VULVOVAGINAL DISEASE INFORMATION

Hope Haefner, M.D.
Professor of Obstetrics and Gynecology
Co-Director, The University of Michigan Center for Vulvar Diseases
Michigan Medicine

Handout developed in conjunction with:

Lynette J. Margesson, M.D.
Assistant Professor of Obstetrics and Gynecology and Medicine (Dermatology)
Dartmouth Medical School

This handout and additional information available at

Disclosures:

Hope Haefner, MD is on the Advisory Board of Prestige, Inc.

Lynette Margesson, MD has no relevant financial relationships with any commercial interest relative to the subject of this lecture.

Handout available at:

https://medicine.umich.edu/dept/obgyn/patient-care-services/womens-health-library/center-vulvar-diseases/resources-providers
or search Google for Resources for Providers University of Michigan

Revised 3-26-2019
A variety of dermatologic conditions affect the vulva and the vagina. It is important to become familiar with the appearances and treatments of the numerous vulvovaginal conditions that you may see in your patients.

### Nonneoplastic Epithelial Disorders

<table>
<thead>
<tr>
<th>1975-1986</th>
<th>1987-present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichen sclerosus et atrophicus</td>
<td>Lichen sclerosus</td>
</tr>
<tr>
<td>Hyperplastic dystrophy</td>
<td>Squamous cell hyperplasia/lichen simplex chronicus</td>
</tr>
<tr>
<td>Mixed dystrophy</td>
<td>Other dermatoses</td>
</tr>
</tbody>
</table>

#### Lichen sclerosus

Lichen Sclerosus – is chronic, autoimmune disease affecting the genital skin causing whiteness, tissue thinning and scarring. It is the most common chronic vulvar condition.

Histology - blunting or loss of rete ridges, hyperkeratosis and loss of melanocytes are seen with a zone of pallor and often a dense interstitial lymphocytic infiltrate.

Pathophysiology: Unknown. Various genetic, autoimmune, infectious and local factors are implicated. The cause is probably multifactorial with a genetic, environmental and possibly infectious input. Often associated with other autoimmune diseases. Thyroid disease is the most common. It can be associated with psoriasis and less commonly lichen planus, morphea, vitiligo, pernicious anemia, inflammatory bowel disease and diabetes. Familial cases have been reported.

Age of onset - middle age (about 40 years – perimenopause) but range is from less than one year to > 80 years

Prevalence: 1:300 to 1:1000

Symptoms - Pruritus is present in up to 90% of cases and it can be severe and intolerable. Scratching causes secondary changes and open areas that cause dysuria, burning and dyspareunia. Scarring leads to dyspareunia, and at times, apareunia. Lichen sclerosus may be asymptomatic and be associated with asymptomatic vulvar scarring.
Physical exam – Scattered or confluent papules forming plaques of ivory white with cellophane-like sheen on the surface. Found anywhere on the vulva from the clitoris and periclitorally to the gluteal cleft. The involvement may be patchy or generalized in various patterns, classically a “figure-of-eight”. It can involve any cutaneous surface but most commonly is found on the vulva in women. Extragenital disease occurs in 15% of patients. LS typically does not involve the vagina. Rarely, it is in the mouth.

Secondary changes - excoriations, purpura, erosions, thickening (lichenification) crusting, and scarring, ranging from loss of labia or burying of the clitoris to loss of all normal vulvar structures.

Differential diagnosis - sexual abuse in children, vitiligo, lichen simplex chronicus, lichen planus, cicatricial pemphigoid, psoriasis

Cancer risk - about 4-5% develop associated SCC
Treatment: Chronic treatment needed for best long term control. Long term treatment decreases risk of cancer.

- Biopsy to confirm diagnosis if needed – (however, not in children)
- Photodocument as is possible
- Educate the patient
- Stop irritants
- Recommend cool, ventilated clothing
- Topical superpotent steroids (various regimens exist)

A variety of topical steroid regimens exist.

1. Clobetasol propionate or halobetasol 0.05% ointment qd to bid for 8-12 weeks – until tissue is as normal as possible – not just for symptom control. Severity will indicate the strength of topical steroid needed long term. If doing well, decrease application to M-W-F or 1-2 times a week. Consider a milder steroid like mometasone 0.1% ointment.

2. Clobetasol propionate 0.05% ointment bid x 1 month, then qhs x 2 months, then decrease to a mid dose topical steroid, such as triamcinolone acetonide 0.1% ointment nightly, with decrease over time to triamcinolone acetonide 0.025% ointment nightly when possible.

Follow up at 6-12 weeks then regularly at 6-12 month intervals

Duration of treatment: lifelong 1 - 7d / week NOTE: LS can be symptom free with ongoing scarring.

Treat associated Candida or secondary bacterial infection
Stop scratching as this keeps LS active. Give 10 mg of hydroxyzine or doxepin at 6 to 7 PM to stop nightly scratching. Scratching flares and spreads LS. (See Lichen Simplex Chronicus below)

For thick lichen sclerosus consider intralesional steroid (triamcinolone 3.3 to 10 mg/mL into thickening area)*. The dose is dependent on the location and thickness of the skin
that is being injected. This can be repeated monthly for 2-3 months. Do not inject high steroid doses into thin skin or in small areas because the tissue can slough.
If constantly scratching use oral prednisone using a 15 day to 3 week taper or IM triamcinolone 1 mg/kg up to 80 mg/dose**. Never give over 80 mg of triamcinolone acetonide IM per month. This can be repeated once a month for 3 months with a maximum of 4 doses a year.

*To clarify the intralesional steroid and intramuscular steroid use for all conditions mentioned in this handout:
For intralesional steroid, dependent on the size of the lesion, the dilution of the triamcinolone 10 mg per mL (Kenalog 10®) will vary. For areas of thin skin use lower doses 3.3 mg per mL. Dilute triamcinolone 10 mg/mL 1 part with 2 parts of saline for injection = 3.3 mg/mL. For thicker areas use higher doses intralesionally (5 up to 10 mg per mL). Never give more than 40 mg of triamcinolone subcutaneously over the entire vulva at one time. These intralesional injections can be repeated monthly for 2 to 3 months.

**For intramuscular steroid use, use triamcinolone 40 mg per mL (Kenalog® 40). Inject deep into muscle IM 1 mg per kg, not to exceed 80 mg in one injection. This can be repeated monthly for up to 4 doses a year.

Add topical estrogen 3-5 days / week to assess compliance with lifelong treatment as indicated to improve barrier function.

Tacrolimus 0.1% ointment and pimecrolimus 1% cream have been used for the treatment of vulvar lichen sclerosus. Burning may occur with these medications.

Tazorac 0.1% gel (can also use 0.05% or 0.1% cream for lower strength) may be used for lichen sclerosis when the skin is very thick or unresponsive to topical steroids. Apply to skin qhs with gradual decrease to two to three times a week.
Acitretin (Soriatane) is a retinoid that may be used for lichen sclerosus unresponsive to topical steroids (and in some cases lichen planus). It is most beneficial for thickened skin. Take 10 mg every 1-2 days for a dose of 30-70 mg per week. It must be taken with fatty food. The patients must not become pregnant, as it is teratogenic like isotretinoin. (expensive, but less costly in Canada).
Alternate treatments to consider – hydroxychloroquine 200 mg bid, methotrexate 10-15 mg / week subcutaneous or oral plus folate 2 mg / d, cyclosporine 4 – 5 mg / kg / d

Surgery is done on occasion to improve function or for scarring.

In all patients with lichen sclerosus:
Arrange follow-up always – indefinitely.
Regular follow-up is needed to make sure there is ongoing treatment because there is an increased risk of developing squamous cell carcinoma (SCC) (<5 % in women). If not responding to treatment - look for concurrent conditions and biopsy and rebiopsy, as needed.
Note – LS involves the vulva not the vagina unless prolapse. Scarring is not reversible by any medical therapy.

Lichen sclerosis affects children in 7-10% LS cases. It usually starts with itching and constipation. Treatment is the same but compliance with long term therapy can be a challenge.

**LICHEN SIMPLEX CHRONICUS (LSC )**

**Synonyms:** Squamous cell hyperplasia, neurodermatitis, pruritus vulvae, hyperplastic dystrophy

“LSC” – The end stage of the itch – scratch – itch cycle. It is usually part of the atopic dermatitis (eczema) spectrum. It can be associated with underlying, secondarily scratched and thickened psoriasis or contact dermatitis or the end stage of several itchy vulvar conditions (e.g. LS). Scratching “feels good” especially for patients with atopic dermatitis (patients with a background of allergies, eczema, hay fever or asthma). Stress makes all of this worse.

**Causes of LSC:**

- **Infection:** Candida and dermatophytosis
- **Dermatoses:** Atopic dermatitis, Psoriasis
- **Lichen Sclerosis**
- **Lichen Planus**
- **Metabolic:** Diabetes and iron deficiency anemia
- **Neoplasia:** Vulvar intraepithelial neoplasia

The most important causes are atopic dermatitis, contact dermatitis or both. Less common causes – psoriasis, LS

Pathophysiology – in this condition there is an altered skin barrier with varying combination of allergens, irritants and skin pathogens that result in a changed immunoregulatory process. Stress further alters the skin barrier function, making all of this worse. This condition is defined by relentless pruritus. These patients scratch in their sleep ruining the effectiveness of their daytime treatments. The chronic scratching causes the skin to thicken and feel firm.

**Clinical Presentation:**

- Relentless pruritus
- Chronic – years of “chronic itch”
- Worse with heat, stress, menstruation
- “Nothing helps”
- Marked lichenification

- Pigmentation changes
- Unilateral or bilateral
- Hair loss from scratching
- Excoriations + crusts
- Diagnosis – clinical biopsy may be needed

Note: Scratching makes erosions with serosanguinous crusts; repeated rubbing causes skin thickening (lichenification). In LSC, you can see both erosions and lichenification.

**Treatment:**
Rule out other conditions
Stop all irritants
Consider Patch testing looking for an allergen
Stop itch/scratch/itch cycles
Topical superpotent steroids, halobetasol or clobetasol 0.05% ointment, bid for two weeks, qhs for two weeks, then M-W-F for two weeks. (For severe disease, a longer duration of a mid dose topical steroid may be required.)
Oral steroids may be required for a short duration (dose varies dependent on disease severity; consider prednisone 40 mg po q am x 5, then 20 mg po q am x 10, however a longer taper may be required)
IM triamcinolone 1 mg/kg (up to 80 mg total) can be used instead of prednisone for severe, itchy or extensive LSC. Repeat is seldom necessary. If repeat is necessary, it can be repeated monthly x 3 total doses.
Intralesional triamcinolone can be used to thin the thick / lichenified skin as for LS above.
Treat infections, bacterial and yeast
- Cefadroxil 500 mg bid for 7 days
- Fluconazole 150 mg po q week x 2
Sedate
- Doxepin or hydroxyzine 10 to 75 mg qhs for nighttime itching
- Citalopram or fluoxetine or sertraline in the morning for daytime itching
- Amitriptyline is also used at times for sedation (25 mg po qhs; can increase to 50 mg po qhs) in patients with severe itch scratch cycle. It puts the patient in a deeper sleep cycle than the other sedation agents listed above. Do not combine amitriptyline with the other sedation agents above. Give early in evening so not sleepy in morning (6 - 8PM). Caution for use in the elderly population. Check for other drug interactions.
Sitz baths or cold soaks
White cotton gloves at night

Note: If skin is very raw the topical steroids will burn. Start with plain Vaseline, oral antibiotics, anti-yeast medication and nighttime sedation for 2-3 days, then start the topicals.
LSC reoccurs due to sensitive skin in the area so it will need repeated management.

LOOK FOR MORE THAN ONE CAUSE OR A COMBINATION OF CAUSES as it is not uncommon to have psoriasis, contact dermatitis and lichen simplex chronicus in the same patient.

Protocol/Patient handout

Severe Itch Scratch Itch Cycle Tips

1. Night time deep sleep with Elavil 25 mg po qhs 2 hr before bedtime (check for medication interactions, do not use in elderly; only one drink of alcohol per night); if needed can increase by 10 to 25 mg increments weekly, not to exceed 150 mg po qhs. Another option is to use hydroxyzine 25 to 50 mg qhs. Can also use neurontin starting at 300 mg with gradual increase. Start at 300 mg daily by mouth for 3 days then 300 mg po bid for 3 days, then 300 mg po tid. It
can be increased gradually by 300 mg weekly, not to exceed 1200 mg po tid.

