Vulvar Disease for Diagnoses and Management

John Willems, MD

Vulvar Disease for Generalists

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Objectives:

- Identify the major forms of vulvar pathology
- Describe the appropriate setup for vulvar biopsy
- Describe the most appropriate management for commonly seen vulvar conditions
## Faculty Disclosure

<table>
<thead>
<tr>
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<th>Nature of Affiliation</th>
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<td>Warner Chilcott</td>
<td>Speakers Bureau</td>
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Classification of Vulvar Disease by Clinical Characteristic

- Red lesions
- White lesions
- Dark lesions
- Ulcers
- Small tumors
- Large tumors

Red Lesions

- Candida
- Tinea
- Reactive vulvitis
- Seborrheic dermatitis
- Psoriasis
- Vulvar vestibulitis
- Paget’s disease
Vulvar Disease for Diagnoses and Management

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Candidal vulvitis
Superficial grayish-white film is often present

Thick film of candida gives pseudo-ulcerative appearance.
Acute vulvitis from coital trauma
Contact irritation from synthetic fabrics
Nomenclature

Subtypes of Vulvodynia:

- Vulvar Vestibulitis Syndrome (VVS)
  also known as:
  - Vestibulodynia
  - localized vulvar dysesthesia

- Dysesthetic Vulvodynia
  also known as:
  - “essential” vulvodynia
  - generalized vulvar dysesthesia

Dysesthesia

- Unpleasant, abnormal sensation
  - examples include:
    - Burning
    - rawness

- Can be spontaneous or evoked

- Includes allodynia and/or hyperalgesia
  - Allodynia:
    - Pain due to a stimulus that does not normally evoke pain
  - Hyperalgesia:
    - Increased response to a stimulus that IS normally painful
Incidence of Dyspareunia

- National Health & Social Life Survey
- Adult Sexual Behavior
- 1749 women - 18 to 59
- 7% incidence of dyspareunia

_JAMA_ 1999;281,6:537-544

Early Descriptions:

Hyperaesthesia of the Vulva

1880

"...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..."


1888

"This disease...is characterized by a 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’s surgical notes state: “The sensitive tissue has been dissected off and relief obtained for a time, the hyperesthesis returning, however, as before the operation.”

1942 Minor vestibular glands identified by Hunt
1976 Erythematous Vulvitis in Plaques (Pelisse & Hewitt)
1983 Extensive perineoplasty advocated by Woodruff & Parmely
1987 Vulvar vestibulitis syndrome coined and defined by Friedrich
1988 Histopathology – chronic periglandular inflammatory response without direct glandular inflammation (Pyka)
NIH Holds First Symposium

Vulvodynia Workshop:

*Current Knowledge and Future Directions*

- April 2-3, 1997
- More than 200 medical specialists attended
- Led to first federal funding of vulvodynia research in FY 2000

Coexisting Medical Conditions
Results from a self-report survey of vulvodynia patients administered by the National Vulvodynia Association

<table>
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<th>Disorder</th>
<th>Number surveyed</th>
<th>Have It</th>
<th>Suspect It</th>
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<tr>
<td>Chronic Fatigue</td>
<td>1566</td>
<td>12.6%</td>
<td>19.9%</td>
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<td>Endometriosis</td>
<td>1452</td>
<td>15.6%</td>
<td>4.4%</td>
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<td>Fibromyalgia</td>
<td>1547</td>
<td>20.0%</td>
<td>15.4%</td>
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<tr>
<td>Interstitial Cystitis</td>
<td>1662</td>
<td>25.2%</td>
<td>22.0%</td>
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<tr>
<td>Irritable Bowel</td>
<td>1675</td>
<td>34.9%</td>
<td>15.8%</td>
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<td>Low Back Pain</td>
<td>1729</td>
<td>55.5%</td>
<td>-</td>
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<tr>
<td>Migraine Headaches</td>
<td>1564</td>
<td>31.2%</td>
<td>-</td>
</tr>
<tr>
<td>Chemical Sensitivities</td>
<td>1595</td>
<td>27.2%</td>
<td>18.2%</td>
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<tr>
<td>Other Chronic Pain</td>
<td>2150</td>
<td>40.5%</td>
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Vulvar Vestibulitis: Associations

- Allergies
- Chronic Fatigue
- Fibromyalgia
- Interstitial cystitis
- Irritable Bowel
- Sensitive Skin
- Multiple Chemical Sensitivities
Vulvar Vestibulitis Syndrome (VVS)

Also known as:
- localized vulvar dysesthesia
- vestibulodynia
VVS: Diagnosis

- Rule out infection, dermatoses (biopsy or colposcopy may be necessary) and any other cause of pain

- Diagnosed using Friedrich’s Criteria:
  - Severe pain on vestibular touch or attempted vaginal entry
  - Tenderness to pressure localized within the vulvar vestibule
  - No evidence of physical findings except for varying degrees of erythema


