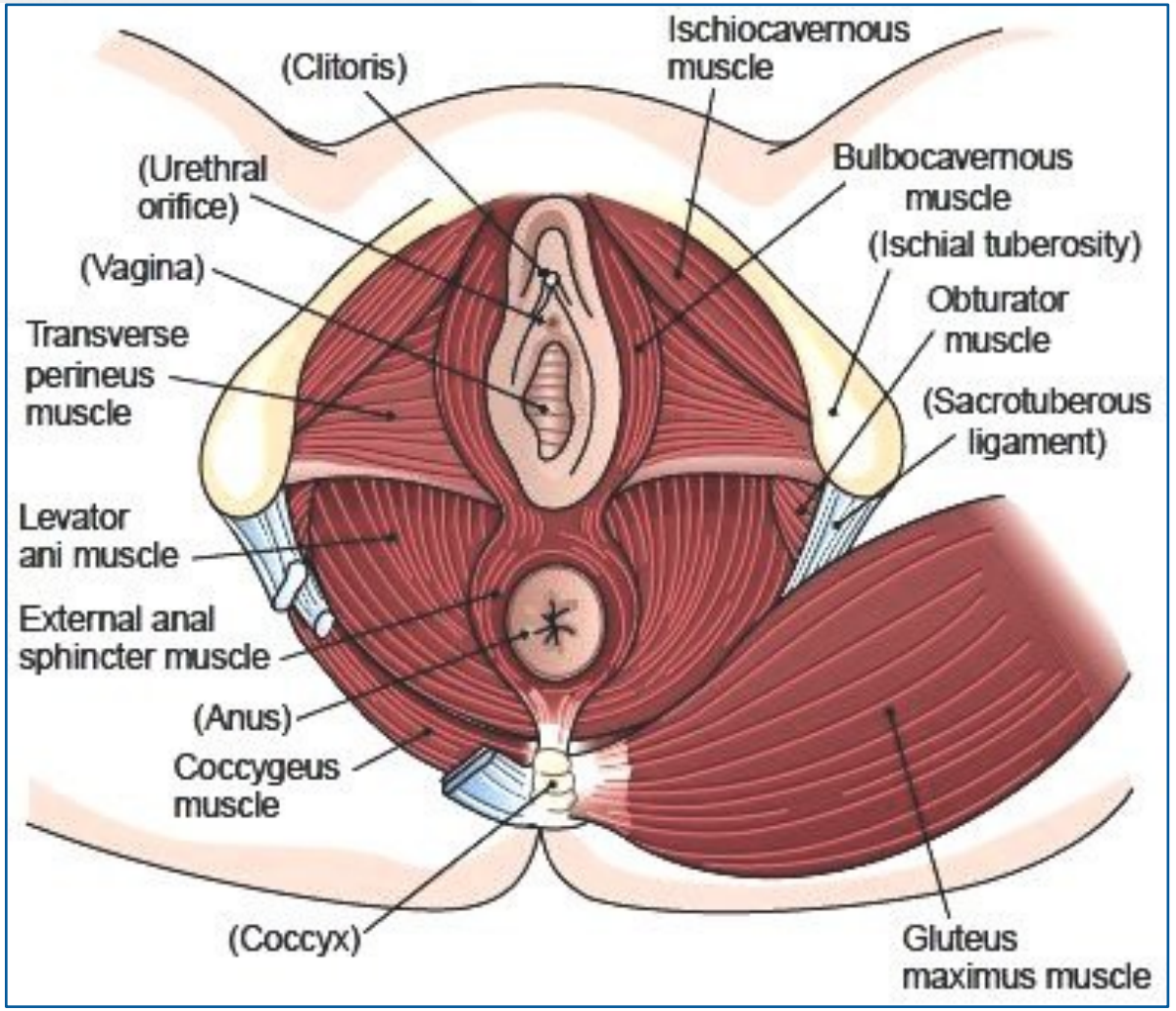


Farage 2012



Images courtesy of Drs. Denniz Zolnoun and Georgine Lamvu

PELVIC FLOOR MUSCULATURE



Terminology and Classification

ISSVD Classification: Vulvar Pain and Vulvodynia

Other Terms

ISSVD CLASSIFICATION: VULVAR PAIN

Vulvar pain related to a specific disorder, i.e., NOT vulvodynia

- Infectious (recurrent candidiasis, herpes)
- Inflammatory (lichen sclerosus, lichen planus, immunobullous disorders)
- Neoplastic (Paget's disease, squamous cell carcinoma)
- Neurologic (post-herpetic neuralgia, nerve compression or injury, neuroma)
- Trauma (female genital cutting, obstetrical)
- Iatrogenic (post-operative, chemotherapy, radiation)
- Hormonal deficiencies (genito-urinary syndrome of menopause, lactational amenorrhea)

ISSVD CLASSIFICATION: VULVODYNIA

Vulvodynia is vulvar pain of at least 3 months duration, without a clear identifiable cause, which may have potential associated factors*.

Descriptors:

- Generalized (multiple areas of the vulva involved), localized (one area of the vulva involved, e.g., clitorodynia, hemi-vulvodynia) or mixed (localized and generalized)

- Provoked (insertional, contact), spontaneous or mixed (provoked and spontaneous)
  - Provoked pain local to the vestibule: "***provoked vestibulodynia***" ***(previously vulvar vestibulitis syndrome)***

- Onset (primary or secondary)

- Temporal pattern (intermittent, persistent, constant, immediate, or delayed)

OTHER TERMS - CONFUSION IS COMMON

Generalized Vulvodynia	Provoked Vestibulodynia
• Hyperaesthesia of the vulva • Dysesthetic Vulvodynia • Vulvar Dysesthesia • Essential Vulvodynia	• Vulvar Vestibulitis Syndrome • Vestibular Adenitis • Minor Vestibular Gland Syndrome • Localized Provoked Vulvodynia

Pathophysiology

Potential Factors Associated with Vulvodynia • Pain Transmission

Neuroproliferation • Mast Cells

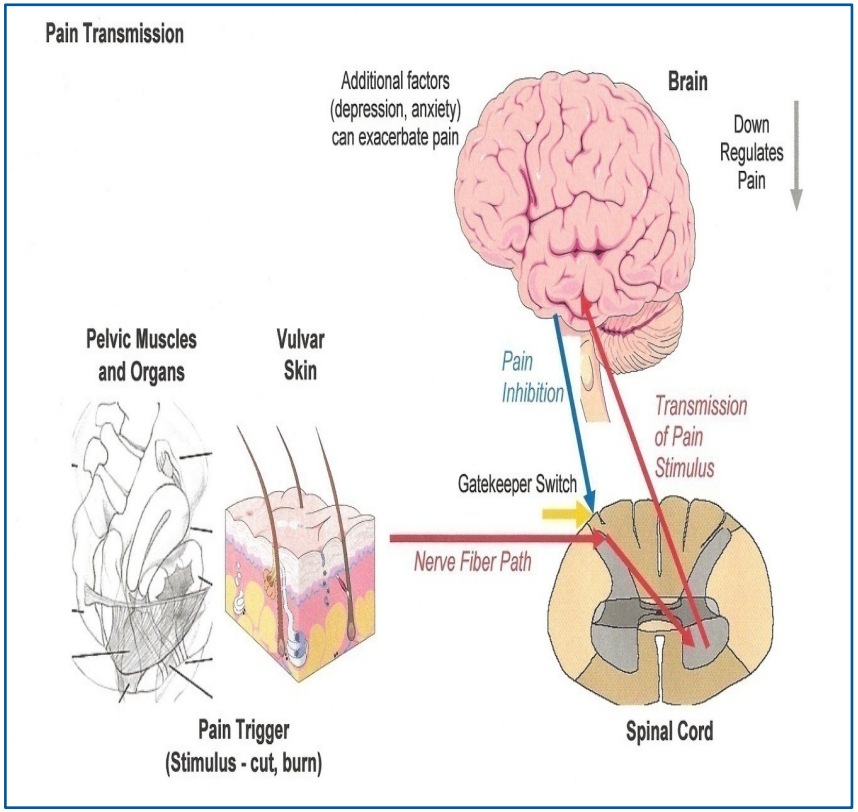
POTENTIAL FACTORS ASSOCIATED WITH VULVODYNIA

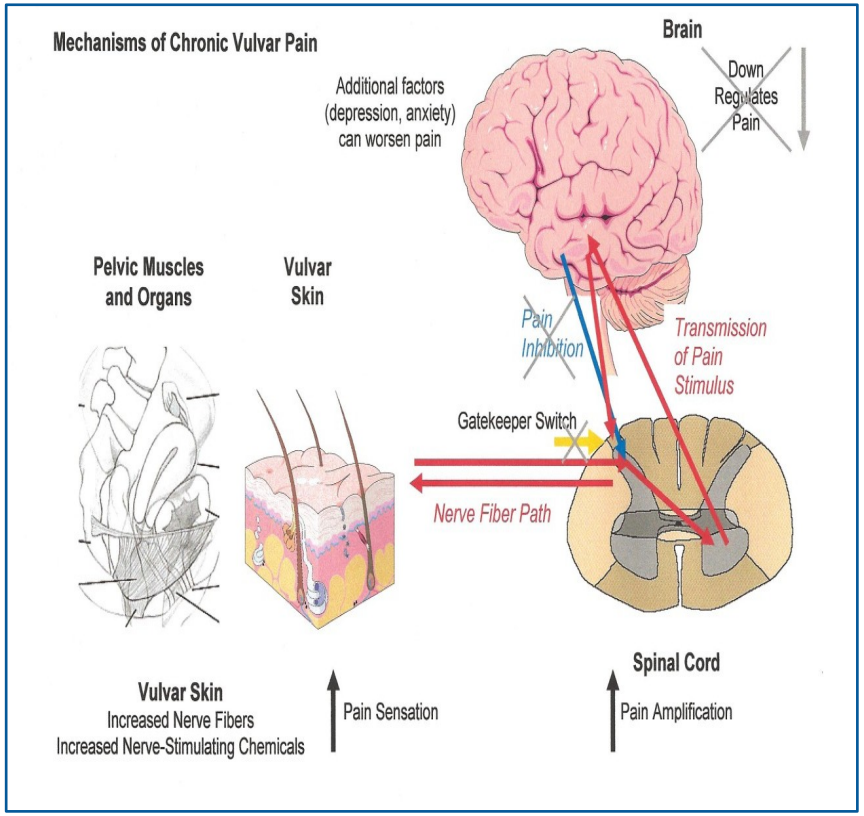
Potential Factor*	Level of Evidence
Co-morbidities and other pain syndromes (eg, painful bladder syndrome, fibromyalgia, irritable bowel syndrome, temporomandibular disorder)	2a
Genetics	2b
Hormonal factors (eg, pharmacologically induced)	2b
Inflammation	2b
Musculoskeletal (eg, pelvic muscle overactivity, myofascial, biomechanical)	2b
Neurologic mechanisms: central (spine, brain) and peripheral	2b
Neuroproliferation	2b
Psychosocial factors (eg, mood, interpersonal, coping, role, sexual function)	2b
Structural defects (eg, perineal descent)	2b

Bornstein 2016

*The factors are ranked by alphabetical order.

NORMAL PAIN TRANSMISSION VS. PROPOSED MECHANISMS OF ALTERED PAIN TRANSMISSION IN VULVODYNIA





NEUROPROLIFERATION

One possible pathophysiologic mechanism of vestibulodynia is neuroproliferation (Bornstein 1997, Bornstein 2008).

Subepithelial and intraepithelial nerve fibers have been detected in patients with vestibulodynia.

Branching of the nerve fibers within the epithelium is rarely seen.

MAST CELLS

In vestibulodynia, there is frequently an increase in mast cell number and activity.

Mast cells show degranulation.

The discharged granules contain tryptase, histamine, serotonin, bradykinin, heparanase, nerve growth factor, etc.