2. Prednisone 40 mg po q am x 5 then 20 mg po q am x 10. If those fail consider a longer oral steroid taper. May require 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. Use steroids with caution in diabetics.

3. Cefadroxil 500 mg po bid x 10 days (to treat secondary inflammation)

4. Do a yeast culture, identify species. If positive, and patient on Elavil, use topical antifungals rather than amitriptyline.

5. Cotton gloves at night

6. Nightgown without underwear versus cotton pajama pants c string

7. Tap water soaks in tepid water after bath, vaseline or other white hand cream that does not pour, such as eucerin cream

8. For daytime itching can use a ssri such as citalopram 20-40 mg q am (don't use with elavil)

After 4 or 5 days, when the skin is not so raw, topical steroids can be used. Start clobetasol propionate ointment 0.05% qhs Disp 30 grams. Then decrease to triamcinolone acetonide ointment 0.1% qhs to bid.

If she is still itchy, can change to Protopic 0.03% or 0.1% alternating days with topical steroid.

**LICHEN PLANUS (LP)**

Lichen planus is an autoimmune, mucocutaneous hypersensitivity disorder with altered cell mediated immunity in older women affecting the skin and mucous membranes.

**Etiology:** It is a disorder of altered T-cell mediated immunity to exogenous antigens targeting the basal keratinocytes of the epidermis. Non-specific mechanisms are also involved plus genetic factors.

The diagnosis is often missed on the vulva and in the vagina.
It tends to occur in menopausal women (age 40-60 years).
It affects skin and mucous membrane – mouth, vulva, vagina, nails, scalp, esophagus, nose, conjunctiva of the eye, ears, and bladder.
Oral and genital LP onset together in 50% cases and oral starts first in 33%.
Painful LP is usually erosive; patient can have LP plus chronic vulvar pain.

**Clinical Presentation:**
1. Papulosquamous – typical papules and plaques with white lacy pattern on the vulvar trigone and periclitoral area. It may be part of
generalized LP. This can be itchy. It tends to respond to topical steroids.

2. Hypertrophic – least common with extensive white scarring and destruction (looks like LS)
   – can be very itchy. Tends to be resistant to treatment.

3. Erosive (vulvovaginal gingival syndrome) – Most common pattern on vulva. This is a destructive, scarred form of lichen planus on the mucous membranes and vulva with a desquamative vaginitis, variable erosions plus atrophy, usually pain, burning and irritation rather than itch. The skin of the vulva often has a glazed erythema. Treatment tends to be resistant.

Note – LP generally involves the vulva and vagina, It may only be in the vagina.

Erosive LP (vulvovaginal gingival syndrome)

Symptoms:
- Severe pain and burning
- Depression + anger
- Dysuria
- Dyspareunia / apareunia

Signs – painful, glossy red erosions (glazed erythema) and scarring are seen around the labia minora and vestibule. The borders may be white to smudgy or smoky gray. The scarring causes flattening of the vulva and loss of the labia minora.
- May see desquamative inflammatory vaginitis
  - Vaginitis with vaginal erosions, atrophy, purulent malodorous discharge, vaginal synechiae and scarring. The vagina may be obliterated.

Note: up to 70% of women with vulvar LP have vaginal involvement.

This can be a chronic, destructive, debilitating and difficult condition.

Diagnosis: Look at mouth and skin for evidence of LP
- Biopsy for H&E and immunofluorescence unless there is the classic lacy pattern

Note - Biopsies may be nonspecific

Typical histology of lichen planus, found in 70% include:
- Irregular acanthosis of the epidermis
- Vacuolar change of the basal cell layer
- A band-like dermal infiltrate of lymphocytes in the upper dermis and often plasma cells
- Apoptotic keratinocytes scattered within the epidermis
- Immunofluorescent staining of the basement membrane zone, shows an irregular deposition of fibrinogen, IgM, cytoid bodies, and, occasionally, granular IgG or IgA.

Differential diagnosis: Lichen sclerosus, drug eruption, cicatricial pemphigoid, graft vs. host disease

Treatment:
- Stop irritants
- Pain control
- Bland therapy for ulcers
- Sedation
- Superpotent steroid ointment (clobetasol) topically once to twice a day.
Intralesional steroid – triamcinolone 3.3 up to 10 mg/mL q 3-4 wks x 3 (do not give high dose in small area-erosions and ulcers may occur)

Intravaginal steroid – hydrocortisone acetate foam 40-80 mg qhs
or 25 to 200 mg compounded suppository qhs (if using high dose steroids, use for short term use, then gradually decrease the dose).
If severe – hydrocortisone acetate 10% compounded in a Replens like base –3 to 5 grams (300 mg to 500mg/dose) nightly for 14 days then 3 nights a week and continue to decrease dose as per response. (Some prefer to use every other night initially, and then gradually decrease the dose)
Note: adrenal suppression and risk of candidiasis

IM Triamcinolone (Kenalog 40) 1 mg/kg every 4 weeks for 3 doses. (Dose up to a maximum of 80 mg total per dose) Repeat monthly for up to 3 months. Max 4 doses per year
Prednisone 30-60 mg a day with taper
Methotrexate 5 -15 mg po or subcutaneously in abdomen or thigh, once a week with folate 2 mg daily
Mycophenolate mofetil 250 mg/day building up to 3gm/day (pregnancy must be prevented)
Hydroxychloroquine 200 mg bid
Acitretin 10 -20 mg/d 3-7 days a week with fatty food for erosive disease. Counsel on no pregnancy as this is a teratogen. (see above for lichen sclerosus)
Cyclosporine 3-4 mg / kg per day
Azothioprine – 50-100 mg bid
Adalimumab 80 mg then 40 mg every 2 weeks.
Patient education and support needed
Dilators
Surgery for scarring followed by intravaginal treatment with steroids

Other Treatments:
- Clobetasol propionate 0.05% ointment virginally using 1-2 grams nightly via a “Premarin type applicator”
- Clobetasol propionate 0.05% ointment/Nystatin 100,000 units/gram/3% oxy-tetracycline in cream base
- Pimecrolimus (Elidel) 1% cream bid for mild LP
- Topical tacrolimus (Protopic) 0.03 or 0.1% ointment (burns) as a steroid sparer
- Etanercept (see below)

Course: uncertain - often very chronic-10% resolve, 50% asymptomatic and 15% do poorly
Risk of squamous cell carcinoma 4-5% - biopsy any suspicious area.
What are the various treatments for Lichen Planus?
Papular lichen planus tends to respond to topical corticosteroids. Triamcinolone acetonide 0.1% ointment for mild disease and clobetasol propionate 0.05% ointment for severe disease.

For erosive disease the following table contains many medications that have been tried for LP treatment. It is important to note that many of these medications are formulated for off label use.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long term Anti-inflammatory antibiotics</td>
<td>This treatment works best for early erosive lichen planus. Doxycycline or clindamycin used long-term. Consider adding weekly fluconazole to prevent yeast infection.</td>
</tr>
<tr>
<td>Steroids are often used for lichen planus</td>
<td>Vaginal LP: Anusol HC 25 mg vaginal suppositories are used in the following manner: 1/2 of a Anusol HC suppository per vagina twice daily for 2 months, then daily for 2 months, then maintenance treatment at 1 to 3 times per week. However, many patients do not experience significant long-term response to intravaginal steroids. The vaginal vault tends to continue to scar. To keep the vault open and prevent adhesions it often will be necessary to use vaginal dilators. The dilator may be lubricated with a hydrocortisone cream. At times a stronger steroid may be required for vulvar LP (see text). Topical: Clobetasol propionate (Temovate®) 0.05% ointment. Intralesional: triamcinolone acetonide 5-10 mg/mL. As above, for stronger treatment: – hydrocortisone acetate foam 40-80 mg qhs or 25 to 200 mg suppository qhs (if using high dose steroids, use for short term use, then gradually decrease the dose). If severe – hydrocortisone acetate 10% compounded in a Replens like base –3 to 5 grams (300 mg to 500mg/dose) nightly for 14 days then 3 nights a week and continue to decrease dose as per response. (Some prefer to use every other night initially, then gradually decrease the dose) Oral: Oral prednisone may be required until healing has occurred. 30-40 mg q am with food for 3 weeks then slowly taper. As the skin heals, topical corticosteroids may be added as the prednisone is tapered. IM steroids (place into muscle in anterior thigh). Used for moderate disease. Dose 1 mg/kg (not to exceed 80 mg) every 4 weeks to every 8 weeks for up to 3 or 4 months. For Oral LP: pat area dry with tissue then apply Clobetasol propionate (Temovate®) gel or ointment 0.05% to affected area up to qid. Apply on a cotton ball in mouth for 5 min. Best to use in a dental tray for 15-30 min bid for gums. Some providers use dental molds to hold in medications in patients with gingival LP</td>
</tr>
</tbody>
</table>
| Tacrolimus and Pimecrolimus | Tacrolimus (Protopic) 0.1% ointment bid to qid.  
Apply on a cotton ball in mouth for 5 min  
Vaginal medication (made by compounding pharmacy)  
tacrolimus vaginal suppositories  
Insert one suppository per vagina (2 mg tacrolimus per 2 gram supp) qhs  
Dispense 50  
Or 0.1% vaginal cream (compounded in a vaginal cream / Replens like base) 2-5 g = 2 - 5 mg/dose for 2 weeks then Mon-Wed-Fri for 2 weeks and slowly decrease Dispense 100 grams  
Vulvar medication  Apply to skin bid  
Tacrolimus 0.1% ointment Available in 30 or 60 gram tubes  

**Calcineurin inhibitors (steroid sparing)**  
pimecrolimus (Elidel) 1% cream bid for mild LP  
topical tacrolimus (Protopic) 0.03%, 0.1% oint  

Note – can burn especially on raw areas  
Long term safety unknown |
<table>
<thead>
<tr>
<th>Less frequently used medications</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hydroxychloroquine</strong> <em>(Plaquenil)</em></td>
<td>Occasionally used. Dose is 200 mg po bid.</td>
</tr>
<tr>
<td><strong>Retinoids</strong></td>
<td>There is no documented successful use of retinoids for vulvovaginal lichen planus. There is only personal experience with Acitretin (Soriatane). It can work well in low dose 30-70 mg/week. (Isotretinoin has been used to treat oral lichen planus; however, discontinuation of the medication results in recurrence of the oral lesions.) Long-term use of retinoids may result in liver dysfunction, but not in the small doses recommended here. Liver function tests, cholesterol, triglycerides and complete blood cell counts should be monitored since laboratory changes are associated with the use of oral retinoids. Patients should be counseled concerning teratogenicity and need for optimal contraception. Acitretin is a strong teratogen that remains in the body for at least three months after the last dose. Topical retinoids (tazarotene - Tazorac®) are often too irritating for this vulvar condition but have been used.</td>
</tr>
<tr>
<td><strong>Cyclosporine</strong></td>
<td>Used topically and systemically. Topical cyclosporine provides a safe and often effective but very expensive alternative for mucous membrane disease. Pelisse et al. described the use of the oral or injectable form of the medication in 100 mg amounts directly to the affected skin four times a day initially. If several mucous membranes were affected for example, 100 mg was applied to the vulva, 100 mg inserted into the vagina, and 100 mg held in the mouth for as long as tolerated before spitting. As disease is controlled, the frequency of application can be tapered. Systemically it is dosed at 4-5 mg/kg/day for 3 months (used in severe disease). Occasionally, in patients with debilitating and painful disease not adequately treated by therapies discussed above, oral cyclosporine may be used. This medication should be used only by health care providers experienced in its use.</td>
</tr>
<tr>
<td><strong>Cyclophosphamide</strong></td>
<td>Systemic antimetabolite</td>
</tr>
<tr>
<td><strong>Azathioprine</strong></td>
<td>Systemic antimetabolite</td>
</tr>
<tr>
<td><strong>Etanercept</strong> <em>(Enbrel)</em></td>
<td>This is used SQ (50 mg subcutaneously 2x/week until symptoms improve, then 25 mg 2x/week))</td>
</tr>
<tr>
<td><strong>Mycophenolate mofetil</strong> <em>(CellCept)</em></td>
<td>Oral use 250mg -3 g/d in divided dose</td>
</tr>
<tr>
<td><strong>Methotrexate</strong></td>
<td>Oral or subcutaneous injection weekly. 7.5 to 15 mg oral or subcutaneously weekly using a 27 or 30 gauge needle. Need to give folate with this medication- 1 mg/d</td>
</tr>
</tbody>
</table>
Lichen Planus and Surgery

For scarred LP of the vagina - post surgery information

I. For dilation:

Dilation is vital to keep the vagina open in patients with vaginal lichen planus. Patients need specific instructions on size of dilator and how to use dilators. They may need a set of dilators and can buy the dilator set from www.vaginismus.com. Start with the largest size that will fit, determined by surgery. Leave the dilator in once or twice a day for 15-20 minutes. For lubricating the dilator use either Vaseline or mineral oil. Hydrocortisone acetate cream or Estrace 0.01% vaginal cream can be used later.