Vulvar Vestibulitis: Patient Profile

67 Patients

Average age at onset 25
Caucasian 100%
Nulliparous 49%
Prior abortions 26%
Primiparous 11%
Multiparous 13%
Onset - Acute 80%
  - Gradual 20%

Peckham 1986
Vulvar Vestibulitis: Etiology

57 Women with Vulvar Vestibulitis

- Gonorrhea: 0.0%
- Chlamydia: 0.0%
- Trichomonas: 0.0%
- Mycoplasma: 0.0%
- Gardnerella: 14.0%
- Candida: 8.8%
- HPV DNA: 5.3% (by PCR)

Bazin et al. 1994

Vulvar Vestibulitis: Etiology

Vulvar Vestibulitis is rarely associated with HPV infection.

Wilkinson et al. 1993
Vulvar Vestibulitis: Etiology

31 Women with Vulvar Vestibulitis

- 32% had a female relative with dyspareunia or tampon intolerance
- 21% date symptoms to postpartum period

Goetsch 1991
Vulvar Vestibulitis: Etiology

The Candidal Trigger

63% Friedrich (1988)

67% Peckham (1986)

80% Mann (1992)

Antigens of Candida Albicans
cross-react with certain
vulvovaginal tissue antigens
in predisposed patients.

Ashman & Ott 1989
The Telephone is Neither a Diagnostic Nor a Therapeutic Tool, and the Temptation to Use it as Such Should be Resisted.

Eduard G. Friedrich, Jr, MD

If the Treatment isn’t Working, Reconsider the Diagnosis.
Rules for the Evaluation of Vulvar Symptoms

- Rule #1
  - Everything feels like a yeast infection

- Rule #2
  - Not everything that feels like a yeast infection is a yeast infection

- Rule #3
  - Remember Rule #1

VVS: Treatment

- Eliminate irritants
- Topical estradiol may decrease severity of symptoms
- Tricyclic antidepressants (e.g. amitriptyline) or anti-convulsants (e.g. neurontin) may be helpful for their pain-blocking qualities
- Counsel patient on vulvar self-care and self-help tips
- Topical anesthetics (e.g. lidocaine)
- Pelvic floor therapy (for those who have pelvic floor muscle abnormalities as measured by surface electromyography)
- Physical therapy
- Surgery (vestibulectomy with vaginal advancement) usually used after more conservative therapies are exhausted (high success rates of 70%+)
- Interferon injections – not recommended
- CO2 LASER VAPORIZATION NO LONGER RECOMMENDED
Vulvar Vestibulitis: Therapy

“The biases of eminent men are still biases.”

M. Crichton 1971

Vulvar Vestibulitis: What Does Not Work

Laser
Topical steroids
5 Flurouracil (Efudex)
Trichloroacetic acid (TCA/BCA)
Interferon
? Surgery
Vulvar Vestibulitis: Therapeutic Approach

- Topical estrogen b.i.d.
- Biofeedback
- Antihistamines
- Reduced oxalate diet
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**Vulvar Vestibulitis: Topical Estrogen**

*Effect of Topical Estrogen on the Vulvar Vestibule*

Thirty-nine postmenopausal, unestrogenized women evaluated for sensory threshold by mechanoreceptor analysis

“lowering the mechanoreceptor threshold of the vulvar vestibule results from a rapid-acting, direct effect of topical estradiol cream upon mechanoreceptive nerve fibers” *Foster - ISSVD abstract 1997*

**Vulvar Vestibulitis: Current Results**

971 Consecutive Vestibulitis Patients

- Follow-up from 3 months to 23.2 years
- Average follow-up – 11.1 years
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**Vulvar Vestibulitis: Current Results**

**Diagnostic Criteria**

- Severe pain on vestibular touch or attempted vaginal entry
- Tenderness to point pressure localized within the vulvar vestibule
- Physical findings confined to vestibular erythema of various degrees

*J Reprod Med 1987;32: 110-114*

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**Vulvar Vestibulitis: Current Results**

**971 Consecutive Vestibulitis Patients**

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Caucasian</td>
<td>949</td>
<td>97.7%</td>
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<td>Premenopausal</td>
<td>806</td>
<td>83.0%</td>
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<tr>
<td>Nulliparous</td>
<td>487</td>
<td>50.2%</td>
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<td>Prior abortions</td>
<td>105</td>
<td>10.8%</td>
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<tr>
<td>Primiparous</td>
<td>126</td>
<td>13.0%</td>
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<tr>
<td>Multiparous</td>
<td>252</td>
<td>26.0%</td>
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Vulvar Vestibulitis: Current Results

