Disclosures

Hope Haefner, MD was previously on the advisory board of Merck Co., Inc.
Objectives

1. Identify clinical features of a spectrum of vulvovaginal diseases... some very unusual!
2. Establish therapeutic strategies for a variety of vulvovaginal diseases
Colposcopy
Clinical Pitfalls of Vulvar Colposcopy

- Not all patients require magnification or acetic acid
- Acetowhiteness is nonspecific
- Marked acetowhite changes in up to 65% of normal women
- Normal anatomic variants – such as vestibular micropapillae – often confused with HPV on colposcopy and histopathology
Colposcopic Techniques

- 3% to 5% acetic acid
- Soak initially for 3-5 minutes
- Use copious amounts
- Reapply often
- Avoid using in presence of breaks in epithelium or inflammation

Anesthesia
• 1% lidocaine (with or without epinephrine)
• Sodium bicarb
• 27-30 gauge needle to inject 1-3 cc's of anesthetic agent
• Inject subepidermally

Biopsy
• Keyes punch
  • 3-5 mm diameter dermatologic instruments (usually 4 mm)
• Fine suture (3.0 or 4.0 Vicryl Rapide) vs. Monsel's or silver nitrate
Cervical biopsy instruments that can also be used for vulvar biopsy
Make Your Selection

A

B

C

D
Your Diagnosis Is?

A. Candida albicans infection
B. Non albicans Candida infection
C. Gonorrhea
D. None of the above
An Unfortunate Patient with Rare Fungal Infection

- 55 y.o. female admitted for nausea, vomiting, diarrhea, and hyperbilirubinemia
- She had been hospitalized for about 3 weeks for complications after bone marrow transplant for AML
- Developed vulvar pain
Rhizopus
Rhizopus

- Mucormycosis (sometimes called zygomycosis) is a serious but rare fungal infection caused by a group of molds called mucormycetes
- Fungi live in soil and in association with decaying organic matter, such as leaves, compost piles, or rotten wood
- Examples of the types of fungi that most commonly cause mucormycosis are: *Rhizopus* species, *Mucor* species, *Cunninghamella bertholletiae*, *Apophysomyces* species, and *Lichtheimia* (formerly *Absidia*) species

Rhizopus

- 13/1500 transplant patients developed this infection in study from 1993
- Surgical resection for cure
- Antifungals-liposomal amphotericin B
- Dressing changes/amphotericin B
80 y.o. woman presents with a 2 year history of vulvar itching and irritation
• Vulvar biopsy negative other than fungal elements
• Triamcinolone 0.1%, 2% lidocaine gel, nystatin, clobetasol 0.5%, Vagisil, diphenhydramine, hydrocortisone, and a oral steroids

Past Medical History
• Significant for hypertension, angina, asthma, thyroid disease and reflux
Itch Scratch Regimen

University of Michigan Center for Vulvar Diseases
Website
(steroids, antibiotics, night-time sedation, cool gel packs, cotton gloves at night, no trauma to vulva, tap water soaks/vaseline...)
Information Regarding Vulvar Diseases

Information regarding Vulvar Diseases

- Patient Education Brochure: This booklet describes various vulvar conditions as outlined below
  - Diseases of the Vulva
  - Some suggested vulvar pain and itching measures
  - Vulvar Self Exam
  - Yeast Infections
  - Lichen Sclerosus
  - Lichen Planus
  - Vestibulitis
  - Squamous Cell Hyperplasia
  - Vulvar Infundibulovaginal Fibrosis
  - Paget's Disease of the Vulva
  - Sexuality and Pain
- Center for Vulvar Diseases (In-Patient Questionnaire)
- Proctology Information (PDF)
- Vulvar Care Tips (PDF)
- Deep Laser Intracavity (PDF)
- Hymenectomy (PDF)
- Hymenectomy VII (PDF) • Updated 10/2015
- Hymenectomy Supportive • A Focus on Surgical Care • Presentation to Recovery (PDF)
- Hymenectomy Videos
- Advice for Hymenectomy (PDF) • Updated 10/2015
- Lichen Planus and Vulva (PDF)
- Tips and tricks of Safe Tricks (PDF)
- Tips and Tricks (PDF)
- Researchy (PDF) • Updated 10/2015
- Protocol for Vulvar Infections (PDF)
- Testicular Infection (PDF)
- EVDI UserGuide (PDF) (Copyright EVDI 2015)

Published papers:
- The Whipple Procedure (PDF)

Severe Itch Scratch Itch Cycle Tips

1. Night time deep sleep with Elavil 25 mg po qhs 2 hr before bedtime; if needed can increase by 10 to 25 mg increments weekly, not to exceed 150 mg po qhs. Can also use neurontin (see protocol). Can also use atarax.

