Vulvodynia
Causes and Management

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Professor, University of Michigan Health System
Ann Arbor, Michigan USA
Prague, September 2016

Disclosures
I have no financial relationships to disclose
Throughout time, numerous controversies in vulvodynia have existed...some remain
Learning Objectives
At the end of this presentation, the participant will:

• Understand the current classification system for vulvar pain (2015 Consensus Terminology and Classification of Persistent Vulvar Pain)
• Explore the various causes of vulvodynia
• Gain knowledge on the treatments utilized for localized and generalized vulvodynia

Written Information Available:

University of Michigan Center for Vulvar Diseases (Google)

Then, click on Information on Vulvar Diseases
University of Michigan Center for Vulvar Diseases

There are many reasons for seeking a vulvar disease specialist at the University of Michigan Center for Vulvar Diseases, treating is not only part of their mission. Our multidisciplinary approach at the center means we can provide women with total care, from cutting-edge treatment options to education and counseling to meet every individual's needs.

The Center for Vulvar Diseases was created in 1993 to better serve and treat women with diseases of the external genitalia. Our center is one of only a handful of clinics that specialize in treating these conditions. We focus on the multidisciplinary approach to help patients improve their health.

This team approach allows us to provide a higher intensity of care and expertise to women who have already demonstrated a resilient and chronic illness or an unresolved vulvar condition.

Many women experience different forms of vulvar pain, including vulvodynia. Vulvodynia is pain on the lips of the vulva or upon intercourse with a normal appearing vulva. It is a burning, stinging sensation. Some patients are unable to accept sexual penetration due to muscle spasm and tenderness. Other conditions associated with vulvar pain include:

- Lichen sclerosus or lichen planus—chronic inflammatory skin disorders
- Vulvar intraepithelial neoplasia—a precancerous condition, often associated with HPV, the human papilloma virus (HPV)
- Vulvar vestibulitis syndrome—a disease of the vestibule and vulva, with pain and discomfort in the vulva
- Bartholin's cysts—fluid filled cysts at the base of the vestibule

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SOGBA Argentina, NY, December, 2015

- Surgery for Vestibulodynia (PPT PDF)
- References - Surgery for Vestibulodynia (PDF)
- Vulvodynia (PPT PDF)
- Vulvodynia Handout (PDF)
- Clinical Aspects of HPV Infection (PPT PDF)

ASCCP, New Orleans, April, 2016

- Puzzling Cases (PPT PDF)
- Case Test (PPT PDF)
- Comparison of Diagnostic Testing for Trichomonas (PDF)
- Costs/Methods of Detecting T. Vaginalis (PDF)

ACOG, Washington DC, May, 2016

- Your Diagnosis Is (PPT PDF)
- Vulvar Diseases: What Do You Know? (PPT PDF)
- Vulvar Diseases: What Do You Know - Handout (Word PDF)
- Erosive and Ulcerative Diseases of the Vulva - Edwards (PPT PDF)

ACOG District XII, Orlando, August, 2016

- Update on Vulvar Dermatology (PPT PDF)

IMS Prague September, 2016

Vulvodynia Causes and Management
Definition of Vulvodynia

International Society for the Study of Vulvovaginal Disease (ISSVD)

Chronic discomfort
Burning
Stinging
Irritation
Rawnness

8.3% of women have vulvodynia

By age 40 years, 7-8% in Boston and Minneapolis/St. Paul reported vulvar pain consistent with vulvodynia.