Some of these enzymes may participate in the pathogenesis of vestibulodynia (Bornstein 2004).

Differential Diagnosis

Disorders known to cause vulvar pain (rule-out diagnoses)

vs.

Vulvodynia

POSSIBLE RISK FACTORS FOR VULVODYNIA

Postulated risk factors reported in the literature to date:

Vulvovaginal infection

Oral contraceptive use

Genetic variability

Dysmenorrhea, chronic pain in other areas of the body

Autoimmune disease, altered immuno-inflammatory response

Allergies, vulvar dermatologic disorders

Early age of first intercourse, pain with first intercourse, pain with/after sex

Early menarche

Nulliparity

Childhood enuresis, nocturnal urination, Urinary burning, pain with wiping

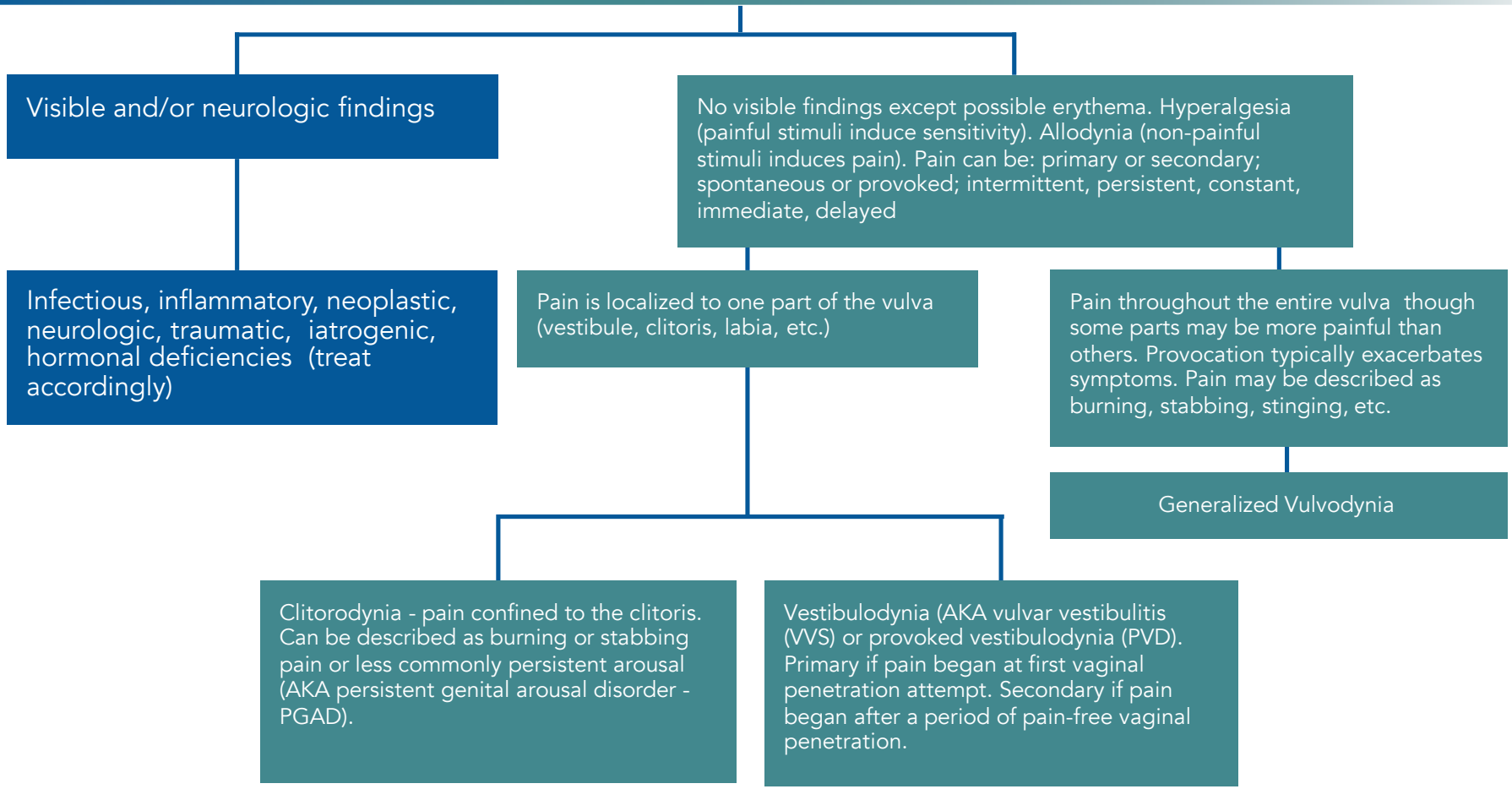
Pain with bike riding

Difficulty or severe pain with first tampon use

Adverse life experiences

RULE-OUT DIAGNOSES

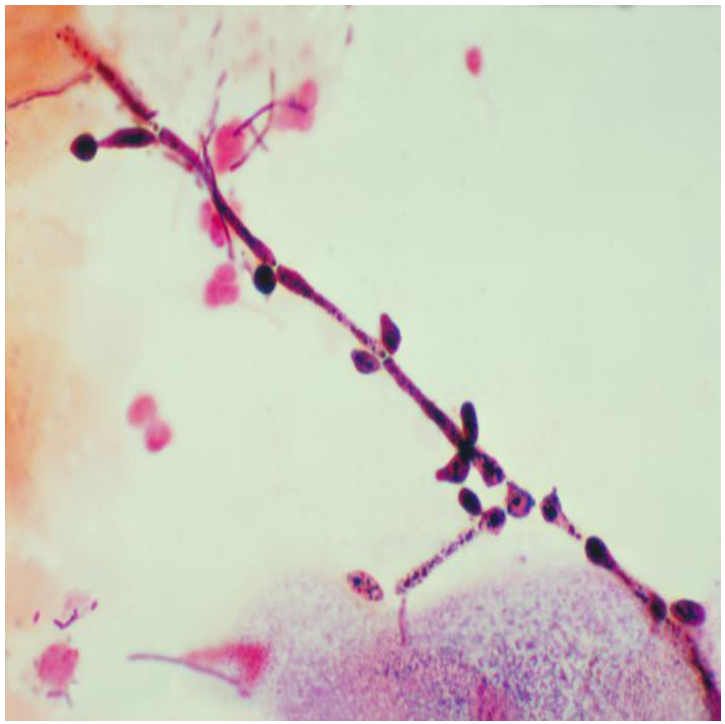
CHRONIC VULVAR PAIN



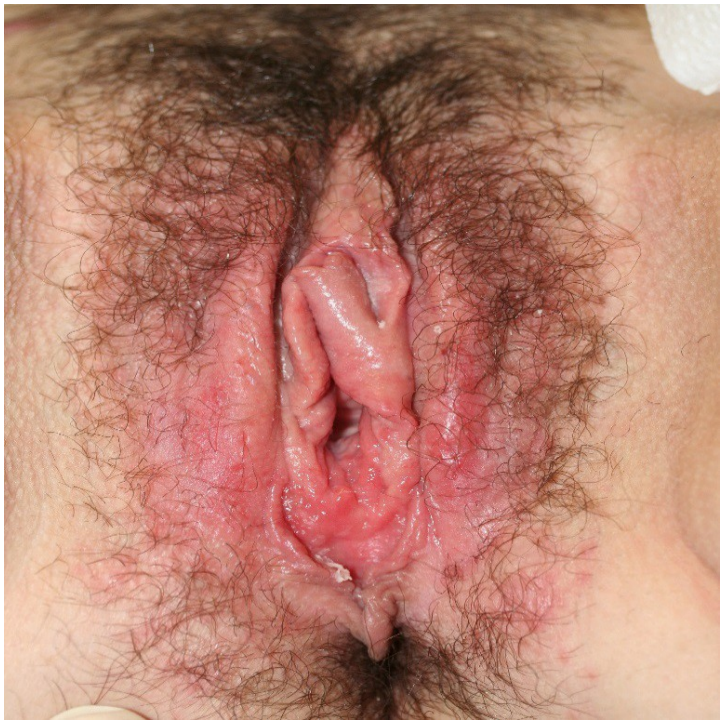
Haefner 2007, Bornstein 2016

RULE-OUT DIAGNOSES
INFECTIOUS DISORDERS

Vulvovaginal Candidiasis



Courtesy of CDC Public Health Image Library

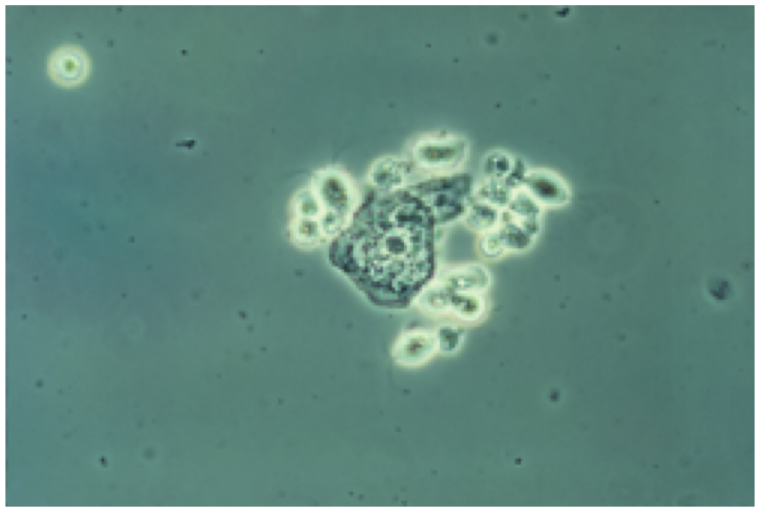


Courtesy of Dr. Andrew Goldstein

For information on diagnosis and treatment, see Ledger 2007 and Nyirjesy 2008.

RULE-OUT DIAGNOSES
INFECTIOUS DISORDERS

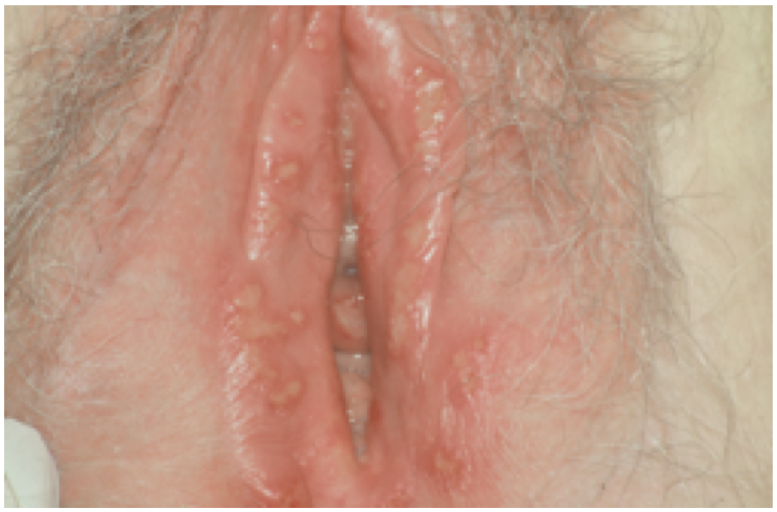
Trichomoniasis



Courtesy of CDC Public Health Image Library

For information on diagnosis and treatment, see Ledger 2007, Soper 2004 & Schwebke 2004.

Genital Herpes



Courtesy of Dr. Libby Edwards

For information on diagnosis and treatment, see Ledger 2007 & Kimberlin 2004.