2. Medrol dose pack vs prednisone 40 mg po q am x 5 then 20 mg po q am x 10. If those fail consider triamcinolone 1 mg/kg up to 80 mg IM using a 1.5 inch needle in buttock (gluteus muscle); repeat in 1 to 2 months if necessary, up to 3 times. There are rarely any problems with depression or emotional instability. It does take 48 hours to start working and it can cause irregular periods with spotting for the next month. The injection must be given into the muscle.
Your Thoughts on Black Discoloration?
Recently Diagnosed with Idiopathic Thrombocytopenia (ITP)

• Unusual presentation is all related to her ITP condition

Puzzling Prepuce/Clitoris Cases

A 39-year-old woman was referred for consultation for a vulvar mass which has been bothering her for several years. It had been aspirated a few years ago but reoccurred. She complains of pain to the slightest touch.
Your Diagnosis Is?

A. Clitoromegaly
B. Prepuce cyst
C. Lymphedema
D. Hidradenitis suppurativa

Which of the Following Does NOT Cause Prepuce Cysts?

A. Female genital cutting
B. Lichen sclerosus
C. Steroid overuse
D. Congenital malformations
How Many Women Around the World Have had Female Genital Cutting?

A. 100,000-200,000  
B. 1-2 million  
C. 50-70 million  
D. 100-140 million
A 69-year-old woman is referred to your clinic, presenting with a mass (3.6 cm x 2.5 cm) between her clitoris and urethra. She complains of some vulvar pain which interferes with horseback riding. The mass was aspirated by her gynecologist, but it reformed. The histology showed only proteinaceous debris.
• Her medical history is positive for cervical dysplasia, and a hysterectomy in 2005
• Pelvic/vulvar CT and MRI were done showing a cyst 3.6 x 2.8 x 2.5 cm

• On physical evaluation the mass is fixed to the inferior aspect of her pubic symphysis
• She was seen by an orthopedic surgeon who did not feel comfortable treating her
• What is your diagnosis?
• What would you suggest?
Pathology report – the histologic findings are not specific, the tissue is indicative of a fibrotic cyst wall, most likely an inclusion cyst adherent to the bone.
Healing Aphthous Ulcer and ?
A 58-year-old woman is referred to your clinic for inability to have intercourse and difficulty with urination.
What Do You Think Her Diagnosis Is?
What Are Your Recommendations?
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Dosing</th>
<th>Timing</th>
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<tbody>
<tr>
<td>Intravaginal corticosteroids</td>
<td></td>
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</tr>
<tr>
<td>Hydrocortisone 100 mg/g in emollient cream base</td>
<td>300 mg (3 g) per vagina OHS</td>
<td>First week postoperatively</td>
</tr>
<tr>
<td></td>
<td>400 mg (4 g) per vagina OHS</td>
<td>Second week postoperatively</td>
</tr>
<tr>
<td></td>
<td>500 mg (5 g) per vagina OHS</td>
<td>Third week postoperatively</td>
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<tr>
<td></td>
<td>400 mg (4 g) per vagina OHS</td>
<td>Fourth week postoperatively</td>
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<tr>
<td></td>
<td>300 mg (3 g) per vagina OHS</td>
<td>Fifth week postoperatively</td>
</tr>
<tr>
<td></td>
<td>200 mg (2 g) per vagina OHS</td>
<td>Sixth week postoperatively</td>
</tr>
<tr>
<td></td>
<td>100 mg (1 g) per vagina OHS</td>
<td>Starting week 7, indefinitely*</td>
</tr>
</tbody>
</table>

Dilators**

| Largest size tolerated | GHS for 20–25 min for 6 mo (with silicone lubricant), then consider daily dilation with a water-soluble lubricant in the shower (dilator placed into vagina and immediately removed to prevent adhesion formation) |

* Depending on disease activity, patients may eventually decrease to 50 mg hydrocortisone suppositories nightly per vagina if tolerated and then 25 mg hydrocortisone suppositories nightly per vagina. The long-term goal is to utilize hydrocortisone suppositories 2–3 times per week. * Any medical-grade dilator set is acceptable. ** Enriched surgical management of vulvomycelial agglutination due to lichen planus. Am J Obstet Gynecol 2016.
15 year-old girl who had sudden onset of dysuria and severe vulvar burning
    She was feeling tired
    She has a cough, a low grade fever and malaise.
Her doctor diagnosed her with acute HSV and started her on acyclovir and sent her to be seen.
    This is day 3
Your Diagnosis Is?