**Diagnosis of Vulvodynia**

Define disease
- Cotton swab test
- Vulvoscopy?
- Duration of pain
Diagnosis of Vulvodynia

Define disease
   Cotton swab test
   Vulvoscopy?
   Duration of pain
Diagnosis of Vulvodynia

Define disease
- Cotton swab test
- Vulvoscopy?
- Duration of pain

Various Terms Utilized for Vulvar Pain Prior to 2003

- Essential vulvodynia
- Dysesthetic vulvodynia
- Vulvar vestibulitis syndrome
- Vulvar dyesthesia (generalized or localized)
- Provoked vulvar dyesthesia
- Spontaneous vulvar dyesthesia

CONTROVERSY!
2003 ISSVD Terminology
and Classification of Vulvar Pain
Salvador, Brazil

Vulvar pain related to a specific disorder

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

Vulvodynia

**Generalized**
- **Provoked** (sexual, nonsexual, or both)
- **Unprovoked**
- **Mixed** (provoked and unprovoked)

**Localized** (vestibulodynia, clitorodynia, hemivulvodynia, etc.)
- **Provoked** (sexual, nonsexual, or both)
- **Unprovoked**
- **Mixed** (provoked and unprovoked)
April 2015

2015 Consensus terminology and classification of persistent vulvar pain
Jacob Bornstein MD, MPA, Andrew Goldstein MD, and Deborah Coady MD
for the consensus vulvar pain terminology committee

From the International Society for the Study of Vulvovaginal Disease (ISSVD),
the International Society for the Study of Women’s Sexual Health (ISSWSH),
and the International Pelvic Pain Society (IPPS)

Support from the National Vulvodynia Association

2015 Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia

A. Vulvar pain caused by a specific disorder*
   • Infectious (eg, recurrent candidiasis, herpes)
   • Inflammatory (eg, lichen sclerosus, lichen planus, immunobullous disorders)
   • Neoplastic (eg, Paget disease, squamous cell carcinoma)
   • Neurologic (eg, postherpetic neuralgia, nerve compression or injury, neuroma)
   • Trauma (eg, female genital cutting, obstetric)
   • Iatrogenic (eg, postoperative, chemotherapy, radiation)
   • Hormonal deficiencies (eg, genitourinary syndrome of menopause [vulvovaginal atrophy], lactational amenorrhea)
B. Vulvodynia—Vulvar pain of at least 3 months' duration, without clear identifiable cause, which may have potential associated factors

The following are the descriptors:
   • Localized (eg, vestibulodynia, clitorodynia) or Generalized or Mixed (Localized and Generalized)
   • Provoked (eg, insertion, contact) or Spontaneous or Mixed (Provoked and Spontaneous)
   • Onset (primary or secondary)
   • Temporal pattern (intermittent, persistent, constant, immediate, delayed)

* Women may have both
2015 Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia

Appendix: Potential Factors Associated with Vulvodynia
• Comorbidities and other pain syndromes (e.g., painful bladder syndrome, fibromyalgia, irritable bowel syndrome, temporomandibular disorder; level of evidence 2)
• Genetics (level of evidence 2)
• Hormonal factors (e.g., pharmacologically induced; level of evidence 2)
• Inflammation (level of evidence 2)
• Musculoskeletal (e.g., pelvic muscle overactivity, myofascial, biomechanical; level of evidence 2)
• Neurologic mechanisms
  • Central (spine, brain; level of evidence 2)
  • Peripheral: neuroproliferation (level of evidence 2)
• Psychosocial factors (e.g., mood, interpersonal, coping, role, sexual function; level of evidence 2)
• Structural defects (e.g., perineal descent; level of evidence 3)

a The factors are ranked by alphabetical order.

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Etiologies

Topical review
Vulvodynia: Current state of the biological science

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1 Department of Anesthesiology/Division of Pain Management, University of Alabama at Birmingham School of Medicine, Birmingham, AL, USA
2 Department of Neurology, University of Alabama at Birmingham School of Medicine, Birmingham, AL, USA
3 Department of Obstetrics and Gynecology, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA
Theories on Etiologies

- Embryologic derivation
- HPV
- Oxalates
- Hormonal changes

- Chronic inflammation
- Altered immuno-inflammatory process/genetics
- Nerve pathways
Theories on Etiologies

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- **Hormonal changes**
- **Chronic inflammation**
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**Hormonal Changes**