RULE-OUT DIAGNOSES
INFLAMMATORY DISORDERS

Lichen Sclerosus

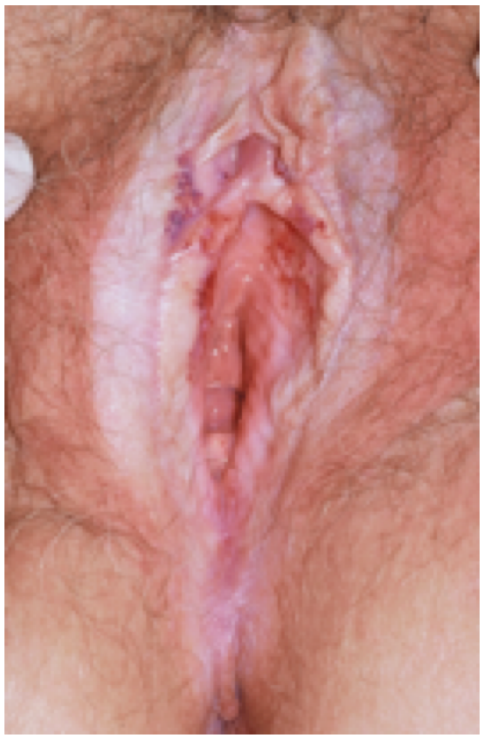


Image courtesy of Dr. Libby Edwards

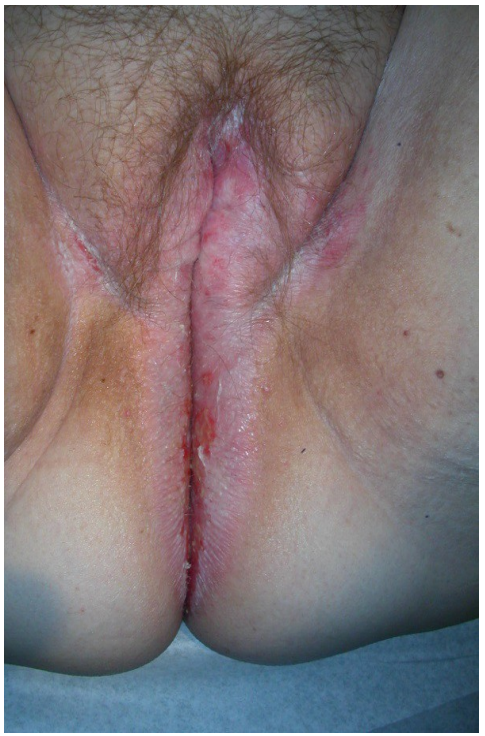


Image courtesy of Dr. Andrew Goldstein

For information on diagnosis and treatment, see Chi 2012, Moyal-Barracco 2014.

RULE-OUT DIAGNOSES
INFLAMMATORY DISORDERS

Lichen Planus

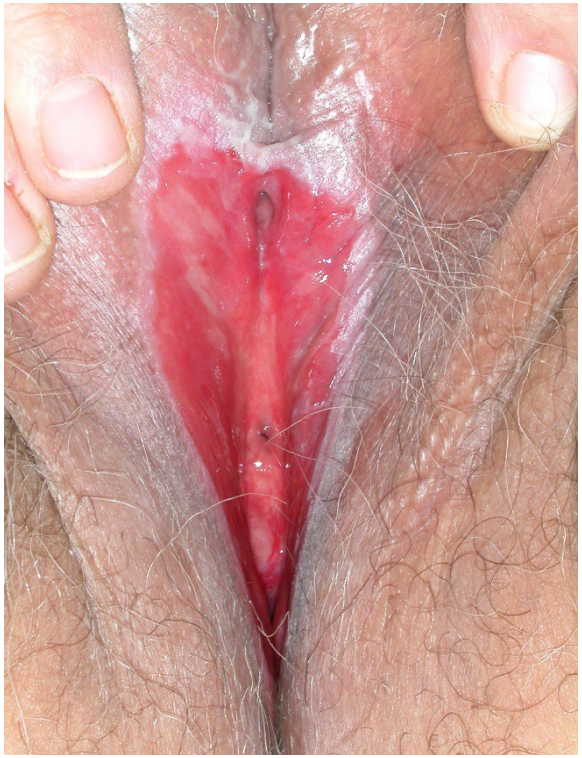


Image courtesy of Dr. Andrew Goldstein

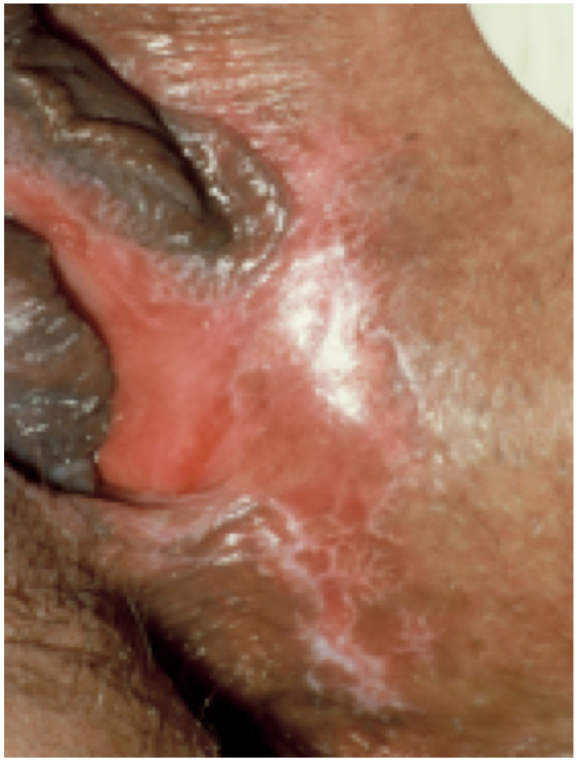
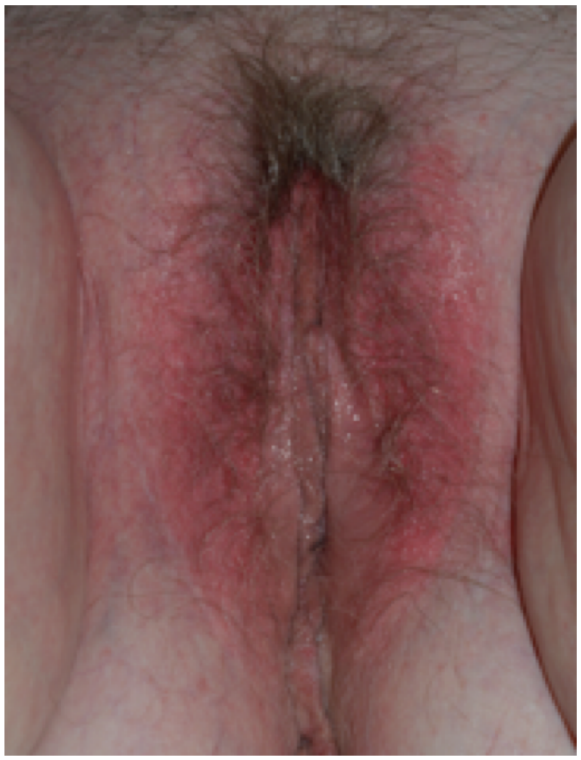


Image courtesy of Dr. Libby Edwards

For information on diagnosis and treatment, see Lewis 2013, Moyal-Barracco 2014, Burrows 2008.

RULE-OUT DIAGNOSES
INFLAMMATORY DISORDERS

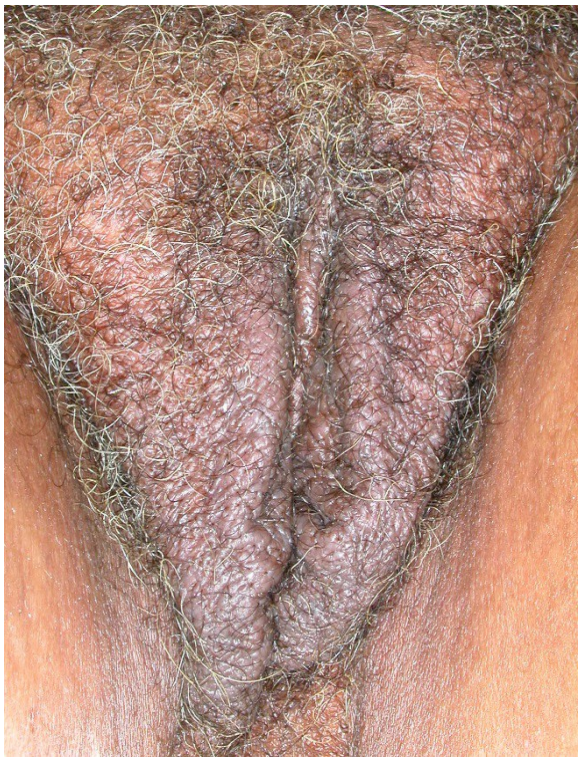
Contact Dermatitis



Courtesy of Dr. Libby Edwards

For information on diagnosis and treatment, see Burrows 2008 & Margesson 2004.

Lichen Simplex Chronicus

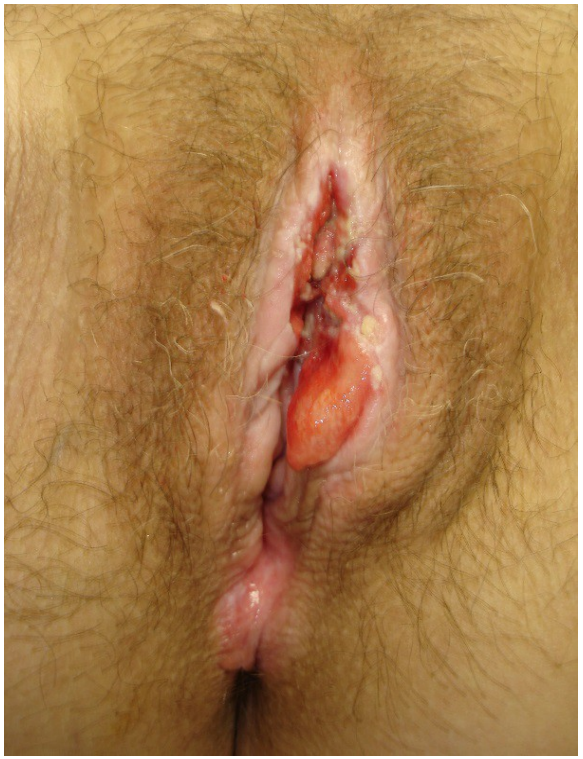


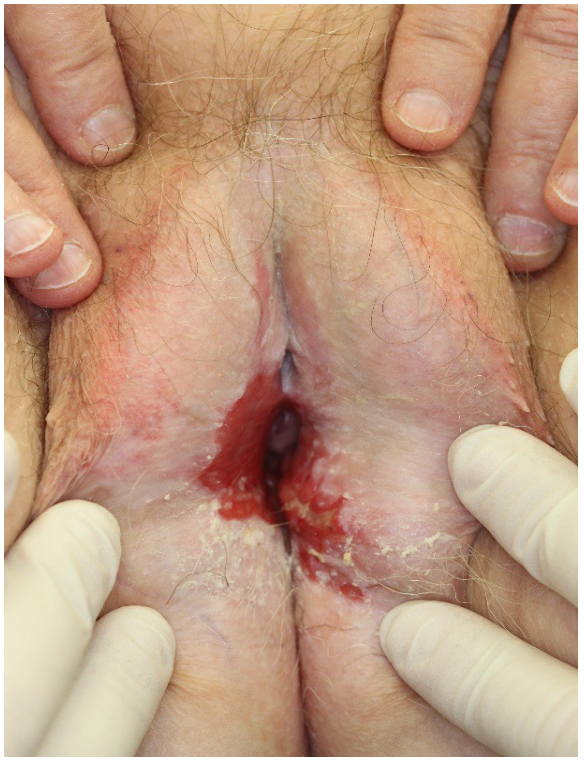
Courtesy of Dr. Andrew Goldstein

For information on diagnosis and treatment, see Moyal-Barracco 2014.