II. To stop inflammation:

If not too severe 2-3 days preoperatively use prednisone 15-30 mg/d AM, with food, plus topical steroid. Keep on prednisone for 1 week post operatively then taper slowly at 5 mg/week. Use with the topical steroid (see below).

For more severe disease consider using a dose of intramuscular triamcinolone 1mg/kg up to a total of 80mg/dose to be given two days after surgery and repeat this monthly for up to three months. Follow and assess her to see if she is going to need other long-term systemic medication, cyclosporine, mycophenolate, methotrexate, etc. Once she is healed she may need a systemic anti-inflammatory. The medication will depend on the case. These medications can be used with intermittent doses of IM triamcinolone, also depending on the case.

A. For the vagina

Two days after surgery, when the stent is removed, the patient needs to start dilating with Vaseline on the dilator twice a day. Dilators must be used nightly. In 1 to 2 weeks if healing then consider 10% hydrocortisone acetate in a vaginal cream 300mg (3g) to 500 mg (5gms) nightly for a week then gradually decrease weekly to 1-3gram Mon-Wed-Fri depending on response. (The compounded prescription is 10% hydrocortisone acetate in vaginal cream base 100 g with 2 refills) (Some providers start this high dose intravaginal steroid 48 hours after surgery, once the vaginal dilator is removed in the clinic). As a steroid sparer consider tacrolimus 2 mg compounded suppository nightly, or 0.1% tacrolimus compounded vaginal cream 2 grams/dose. Note – tacrolimus can cause a burning sensation. Use fluconazole 150 mg weekly to prevent yeast as needed.

B. For the vulva - to start two days after surgery, if not very eroded, topical clobetasol 0.05% ointment in a thin film PM. If eroded use plain Vaseline for 2 weeks and then restart clobetasol. If tolerated consider using tacrolimus 0.1% ointment twice a day as a steroid sparer note - as above, it can cause a burning sensation.
Follow up- patient needs to be seen often for support and to adjust treatment. Avoid sexual intercourse until well healed with adequate size.

**Atrophic Vulvovaginitis**
Postmenopausal women not on estrogen replacement experience thinning of the vulvar and vaginal epithelium. They may also have thinning of the pubic hair and smoothness and thinning of the vulvar skin. The labia minora and majora lose substance and become more wrinkled; complete resorption of the labia minora occurs in some and may mimic the end stage of lichen sclerosus. Patients may be asymptomatic, but many are aware of a sensation of dryness that sometimes makes intercourse uncomfortable. Some patients complain of dysuria, urgency, and frequency as a result of atrophic urethritis. The diagnosis of atrophic vulvovaginitis is by clinical examination and a history of estrogen deficiency. Vulvovaginal atrophy from lack of estrogen can be seen with use of BCP, Depo-Provera, nursing etc. Atrophic vaginitis is suspected when parabasal cells and inflammatory cells are seen on wet prep in a symptomatic patient. Atrophic vulvovaginitis complicates all vulvovaginal conditions. Without estrogen the barrier functions are weaker and the tissues more susceptible to irritation from day to day hygiene practices, sexual activity etc. This can be further compounded by an already disrupted barrier in lichen sclerosus, lichen planus, even VIN. Estrogen topically and, if appropriate, systemically can make a big difference. Consider adding topical estrogen to the vulva 2 to 7 days/week for postmenopausal lichen sclerosus and lichen planus.

**CONTACT DERMATITIS**

Contact dermatitis is an inflammation of the skin resulting from an external agent that acts as an irritant or allergen. This reaction may be acute, subacute or chronic.

**Primary irritant contact** dermatitis results from prolonged or repeated exposure to a caustic or physically irritating agent. (e.g. urine, feces, soap residue) Anyone exposed to such a product often enough will have a reaction. This is a non-immunologic reaction. The skin is directly damaged. Top three causes –

1. Over-washing (some patients become obsessed with cleanliness and wash the area with soap and water multiple times each day, causing irritation. Some may become fixated on symptoms and even use harsh cleansers. Patients may remain secretive and not report these habits.)
2. Use of creams with drying bases
3. Wetness (urine, feces, menstruation)

**Allergic contact dermatitis** results from a frank allergic reaction, to a low dose of a substance (e.g. poison ivy, neomycin or benzocaine). This is a type IV delayed hypersensitivity reaction. Top three causes – Neomycin, benzocaine and preservatives.

**Note:** Irritant contact dermatitis is immediate; allergy takes 1-2 days.

Clinical Presentation: The same for both types of reactions

Varying degree of itch, burning and irritation; can be acute or chronic. With an irritant there is a history of repeated exposure, e.g. repeated use of soaps, cleansers, chronic incontinence. Allergic contact dermatitis can be more acute with sudden onset of symptoms of itching and burning that can be more intense. On physical exam there can be an acute blistered erosive eruption but most of the time there are subacute or chronic changes with evidence of
excoriation, honey colored crusting (with or without secondary infection) or just dryness, scaling and erythema. There may be altered pigmentation.

Diagnosis: Morphology of rash plus history of an irritant substance or an allergen. Biopsy may be needed to sort this out. To define allergic etiology, patch testing must be set up by a dermatologist or allergist.

TIPS ON VULVAR CONTACT DERMATITIS
1. Irritant contact dermatitis of the vulva is common. Factors that promote vulvar irritation with disruption of barrier function are:
   a. Lack of estrogen that causes the epidermal barrier to be weakened/thinned and less moist and pliable. The result if cracking/fissuring, etc.
   b. Overzealous hygiene with excessive washing with a washcloth or sponge using caustic soaps results in dry cracked and burned skin. Beware of the “dirty” vulva. Women are convinced that the area is dirty and needs to be scrubbed.
   c. Excess maceration of the area from:
      Sweat, urine, wet pads of any type results in irritation
      Incontinence is a hidden epidemic
      Note – urine and feces burn enzymatically and/or chemically
   d. Existing dermatoses, infection or tumors, e.g. lichen sclerosus, lichen planus, candidiasis are susceptible to irritants.
2. History of contactants may be difficult to elicit
3. Always stop all unnecessary vulvar contactants
4. Suspect allergic contact dermatitis with a sudden onset of intense itching and/or vesiculation and weeping
5. Always set up patch testing to rule out possible common allergens for patients with chronic or recurrent, poorly responsive vulvar dermatoses. Work with a dermatologist or allergist who can do the patch testing. The best screen is the North American Patch Test series (about 60 or more allergens) not the True Test Series as it may test for too few allergens – 25 to 35.
6. Reassess you vulvar patients for contact dermatitis as women commonly self-treat themselves to “wash away” or “clean up” their itchy or burning vulva. Contact dermatitis can complicate all vulvar conditions.

Treatment:
- Stop the irritant or allergen exposure
- Topical corticosteroids – clobetasol 0.05% or halobetasol 0.05% ointment bid x 5-7 days, then daily x 5-7 days (avoid long term use)
- Bland emollients such as petrolatum or mineral oil and nighttime use sedation for sleeping
- Antibiotics are needed for secondary infection – see lichen simplex chronicus above
- If very severe, prednisone 1 mg/kg decreasing over 14 – 21 days or 1 dose of triamcinolone acetonide IM 1 mg/kg (anterior thigh) (do not exceed 80 mg total IM)
Caution in patients with diabetes- high dose steroids can interfere with their glucose control.

Common Vulvar Irritants:
Soaps/cleansers Douches
Medications -Trichloroacetic acid, 5FU Spermicides
Sweat, urine, feces     Panty liners

Common Vulvar Allergens:
Benzocaine (Vagisil®)     Preservatives (parabens and propylene glycol)
Neomycin (Neosporin®)    Condoms – latex
Chlorhexidine (KY jelly®)    Lanolin
Perfume                  Nail Polish

Some wipes and paper products contain the preservative methylchloroisothiazolinone/methylisothiazolinone and this can cause an allergic contact dermatitis.

**Crohn’s Disease**

Crohn’s disease is a chronic inflammatory bowel disease. It is an autoimmune disorder affecting the gastrointestinal tract from mouth to the anus. It affects over 300,000 women in North America. The onset for women is between 15 and 30 years of age. It is diagnosed by biopsy of the skin or the GI tract. This shows a diffuse lymphohistiocytic infiltrate with loose non-caseating granulomas. These granulomas are considered the hallmark of Crohn’s disease but they are found in only 30-90% of biopsies of Crohn’s patients, whether in bowel or skin.

The most common symptoms of Crohn’s disease are abdominal pain, cramping and diarrhea, often following a meal. There can be rectal bleeding, weight loss, joint pains and fever. Anemia is not uncommon. Patients often develop sores in the anal area and sometimes fistulae.

It is reported to be rare in the vulva though the prevalence is not known. There have been 145 reported cases on vulvar involvement since 1965 and recently these were summarized by Barrett et al., in Crohn’s Disease of the Vulva, J Crohn’s Colitis (2014) and Vulval Crohn's disease: a clinical study of 22 patients in Colitis, Laftah Z et al. 2015.

Vulvar Crohn’s disease is still considered rare. The common features are labial swelling, vulvar ulcers and hypertrophic lesions.

Patterns of Crohn’s disease on the vulva:

**Specific:**
1. Contiguous – Direct extension to the skin from GI fistulae, usually perianal fistulae, rarely rectovaginal fistulae.
2. Metastatic Crohn’s disease (MCD) on the vulva causes 90% of vulvar lesions. This is a granulomatous inflammation of the vulvar skin with swelling and induration of the labia unilateral or bilateral, with or without ulcers, and can have any of the following:
   a. Classic “knife cut ulcers”, linear ulcers, and fissures with linear ulcers in any of the creases of the perineum or perianal area such as inguinal folds, interlabial sulci, periclitorally, perineum, and/or gluteal cleft. These can be associated with scattered ulcers, edema of the skin, drainage and pain (note only 38% show granulomas on biopsy) Ulcers are seen in 40%.
b. Swelling and edema of labia majora, labia minora that is unilateral or bilateral. This can be associated with granulomatous infiltration and/or lymphangiectasia and there can be frank lymphangiomias with cobbling, even verrucous changes of the skin referred to as pseudo-condyloma acuminata

c. Perianal skin tags – these are often the harbinger of Crohn’s disease in 40-70% of cases. They often look like hemorrhoids. They develop from localized lymphatic obstruction. These are classic and found in most cases of Crohn’s disease.

Reactive:
1. Aphthae - these ulcers can be genital and/or oral, single or multiple. These can be associated with “knife cut ulcers”. These can be totally asymptomatic or tender.
2. Suppurative lesions - hidradenitis suppurativa (HS) is associated with Crohn’s disease in about 17% of HS patients.