**Controversy!**

Variation in pain occurs over the menstrual cycle

OCP use and vulvodynia

Variation in pain premenopause and postmenopause
Estrogen Receptor Expression

Study group showed a significant decrease in estrogen receptor expression, and 50% of the samples did not exhibit any receptor expression

Eva LJ, MacLean AB, Reid WM, Rolfe KJ, Perrett CW

Steroid receptor expression and morphology in provoked vestibulodynia

Ulrika Johannesson Karolinska Institutet,
Danderyd Hospital, Sweden
Co-authors; Lena Sahlin, Britt Masironi, Bo Blomgren,
Marita Hilliges, Eva Rylander, Nina Bohm-Starke
Conclusion

- Increased expression of ERα in the vulvar vestibular mucosa in patients with provoked vestibulodynia in the absence of an altered epithelial morphology
For women aged <50 years of age, OC use did not increase the risk of subsequent vulvodynia.

Polymorphisms of the Androgen Receptor Gene and Hormonal Contraceptive Induced Provoked Vestibulodynia Goldstein et al. 2014

- Women who developed vestibulodynia while taking combined hormonal contraceptives and a control group of women were tested for polymorphisms of the gene coding for the androgen receptor (AR) that is located on the X chromosome
- DNA from 30 women who developed vestibulodynia while taking CHCs and 17 control women were tested for the number of cytosine-adenine-guanine (CAG) trinucleotide repeats in the androgen receptor. Serum-free testosterone was tested in both groups.
Conclusion

- Women who developed vestibulodynia while taking CHCs are more likely to have longer CAG repeats in the androgen receptor than women who took the same type of CHC but did not develop vestibulodynia
- Risk of developing CHC-induced vestibulodynia may be due to lowered free testosterone combined with an inefficient androgen receptor that predisposes women to vestibular pain

Unprovoked Vestibular Burning in Late Estrogen-Deprived Menopause: A Case Series

Goetsch MF. JLGTD 2012; 16:442-446

- 7 menopausal women range 1-4 years of pain (1 patient on oral estradiol)
- 3 developed pain after aromatase inhibitor
- Utilized lidocaine, local estrogen to vestibule and physical therapy
Theories on Etiologies

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Vulvodynia: The Role of Inflammation in the Etiology of Localized Provoked Pain of the Vulvar Vestibule (Vestibulodynia)

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¹Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of California, Los Angeles, California
²Department of Obstetrics and Gynecology, David Geffen School of Medicine at UCLA, University of California, Los Angeles, California

Address for correspondence Andrea J. Rapkin, MD, Department of Obstetrics and Gynecology, David Geffen School of Medicine at UCLA, University of California, 10833 Le Conte Avenue, Room 27-139 CHS, Los Angeles, CA 90095-1740 (e-mail: arapkin@mednet.ucla.edu).
Mast Cells

- Bornstein et al. (2004) found significant increase in inflammatory infiltrate, number of mast cells and degranulated mast cells in vestibulitis patients (N=40) compared to normal controls (N=7, ages 18-48)
- Regauer et al. (2015) evaluated 35 patients with vulvodynia
  - Median age was 24 years (ranged from 18 to 70 years).
  - Control tissues obtained from autopsies (? number)
  - Only 20/35 vulvodynia specimens showed a T-lymphocyte dominant inflammatory infiltrate on HE-stained sections, but all showed mast cells. 4/35 biopsies showed <10 mast cells/mm², 15/35 specimens 40–60 mast cells/mm² and 16/35 specimens >60 mast cells/mm² (average 80/mm²). Control tissue contained typically <10 mast cells.