RULE-OUT DIAGNOSES
NEOPLASTIC DISORDERS

Squamous Cell Carcinoma





Images courtesy of Dr. Andrew Goldstein

For information on diagnosis and treatment, see Alkatout 2015.

Pudendal, Genitofemoral and/or Ilioinguinal Nerve Injury

Can be caused by several different insults including: childbirth, sports injuries, trauma and surgery (for incontinence or for vaginal vault prolapse) (see Paulson 2011, Masata 2012, Parnell 2012, Bekker 2012)

RULE-OUT DIAGNOSES
NEUROLOGIC DISORDERS

Pudendal Neuralgia due to Nerve Entrapment* (see Peng 2009, Insola 2010)

Diagnosed by presence of all five Nantes Criteria: 1) pain in the anatomical territory of the pudendal nerve, 2) worse on sitting, 3) not usually waking the patient at night, 4) not accompanied by any objective perineal sensory loss, with 5) a positive anesthetic block of the pudendal nerve at the ischial spine (Labat 2010)

Patients often present with associated urinary, anorectal, sexual, neuromuscular, and hypersensitization signs, which can complicate the diagnostic approach and therapeutic management (Labat 2010).

*These disorders are many times also diagnoses of exclusion, and can, therefore, be difficult to definitively differentiate from vulvodynia.

RULE-OUT DIAGNOSES
NEUROLOGIC DISORDERS

Peripheral Neuropathy/Neuralgia*

Neuropathy induced by diabetes, chemotherapy, multiple sclerosis (see Stavraka 2012, Loprinzi 2008)

Herpes zoster virus can lead to post-herpetic neuralgia masking as vulvodynia (see Oaklander 2002).

Pharmacologic toxicity, eg, nitrofurantoin (see Tan 2012)

*These disorders are many times also diagnoses of exclusion, and can, therefore, be difficult to definitively differentiate from vulvodynia.

RULE-OUT DIAGNOSES
NEUROLOGIC (AND OTHER) DISORDERS

Sacral Meningeal (Tarlov) Cysts (see Hiers 2010, Van de Kleft 1991)

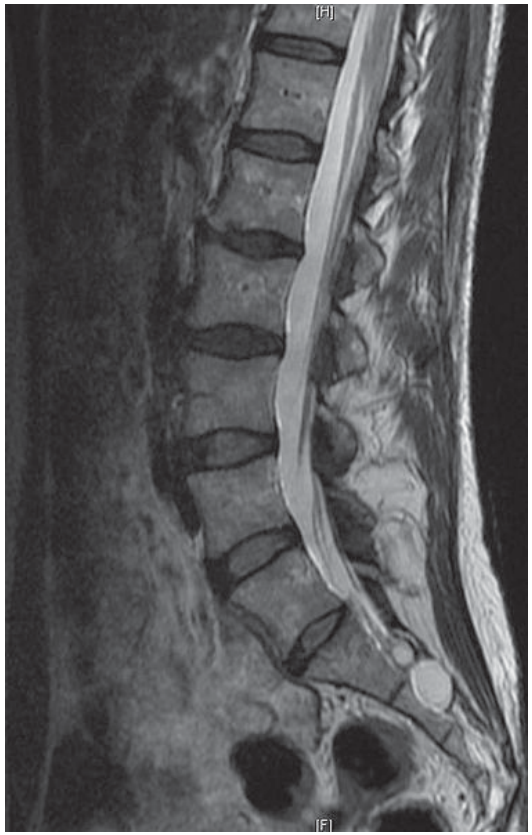


Image courtesy of Wikimedia Commons

Referred pain from ruptured disc or scarring around sacral nerve roots after disc surgery, pelvic floor muscle dysfunction and/or orthopedic condition, e.g., labral hip tear (image below)

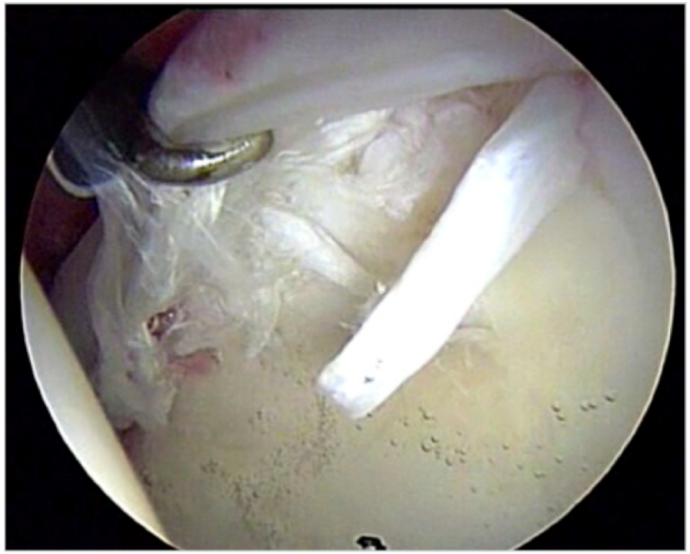


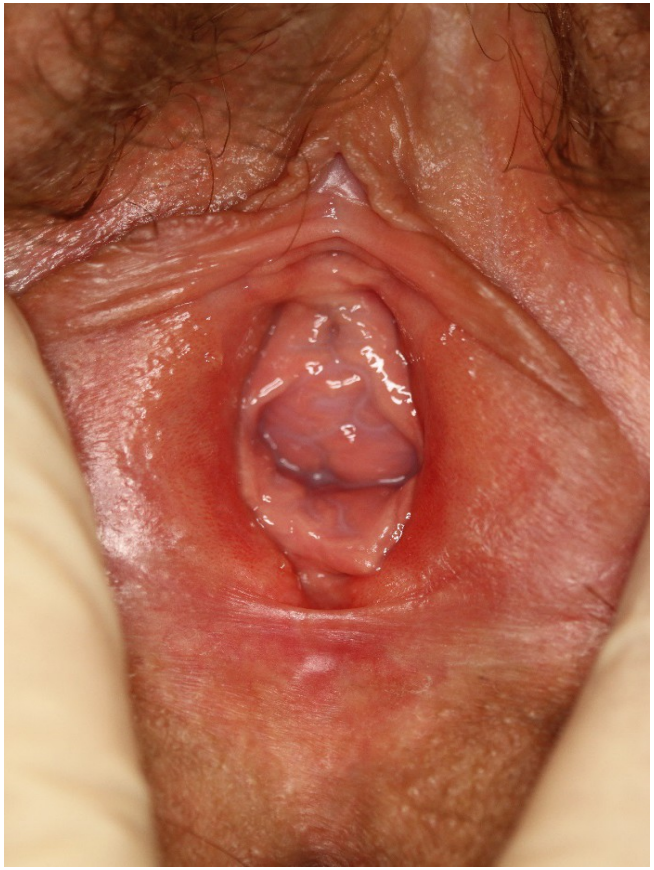
Image courtesy of Deborah Coady

RULE-OUT DIAGNOSES
TRAUMA

Trauma to the vulva may lead to chronic vulvar pain.

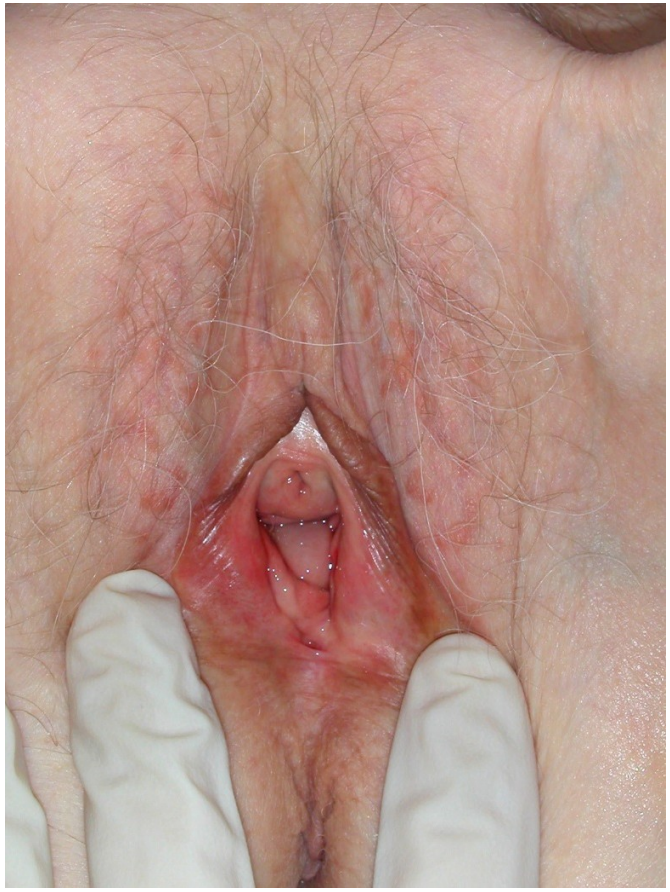
- Female genital cutting
- Perineal trauma
- Straddle injuries
  - Bicycles
  - Falls from climbing
- Injuries to pelvis
  - Motor vehicle accidents

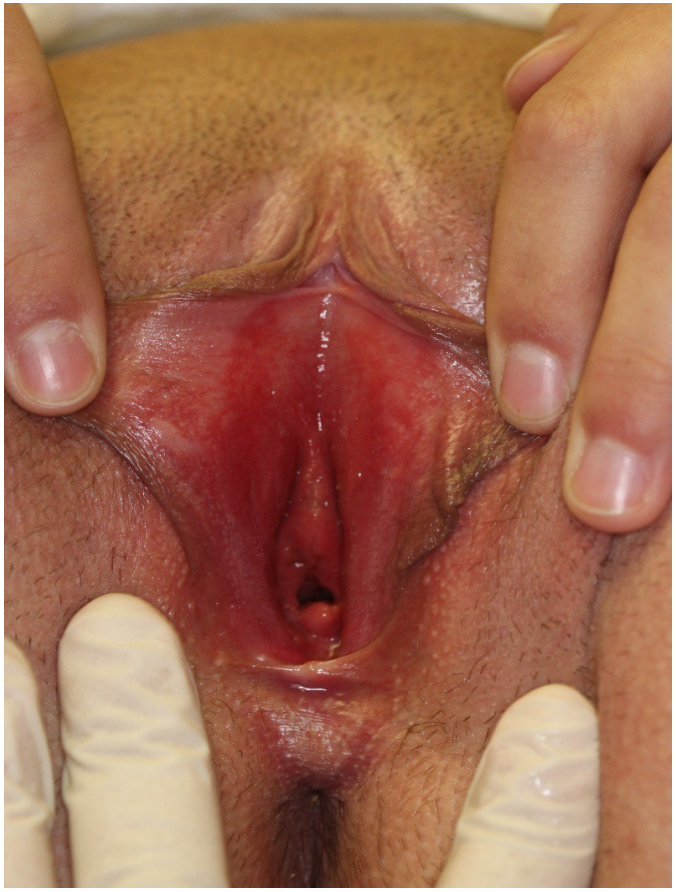
RULE-OUT DIAGNOSES
HORMONAL DEFICIENCIES