Extra-intestinal manifestation of Crohn’s disease include:
- Arthritis - Spondyloarthopathies
- Ocular - conjunctivitis, uveitis, episcleritis
- Hepatobiliary - primary sclerosing cholangitis
- Skin - Erythema nodosum
  - Pyoderma gangrenosum – in 1% of CD
  - Cheilitis, oral swelling - oral disease can be found in 8% of patients
    - cheilitis, cobblestoning of the buccal mucosa, lip swelling
    - Psoriasis
    - Vasculitis usually on lower legs
    - Epidermolysis bullosa acquisita

The anal area is often involved with:
- Perianal abscesses and fistulae
  - Fissures in 25-35%
  - Fistulae 6 -35%
  - Ulcers 5% - these can be very large
- Skin tags - these anal tags are due to lymphedema. They can be:
  a. Large hard tag-like lesions that develop in healed anal fistula ulcers
  b. The “elephant ear” type which are described as broad, soft and sometimes can resolve

Note: 25% of patients present with vulvar manifestations of Crohn’s disease before developing GI disease. The GI disease may not show up for many years.

Think of possible Crohn’s disease with the following vulvar lesions:
1) Vulvar swelling/edema, lymphedema with lymphangiectasia. The labia may be hypertrophic and pseudocondylomata can be very dramatic. This is due to granulomatous infiltration and impaired lymphatic drainage due to chronic inflammation from the Crohn’s disease. Recurrent cellulitis results in lymphatic vessel destruction and obstruction and more swelling
2) Ulcerations - knife cut ulcers, aphthous ulcers
3) Suppuration with hidradenitis suppurativa-type lesions
4) Perianal disease with swelling, fissures, anal and perineal tags

Diagnostic Workup
1) Biopsy - skin, bowel (GI workup always needed)
2) Consider differential diagnosis ruling out infectious diseases - Candida albicans, bacterial vaginosis and trichomoniasis. Note: Crohn’s disease can be associated with a desquamative inflammatory vaginitis (personal observation).
3) Rule out other
   a. Infections: lymphogranulomatosis, tuberculosis, syphilis, HSV in an immunosuppressed patient, HIV, rare causes of infectious ulcer - see section on vulvar ulcers.
   b. Inflammatory conditions such as sarcoidosis, hidradenitis suppurativa, foreign body reaction, contact dermatitis. Rule out infiltrative conditions e.g. squamous cell Ca
   c. Causes of chronic lymphedema: See section on lymphedema.
   d. Causes of lichen planus vulvar ulcers: See section on vulvar ulcers. Note: Granuloma inguinale and Langerhans cell histiocytosis both cause linear ulcers. Specific investigations will depend on screening for appropriate conditions.

Treatment  A multidisciplinary approach is needed.
Most important aim is to control the bowel disease
1) First line treatment usually is systemic corticosteroids. Corticosteroids are the cornerstone of treatment but are not always well tolerated. Prednisone may be combined with metronidazole or azathioprine. Intralvesional triamcinolone 10 mg/mL (up to 40 mg total on the vulva) can be helpful (personal experience).
2) Further treatment can include, methotrexate or mercaptopurine.
3) In more severe disease the usual treatment is with infliximab or adalimumab or, less commonly, certolizumab pegol or ustekinumab. Combination therapy is common.
4) In some patients surgery is necessary to debulk the significant edema and lymphangiectasia but this is not curative. Surgery should be considered especially if there are strictureal complications or difficult draining lesions.
5) For local treatment for limited disease - superpotent steroids with clobetasol 0.05% ointment or halobetasol 0.05% ointment can be used for short periods of time for two weeks. Patients can be switched to the calcineurin inhibitor tacrolimus (Protopic®) 0.1% ointment twice a day if there is no burning. For thick perianal tags triamcinolone 5 to 10 mg/mL can be injected every three to four weeks. (See section on edema below).

**HIDRADENITIS SUPPURATIVA**

**Definition** – Hidradenitis suppurativa is a chronic follicular occlusive disease, characterized by recurrent painful, deep-seated nodules and abscesses located primarily in the intertriginous areas of the axillae, groins, perianal, perineal and inframammary regions. The Second International HS Research Symposium (San Francisco March 2009) adopted the following consensus definition. “HS is a chronic, inflammatory, recurrent, debilitating, skin follicular disease that usually presents after puberty with painful deep seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axilla, inguinal and anogenital region”. HS is frequently misdiagnosed as “boils”. This results in delayed diagnosis, fragmented care, and progression to a chronic, disabling condition that has a profoundly negative impact on quality of life.
The prevalence of hidradenitis suppurativa (HS) is 1 to 4%. Women are more commonly affected than men. Some studies have described a predilection in patients of afro-carib descent, but this has not been confirmed in all. 25% of patients present between the ages of 15 and 20 and 53% are aged 21 to 30. Female to male ratio is 3.3:1. Prepubertal cases are rare, but occasional onset in neonates and infants has been described. Women are affected under the breasts (22%) and in the groin (93%).

HS has been erroneously linked to the apocrine sweat glands. The first pathogenic change is in the follicular portion of the folliculopilosebaceous unit (FPSU).

HS is characterized by recurrent inflamed deep-seated acneform nodules that result in abscesses and chronic draining sinus tract formation leading to scarring, disfigurement and life-altering disability. The lesions occur in areas of the skin that contain folliculopilosebaceous units.

Diagnosis relies on the following diagnostic criteria:
1. Typical lesions: either deep-seated painful nodules (blind boils) in early primary lesions or abscesses, draining sinuses, bridged scars and “tombstone” open comedones in secondary and late-stage lesions.
2. Typical topography: axillae, groin, genitals, perineal and perianal region, buttocks, or infra- and inter-mammary fold
3. Chronicity and recurrences.

These three criteria must be met to establish the diagnosis.

Multiple skin abscesses occur, with draining subcutaneous sinus tracts. Scarring and deformity are present in many individuals. Although biopsy is not absolutely required for diagnosis of HS, you may send tissue to pathology indicating that the clinical picture is consistent with HS. The characteristic findings include follicular hyperkeratosis, active folliculitis or abscess, fragments of epithelialized sinus tract, fibrosis, foreign body granuloma formation, intact apocrine and eccrine structures showing stasis and surrounded with inflammation, fibrosis, fat necrosis, inflammation of the subcutis, loss of 80% of sebaceous gland volume, and a psoriasiform acanthosis of the inter-follicular epidermis.

The basic problem seems to be a structural defect. People with HS appear to have genetically ‘weak-walled follicles’ that rupture easily. New histologic findings show that the connective tissue support tissue around the follicular tube is weak to non-existent at the point where the sebaceous glands attach to the follicle (the sebofollicular junction).

This defect leads to the following sequence of events:
1. The problem starts with endogenous and exogenous androgens acting on the follicle duct lining cells so that the cells build up and occlude the ducts. It is hypothesized that dietary factors that elevate insulin and insulin-like growth factor-1 sensitize the FPSU’s androgen receptors, creating the increase in end organ responsiveness that leads to follicular occlusion and an accompanying seborrhea. Exogenous androgens, androgenic progestins and drugs like lithium can
also make things worse. Smoking is strongly associated with HS. It promotes follicular plugging in HS as it does in acne and is also responsible for poor healing. High glycemic load diets plus the casein and whey in milk and milk products increase androgen sensitivity, increasing follicular plugging.

2. The follicular duct content expands as keratinocytes accumulate and the wall of the follicle eventually ruptures due to the weakness in the follicle support. A number of genetic defects may play a role here.

3. Follicular rupture results in the release of numerous inflammatory stimuli and antigens, including keratin fragments, bacteria and yeast that trigger ever more numerous elements of the innate and adaptive immune systems, leading to the development of an acute inflammatory response in the surrounding tissue. Extensive research has been done on the acute and chronic phase cellular and cytokine reactants in an effort to focus treatment appropriately for more effective therapy.

4. Attempted healing creates chronic inflammation and results in chronic tissue destruction through a foreign body-like reaction and subsequent resolution by scarring.

5. Mechanical factors are important because any friction or shearing force, from tight clothing to pinching the area can make it worse. Obesity does not cause HS but the resulting sweating, maceration and friction can make the situation worse.

6. When the pores rupture, follicular stem cells can be released into the subcutis where they appear to trigger the formation of cysts and epithelialized sinuses. Chronic cases appear to be due to the production of an invasive proliferative gelatinous mass (IPGM) consisting of a gel in which are embedded both inflammatory cells and, it is postulated, the stem cell-derived precursors of the epithelialized elements described above. Continuous growth of these hormonally stimulated remnants beneath the surface creates and perpetuates the communicating sinuses and inflammatory mass and provides increasing volumes of invading material. The inflammation in the dermis and subcutis will not settle until this material is eliminated.

In summary - genetically weak-walled follicles, distended under the influence of hormones and subject to friction and pressure, rupture, release materials that stimulate the innate and adaptive immune systems that create the painful inflammatory subcutaneous nodules.

Etiology
The development of HS depends upon a combination of factors.

Genetic factors
A 35-40% positive family history may reflect inadequate family reporting and / or variable penetrance and expressivity. An autosomal dominant inheritance pattern has been noted, but no consistent specific genetic defect has been found. Von der Werth suggests that HS is most likely a heterogeneous disease, probably with several genes involved.

Infection
Bacteria have long been considered in the pathogenesis of HS. It is generally agreed that bacteria do not have a major direct role in the etiology of HS but, as secondary invaders, may share in the
pathogenesis of the chronic relapsing lesions causing some of the destructive processes that are seen. While local cellulitis is not uncommon as a cause of part of the inflammatory activity, septicemia and systemic illness in this disorder are exceptionally rare.

Hormonal factors
A strong relationship exists between sex hormones and HS. The female preponderance suggests a greater sensitivity of females to androgens. There are no elevations in serum androgens in the vast majority of HS patients. End organ sensitivity, presently not measurable, is likely responsible. Increased access to the androgen receptor is mediated by insulin and insulin-like growth factor-1 (IGF-1), both chronically raised by dietary factors.
In women, HS onsets around menarche, flares premenstrually and following exposure to androgenic progestins like medroxyprogesterone acetate or levonorgestrel, but improves with pregnancy. While it usually fades after menopause, the drop in estrogen has been responsible for post-menopausal onset in a minority of cases.
Anti-androgen therapy helps HS patients of both sexes. Finasteride, a selective inhibitor of the type II isomer of 5α-reductase, reduces levels of 5α-DHT. It was used to improve six of seven adults with HS and three children, one with premature adrenarche and one with polycystic ovarian syndrome.

Immune factors
The disease does not usually produce acute systemic inflammatory effects. There is no fever, rare lymphadenopathy, rare septicemia, occasional local cellulitis, cultures are usually sterile and, if the offending material beneath the surface is removed, the disease heals without further difficulty and without antibiotics. This is strongly suggestive of inflammation mediated on the local level by the innate immune system. Consider a simple ingrown hair. Flick out the ingrown hair and the inflammation fades.
The immune systems accelerate the disorder. Pathologic examination of excised early lesions demonstrates a wide variety of immune responses involving the innate and acquired (adaptive) immune systems. A vast catalogue of T-lymphocytes and cytokines are assembled. Unfortunately, cooling the inflammation does not cure the disease.

Mechanical Factors
Weakness in the support structure of the follicular portion of the FPSU likely predisposes to follicular rupture caused by local trauma. Patients worsen their lesions by pinching them. Obesity contributes to these increases in pressure and shear forces, but more important is the relationship of obesity to dietary habits that raise plasma glucose and insulin levels. This sensitizes the androgen receptors, increases the plugging of pores, causes insulin resistance and enhances obesity. HS affects thin people but overweight patients may have more severe disease.

Smoking
Smoking is strongly associated with HS. Smokers are generally more severely affected than non-smokers. Nicotine promotes follicular plugging and interferes with healing, a major problem in a disorder that characteristically heals poorly.
Diet
The androgen receptors that control growth are normally closed to circulating androgens. Elevated insulin (from the combination of high glycemic carbohydrate load and dairy whey) and IGF-1 (induced by casein in milk) open these receptors and expose them to circulating androgens. Androgens from any source can then access previously inaccessible androgen receptors. Stimulation of follicular androgen receptors results in ductal keratinocyte overproduction, failure of terminal differentiation of the keratinocytes and retention hyperkeratosis (result – plugged / blocked pores that can easily rupture). Androgen sources include the adrenals, ovaries and testes, 5α-reduced molecular precursors of DHT in dairy products, the androgenic progestins in birth control pills, the levonorgestrel-containing IUD, intramuscular medroxyprogesterone acetate (MPA) injections and contraceptive implants.