971 Consecutive Vestibulitis Patients

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count (n)</th>
<th>Percentage</th>
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<tr>
<td>Urologic Symptoms</td>
<td>436</td>
<td>44.9%</td>
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<tr>
<td>Yeast History</td>
<td>667</td>
<td>68.7%</td>
</tr>
<tr>
<td>HPV History</td>
<td>119</td>
<td>12.3%</td>
</tr>
<tr>
<td>Irritable Bowel</td>
<td>166</td>
<td>17.1%</td>
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<tr>
<td>Fibromyalgia</td>
<td>249</td>
<td>25.6%</td>
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</table>

- 64 with prior perineoplasty
- 41 with prior laser surgery to vestibule
- 15 with multiple vestibular surgeries
- 8 with multiple laser surgeries to the vestibule
- 27 with combinations of laser and scalpel surgery
- 23 with prior topical 5-flourouracil exposure
- 15 with prior vestibular interferon injections
**Vulvar Vestibulitis: Current Results**

*Definition of Response*

- Complete response: substantially improved
  - Full activities of daily life
  - Able to wear fitted clothing
  - Urinary symptomatology cleared

- Partial response: moderately improved
  - Comfortable coitus at least one third of the time
  - Quality of life significantly better

*Objective Correlates of Response*

- Q-tip testing normalized
- Vestibular erythema absent
- Pelvic floor muscle tension reduced
- Enhanced voluntary control of the pelvic floor musculature
- Pelvic musculature non-tender to palpation
### Vulvar Vestibulitis: Current Results

**971 Consecutive Vestibular Patients**

**884 Evaluable Patients**

- **711 patients (80.4%)** - complete response
- **150 patients (17.0%)** - partial response
- **23 patients (2.6%)** - no response
- **87 patients (9.0%)** - lost to follow up

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**Vulvar Vestibulitis: Current Results**

**971 Consecutive Vestibulitis Patients**

**884 Evaluable Patients**

- **711 Responders**
  - **63.7%** - topical estradiol & biofeedback & reduced oxalate diet / oral calcium citrate
  - **34.9%** - topical estradiol & biofeedback
  - **1.4%** - biofeedback & reduced oxalate diet / oral calcium citrate
**Vulvar Vestibulitis: Current Results**

- 249 Patients with fibromyalgia
  - no response in 9 (3.5%)
  - partial response in 104 (41.9%)
  - complete response in 136 (54.5%)

- 2 Patients with reflex sympathetic dystrophy
  - no response in 1
  - partial response in 1

**Vulvar Vestibulitis: Beyond 2011**

**Research Directions**

- Genetic Basis
  - Further familial evaluation
  - Human genome project

- Mast cell management - linolenic acid
- Improved neuropharmaceutical agents
- Improved combined topical therapies
- Urinary symptomatology and oral heparinoids
Lichen Simplex Chronicus (LSC)

LSC: General Information

- End stage of itch-scratch-itch cycle in predisposed patients due to:
  - Irritants
  - Infections
  - VIN
- Patients often frustrated by long course of symptoms and having seen many physicians
- Recurrence is common
LSC: Diagnosis

- Patient reports intense pruritus with relief upon scratching
- Thick, lichenified skin – often reddened
- May exhibit erosions or fissuring
- Culture for yeast and bacteria

LSC – Classic Presentation

Usually, the skin abnormalities of lichen simplex chronicus (aka eczema, atopic dermatitis, neurodermatitis) are caused by rubbing or scratching, as can be seen from the rubbed and thickened skin in this woman.
**LSC: Treatment**

- Treat any underlying infection
- Remove potential irritants or allergens; stop all topicals, soaps, douches, etc.
- Sitz baths or compresses 1-2x/day for 10-15 minutes
- Mid-to-high potency topical corticosteroid
- Counsel patient about vulvar self-care measures to minimize risk of recurrence

**White Lesions**

- Dystrophy
  - Lichen sclerosus
  - Squamous cell hyperplasia
  - Mixed/other dermatoses
- Vitiligo
- Leucoderma
- Cancer in situ
**Classification of Vulvar Dystrophy (ISSVD - 1975)**

- Hyperplastic dystrophy
  - Without atypia
  - With atypia
- Lichen sclerosus
- Mixed dystrophy - lichen sclerosus with epithelial hyperplasia
  - Without atypia
  - With atypia

**Classification of Vulvar Dystrophy (ISSVD - 1987)**

- Squamous cell hyperplasia (formerly hyperplastic dystrophy)
- Lichen sclerosus
- Other dermatoses
Vulvar Dermatoses