A. Aphthous Ulcers
B. Atypical Herpes Simplex Virus
C. Drug Rash
D. Trauma - Abuse?

The most common cause of acute vulvar ulcers in the world is:

A. Behcet’s disease
B. Syphilis
C. Aphthous ulcers
D. Herpes simplex virus in the immunosuppressed
Vulvar Aphthous Ulcers

Canker sores on the vulva
Acute painful ulcer(s) of sudden onset
Common as acute reactive ulcers
in younger patients - often missed

Synonyms:
- Ulcus vulvae acutum
- Lipschütz ulcers
- Reactive nonsexually related acute genital ulcers*
Vulvar Aphthous Ulcers

“Canker Sores” on the Vulva

- Average age is 14 (9-19) yrs
- Sudden onset
- Usually multiple, painful, well demarcated punched-out ulcers
- Size: most <1cm; can be 1-3 cm
- Prodrome - flu-like with mild fever, headache, malaise
- Duration 1-3 weeks, can last months
- One episode, less common recurrent
- Past history of oral aphthae – canker sores
- Rarely Behcet’s in North America
Aphthous ulcers can be associated with all the following conditions except:

A. Hepatitis C  
B. Epstein Barr Virus  
C. Crohn’s Disease  
D. Mycoplasma Pneumonia

APHTHAE - Associations

**Acute** (more common) - can recur  
- usually a prodrome - fever, headache, malaise, GI upset  
- EBV, Mycoplasma pneumoniae, viral upper respiratory infection (parvovirus, influenza, paramyxovirus) or gastroenteritis (salmonella), toxoplasmosis gondii, Strep, mumps, CMV, Lyme

**Chronic or Recurrent / Complex** (recurrent oral and genital aphthae)  
Inflammatory Bowel disease - Crohn’s, Ulcerative colitis, Celiac disease  
Behcet’s disease  
Medications - cytotoxic, NSAIDs  
Myeloproliferative disease, cyclic neutropenia, lymphopenia  
HIV

**Syndromes** – rare  
Sweet’s Syndrome  
PFAPA – periodic fever, aphthae, pharyngitis, adenitis  
MAGIC – mouth and genital ulcers with inflamed cartilage
Evaluation Vulvar Aphthae

Thorough history and physical – eye, oral, genital
Always test for HSV

Lab tests to consider –
  - CBC, diff
  - Serology for HSV, HIV, EBV, syphilis, CMV, *Mycoplasma pneumoniae*
  - Influenza – swab PCR
  - HSV - swab for PCR - **ALWAYS R / O HSV**
  - For Strep -throat swab and antistreptolysin O titer

No Biopsy for children

Gi investigations –
for inflammatory bowel disease and celiac disease

Diagnosis of exclusion - etiology often not found

The best treatment for acute painful aphthous ulcers is:

A. Cyclosporine
B. Prednisone
C. Clobetasol ointment 0.05%
D. Clindamycin oral
Vulvar Aphthae - Therapy

- **Pain control** - topical, systemic
- **Prednisone** 40 - 60 mg each morning until pain resolves (5 - 7 days, then ½ dose 5 - 7 days)
  - ultrapotent corticosteroid
- **Educate** - Most often a one-time event, can recur
  - **If not controlled:**
    - Intralesional triamcinolone 5-10 mg/ml
  - **doxycycline 50-100 mg bid**
  - **colchicine** 0.6 mg bid-tid if tolerated
  - **dapsone** 50-150 mg per day
  - **dapsone + colchicine**
  - **pentoxyfylline** 400 mg tid
  - **cyclosporine** 100 mg 1-3/d
  - **thalidomide** 100-150 mg per day

Ulcer iphone app
www.issvd.org

A Decision-Support Tool & Novel Mobile Application
A 63 year old woman is referred for consultation for vulvar pain, irritation and a non healing lesion. She’s known to have lichen sclerosus, treated with both topical and IM steroids, tacrolimus, estrogen cream and various other medications.

She’s been also diagnosed with GI Crohn’s disease, treated with Imuran.
She had biopsies taken several times, the most recent is 5 months prior to her visit to see you. Biopsies from the vestibule, lower vaginal wall and right labium minus revealed spongiosis with hyperkeratosis and hypergranulosis with squamous atypia and underlying chronic inflammation. Several areas appeared reactive and were felt to represent a chronic eczematous process or cutaneous reaction to the underlying Crohn's
Part 1
Would you consider a biopsy/ies?