Courtesy of Dr. Andrew Goldstein

RULE-OUT DIAGNOSES
IATROGENIC

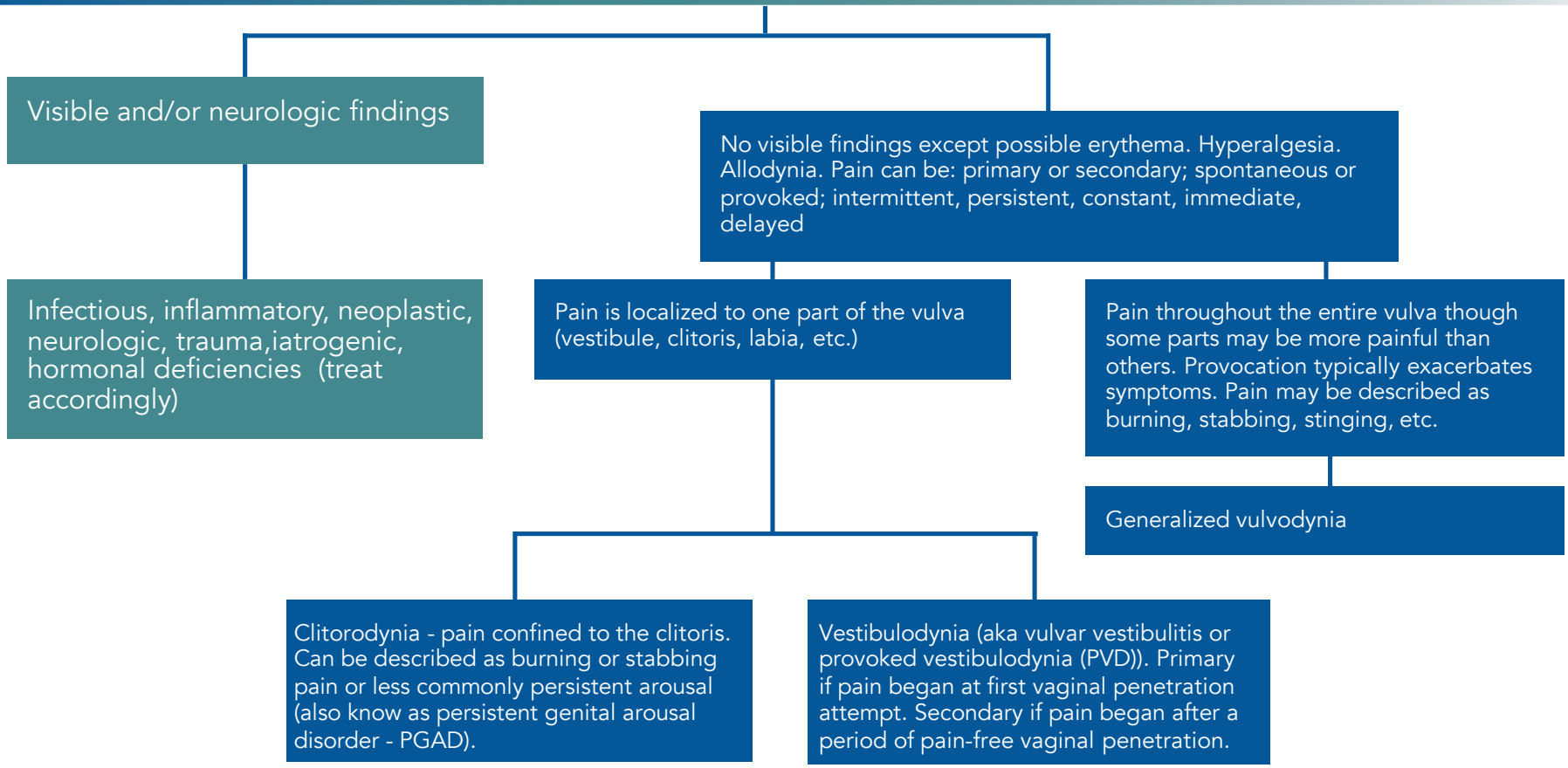




Images Courtesy of Dr. Andrew Goldstein

VULVODYNIA ASSESSMENT

CHRONIC VULVAR PAIN



Haefner 2007, Bornstein 2016

VULVODYNIA ASSESSMENT
SCREENING QUESTIONS

Four Questions Highly Predictive of a Clinical Diagnosis

1) Experience genital "pain"?

2) Experience genital burning > 3 months?

3) 10 or more episodes of pain on contact with tampon insertion, sexual intercourse or gynecological exam?

4) Does pain on contact limit/prevent intercourse?

2015 ISSVD, ISSWSH, IPPS CONSENSUS TERMINOLOGY AND CLASSIFICATION OF VULVODYNIA

Vulvodynia is vulvar pain of at least 3 months duration, without a clear identifiable cause, which may have potential associated factors.

Descriptors:

- Localized (e.g., vestibulodynia, clitorodynia), generalized or mixed (localized and generalized)
- Provoked (eg, insertional, contact), spontaneous or mixed (provoked and spontaneous)
- Onset (primary or secondary)
- Temporal pattern (intermittent, persistent, constant, immediate, delayed)

Bornstein 2016

VULVODYNIA ASSESSMENT
COMPONENTS OF THE EXAMINATION

After all infectious, inflammatory, neoplastic, neurologic, and other disorders are identified and treated, women are assessed for vulvodynia through a five-step examination, as described in the following slides.

Step 1: Visual Examination

Step 2: Cotton-Swab Examination of the Vulva and Vulvar Vestibule

Step 3: Neurosensory Examination

Step 4: Pelvic Floor Muscle Examination

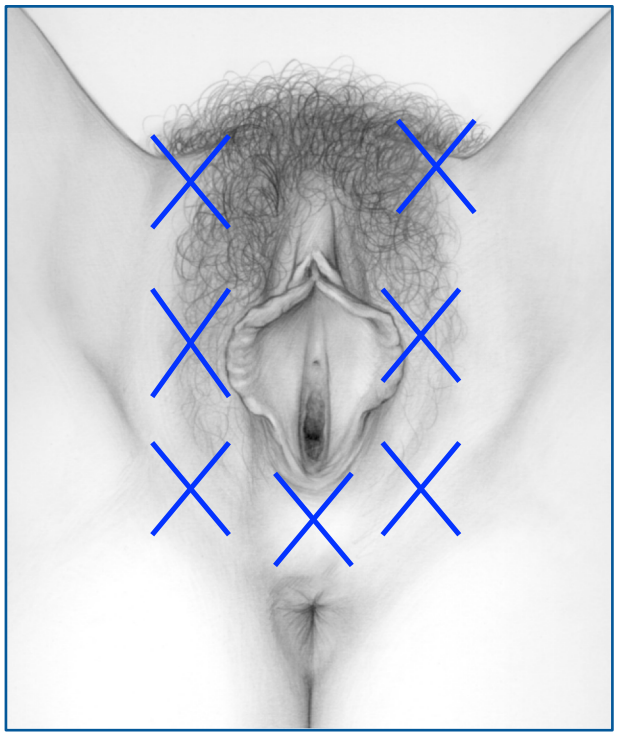
Step 5: Evaluation of Pain Comorbidity & Contributing Factors

VULVODYNIA ASSESSMENT

SUBJECTIVE FINDINGS: "WHERE DOES IT HURT?"

Generalized Vulvodynia

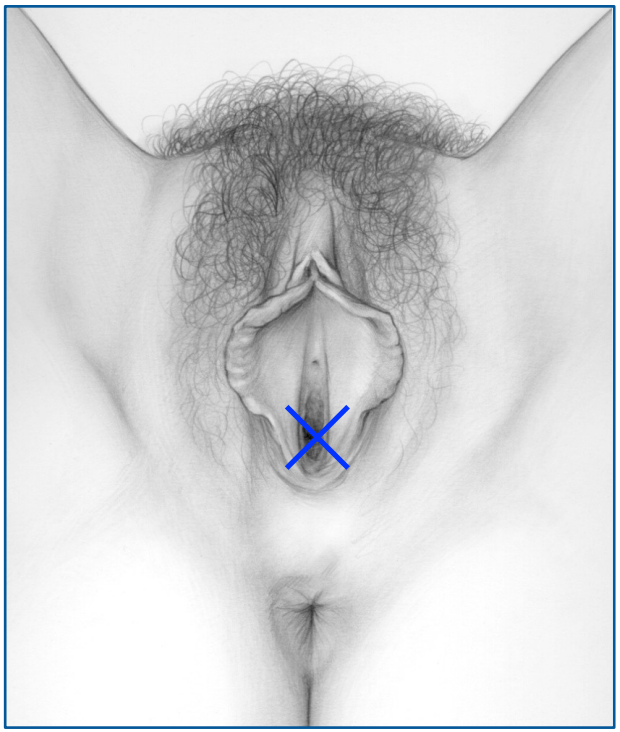
"It hurts all over, all of the time."



Less prevalent (20%) subtype

Provoked Vestibulodynia

"It hurts at the opening only with touch or pressure."

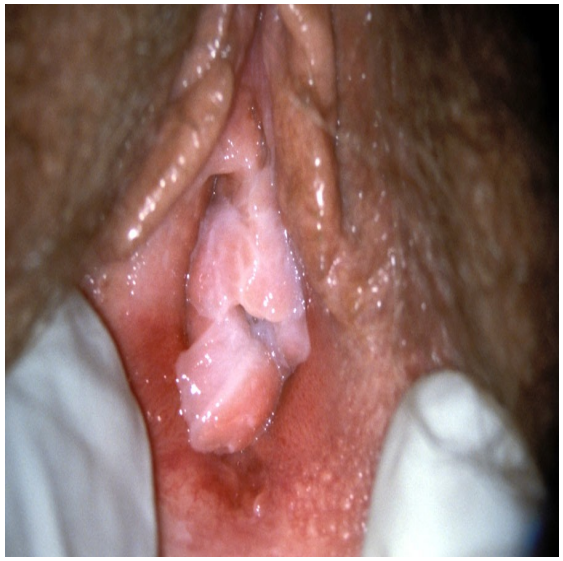


More prevalent (80%) subtype

VULVODYNIA ASSESSMENT
STEP 1: VISUAL EXAMINATION

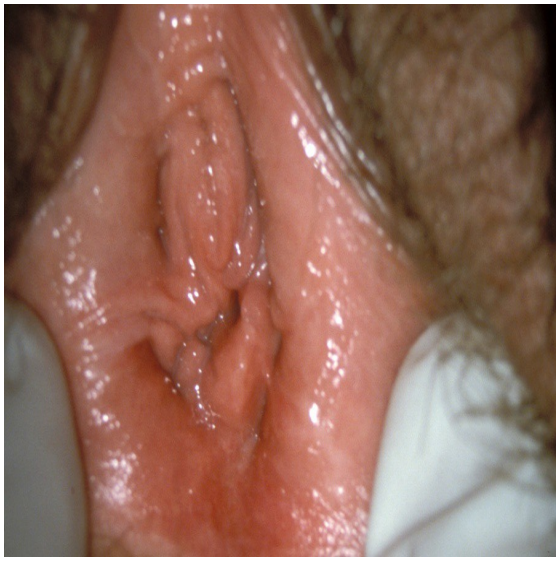
Patient #1

Severe Erythema



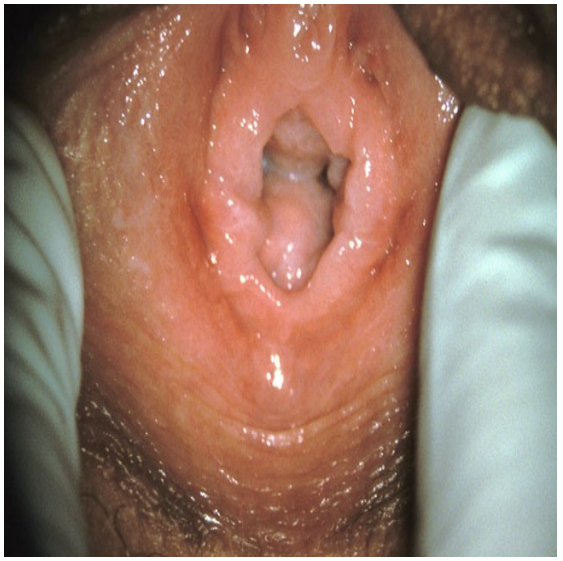
Patient #2

Moderate Erythema



Patient #3

Minimal Erythema Severe Pain



Pain severity and subsurface inflammation do not consistently correlate with the amount of erythema observed (Bergeron 2001, Farage 2009).

Reprinted with permission from Ledger, W.J. and Witkin, S.S., Vulvovaginal Infections, Manson Publishing, London, 2007, page 103.