Vestibular Mast Cell Density in Vulvodynia: A Case-Controlled Study

- No difference in mast cell density in biopsies of the vestibule found between white cases and racially matched controls
- Black control women have a lower mast cell density compared with white control women

Papoutsis D, Haefner HK, Crum CP, Opipari AW, Reed BD. J Lower Genit Tract Dis 2016;20: 275-9
Theories on Etiologies

- Embryologic derivation
- HPV
- Oxalates
- Hormonal changes
- Chronic inflammation
- Altered immunoinflammatory process/genetics
- Nerve pathways

Genetics

- Inflammatory response Candida
  - Mannose binding lectin
  - NALP3 expressed in macrophages
- Neurotransmitters
  - Guanosine triphosphate cyclohydrolase (GCH1)
- G protein coupled-receptors
  - Melanocortin-1 receptor
- Neuroinflammatory (cytokines)
  - Interleukins (IL)
- MicroRNA
- New thoughts
  - Dectin 1
  - Familiality
Genetics

- Inflammatory response
  - Candida
    - Mannose binding lectin
    - NALP3 expressed in macrophages
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- New thoughts
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  - Familiality
Proposed neuroimmunological mechanism of the allodynia/hyperpathia of vulvodynia

**Potentially inciting factors:**
- Infections
- Irritants
- Toxins
- Medications
- Other

**Increased proinflammatory cytokines:**
- IL-1, IL-6, IL-8
- IFN-α
- TNF-α

**IL-12 and IL-18**

**Substance P**

**CGRP**

**Nerve growth factor increased**

**Mast cell accumulation**

**Distal nerve sprouting**

**Allodynia and hyperpathia**

**IL-4**

**Legend:**
- = stimulatory
- = inhibitory

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**Theories on Etiologies**

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Question 3

The nerve which supplies the major portion of the vulva is the
1. Ilioinguinal nerve
2. Genitofemoral nerve
3. Perineal nerve
4. Pudendal nerve

Pudendal Nerve

Originates from S2, S3, and S4 foramina
Vulvodynia Management

Evaluating Vulvodynia Patients
A Team Approach
Tender, or patient describes area touched as area of burning

Yeast culture negative or inadequate relief with antifungal rx

1. Vulvar care measures
2. Topical medications
3. Oral medications
4. Injections
5. Biofeedback/Physical therapy
6. Cognitive and behavioral therapy

Vulvar Care Measures

No soap on the vulva

Shower heads for rinsing and…
Cool Gel Packs

Replens
Astroglide
KY Liquid
Probe
Slippery stuff
Jo Premium
… etc.

Vaginal Lubricants
Topical Anesthetics

- 5% Lidocaine (Xylocaine®) ointment safe, effective short-term symptom relief for vestibulodynia (pre-intercourse)
  - Benzocaine (Vagisil®) not recommended; it is a sensitizing agent, causing rebound vasodilation and pain
- Doxepin (Zonalon®)
- Topical amitriptyline 2% with baclofen 2% in WWB (water washable base)- squirt ½ cc from syringe onto finger and apply to affected area WWB. Apply qhs with increase not to exceed tid
- Topical ketamine 2%, topical gabapentin 6%, topical baclofen 2% in WWB. Apply qhs with increase not to exceed tid

Oral Medications
Tricyclic Antidepressants

- Useful for neuropathic pain syndromes such as postherpetic neuralgia and vulvar dysesthesia
- Doses for pain management less than for depression
  - Tricyclics
  - SSRIs
  - SSNRI’s (venlafaxine, duloxetine)

Tricyclic Antidepressants

Amitriptyline or desipramine
  - Advise regarding rationale
  - Start at low dose two hours before bedtime and increase up to 150, until comfortable, or intolerable side effects
  - One drink of ETOH per day
  - Advise slow benefit
Tricyclic Medications

Adverse effects
- Drowsy (amitrip > desip) or
- Jittery (desip > amitrip), tachycardia
- Dry mouth, eyes
- Increased appetite
- Constipation

Other Antidepressants
- Venlafaxine (Effexor)
- Duloxetine (Cymbalta)
Anticonvulsants and Pain Control

The role of anticonvulsant drugs in the treatment of neuropathic pain is evolving and has been clearly demonstrated

- Gabapentin
- Pregabalin
- Topiramate
- Tiagabene
- Lamotrigine

Gabapentin

- 64% of 152 generalized vulvodynia patients improved by 80% in a retrospective chart review