Drugs
Hidradenitis suppurativa can be triggered or flared by lithium and by androgenic progestins in BCPs and IUDs.

Systemic Associations of HS
Obesity and metabolic syndrome.
The diet responsible for metabolic syndrome has the same metabolic drivers causing androgen-driven overgrowth of individual keratinocytes (causing plugged / blocked pores as above). A number of recent studies show increased prevalence of metabolic syndrome and insulin resistance in HS patients, particularly younger patients. These HS patients may have diabetes, lipid abnormalities (with increase in gall stones), cardiovascular diseases and hypertension. HS is also associated with polycystic ovarian syndrome.

Autoimmune diseases.
HS is associated with inflammatory bowel disease, arthritis and spondyloarthropathy

Follicular occlusive diseases.
Follicular occlusive triad (acne, pilonidal sinuses, dissecting cellulitis scalp)
SAPHO (Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis) and its relatives

Quality of life
HS has a profoundly negative impact on patients' physical, social, and economic lives. Many patients become socially isolated or reclusive due to the pain, malodorous discharge, intimate sites of eruptions, inappropriate medical care due to incorrect diagnosis, the numerous lesions, long and continuous duration, and pelvic area involvement. Medical, dietary, emotional and peer support are vital for these patients.

Differential diagnosis –Multiple conditions are to be considered in the differential diagnosis of hidradenitis suppurativa.

Infections
Bacterial - Carbuncles, furuncles, abscesses, ischiorectal/perirectal, Bartholin’s duct abscess
Mycobacteria – TB
STI– granuloma inguinale, lymphogranuloma venereum, syphilis
Deep fungi – blastomyces, nocardia
Tumors Cysts – epidermoid, Bartholin’s, pilonidal
Miscellaneous - Crohn’s, anal or vulvovaginal fistulae

Clinical features – The early/primary lesions are single, painful, deep-seated nodules 0.5-2cm, round, showing no tendency to “pointing” that may progress to drainage and resolution. Lesions persist as a “silent” nodule that can recur, form an abscess and drain, and often will recur even if surgically drained. With time these progress to form chronic, recurrent and extending lesions at same site, coalescing with fibrosis and sinus formation. Lesions persist for months with pain and drainage with foul odor. These can result in tertiary lesions with hypertrophic fibrous scarring with “bridged scars” forming rope-like bands mixed with active, painful, inflammatory nodules and sinus tracts forming thick plaques over an area. Thick scarred areas can result in decreased mobility and lymphedema. When severe, there is social withdrawal, depression and major social dysfunction.

Lesion course – most form a persistent variably painful abscess, then rupture and drain purulent material. They may then resolve or recur. A chronic sinus may form that can drain a seropurulent and/or bloody discharge, or it may ulcerate, burrow and rupture into nearby lesions. Mean age of onset is 22 years old and it lasts on average 19 years but can remit or partially remit with pregnancy and breast-feeding. This all can be variable. Each new painful lesion lasts 10-30 days. There may be one or two outbreaks a year, or per month, with varying severity. Flaring with menses is common, underlining the need for hormonal control.

MANAGEMENT PRINCIPLES

Therapy and prognosis – Planning treatment generally follows severity grading. The first two stages respond to medical treatment and early minor surgical procedures whereas the third stage requires continuation of all preventive measures and hormonal control plus biologics and surgery. All patients will need thorough education and constant reassurance and support.

Prevention – This is Job #1 – Stop New Lesions
The importance of preventing new or additional lesions must be stressed.
Hormone control, environmental control, dietary regulation, complete nicotine avoidance - all must be aggressively pursued while Job #2 is completed in parallel.

Treatment – This is Job #2 – Active Therapy
Define and document the location and frequency of the flares and the intensity of the pain at baseline and at regular intervals once a treatment program is established.
A permanent cure is achieved only with thorough surgical removal of the subcutaneous material that is driving the inflammation.
Cooperative medical and surgical treatment is essential.

**Goals of management of hidradenitis:**
1. To prevent development of new lesions
2. To reduce the extent and progression of the disease and bring it to a milder stage
3. To heal existing lesions while preventing new ones from forming
4. To prevent progression of scars and sinuses in cases of extensive hidradenitis suppurativa

**Hurley’s criteria for Hidradenitis Suppurativa Staging**

Hurley’s criteria for Hidradenitis Suppurativa Staging – used to assess the severity of the single worst area of involvement.

Treatment principles – choose treatment to fit the lesions present at various degrees of severity staging

Stage I: Abscess formation, single or multiple without sinus tracts and cicatrisation/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 abscess

55-70% stay in Stage I
28% progress to Stage II
4-7% progress to Stage III

**General Hidradenitis Suppurativa Treatment**

While there is no single effective treatment or cure for HS, the activity of the disease can be brought to zero with a combination of preventive lifestyle changes and permanent removal of the subcutaneous inflammatory material using surgical procedures ranging from mini-unroofing of individual inflammatory units, through full un-roofing, up to wide surgical excision for very severe HS (Hurley's III). Prevention requires metabolic, medical and surgical strategies and lifelong gentle atraumatic care.

Education, diet and support
Improve environment:
Reduce all trauma, friction in the area, heat, sweating and obesity
Loose clothing, boxer-type underwear
Tampon use if appropriate / avoid pads
Antiseptic washes are optional
Consider anti-androgen treatment
Stop smoking and all other nicotine
Hair removal laser for local lesion reduction

Zero dairy diet with low glycemic load diet, 
**because the same diet that causes HS is a major contributor to obesity.**
At all stages – especially if weight is an issue – consider use of metformin (500mg to start up to 500mg tid) to improve sensitivity to insulin in patients on high glycemic load diets. Lowering chronic hyperglycemia reduces insulinemia and so decreases the impact on androgen receptors, with a positive outcome.

**Treatment - Hurley’s Stage I**
“Abscess formation, single or multiple without sinus tracts and cicatrisation/scarring.”

This is the most limited form of disease and is generally responsive to combined lifestyle modification and medical therapy.
The majority of patients with Stage I have a few flares a year; however, they can be well controlled.

**Medical Treatment for Stage I Hidradenitis Suppurativa**
Topical antibiotics
   - Clindamycin 1% lotion bid
Intralesional
   - Triamcinolone acetonide 10 mg/mL, 0.5 to 1 mL injected with a 30g needle into individual, painful, early papules / small nodules to suppress inflammation. Inject through normal skin at the edge of the nodule right into the center of the lesion. Avoid over-filling and bursting.
Systemic Antibiotics (for 7-10 days) - wide choice
   - Doxycycline 100 mg po bid or clindamycin 300 mg po bid, or amoxicillin / clavulanic acid 500mg -1g po q 8h
Adjunct preventive therapy
   - Zinc picolinate 30 mg with copper gluconate 2mg po bid
   - Vitamin C 500 mg tid with food
   - Vitamin D3 2000 – 5000 IU daily with fatty food
Anti-androgens
   - Drospirenone in Yasmin and Yaz Oral Contraceptives
     – consider extended regimen (Yasmin daily x 84 – 126 days)
   - Yasmin or Yaz plus spironolactone
   - Spironolactone alone 50 – 100 – 200 mg/d
   - Finasteride 5 mg/d (Use of finasteride 5 mg per day in women and young girls as an antiandrogen for both therapy and long-term prevention) with obsessive non-androgenic (drospirenone or copper IUD) contraception
Surgical Treatment – mini-unroofing eliminates single follicular unit explosions
   - standard unroofing / deroofing for larger lesions
   - excisional surgery not usually needed for Hurley Stage I

General Care
   Avoid irritants
   Loose clothing
   Stop all nicotine
   Weight loss
   Hair removal laser for lesion reduction

Maintenance
   Continue above as needed

Treatment - Hurley’s Stage II
   “Recurrent abscesses with sinus tract formation and scarring,
   either single or multiple widely separated lesions”

The aim is to clear these patients or at least reduce them to stage I disease.
Sinus tracts and scarring will require combined medical and surgical therapy. For those with little
scarring and much inflammation use antibiotics such as rifampin and/or clindamycin for 3 months
to clear active cellulitis and then decrease to maintenance on doxy- or minocycline, full dose zinc
with copper.

General care and intralesional treatment is the same as for stage I. Antibiotics for at least three
months are usual, with a decreased dose for maintenance. Systemic antibiotics include doxycycline,
as above or, for more extensive disease, clindamycin 300 mg twice a day often combined with
rifampin 300 mg twice a day for three months. (See below for prescribing details) Dapsone 100 mg
per day can be used. (See below for prescribing details ). The same adjunctive therapy with full
dietary restriction, zinc picolinate with copper, anti-androgens and no nicotine must be maintained.

A. Medical Treatment for Stage II
   All preventive measures are continued indefinitely.
   Topical antibiotics
      Clindamycin 1% lotion twice a day
   Systemic Antibiotics
      Amoxicillin and clavulanic acid 3g loading dose on Day 1 then 1g po q8h for 5-7 days for
      acute painful lesions
      Clindamycin 300 mg po bid with / without rifampin 300 mg po bid
      Sulfamethoxasole- trimethoprim (Bactrim DS) 1 tab bid
      Dapsone 50 mg po and then 100 mg po with the appropriate blood work (See below for
      prescribing details).
      Combination of rifampin-moxifloxacin-metronidazole for 6 weeks followed by
rifampin-moxifloxacin (metronidazole 500mg tid, rifampin 10 mg/kg/d, moxifloxacin 400 mg/d) (see references for details)
Maintenance – Doxycycline or minocycline 100 mg bid
Acitretin – a retinoid can be helpful but must be avoided in women of childbearing age (see references)

Adjunct preventive therapy
Zinc picolinate 30 mg with copper 2 mg po bid
Vitamin C 500 mg tid with food
Vitamin D3 2000-5000 IU with fatty meal
Anti-androgens
Drospirenone in Yasmin and Yaz Oral Contraceptives
– consider extended regimen (Yasmin daily x 84 – 126 days)
Yasmin or Yaz plus spironolactone
Spironolactone alone 50 – 100 – 200 mg/d
Finasteride 5 mg/d (Use of finasteride 5 mg per day in women and young girls as an antiandrogen for both therapy and long-term prevention) with obsessive non-androgenic (drospirenone or copper IUD) contraception
Intralesional triamcinolone as in Stage I

B. Surgical Treatment
If there are persistent chronic sinus tracts or cysts then obsessive wide surgical unroofing is necessary. Incision and drainage (I and D) should be avoided except for a tense abscess that is too painful to bear. Acute painful lesions and abscesses may need to be drained for pain relief only but are better managed by unroofing with thorough removal of debris. This must include sinuses, cyst wall remnants, scars that may harbor sequestered cysts and sinuses and careful elimination of all communicating sinuses and all of the invasive proliferative gelatinous mass (IPGM).

C. and D. General Care and Maintenance- as for Stage I

Treatment - Hurley’s Stage III
“Diffuse or almost diffuse involvement or multiple interconnected tracts and abscesses”

This stage is a surgical disease but full supportive concurrent medical treatment is both prophylactic and essential. This requires a staged medical – surgical team approach

A. Medical Treatment
Pre-Op -These patients will need the anti-inflammatory effects of medical treatment to prepare them for surgical treatment.
1. If cellulitis is present, antibiotics are essential, especially in cases being considered for ‘biologic’ therapy. A study of IV ertapenem 1 gm daily for 6 weeks followed by various combinations of moxifloxacin, rifampin and metronidazole significantly improved severe HS. Clindamycin 300 mg po bid with Rifampin 300 mg po bid is more commonly used.

2. Once cellulitis is controlled
Corticosteroids 0.5 – 0.7 mg/kg/d methylprednisolone or prednisone (oral) is classic. TNF-α and IL inhibitors are the newcomers
Infliximab 5 mg/kg IV by infusion Q6 weeks – use with the help of a knowledgeable health care provider
Adalimumab was approved in late 2015 by FDA for management of the signs and symptoms of moderate and severe HS. The dose is 80 mg on Day 1 and Day 8 then 40 mg weekly.
Ustekinumab and Anakinra have also been tried with mixed results

These ‘biologics’ are valuable to decrease swelling, inflammation, pain and discharge pre-operatively, simplifying unroofing and excisional surgery and minimizing the need for extensive or excessive tissue removal. They do not affect either the epithelialized sinus tracts or the invasive proliferative gelatinous mass that is so resistant to therapy. Biologics are not a cure; improvement is rarely permanent.