VULVODYNIA ASSESSMENT

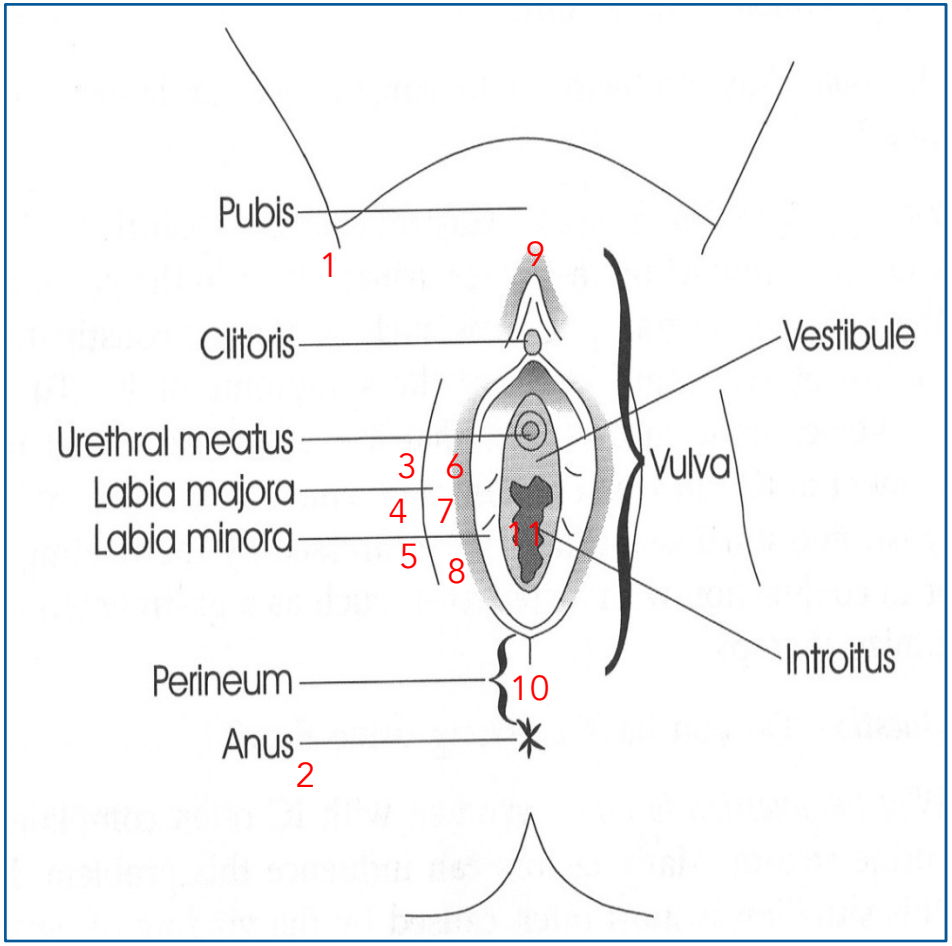
STEP 2: COTTON SWAB EXAMINATION OF THE VULVA

Using a cotton swab, test for allodynia, hypo- and hyperalgesia by applying gentle pressure to the following areas:

- 1-2 inner thigh
- 3-5 labia majora
- 6-8 interlabial sulcus
- 9 clitoris, clitoral hood
- 10 perineum
- 11 sites within vestibule (next slide)

For each site, the patient:

- Rates the pain severity (VAS score)
- Describes the pain character (burning, raw, etc.)



VULVODYNIA ASSESSMENT

STEP 2: COTTON SWAB EXAMINATION OF VULVAR VESTIBULE

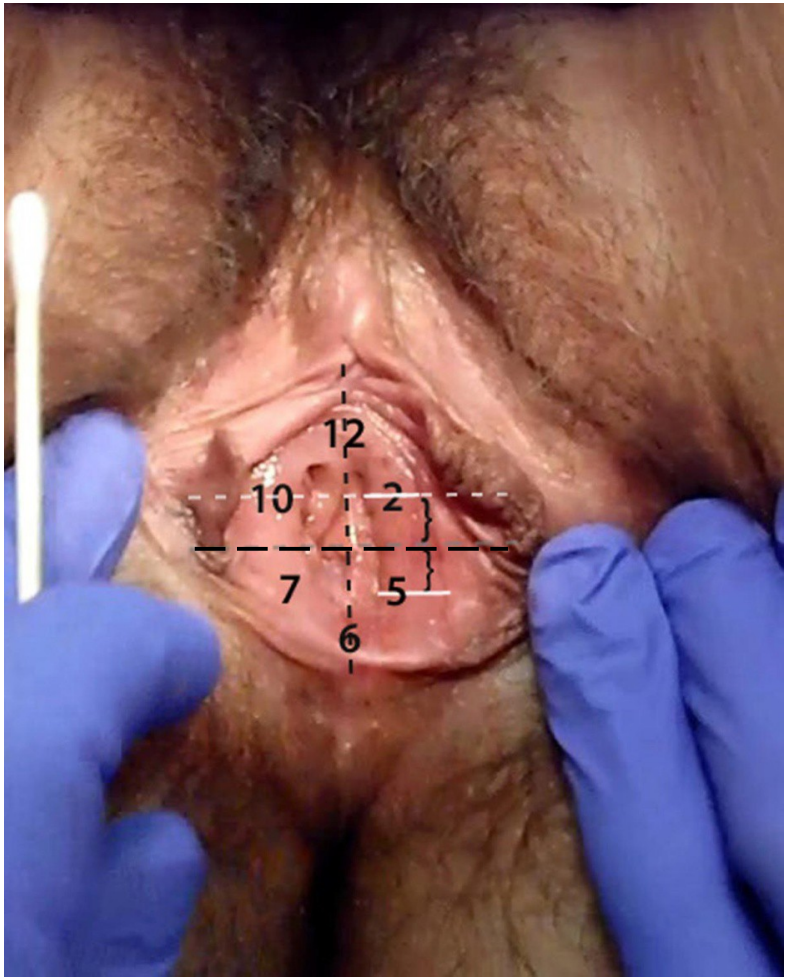
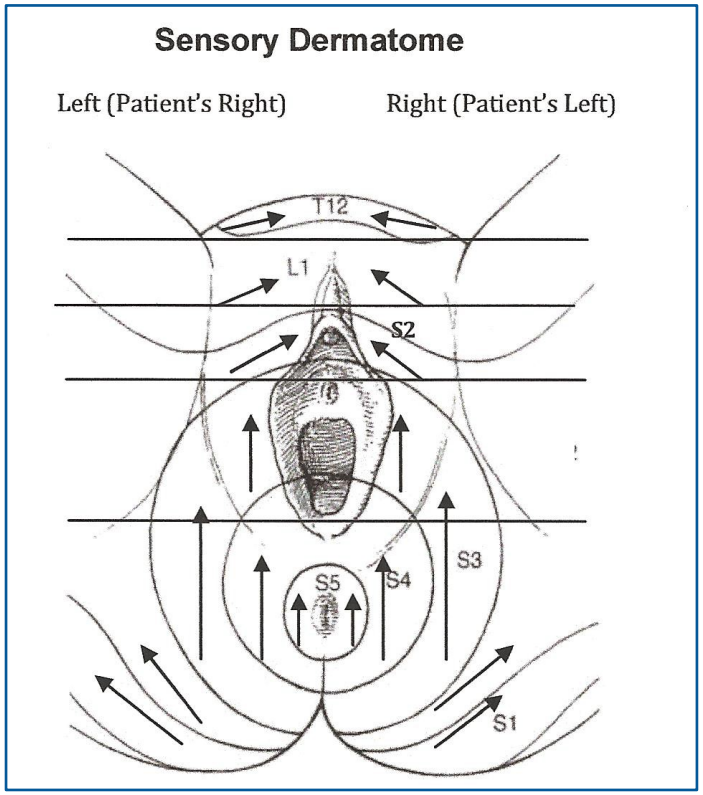


Image courtesy of Dr. Denniz Zolnoun

VULVODYNIA ASSESSMENT
STEP 3: NEUROSENSORY EXAMINATION

- Instruct the patient on 'cotton' vs. 'pin-prick' sensation by touching her outer thigh (just above the knee) with the cotton portion, followed by the wooden portion, of the cotton swab
- Using the cotton swab, gently stroke (upwards) each of the sensory dermatomes
- Note sensation (normal, allodynia, hypo-sensitive), pain score, pain character (eg, sharp, burning, shooting), and right- to left-side differences
- Break the cotton swab in half and repeat exam with the sharp wooden portion of the swab using punctate pressure (apply light pressure for 1 sec) in each dermatome

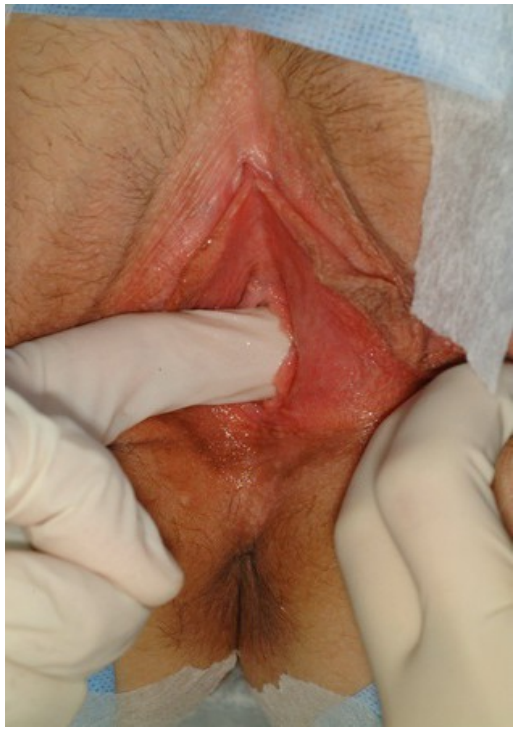
- Note sensation (normal, allodynia, hypo-sensitive), pain score, pain character (eg, sharp, burning, shooting), and right- to left-side differences

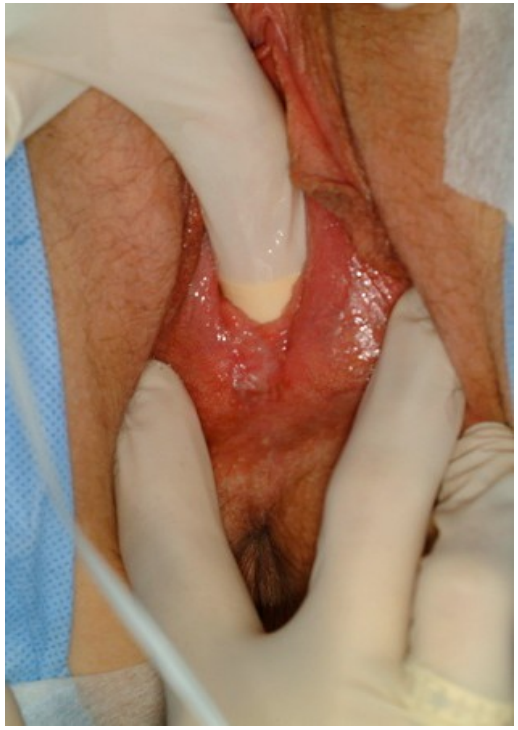


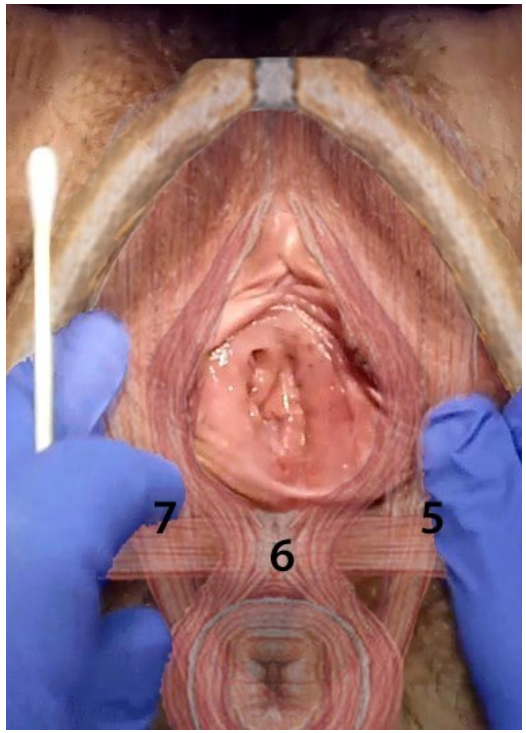
From ongoing NIH Grant 5K23HD053631

VULVODYNIA ASSESSMENT

STEP 4: PELVIC FLOOR MUSCLE EXAMINATION







Images courtesy of Dr. Denniz Zolnoun

VULVODYNIA ASSESSMENT

STEP 5: EVALUATION OF PAIN COMORBIDITY & CONTRIBUTING FACTORS

As a consequence of living with a poorly understood, under-recognized genital pain disorder, women commonly report emotional distress and sexual impairment.