Pregabalin

• Retrospective chart review of 28 women on pregabalin for vulvodynia.
  – 12 reported improvement averaging 62%
  – 10 discontinued due to AEs
  – 4 had no improvement
  – 2 with vestibulodynia had not tested their pain

Aranda J, Edwards L: presented at the 2007 ISSVD World Congress

Anticonvulsants and Pain Control

The role of anticonvulsant drugs in the treatment of neuropathic pain is evolving and has been clearly demonstrated

- Gabapentin
- Pregabalin
- Topiramate
- Tiagabene
- Lamotrigine
Oral Pain Medications

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  - (PATIENT'S DRUG INFORMATION System)
- Trade/Brand Drugs
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- Dosing Tools
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- Patient Literature

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Specific Point Tenderness

- Bupivacaine / triamcinolone acetonide injections
  - Bupivacaine (0.25% or 0.5%) and triamcinolone acetonide (Kenalog®)
  - Draw up triamcinolone acetonide (Kenalog®) first (40 mg/cc) (can use up to 40 mg steroid in single dose per month). CAUTION ON PERINEUM AND SMALL AREAS. 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
  - 50% efficacy

Nerve Blocks

- Pudendal
- Genitofemoral
- Ilioinguinal
- Ganglion impar
Pudendal Nerve Blocks

Originates from
S2, S3, and S4
foramina

Genitofemoral and Ilioinguinal
Nerve Blocks
Genitofemoral and Ilioinguinal Nerve Blocks

Ganglion Impar Block
Treatments for Vaginismus

Counseling

Topical lidocaine

Topical baclofen

Physical therapy

Dilators

Hypnosis
Surgical Treatment

Surgery
New Thoughts and Trends

Novel Therapeutic Approaches

Chemodenervation

Over 1900 reports of botulinum toxin for pain
  Minimizes vaginismus-relaxes levator ani muscles

Medline search August 29, 2016
Chemodenervation
Bulbocavernosus

Neuromodulation

- Peripheral subcutaneous stimulation
- Sacral nerve stimulator
  - Modulation of efferent signals to spinal cord
  - Refractory pain in distribution of specific nerve root (S3 or S4)
Acupuncture

Acupuncture Today 2001;2:1,16.

Hypnosis
www.asch.net

Report on hypnosis for vestibulodynia
## Newer Treatments/Less Commonly Used

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>Rejoice trial (Yuvexxy)</td>
<td>Enoxaparin injections</td>
</tr>
<tr>
<td>Milnacipran (fibromyalgia)</td>
<td>Passiflora incarnata attenuation (rats)</td>
</tr>
<tr>
<td>Leukotriene receptor antagonist</td>
<td>KTP and YAG laser rx</td>
</tr>
<tr>
<td>Topical nitroglycerin</td>
<td>Radiofrequency (pulsed)</td>
</tr>
<tr>
<td>Topical capsaicin</td>
<td></td>
</tr>
<tr>
<td>Fibroblast cream (Neogyn)</td>
<td>Motor cortex stimulation (central)</td>
</tr>
</tbody>
</table>

## The Vulvodynia Guideline


- A guideline for treating vulvodynia is described

www.jlgtd.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)
JLGTD

2013 Vulvodynia Guideline Update

Colleen K. Stockdale, MD
Herschel Lawson, MD

Journal of Lower Genital Tract Disease
2014 Apr;18(2):93-100

Vulvodynia Awareness Campaign
Office of Research on Women’s Health

http://orwh.od.nih.gov/health/vulvodynia.html
General Measures

Written material/handouts
- Patient education regarding the nature and prognosis of vulvodynia
- National Vulvodynia Association
  www.nva.org or 301-299-0775

Online teaching program on chronic vulvar pain http://learn.nva.org

Oceans of Lotions, Potions, and Notions
No “One Simple Cure”

The Human Dimension
Thank You