Yes
No
Part 2
As you are taking her history, she states she only urinates twice a day secondary to the pain she has. When you touch the vesibule it is hard and firm. Would you take a biopsy/ies?

Yes
No
Histopathology reveals:

1. Adenocarcinoma
2. Lichen planus with VIN
3. Squamous cell carcinoma
4. Lichen sclerosus with VIN

Invasive squamous cell carcinoma; depth of invasion is at least 4mm. Carcinoma extends to multiple specimen edges on all three biopsies.
2, 4 mm punch biopsies
MM 1.3 mm in depth

Malignant Melanoma
Vulvar Malignant Melanoma (MM)

- 5% vulvar cancer are MM
- Found in older women > 65 years
- Site – 75% on vulvar mucosa
- Amelanotic 25%, multifocal 20%
- Atypical color – with variably red, white, or blue color: amelanotic MM pink or red
- A late diagnosis

Take home messages:
- Don’t forget to listen to your patients and touch
- Don’t hesitate to re-biopsy if the results are not consistent with the whole picture
51 y.o. G0 presents for evaluation of possible lichen sclerosus
• Biopsy performed at outside facility- lichen sclerosus vs. amyloidosis, favor lichen sclerosus
• September 2015 she noticed some vulvar discomfort
  Initially intermittent … now continuous
IBD Panel

Comments: IBD sgi Diagnostic

TEST RESULT:

**Pattern Consistent with IBD**  Ulcerative Colitis

SEROLOGY RESULT

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<tr>
<th>Assay</th>
<th>Results</th>
<th>Reference</th>
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<tbody>
<tr>
<td>ASCA IgA ELISA</td>
<td>21.3 EU/ml</td>
<td>&lt;8.5 EU/ml</td>
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<tr>
<td>ASCA IgG ELISA</td>
<td>17.2 EU/ml</td>
<td>&lt;17.8 EU/ml</td>
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<tr>
<td>Anti-OmpC IgA ELISA</td>
<td>&lt;3.1 EU/ml</td>
<td>&lt;10.9 EU/ml</td>
</tr>
<tr>
<td>Anti-CBir1 IgG ELISA</td>
<td>15.1 EU/ml</td>
<td>&lt;78.4 EU/ml</td>
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<tr>
<td>Anti-A4-Fla2 IgG ELISA</td>
<td>27.3 EU/ml</td>
<td>&lt;44.8 EU/ml</td>
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<tr>
<td>Anti-FlaX IgG ELISA</td>
<td>38.2 EU/ml</td>
<td>&lt;33.4 EU/ml</td>
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<tr>
<td>IBD Specific pANCA</td>
<td>&gt;100.0 EU/ml</td>
<td>&lt;19.8 EU/ml</td>
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<td>Autoantibody ELISA</td>
<td>Not Detected</td>
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<td>IFA Perinuclear Pattern</td>
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<td>DNase Sensitivity</td>
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GENETIC RESULTS

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<tr>
<td>ECM1</td>
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<td>NKX2-3</td>
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<tr>
<td>STAT3</td>
<td>Variant Detected - Variant Detected: SNP (rs744166) Heterozygous rs744166(A;G) rs744166(G;G)</td>
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INFLAMMATION RESULTS

<table>
<thead>
<tr>
<th>Assay</th>
<th>Results</th>
<th>Reference</th>
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<tbody>
<tr>
<td>ICAM-1</td>
<td>0.32 ug/ml</td>
<td>&lt;0.54 ug/ml</td>
</tr>
<tr>
<td>VCAM-1</td>
<td>0.55 ug/ml</td>
<td>&lt;0.68 ug/ml</td>
</tr>
<tr>
<td>VEGF</td>
<td>155 pg/ml</td>
<td>&lt;345 pg/ml</td>
</tr>
<tr>
<td>CRP</td>
<td>2.6 mg/L</td>
<td>&lt;13.2 mg/L</td>
</tr>
<tr>
<td>SAA</td>
<td>7.4 mg/L</td>
<td>&lt;10.9 mg/L</td>
</tr>
</tbody>
</table>
Colonoscopy Negative

• What to do?

A 29 y.o. G3P3 presents with vulvar irritation
What is your diagnosis?

- Candidiasis
- Bacterial vaginosis
- Group B streptococcus
- Desquamative inflammatory vaginitis

Have you even heard of DIV?