Comorbid pain syndromes are also common, including:

- Interstitial Cystitis | Irritable Bowel Syndrome | Endometriosis
- Orofacial Pain (TMJ) | Chronic Headache (Migraine, Tension Type)
- Fibromyalgia | Chronic Fatigue Syndrome

Assessment of comorbid disorders is important in selecting therapies that target all factors contributing to a woman's current pain state, including:

- Pain (location(s), intensity & interference)
- Emotional Functioning
- Sleep Interference (both falling asleep & staying asleep)
- Physical Functioning
- Sexual Functioning

See Comorbidity References.

VESTIBULODYNIA: A DIAGNOSTIC ALGORITHM
NEUROPROLIFERATION

VESTIBULODYNIA WITH TENDERNESS THROUGHOUT ENTIRE VESTIBULE

NEUROPROLIFERATION

ACQUIRED NEUROPROLIFERATIVE VESTIBULODYNIA

HX: Allergic reaction, chronic yeast infection, polymorphisms in IL1RA, MBL, IL1B, associated with urticaria, hives, sensitive skin

PE: Tenderness of the entire vestibule from Hart's line to the hymen, often with erythema that worsens after touch with cotton swab. Umbilical hypersensitivity in approximately 60% of these women.

LABS: increased density of c-afferent nociceptors if using S-100 of PGP 9.5

CONGENITAL NEUROPROLIFERATIVE VESTIBULODYNIA

HX: Pain since first tampon use, speculum insertion, and coitarche. No pain free sex. Late coitarche > 25 years old.

PE: Tenderness of the entire vestibule from Hart's line to the hymen, often with erythema that worsens after touch with cotton swab. Umbilical hypersensitivity in approximately 60% of these women.

LABS: increased density of c-afferent nociceptors if using S-100 of PGP 9.5

VESTIBULODYNIA: A DIAGNOSTIC ALGORITHM
INFLAMMATORY VESTIBULODYNIA

VESTIBULODYNIA WITH TENDERNESS THROUGHOUT ENTIRE VESTIBULE

INFLAMMATORY VESTIBULODYNIA

HX: Chronic infections, allergic reactions, copious yellowish discharge.

PE: Erythema (redness), leukorrhea (thick discharge), induration (hardening of soft tissue), vaginal mucosal tenderness, cervicitis/ectropion (inflammation of the outer cervix)

CAUSES: Desquamative inflammatory vaginitis, chronic candidiasis, latex allergy/semen allergy

DESQUAMATIVE INFLAMMATORY VAGINITIS

HX: Copious yellow vaginal discharge that ruins underwear or requires a panty liner, vulvar pruritus where discharge dries

PE: Copious leukorrhea, vaginal mucosa erythema, cervicitis, cervical ectropion

CAUSES: Unknown, but current hypothesis is either infection of unknown pathogen, erosive lichen planus, vulvovaginal atrophy, or cervical ectropion.

RECURRENT CANDIDIASIS

PE: Erythema, induration, thin fissures, peri-anal erythema. Discharge is often thin and yellow, not thick and white (cottage cheese-like).

LABS: Hyphae and increased WBCs on wet mount. Positive cultures

CAUSES: Diet high in simple sugars, antibiotics, OCPs

VESTIBULODYNIA: A DIAGNOSTIC ALGORITHM
HORMONALLY ASSOCIATED VESTIBULODYNIA

VESTIBULODYNIA WITH TENDERNESS THROUGHOUT ENTIRE VESTIBULE

HORMONALLY ASSOCIATED VESTIBULODYNIA

PE: Gland ostia are erythematous, mucosal pallor with overlying erythema, decreased size of labia minora and clitoris

LABS: High SHBG, low free testosterone, low estradiol

CAUSES: Hormonal contraceptives, spironolactone, Tamoxifen, aromatase inhibitors, oophorectomy, amenorrhea, lactation

VESTIBULODYNIA: A DIAGNOSTIC ALGORITHM

PELVIC FLOOR MUSCLE DYSFUNCTION AND PUDENDAL NEURALGIA

VESTIBULODYNIA

TENDERNESS ONLY IN THE POSTERIOR VESTIBULE

OVERACTIVE PELVIC FLOOR MUSCLE DYSFUNCTION

HX: 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.

PE: Pain at 4, 8 o'clock if hypertonus of pubococcygeus muscle. Pain at 6 o'clock if hypertonus of puborectalis muscle.

TENDERNESS EXTENDS OUTSIDE OF THE VESTIBULE

PUDENDAL NEURALGIA

HX: Often unilateral pain or significantly worse on one side. Pain can extend to the clitoris, labia, perineum, or anus and the inner thigh. History of coccyx trauma, history of hip pain or labral tear. Pain is usually better with lying prone or standing, worse with sitting. Pain improves temporarily with pudendal nerve block.

PE: The pudendal nerve is tender when palpated at ischial spine on vaginal exam. The obturator internus muscle is usually very tender, unilateral or significantly greater on one side.

Individualized Multidisciplinary

GENERAL PRINCIPLES

Scientific level of evidence for almost all treatments is poor with very few RCTs.

Individualized, Multidisciplinary Treatment Regimen Recommended

- Components of an individualized, multidisciplinary, biopsychosocial treatment approach are selected after identifying vulvodynia subtype and contributing factors (Jodoin 2011, Spoelstra 2011, Stockdale 2014).
- Multidisciplinary treatment results in reduced pain level, improvement in sexual functioning as well as increased patient knowledge, gain of tools/skills, improved mood and psychological well-being, gain of validation and support, and empowerment (Sadownik 2012, Brotto 2015).

See Andrews 2011 for an evidence-based review.

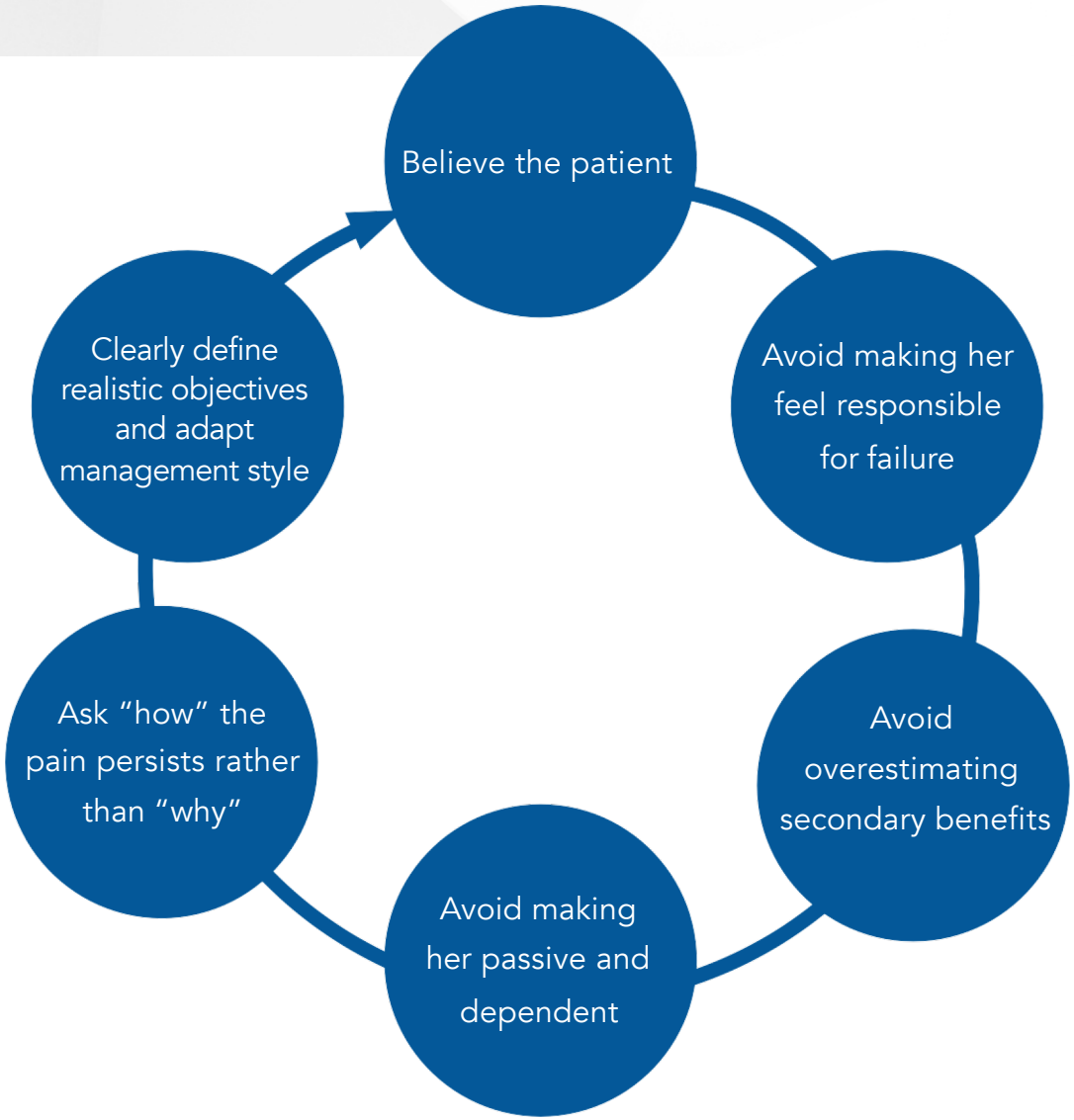
GENERAL PRINCIPLES

Treatment Outcome Varies, but Majority Improve with Treatment

- Treatment response varies among patients, likely due to heterogeneity of underlying etiology.
- There is currently little knowledge to predict treatment outcome, although studies are ongoing.
    - Heddini (2012) found that successful treatment was more likely in women with fewer concomitant pain disorders, and lower response rates were found in women with primary, rather than secondary, PVD.
- As such, it can take many months to identify a treatment regimen that is helpful, but the majority of women will improve with treatment for variable periods of time (Ventolini 2009).
    - Remission rates differ among women, underscoring the heterogeneity of vulvodynia, and remission may occur without treatment (Davis 2013, Nguyen 2015).

See Andrews 2011 for an evidence-based review.