Note – Medical treatment at this stage is only palliative and temporary. Patients must avoid nicotine after surgery in order to prevent new lesions and follow the dietary recommendations. Anti-androgens may still be needed.

B. Surgical Treatment
Wide surgical unroofing and debriding of all cysts and sinuses and scarred tissue can be accomplished by a knowledgeable surgeon. Healing can be by secondary intention or it may be accelerated with mesh grafting. Primary closure is avoided in active disease. At times, flaps and grafts are required.

Local Unroofing Surgery
Unroofing is simple surgery, an old technique that has been ignored for years. Recently revived, it deserves wide use. It is practical for lesions from the early hot nodules of Stage I to the advancing, branching lesions of Hurley Stage III. Removing early lesions and taking the tops off the deep epithelialized subcutaneous sinus tracts of HS/AI is invaluable. It requires nothing more than sturdy scissors, blades held parallel to the skin surface. Alternatively, laser and electrosurgery have been used. It is far more effective than prolonged antibiotics and anti-inflammatory therapy.
Unroofing is not technically difficult, can be performed in the office setting under local anesthesia, and so is easily adapted to the Emergency Room.
This is the technique that we recommend to replace “I&D” of fluctuant masses and other manifestations of HS/AI. Every opportunity to perform I&D should be converted into an
opportunity to unroof the lesion. It provides superior drainage and pain control, eliminates the risk of inadequate ‘wound toilet’ that leaves behind the invasive proliferative gelatinous mass (IPGM) and fragments of the exploded FPSU. These are the sources of recurrences.

I&D is a temporary ‘solution’; unroofing is almost always permanent. It requires very simple post-operative dressings and post-operative pain is remarkably easy to manage.

Lidocaine 1-2% anesthesia with epinephrine is used. Controlled volumes are injected peripherally, avoiding leakage through sinuses. Time for vasoconstriction reduces pain and blood loss. Tumescent anesthetic technique is highly effective in dealing with entire involved anatomical units, and may spare some the need for general anesthetics.

A single inflamed follicular unit requires only urgent mini-unroofing (not I&D). A biopsy punch of appropriate diameter (5-8mm) is centered over the involved FPSU and a twisting incision removes the central damaged material. This is then debrided with digital pressure, curettage with gauze wrapped around a cotton applicator, and then ferric chloride hemostasis is applied with a cotton-tipped applicator.

Fluctuant masses are best initially incised and drained to reduce pressure. The central linear incision is extended to the edge of the loose tissue over the fluctuant area and the incision is extended through 360 degrees at the edge of the ‘roof’, beveling the edges with scissors. The base of the wound is then scrubbed with coarse gauze. Curettage with a spoon or bone curette may be needed to remove the IPGM. Excision of fat at the base of the wound is unnecessary and counterproductive. All depths and margins are explored digitally, visually, and with scissors tips. Any linear fibrous tissue is suspect as a possible sinus track and is best removed. Communicating sinuses once detected are unroofed. They can be surprisingly extensive and must be totally unroofed. Remove all tissue that is involved with active disease, devitalized or, if left behind, would interfere with healing. The wound base and small bleeders are dried and sealed with ferric chloride solution. Electrodesiccation or electrocautery are rarely needed. Scars are normally soft, contract to a much smaller area than that unroofed, and are quite acceptable to the patients.

Post-operatively, the wound is dressed with a thick coat of simple petrolatum. Running water only, no anti-bacterial soaps and no washcloths are used. Thick layers of petrolatum on cotton or soft gauze are re-applied once or twice daily or as needed. Patients (and wound care staff) must avoid debriding the wound. Healing by secondary intention and epithelialization will proceed only if the fresh epidermis is allowed to cover the wound and is not debrided away.

HS is not an infection; the inflammation is caused by the material removed by this procedure, so antibiotics are rarely necessary and are best avoided to minimize overgrowth of yeast and resistant bacteria.

Unroofing also eliminates the risk and costs of hospital or ambulatory surgical center care, laser, general anesthesia, graft donor sites, dehiscence, infection, the burying of residual inflammatory foci, post-operative antibiotics, time lost from work, and the need for travel to major centers. When performed correctly it stops forever the progression of the lesion treated.

For extensive Stage 3 vulvar hidradenitis suppurative, total vulvectomy with skin grafts may be required. For further information on this, go to the University of Michigan Center for Vulvar Diseases Website and search for hidradenitis suppurativa.
Specific Drug Information for Medications Used in the Treatment of Hidradenitis Suppurativa

CLINDAMYCIN
In hidradenitis, clindamycin is used as an anti-inflammatory medication.
– helps settle down the redness, swelling, etc.
It is also a very effective medication for bacterial infections.

Side effects
Bowel inflammation can occur due to an overgrowth in the bowel of bacteria (C. difficile) that release a toxin. This can occur in a few patients. If there is any problem with diarrhea, stop the medication. Other side effects include upset stomach, vomiting, and skin rashes. Clindamycin can be taken with the rifampin or used separately.
Dose – 150 - 300 mg po twice a day - to be taken with food. Use for 3-6 months.
Interactions – can interact with birth control pills

AMOXICILLIN / CLAVULANATE
Used as an anti-inflammatory
Dose – For acute nodules and incised abscessed lesions - amoxicillin and clavulanic acid 3g loading then 1g po q 8h for 5-7 days (taken with food). For indolent nodules, 500 mg po tid for 1-2 weeks.
Side effects – allergy, GI upset, nausea, diarrhea, yeast, rashes
Contraindications – hypersensitivity
Indications – For acute nodular flares.

ZINC GLUCONATE
Zinc gluconate is anti-inflammatory and helps in wound healing.
Dose is 50 mg po bid or 30 mg po tid. This is suppressive rather than curative.
A preparation balanced with copper is preferred
– 30 mg zinc picolinate and copper 2 mg taken once or twice daily.
Side effects are occasional GI upset with nausea and / or diarrhea. Zinc sulfate is avoided for this reason.
High doses can affect iron in the body with resulting anemia and drop in white count.
Do not increase the dose of zinc.

RIFAMPIN
Rifampin 150 and 300 mg tablets – this is an antibacterial agent that is used for bacterial infections, both common ones and mycobacteria including tuberculosis. This medication is used in hidradenitis suppurativa as an anti-inflammatory and is usually combined with other medications.
Dose - 150 – 300 mg po twice a day. Take on an empty stomach. It is occasionally given as 600 mg in one dose. It can be given with other medication such as clindamycin taken in two doses daily or may be given as a single dose with a large glass of water at 4 AM to prevent any interaction with the other medicines.
Monitoring blood tests for Rifampin - baseline CBC, renal and liver function tests should be taken. Caution should be taken if there is pre-existing liver disease or liver function abnormalities. Repeat blood tests at 2-4 week intervals as needed.
Drug interactions – many may occur
Birth control pills – decreases effect of BCP (only antibiotic proven to do this)
  Blood thinning drugs – increases INR / clotting time
  Heart drugs – digoxin, quinidine
  Beta-blockers – verapamil
  Anti-convulsants – phenobarbital, phenytoin
  Anti-fungal drugs – ketoconazole
  Bronchodilators – theophylline
  Immunosuppressant drugs – cyclosporine
  Corticosteroids
  Sulfonylurea and other hypoglycemic medications
  Miscellaneous – acetaminophen, dapsone.
  Enalapril can result in an increase in blood pressure.

Side effects
  Urine discoloration – orange red
  Permanent staining of soft contact lenses

Allergic reactions
  Flu-like syndrome with fever, chills, headache, dizziness & rashes
  Skin rashes – itching, hives, pimply reactions, and blisters,
    rarely erythema multiforme or toxic epidermal necrolysis
  Dizziness, headache and fatigue can occur
  Rarely anemia and hepatitis

DAPSONE
This is used as an anti-inflammatory. It reduces PMN/WBCs in tissue
Dose – 50 - 100 mg orally per day. Start at 50 mg/day for first 2-4 weeks
Caution – Glucose-6 phosphate dehydrogenase must be measured prior to therapy. If this is low dapsone is usually contraindicated because there is a serious risk of blood problems such as hemolytic anemia.
This can be more of a problem for some African Americans and Asians resulting in a more toxic reaction from the dapsone. Dapsone affects red blood cells so that they do not “live as long”. Usually red blood cells last for 120 days but when a patient is on dapsone this can decrease to 80 days causing the hemoglobin, to drop. This can be a problem in patients with heart, liver and kidney disease. A thorough history and physical with attention to the heart, liver and renal function is important. Patients must be checked to be sure there is no pre-existing anemia.
Contraindications to the use of dapsone include prior hypersensitivity and agranulocytosis. Patients with severe allergy (hypersensitivity) to sulfonamides may be allergic to dapsone. If a mild allergy to sulfonamides, this is less likely.
Relative contraindication would be significant cardiopulmonary disease, G-6PD deficiency, and severe sulfonamide allergy.
Monitoring blood tests for patients for dapsone
  1. G-6PD level must be assessed.
  2. CBC with differential, liver function tests, BUN, creatinine and urinalysis.
3. Repeat blood work - CBC with differential, WBC and reticulocyte count every week for 4 weeks and then every 2 weeks for 8 weeks and then about every 3-4 months. Check reticulocyte count to assess response to Dapsone hemolysis.

4. Liver function and renal function tests every 4 months for maintenance.

**Drug interactions**
1. Dapsone levels are increased with trimethoprim, probenecid
2. Dapsone levels are decreased with rifampin
3. Dapsone, if combined with hydroxychloroquine and sulfonamides, yields more red blood cell toxicity

**Cross Reactions**
Other sulfonamide type drugs - patients with severe allergic reactions to sulfonamide medications may be allergic to Dapsone. This is very rare.

**Adverse Effects**
1. Hemolytic anemia, methemoglobinemia – symptoms headache, lethargy
2. Hepatotoxicity – mono-like syndrome
3. Peripheral neuropathy
4. Allergy – rashes etc.
5. GI upset

**Behçet's Disease**
Is a very rare condition. It is common in the Middle East but distinctly uncommon in North America. Behçet's disease was first described in 1937 by Hulusi Behçet, a Turkish dermatologist. It is defined by a triad, classically of oral ulcers, genital ulcers and uveitis. Oral ulceration is the most common cutaneous finding in Behçet's disease. The most common sites of involvement are the buccal mucosa, gums, tongue, lips, and pharynx. In order to make a diagnosis of Behçet's, a patient must experience oral ulceration occurring at least three times in one year and fulfill the other criteria discussed below. The lesions tend to be painful, shallow to deep, and have erythematous borders with yellow, fibrinous bases. Ten percent of patients, however, develop major aphthous ulcerations, which are lesions that are larger, more persistent, and may heal with scarring. Vulvar lesions are quite common. Involvement of the vagina and/or cervix may also occur. Pathergy is one of the diagnostic criterions for Behçet's and consists of development of a small pustule within 24 to 48 hours after the skin has been pricked by a blunt sterile needle. Although helpful if positive, its sensitivity is debatable with some studies finding it as low as 10 percent (Davies PG,

**International study group criteria for the diagnosis of Behçet's disease**

<table>
<thead>
<tr>
<th>Major criteria (need 1)</th>
<th>Recurrent oral ulceration</th>
<th>Minor aphthous, major aphthous, or herpetiform ulceration observed by health care provider or patient that recurred at least three times over a 12-month period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor criteria (need 2)</td>
<td>Recurrent genital ulceration</td>
<td>Aphthous ulceration/scarring observed by health care provider or patient</td>
</tr>
<tr>
<td></td>
<td>Eye lesions</td>
<td>Anterior or posterior uveitis or cells in vitreous on slit lamp examination; or retinal vasculitis observed by ophthalmologist</td>
</tr>
<tr>
<td></td>
<td>Skin lesions</td>
<td>Erythema nodosum observed by health care provider or patient, pseudofolliculitis or papulopustular lesions; or acneiform nodules observed by the health care provider in a postadolescent patient who is not receiving corticosteroid treatment</td>
</tr>
<tr>
<td></td>
<td>Positive pathergy test</td>
<td>As interpreted by health care provider at 24 to 48 hours</td>
</tr>
</tbody>
</table>


Treatments that have been utilized in the treatment of Behçet Disease

<table>
<thead>
<tr>
<th>Class 1 or II topical steroids</th>
<th>Dapsone</th>
<th>Cyclosporine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intralesional triamcinolone acetonide</td>
<td>Systemic steroids</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Topical anesthetics</td>
<td>Methotrexate</td>
<td>Thalidomide</td>
</tr>
<tr>
<td>Colchicine</td>
<td>Azathioprine</td>
<td>Interferon alfa-2a</td>
</tr>
</tbody>
</table>

**DIFFERENTIAL DIAGNOSIS OF VULVAR EDEMA**

Swelling can be due to any of these conditions or combinations of inflammation, infiltration and lymphatic disruption or obliteration

**Inflammatory Edema**

1. Allergic/Immune
   1. Allergic Reaction
      a. Angioedema with or without urticaria
      b. Allergic Contact Dermatitis
   2. Granulomatous Inflammation
      a. Crohn’s Disease
b. Melkersson-Rosenthal Syndrome
c. Sarcoidosis

II Infection – edema secondary to local infection
   1. Cellulitis – streptococcal
   2. Abscess – Bartholin’s duct
   3. Candidiasis
   4. Rare – Tuberculosis, actinomycosis, Granuloma Inguinale, Amebiasis, Blastomycosis, Schistosomiasis

III Other
   1. Direct Trauma
   2. Hidradenitis suppurativa (HS)
   3. Amyloidosis
   4. Infiltrative neoplasm – inflammatory breast CA

Note – all infections, Crohn’s and HS can cause inflammatory edema the scarring and secondary obstructive lymphedema.