Lichen Sclerosus (LS)
LS: General Information

- Etiology unknown, generally believed to be autoimmune
- Occurs on genital skin in about 80% of cases
- Females of any age can develop LS, including young children, toddlers and infants (as can males) but most symptomatic are post-menopausal women
- Childhood LS can resolve at puberty (children should be followed very carefully throughout adolescence – do not assume that no symptoms equals no disease)
- Sometimes improves during pregnancy (usually 2nd tri)
- Often misdiagnosed as yeast infections, herpes or vitiligo
- 2-5% risk of developing vulvar squamous cell carcinoma

LS: Diagnosis

- Pathognomonic sign is texture change – crinkling, occasionally looks waxy
- Punch biopsy typically used
  - in women with severely fragile skin or in children, treatment is sometimes initiated without a biopsy
- Histological findings:
  - hallmark is liquefaction degeneration of the basal cell layer with homogenization of collagen in the dermis (epidermis can be atrophic or thickened)
- Hypo-pigmentation – “butterfly” or “keyhole” appearance
- Pruritus, sometimes burning or pain
- Atrophy and increased risk of fissures
- In advanced or untreated cases: clitoral hood fuses; labia minora fused to majora; narrowing of the introitus; dyspareunia
LS – Classic Presentation

Severe lichen sclerosus is itchy and it can be identified by the white color and easy bruising and tearing when rubbed, obviously a cause of symptoms.

LS: Treatment

- Topical clobetasol propionate 0.05% 1-2x/day
  - Reduce frequency and/or potency when texture and/or symptoms normalize
- Testosterone and progesterone do not work better than petrolatum ointment (Vaseline) alone
- Some are beginning to prescribe topical tacrolimus with good results – research is needed
- Dilator and/or sex therapy may be helpful for women who experience dyspareunia
  - first treat the vulvar skin to help restore elasticity – and recommend using lubrication
- Counsel patient on vulvar self-care measures
- Skin grafting not recommended due to high rate of recurrence
Suggestions for instructing patients in applying topical treatments

Some topical treatments are very effective, however caution should be used in their application.

Give specific instructions for applying topical treatments for the vulva:

- **Amount of cream**
  - Squeeze correct amount of treatment sample on your own finger during office visit

- **Application site**
  - Some women will have never seen their vulva
  - Shade in or point to areas on a vulvar diagram to indicate correct application site
  - Have patient apply treatment during visit, using a mirror for clarity
Lichen Planus (LP)

LP: Diagnosis

- Differentiating LS & LP can be difficult; can also co-exist
- A biopsy is helpful in diagnosing LP but histological findings are sometimes non-specific
- May be associated with slightly increased risk of cancer
- Histological findings:
  - Hallmark is a dense chronic inflammatory infiltrate hugging and obscuring the basal cell layer with occasional necrotic keratinocytes
  - Classic Non-erosive Lichen Planus
    - white lacy or fern-like papules
  - Erosive Lichen Planus
    - Clearly demarcated red plaques on oral and/or genital membranes with white “lacy” edges
    - Erythematous lesions in the vestibule & up into vagina
    - Burning pain; dyspareunia
    - May resemble lichen sclerosus, particularly when late agglutination of architecture occurs
LP: Classic Presentation

Lichen planus with irregular white lines is classic, and the deep red areas are painful erosions.

LP: Subtle Presentation

Even subtle lichen planus can hurt, as it does in this woman who has mild white streakiness towards the posterior fourchette, and small posterior vestibular erosions.
LP: Treatment

Options include:
- Ultrapotent corticosteroids with careful follow-up for vulva; hydrocortisone foam for vagina
- Tacrolimus (be careful – absorbed from vagina)
- Hydroxychloroquine
- Anti metabolites
- Systemic retinoids
- Vaginal dilator therapy for women with introital stenosis and/or labial adhesions
**Dark Lesions**

- Lentigo
- Nevi
- Melanoma
- Ca-in-situ
- Seborrheic keratosis
Unifocal lentigo

Unifocal carcinoma in situ
Unifocal lentigo

Spreading melanoma (Courtesy Dr. F.J. Fleury)
Compound nevus

Junctional nevus
Intradermal nevus

Melanoma
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Ulcers

- Herpes
- Syphilis
- Behçet’s disease
- Crohn’s disease
- Hidradenitis
- Chancroid
- Granuloma inguinale
- Spider bite
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Mild herpetic ulcerations

Severe herpetic vulvitis
Localized recurrent herpes

Confluent herpes vesicles
Atypical localized herpes

Atypical large herpetic ulcers
Small Tumors

- Condylomata acuminata
- Molluscum contagiosum
- Epidermal cysts
- Angiomata
- Mucus cysts
- Acrochordon
- Hidradenoma
Large Tumors

- Bartholin duct obstruction
- Trauma
- Lymphogranuloma venereum
- Squamous cell carcinoma
Resources

- Benign Diseases of the Vulva & Vagina
  - Kaufman, Friedrich, Gardner

- Genital Dermatology – Lynch & Edwards

- Vulvar Disease – E. Friedrich