COMPONENTS OF THE PROVIDER/PATIENT RELATIONSHIP



Labat 2010

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

First step is vulvar* self-care, eg, avoid all vulvar irritants, and chronic pain self-care

Oral "Pain-Blocking" Medications (1) ^

- Tricyclic antidepressants (amitriptyline, nortriptyline) (1, 2-4, 28, 32, 33, 91) **
- Anticonvulsants (gabapentin, pregabalin, lamotrigine, topiramate oxcarbamazepine) (1, 5-9, 105, 106)
- SSNRIs (duloxetine, venlafaxine, milnacipran) (1, 132)
- In severe cases, or to manage symptoms while the dose of a long-term medication is titrated upward, other pain-relieving medications (eg, short-term opioids) can be used

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

Topical Formulations

- Compounded topical formulations can be used in conjunction with medications (or other treatments)

- Topicals contain either a single active ingredient or a combination of ingredients (anesthetic, antidepressant, anticonvulsant) (1, 10, 30-35, 92, 109, 110, 131)

  -Topical use of benzocaine and diphenhydramine should be avoided due to potential sensitization and irritation (108)

  -Topicals not found useful*

- Discontinuation of oral contraceptives (OC) and use of a topically formulated estrogen (and sometimes testosterone) cream is recommended for cases in which OC use is suspected to play a role in symptom development and/or maintenance (1, 97, 103, 104)

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

Nerve Blocks

- Pudendal and/or caudal blocks of local anesthetic, or local anesthetic and steroid, have been used with varying degrees of success (11-15)
- Limited studies of multilevel nerve blocks (subcutaneous, pudendal, caudal) demonstrate efficacy (48, 93, 111)

See Treatment References.

Pelvic Floor Muscle Therapy

Pelvic floor muscle therapy, including various physical therapy techniques, biofeedback training, trigger point injections and use of vaginal dilators, has been found helpful in women who also exhibit pelvic floor muscle abnormalities, eg, spasm, weakness, instability (1, 20-23, 31, 34, 36-46, 94, 112).

The efficacy of botulinum, Type A (BTA) has been evaluated in a double-blind placebo controlled RCT and 2 case series. Petersen et al. found no difference between administration of 100 u BTA versus placebo in level of pain, quality of life and sexual function in 64 women with provoked vestibulodynia (PVD) (82). In contrast, a prospective case series of 20 women with PVD, by Pelletier et al., found that 80% of women reported an improvement in pain and 72% were able to have sexual intercourse following a dose of 100 u of BTA. Quality of life and sexual function also improved (126).

See Treatment References 1-135.

Pelvic Floor Muscle Therapy (cont.)

Similarly, lower doses of Botox (35-50 u) were found to significantly reduce pain and oral medication use, and improve quality of life, in a retrospective study of 19 women with PVD. Botox is not recommended as a first-line treatment for PVD. It may be useful, however, in combination with pelvic floor physical therapy (127).

For a comprehensive review, see References 47, 112.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

Psychotherapy

- Adjunct cognitive-behavioral therapy, psychotherapy (individual or couples) and/or sex therapy focused on pain reduction, sexual rehabilitation and/or relationship enhancement may be helpful (26, 37, 42, 66, 95, 113)

- Eliminating stress may also be a contributing factor in symptom improvement (44)

Neurostimulation

- Case reports of recalcitrant patients show benefit of spinal cord stimulation (16-18)

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

Surgery

Two procedures *exclusively* for women with provoked vestibulodynia:

- Vestibulectomy with Vaginal Advancement
  - Involves the removal of a portion (or all) of the vestibule, with vaginal advancement
  - Surgical technique/images (www.nva.org/shg3)
- Modified Vestibulectomy
  - Only the superficial painful tissue is removed and there is no vaginal advancement.
  - Surgical technique/images (www.nva.org/vestibulectomy)

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

Surgery (cont.)

- Most published results are based on Vestibulectomy with Vaginal Advancement. In this type of surgery, the vagina is pulled and sutured to the perineal skin, halfway between the vulvar introitus and the anus so that the sensitive mucosa-skin junction will not be in the introitus itself (128).

- Overall success rates for both procedures range from 60-96 percent (29, 42, 49-60, 114, 115), but recurrences may occur in an unknown percentage of patients over a variable period of time (96).

- After surgery, physical and dilator therapy are often recommended and appear to help alleviate any remaining pelvic floor myalgia (53, 59).

- Careful patient selection is essential because it increases the likelihood of success with a surgical procedure. Researchers are studying factors that may predict surgical treatment success or failure (42, 52, 55, 59, 61-64, 96, 116).

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

These treatments, some of which are currently the focus of efficacy studies, are occasionally used to manage vulvodynia symptoms, depending on the case.

- **Topical Steroids –** Both improvement and worsening reported (32, 67). Recently, a review article concluded that steroids are not effective (127).
- **Neogyn (cutaneous lysate skin cream containing human cytokines) –** Initial study demonstrated decreased inflammation and intercourse-related pain (102).
- **Subcutaneous Steroid/Anesthetic Injections –** Some improvement noted (71-73). Case report noted improvement following remote foci anesthetic injection (117).
- **Vaginal Diazepam –** Initial case studies showed decreased levator muscle pain and vulvar pain. However, it is uncertain whether the effect is local or systemic (98, 118, 119).

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

Treatments lacking proof of efficacy:

- **Diet Modification -** Although a minority of women claim benefit from a low oxalate/calcium citrate regimen, studies have found no difference in the amount of urinary oxalate excreted by women with vulvodynia and controls (1, 24, 32, 74, 75). A case-control, population-based study found no association between increased consumption of foods with high oxalate content and risk of vulvodynia (25). Some women report that eliminating acidic and/or high sugar foods provides some symptom-relief.

- **Interferon Injections** - Although initial data was promising, recent clinical data indicate a much lower or non-existent efficacy rate (1, 32, 68, 69).

- **Topical Cromolyn** - The initial study found little efficacy in women who had recalcitrant symptoms (70).

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

Experimental treatments that have been the focus of several recent journal publications, but are not widely used at this time, include:

- Leukotriene Receptor Antagonist: One controlled study of women with PVD showed a 50% improvement in symptoms (83)
- Topical Nitroglycerin: Initial report of improvement in pain and dyspareunia, but headache was a limiting side effect (84)
- Topical Capsaicin: Initial report of improvement in pain and dyspareunia (85)
- Enoxaparin Injections: Decreased vestibular sensitivity and dyspareunia (101)
- KTP-nd: YAG Laser Therapy: Initial report showed reduced dyspareunia and improved sexual satisfaction (86)

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

- Photodynamic Therapy - Initial report of reduction in overall symptoms, but no improvement in intercourse-related pain (87)
- Transcutaneous Electrical Nerve Stimulation – Reports of improvement in vulvar pain, intercourse-related pain and sexual functioning (88, 89, 99, 120, 121)

See Treatment References 1-135.

INDIVIDUALIZED MULTIDISCIPLINARY TREATMENT

Additional experimental treatments that have been the focus of several recent journal publications, but are not widely used at this time, include:

- Palmitoylethandamide - Inconsistent effectiveness when used in combination with TENS and other agents (99, 122, 123)
- Sacral Neuromodulation - One case report described sustained pain improvement at 2 years follow-up (90)
- Peripheral Neuromodulation - Case report described pain improvement (with 1 year follow-up) (124)
- Pulsed Radiofrequency - Case report of successful use for chronic vulvodynia (125)
- Transcranial Direct Current Stimulation - One case report of a refractory patient who responded well (19)
- Motor Cortex Stimulation – Two cases showed decreased pain, increased daily activities and quality of life after failure of conventional neuromodulation, eg, spinal cord stimulation (100).
- Alternative Therapies

See Treatment References 1-135.

USING VALIDATED EVIDENCE-BASED TOOLS TO TRACK KEY DOMAINS & TREATMENT OUTCOME

- **Key domains important to assess and track over time include:**
  - Pain (location(s), intensity & interference)
  - Physical, emotional and sexual functioning
  - Sleep interference (both falling asleep & staying asleep)
  - Treatment side effects
- **Female Sexual Function Index* can be used to monitor sexual function and satisfaction.**
- NIH PROMIS^ also has numerous tools using computerized adaptive testing to measure outcomes.
- Several web-based and smartphone apps are currently available online for use by pain sufferers, including those listed below, however, most do not provide information to patients' clinicians.^^

Key Summary Points

- Vulvodynia, defined as chronic vulvar pain of at least 3 months duration that occurs in the absence of a clear identifiable cause, is a widely prevalent, misdiagnosed, and under-researched pain disorder affecting women of all ages and ethnicities. It negatively affects women's physical, emotional and sexual health.

- The vulva contains tissues derived from both the endoderm and ectoderm. It is innervated by the ilioinguinal, genitofemoral and pudendal nerves. Further, its proper functioning relies on both superficial and deep pelvic floor musculature.

Key Summary Points

- Women/adolescents who are likely to have a clinical diagnosis of vulvodynia report: i) genital pain, ii) genital burning for more than 3 months, iii) 10 or more episodes of pain on contact with tampon insertion, intercourse or gynecologic exam, and iv) pain on contact that limits/prevents intercourse.

- Although vulvodynia's pathophysiology remains inconclusive, research supports the theory that multiple mechanisms predispose, trigger and perpetuate symptoms. Heterogeneous mechanism-based subgroups demonstrate variable degrees of peripheral and central nervous system sensitization, vestibular tissue changes and pelvic floor muscle dysfunction.

Key Summary Points

- The vulvodynia subtype is first classified by location: generalized (several areas of the vulva) vs. localized (a specific vulvar region) and then by provocation (provoked, spontaneous or mixed). The two most common subtypes of vulvodynia are generalized vulvodynia (spontaneous pain in several vulvar areas) and provoked vestibulodynia (provoked pain localized to the vulvar vestibule).

- After all known infectious, inflammatory, neurologic, neoplastic and other causes of vulvar pain are ruled out, a thorough vulvodynia assessment includes: i) visual exam of the vulva, ii) cotton swab exam of the vulva and vulvar vestibule, iii) neurosensory exam, iv) pelvic floor muscle evaluation, and v) an evaluation of pain comorbidity and contributing factors.

Key Summary Points

- Components of an individualized, multidisciplinary, biopsychosocial treatment regimen are selected after identifying the vulvodynia subtype and contributing factors. Due to vulvodynia's heterogeneity, treatment response varies among women. As a result, it can take time to identify a helpful regimen, but the majority of women do improve with treatment.

- It is vital to assess and track key pain-related domains over time as women undergo treatment. Several validated easy-to-use tools are currently available to track pain intensity and interference; physical, sexual and emotional function; sleep interference; and treatment side effects.

SELECTED REFERENCES

Selected Journal References available at www.nva.org/articles

- 2015 Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia (Bornstein)
- Medical and Physical Predictors of Localized Provoked Vulvodynia (Bohm-Starke)
- Vulvodynia: Diagnosis and Management (Reed)
- Vulvodynia: An Evidence-Based Approach to Medical Management (Andrews)
- Vulvodynia-An Evidence-Based Literature Review and Proposed Treatment Algorithm (De Andres)
- The Vulvodynia Guideline (Haefner)
- 2013 Vulvodynia Guideline Update (Stockdale)
- Vulvodynia Interventions – Systematic Review and Evidence Grading (Andrews)

SELECTED REFERENCES

Proceedings of the 2003 & 2011 NIH Conferences available at www.nva.org/nihreports

Selected Reference Textbooks available at www.nva.org/bookstore

- Female Sexual Pain Disorders: Evaluation and Management

  (Goldstein, Pukall, Goldstein)

- The Vulva: Anatomy, Physiology and Pathology

  (Farage, Maibach)

PATIENT RESOURCES

Patient Booklets available at www.nva.org/shg

- Self-Help Guide: features important self-help strategies for alleviating vulvar pain and maintaining sexual intimacy
- Conception to Pregnancy Guide: includes information on conception through the postpartum period
- Partner Guide: helps partners to have a better understanding of vulvodynia and the challenge of living with someone who has it
- Disability Guide: provides step-by-step guidance that will help vulvodynia sufferers compile and submit a successful disability claim

NVA Brochure available at www.nva.org/publications/

Self-help tips available at www.nva.org/tips

Reference Books available at www.nva.org/bookstore