Obstructive Lymphedema
I  Congenital
   1. Milroy’s disease (congenital lymphedema)
   2. Lymphangioma

II  Infection with secondary lymphatic damage
   1. Recurrent cellulitis – streptococcal
   2. Lymphogranuloma venereum
   3. Filariasis

III Physical lymphatic obstruction with mass, tumor, or destructive process
   1. Pregnancy
   2. Pelvic or local trauma
   3. Pelvic tumor
   4. Post-radiation scarring
   5. Congestive heart failure

IV Metabolic
   1. Obesity
   2. Renal failure
   3. Hepatic failure

Note – Chronic obstructive lymphedema can result in lymphangiectasia / acquired lymphangiomas.

PROTOCOL FOR LYMPHANGIECTASIA AND CHRONIC LYMJPHEDEMA OF THE VULVA
A. First control infection. Usually it is Strep and occasionally Staph.
   1. Gently cleanse with Cetaphil® or another triclosan-containing antibacterial cleanser morning and
      night, pat dry.
   2. Bleach baths can be very useful in reducing re-infection. Do 2-3 times a week. Add one half cup
      of household bleach (125 mL) to a 10 inch (25 cm) deep tub of comfortably warm bath water. Mix
      well. Soak for 5-7 minutes, ensuring penetration of the solution into all cracks and genital / buttock / skin
      folds, using a plastic cup and bare hands to spread over all involved areas. For sitz bath mix 1 ¼
      teaspoon bleach in 1 gallon of water.
   3. Antibiotic ointment (mupirocin ointment twice a day) and if skin is crusty, debride loose matter
      only. Do not rub.
   4. Penicillin VK 500 mg qid for 2-4 weeks and then tid for 2-3 months, bid at least 6 months or
      more. Any flares, go back to four a day. If patient is doing very well, decrease to one or two a day
      indefinitely, for the next one or two years.
      Cephalexin 500 mg with the same dose may also be used.
      (For intermittent flares, bump up the dose to 500 mg qid.)

B. For the edema:
   1. A brief course of prednisone or prednisolone starting at 20-30 mg in the morning for 2-3 weeks
      and then decreased gradually. Length of use of Prednisone depends on the response. Patients who
      flare acutely may require 30 mg per day for 1-2 weeks, then 15 mg per day for 1-2 weeks.
      Chronic edema may require 20-30 mg per day for 2-3 weeks and a slow stretched-out course
      over 2-3 months, dropping 2.5 mg every 1-2 weeks.
   2. If the edema is very indurated and woody use intralesional triamcinolone acetonide 10 mg/mL
      (Kenalog 10¨) instead of the oral steroid to soften or get rid of fibrosis.
      a. Anesthetize the keratinized skin for one hour with topical
      EMLA or equivalent under occlusion.
      b. If it is somewhat woody / indurated start with 10 mg and if quite woody use up to 40 mg
      total dose monthly (over large surface area). Inject with a 25-26g needle and use about a 1
      cm grid. Inject into the subcutaneous tissue just enough to blanch the area. To soften this
      chronic lymphedema you can utilize it once a month.
   3. Lymphatic massage:
      This may be helpful for the vulva and for the lower legs. Some physiotherapists are trained to
      teach the patient how to do this at home, depending on the complexity of the problem.
   4. For lymphangiomas that remain open and draining:
      A. For extensive involvement excisional surgery to debulk the area may be necessary.
      B. For more localized involvement or those for whom surgery is not an option -
         a. Once you have the infection down and controlled then you can safely use the local
            anesthesia as above – 2.5% lidocaine 2.5% prilocaine in a cream base (EMLA) apply every
            ½ hour for 1 to 2 hours under occlusion, then local anesthesia 2% lidocaine with epinephrine.
         b. To cleanse the area do not use alcohol.
         c. Electrodesiccate on a high setting and put the needle into each one of the small
            lymphangiectatic “fish eggs” and cauterize them until they bubble, turn black and crust.
         d. Post-operatively:
            Soak in tepid water 1-2 times a day
Mupirocin ointment 2 times a day to involved areas.  
Keflex 500 mg qid for 2 weeks then chronic penicillin VK  
Tylenol #2 for pain (acetaminophen and codeine)  
Loose ventilated clothing.  
Consider fluconazole suppression.  
Repeat the destruction when and if needed.

ULCERS OF THE VULVA

Ulcers of the vulvar are diagnostically challenging. It is often very difficult to differentiate them from erosions. Erosions involve loss of the epidermis only, not the dermis, and they appear as deep red, often weeping, patches. Ulcers are deeper, extending into the dermis with a white or yellowish fibrinous base. Most diseases produce either erosions or ulcerations but often these overlap. Erosions can be transformed into ulcers by secondary infection, irritant contact dermatitis, rubbing and other trauma.

The best example is severe herpes simplex virus (HSV) infection. The primary lesion of HSV is an intraepidermal vesicle that becomes a pustule that ruptures, creating an erosion. When severe, these erosions can ulcerate. An ulcer is characterized by loss of both epidermis and dermis.

A diagnosis of a vulvar ulcer based on morphology alone is erroneous 40% of the time. Laboratory testing is usually required.

DIFFERENTIAL DIAGNOSIS

In sorting out these conditions, try to identify the primary process. Is it a pustule within the epidermis as in candidiasis or herpes simplex, an intraepidermal vesicle in acute eczema (contact dermatitis), or a frank bulla (intraepidermal or sub-epidermal) as in the bullous diseases or drug eruptions. All these rupture, resulting in erosions and/or ulcerative disease.

All of these can look much alike and it can be very difficult to differentiate them clinically, especially if there are secondary changes with crusting and bleeding, etc.

A good history is important, as is the understanding that the history may be inaccurate. Many women have problems with discussing the genital area

Note the following factors:

<table>
<thead>
<tr>
<th>Age</th>
<th>Immune status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidemiology and demographics of their community</td>
<td>Systemic disease</td>
</tr>
<tr>
<td>Travel and sexual exposure</td>
<td>History of abuse</td>
</tr>
<tr>
<td>Pattern of recurrence</td>
<td>Previous sexually transmitted diseases</td>
</tr>
<tr>
<td>Previous/present treatment</td>
<td></td>
</tr>
</tbody>
</table>

Note the following factors specific for vulvar ulcers:

| Pain | Systemic symptoms |
| Induration | Lymphadenopathy |
| Friability | Fever |
| Number of lesions (single or multiple) | Malaise |
| Acute or chronic | Headache |
| Speed of onset | Extranatal changes |
Tests for all ulcers:  
- HSV culture  
- CBC  
- Candida cultures  
- RPR (syphilis screen)  
- HIV screen  
Serology as indicated for Epstein Barr virus (EBV) - antiviral capsid antigen – IgM for EBV and Serology for Mycoplasma Pneumoniae  
- Biopsy for H&E +/- immunofluorescence

Consider more extensive workup depending on the case, e.g. cultures, smears and serology.

**Biopsies** are very important. Always biopsy the edge of the lesion – not the necrotic center. A wedge excision of the edge often gives the best information for the pathologist but may be impractical. Two smaller punch biopsies may be more appropriate

Why biopsy? Because it is impossible to guess the cause of most ulcerative erosive conditions – biopsy gives the most information, especially for chronic ulcers. Although it is an uncomfortable procedure it can be made almost painless. One is adding an extra open area to an already tender area but your patient is already very stressed and wants to know the answer.

**Most common causes of primary vulvar ulcers (not erosions):**

**INFECTIONOUS**

**Venereal**
- Herpes simplex (HSV)
- Immunosuppressed

**Chancroid**
- Granuloma inguinale
- Lymphogranuloma venereum
- Syphilis
- Human immunodeficiency virus

**Non Venereal**
- EBV
- Mycoplasma pneumoniae

**NON-INFECTIONOUS**
- Aphthous ulcers
- Behçet’s disease
- Crohn’s disease
- Factorial disease
- Fissures

<table>
<thead>
<tr>
<th>Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
</tr>
</tbody>
</table>

The infectious ulcers are classically due to the STIs. The most common cause of genital ulcers in the world is herpes simplex. HSV in any Immunosuppressed patient can present with ulcers. These can be chronic, severe, punched out, and widespread. These are typically seen in a HIV positive individual. The other conditions are syphilis, Chancroid, granuloma inguinale and rarely Lymphogranuloma venereum. These conditions are all quite uncommon in North America. 

Much more common are the non-infectious ulcers, particularly aphthae, which classically present as punched out, painful ulcers. They are mostly idiopathic but they can be associated with underlying conditions, see below. Aphthous ulcers are also seen in Behçet’s disease, Crohn’s disease and HIV. Crohn’s disease may present with the deep classic “knife-cut” type ulcers. Pyoderma gangrenosum can
cause ulcers. Last in this group are the factitial ulcerations. Tumors, classically squamous cell carcinoma, also ulcerate.

The limitation to this classification is the possibility of missing the less common conditions that could cause vulvar ulcers and erosions such as drugs, irritant contact dermatitis, secondary infected bullous diseases etc.