- Yes
- No
Atrophic Vaginitis

Desquamative Inflammatory Vaginitis

Rule out Trichomonas

D. Birenbaum MD collection
Desquamative Inflammatory Vaginitis (DIV)

- Occurs in 8% of women presenting to a specialty clinic with chronic vaginitis symptoms
- More frequent in Caucasians
- Peak occurrence in perimenopause
- **Diagnosis of exclusion**

Rule Out Lichen Planus
What other conditions does DIV have a similar microscopic appearance to?
Conditions Associated with Inflammatory Vulvovaginitis

- Atrophic vaginitis
- Erosive lichen planus
- Pemphigus vulgaris
- Behçet’s disease
- Collagen vascular diseases
- Traumatic
  - Foreign body, vesicovaginal fistulae
- Allergic vaginitis
- Chemical vaginitis
- Infection
  - Group A Streptococcus, Trichomonas, Cervicitis
  - Degenerating leiomyoma or endometrial polyp
- Idiopathic

DIV
Therapy Options Clindamycin
(Adapted from Reichman and Sobel 2014)

Clindamycin 2% cream 5(g)
One applicator intravaginally qhs x 3 weeks (consider 2 x per week x 2 months)
  Longer suppression time may be required

Clindamycin 200 mg vaginal suppository qhs x 3 weeks
(consider 2 x per week x 2 months)
  Longer suppression time may be required
DIV

Therapy Options Clindamycin
(Adapted from Reichman and Sobel 2014)

Intravaginal hydrocortisone suppositories 25 mg intravaginal bid for 3 weeks (consider 3 x per week x 2 months)
   Longer suppression may be required

Intravaginal hydrocortisone cream 300 to 500 mg intravaginal qhs for 3 weeks (consider 2 x per week x 2 months for maintenance therapy, with gradual dose reduction if possible)

DIV

Other Options

Combine clindamycin cream and hydrocortisone suppositories

Compound a high dose intravaginal corticosteroid and 2% clindamycin
   Hydrocortisone 100 mg/gram in clindamycin in 2% emollient cream base. Insert 5 gram (applicator full) per vagina every other night x 14 doses. This needs to be made at a compounding pharmacy.
DIV Other Options

If not working, reconsider the diagnosis!
(has estrogen been addressed?)

• May need to add estrogen


28 y.o. G4 P0 EAB 4 with vulvar, axillary disease. She has used Yasmin and this has not helped.

GYN Hx

• Positive trichomonas
• HIV negative
• Stage 3 vulvar Hidradenitis c active left axillary hidradenitis s/p resections
Hurley’s Criteria for HS Staging

**Stage I:** abscess formation, single or multiple, without sinus tracts and cicatrization/scarring.

**Stage II:** recurrent abscesses with sinus tracts and scarring, single or multiple, widely separated lesions.

**Stage III:** diffuse or almost diffuse involvement, or multiple interconnected tracts and abscesses across the entire area.

**Other PMH:**
- Negative
- Her past surgical history is significant for the multiple excisions of boils on armpits and buttock
- She has never undergone an extensive resection of the vulva and buttock with skin grafting
  - Tracts have just been I&Ded or single tracts excised without removal of disease in toto
• Hepatitis testing nonreactive A, B, C
• 1-24-14 IBD panel
  – Pattern consistent with IBD Crohn’s Disease

• 2-24-14 Colonoscopy
• Diagnosis: A-C. Terminal ileum, right and left colon, biopsies: No significant abnormality.
What are your recommendations?

- Derm recommended initiating Remicade infusions at 5 mg/kg (at 114 kg, rounded to nearest 100 mg, this is a dose of 600 mg per infusion). Infusions to occur at 0, 2, 6, and 8 week intervals followed by every 8 weeks thereafter.
- Derm recommended initiating concomitant methotrexate (goal dose of 7.5 mg weekly) in an effort to prevent antibody formation against the chimeric Remicade. Folic acid to be taken on non-methotrexate days.
- NOW MAY CONSIDER HUMIRA
• In the interim, recommend wash to affected areas daily
  - Erythromycin solution daily to BID to affected areas as well
  - Continue Ceftin
  - Will likely transition to doxycycline 100 mg po BID to be used simultaneously with the above systemic and topical agents
4 mos post op grafts

2 years after surgery
Extensive Hidradenitis vs. Crohn’s

Recent Admission 2 Years Later
Recommendations if medical management fails-with the potential that this may be Crohn’s?
When patients do not respond to therapy
  – Reconsider the diagnosis
  – Check for infection - fungal, bacterial, HSV
  – Consider contact dermatitis to a medication, over washing, etc.
  – Evaluate for pre-cancer or cancer
If in Doubt, Cut it Out