2. Etiologic classification vulvar ulcers and erosions:

### INFECTIONS

**a) Venereal**
- Herpes simplex
- Chancroid
- Granuloma Inguinale
- Lymphogranuloma venereum
- Syphilis
- Human Immunodeficiency Virus

**b) Non-venereal**
- Candida
- Herpes zoster
- Varicella
- Hand Foot Mouth disease
- Staph & Strep,
- Typhoid & paratyphoid,
- Brucellosis
- Diphtheria,
- Pseudomonas
- Epstein-Barr and Mycoplasma pneumoniae

### Non-Bullous Dermatoses

<table>
<thead>
<tr>
<th>Non-Bullous Dermatoses</th>
<th>Bullous Dermatoses</th>
<th>Premalignant and Malignant Tumors</th>
<th>Infections</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritant contact dermatitis</td>
<td>a) Autoimmune BMM Pemphigoid P. vulgaris Bullous pemphigoid Linear IgA Disease EB Acquisita</td>
<td>Premalignant and Malignant Tumors</td>
<td>H. zoster</td>
<td>Rheumatoid nodule</td>
</tr>
<tr>
<td>Drug Reaction*</td>
<td></td>
<td></td>
<td>Varicella</td>
<td>Gangrene</td>
</tr>
<tr>
<td>Fixed Drug Reaction LE</td>
<td></td>
<td></td>
<td>Vaccinia</td>
<td>Acrodermatitis</td>
</tr>
<tr>
<td>Crohn’s</td>
<td></td>
<td></td>
<td>Hand/Foot/Mouth</td>
<td>Lymphangiectasis</td>
</tr>
<tr>
<td>Darier’s</td>
<td></td>
<td></td>
<td>Staph &amp; Strep</td>
<td>Graft vs. Host</td>
</tr>
<tr>
<td>Behçet’s</td>
<td></td>
<td></td>
<td>Typhoid</td>
<td>Spider bite</td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
<td></td>
<td></td>
<td>Paratyphoid</td>
<td>Hymenal Fissures</td>
</tr>
<tr>
<td>Hidradenitis Suppurativa</td>
<td></td>
<td></td>
<td>Brucellosis</td>
<td>Reiter’s Disease</td>
</tr>
<tr>
<td>Necrolytic Migratory Erythema</td>
<td>b) Non-autoimmune TEN / EM Contact Dermatitis Hailey-Hailey EB Inherited</td>
<td>Extramammary Paget’s Disease</td>
<td>Diphtheria</td>
<td>Wegener’s Granulomatosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pseudomonas</td>
<td>Factitial</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tuberculosis</td>
<td>Female Genital Mutilation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Histoplasmosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Actinomycosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cryptococcosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Leishmaniasis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Schistosomiasis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Amebiasis</td>
<td></td>
</tr>
</tbody>
</table>

*12 meds for known to cause a drug reaction

Antibiotics
Sulfa
Penicillin (PCN) (not as much trouble as before (no polymers attached)
cephalosporins

Cardiovascular
HCTZ
Lasix
Beta-blockers
Ace inhibitors
Dilantin

Miscellaneous
Allopurinol
Vaccines
New biologicals
NSAIDs

Of all this list, the most important causes of ulcers and erosions are, in North America are:

Infections

<table>
<thead>
<tr>
<th>Venereal</th>
<th>Non Venereal</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV</td>
<td>Candida</td>
</tr>
<tr>
<td>Syphilis</td>
<td>EBV</td>
</tr>
<tr>
<td>HIV</td>
<td>M Pneumoniae</td>
</tr>
</tbody>
</table>

Dermatoses

<table>
<thead>
<tr>
<th>Bullous</th>
<th>Non-Bullous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact dermatitis</td>
<td>Aphthosis</td>
</tr>
<tr>
<td></td>
<td>LS</td>
</tr>
<tr>
<td></td>
<td>LP</td>
</tr>
<tr>
<td></td>
<td>Drug</td>
</tr>
<tr>
<td></td>
<td>Contact</td>
</tr>
<tr>
<td></td>
<td>Crohn’s</td>
</tr>
</tbody>
</table>

Tumors  Squamous Cell Carcinoma

APHTHAE (aphthous ulcers)
Canker sores on the vulva
Very common in the mouth and not uncommon on the vulva
Acute painful ulcer or ulcers of sudden onset
Can be recurrent or chronic
Minor or major in size, single or multiple

Painful, non-sexually transmitted ulcers in young girls or women are referred to by many terms and there is no consensus on best term. See list below:
Ulcus vulvae acutum
Lipschütz ulcers
Nonsexually acquired genital ulceration (NSAGU)
Complex Aphthosis or aphthae
Vulvar aphthous ulcers
Acute vulvar ulcers

Clinical:
Average age is 14 (9-19) yrs, but patients can be older
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
There is not always a prodrome especially with recurrent cases in older patients
Duration 1-3 weeks, can last months
One episode, less common recurrent
Often past history of oral aphthae – canker sores
Not Behçet’s
Associated with oral aphthae – complex aphthae

The following associations have been made:
**Acute (more common)** – these can recur
Usually with a prodrome - fever, headache, malaise, GI upset
These have been reported in the literature associated with:
EBV, Mycoplasma pneumoniae, viral upper respiratory infection
(parvovirus, influenza, paramyxovirus) or gastroenteritis, Strep, CMV,
Mumps, salmonella, toxoplasma gondii

**Chronic or recurrent aphthae:**
No prodrome.
Associations:
Bowel disease - Crohn disease, Ulcerative colitis, Celiac disease
Infections – HIV
Behçet’s disease
Medications – cytotoxic, NSAIDs
Myeloproliferative disease, cyclic neutropenia, lymphopenia

**Syndromes with Genital Aphthous Ulcers: rare**
Sweet’s syndrome
Mouth and Genital Ulcers Inflamed Cartilage - MAGIC Syndrome
Periodic Fever, Aphthae, Pharyngitis, Adenitis - PFAPA Syndrome

Note Acute aphthae are probably immune complex related and can be precipitated by infection such as a viral illness. e.g. viral gastroenteritis or upper respiratory tract infection, influenza, CMV. Epstein Barr virus (EBV) could directly infect the skin or cause an immune complex reaction. Mycoplasma pneumoniae can do the same. Streptococcal infection has been found. Most common cause of acute onset aphthae in a 12-20 year old is probably an infection.
For recurrent aphthae and complex aphthosis look for inflammatory bowel disease or, less likely, a lymphoproliferative problem.

**Diagnosis of exclusion**
Cultures negative, biopsies non-specific and blood work non-contributory

Differential diagnosis:
- HSV, Syphilis, HIV, Chancroid, LGV, Granuloma Inguinale
- pyoderma gangrenosum
- trauma
- contact dermatitis

Evaluation of Vulvar Aphthae:
Thorough history and physical – eye, oral, genital
Only testing for HSV may be necessary

**Biopsy rarely needed**
Lab tests that could be considered–
- CBC, diff
- Serology for HSV, HIV, EBV, syphilis, CMV, *Mycoplasma pneumoniae*
- Influenza – swab PCR

**HSV - swab for PCR – always rule out HSV**
For strep -throat swab and antistreptolysin O titer
Tests as indicated for – paratyphoid and typhoid (stool, blood culture), TB enterocolitis, Yersinia
GI investigations –
for inflammatory bowel disease and celiac disease

Note – in HIV + patients with genital ulcers - 60% of genital ulcers are due to aphthae and 40% to HSV

Treatment: depends on the severity. If mild comfort measures may be all that is needed
Local therapy  AGNO3 sticks
Pain control – topical – 5% lidocaine ointment
- systemic – mild, moderate pain – NSAID  severe - opioids

**Immunosuppression -**
Prednisone 40 – 60 mg each morning until pain resolves (3-7 days, then ½ dose 3-7 days) with food
Methylprednisolone (Medrol) 4-8mg bid-tid 3-7 days then ½ dose 3-7days) with food
Clobetasol or halobetasol 0.05% ointment AM & PM
If not sure if HSV use antiviral meds until HSV test report available.

Educate -Most often a one-time event, can recur

For persistent or chronic aphthae:
Oral corticosteroid for initial control - prednisone or methylprednisolone
Intralesional triamcinolone (Kenalog 10 mg/mL) 5-10 mg
doxycycline 50 - 100 mg od
colchicine 0.6 mg bid-tid if tolerated
dapsone 50-150 mg per day
dapsone + colchicine
Cyclosporine  100 mg up to tid decreasing to 100 mg 2-3 doses/week
Pentoxifylline 400 mg tid
Thalidomide 100-150 mg per day (Concern for teratogenesis)
TNF alpha inhibitors- infliximab, adalimumab, etanercept

Prognosis:
Most often a one-time event
Scarring can occur
Occasionally recurrent

**Desquamative Inflammatory Vaginitis - DIV**

Desquamative Inflammatory Vaginitis - DIV is an erosive vulvovaginitis characterized by dyspareunia and a profuse, purulent, vaginal discharge. It is of unknown etiology. It is considered to be due to a primary defect of alteration in vaginal flora. Most commonly it presents in perimenopausal women.

Clinical findings are dyspareunia with pain, burning and a vaginal discharge that can be profuse that can be sometimes gray and green - 90% of cases have purulent vaginal discharge.

On examination there is a spotty, ecchymotic rash on the vestibule. The skin appears thin, sensitive, red and sometimes swollen. On speculum examination there are fine red “dots” scattered through the vagina with the discharge as above. On wet preparation (vaginal smear) there are numerous parabasal cells, many neutrophils (neutrophil/epithelial cells greater than 1:1 in at least 4 HPF’s), pH is increased > 4.5. Lactobacilli are decreased or absent. There can be increased Gram positive cocci and Gram negative bacilli.

**Diagnosis:**
Requires all of the following criteria:
1. At least one of the following symptoms - vaginal discharge, dyspareunia, pruritus, burning or irritation.
2. Vaginal inflammation with spotty ecchymotic rash and redness.
3. Vaginal pH > 4.5.
4. Wet preparation showing increased para basal cells and white cells.

Causes of inflammatory vaginitis that must be excluded are bacterial vaginosis, N. gonorrhoeae, C. trachomatis and T. vaginalis.

An inflammatory vaginitis can be seen with vulvovaginal atrophy with lack of estrogen, Crohn’s disease and rarely with the chronic bullous disease, cicatricial pemphigoid and pemphigus.

**Treatment:**
Treatment varies among providers. Some prefer intravaginal clindamycin, while others prefer intravaginal steroid such as hydrocortisone at 25 mg doses while others combine clindamycin with hydrocortisone per vagina.

**Therapy Options Clindamycin and/or Hydrocortisone (Adapted Sobel 2015)**
- Clindamycin 2% cream 5 grams - one applicator intravaginally nightly for four to six weeks with reassessment and if not clear treatment is continued then gradually tapered to 3x a week, 2x a week, etc.
- Clindamycin 200 mg vaginal suppositories nightly for four to six weeks then gradual taper as above.
- Intravaginal hydrocortisone suppositories 25 mg twice a day for four to six weeks (consider 3x a week for two months for suppression). Longer treatment may be necessary.
- Can combine clindamycin cream and hydrocortisone suppositories every other night for four to six weeks and then suppression if needed.
- 10% intravaginal hydrocortisone cream (100 mg/gram) 300 to 500 mg intravaginally, inserted nightly for four to six weeks and then gradually taper as above.
- Compound intravaginal hydrocortisone in 2% clindamycin using 10% hydrocortisone (100 mg/gram) with clindamycin 2% in a vaginal cream base inserting 3 to 5 grams vaginally for two to four weeks and gradually taper. This needs to be made in a compounded pharmacy.
- If not working, reconsider diagnosis.
- Estrogen replacement needs to be addressed and yeast suppression with fluconazole may be necessary.

**HERPES SIMPLEX VIRUS (HSV)**  
(adapted from CDC STD Treatment Guidelines)

This is a common sexually transmitted disease worldwide and it is the most common cause of vulvar ulcers. A history of HSV is unreliable. Primary HSV is uncommon. The majority of patients present with non-primary recurrent disease.

Infection is usually from sexual contact. Most transmission occurs during periods of asymptomatic viral shedding. Most persons infected with HSV-2 have not been diagnosed with genital herpes. Many people have mild or unrecognized infections but they shed the virus intermittently in the genital tract. Thus, the majority of genital herpes infections are transmitted by persons unaware that they have the infection or who are asymptomatic when transmission occurs.

**Symptoms:**

Primary HSV - Paresthesia for 2-3 days, followed by fever, malaise, headache and myalgia
There can be pain, moderate to severe (“deep boring pain” reflecting nerve involvement)
Recurrent infection - there is more tingling, itching and burning before the onset of vesiculation

**Physical Examination**

Can be seen anywhere on the vulva, vagina, over cervix, anus, buttocks and thighs.
Primary – red swollen vulva with extensive vesiculation, rapidly becoming pustular with open tender erosions lasting two weeks.
Recurrent infection – lesions are less extensive and are clear in 5-7 days with only mild swelling.

Note – Over 90% of HSV 2 carriers are unaware of their infection yet 80% have symptoms. Women think they have: Vaginitis, GU infection, clothing irritation or hemorrhoids
Symptoms can occur with no rash and no blistering in HSV sine eruption – herpes simplex without visible eruption
Immunosuppressed HSV – chronic ulcers that gradually extend at the periphery. There may be varying degrees of necrosis. These are painful and indolent.

Diagnosis: Cultures can be unreliable. Keep viral media refrigerated, on hand, and up to date. Failure to detect HSV by culture or PCR does not indicate an absence of HSV infection, because viral shedding is intermittent.

Virologic Tests
Cell culture and PCR are the preferred HSV tests
PCR assays for HSV DNA are more sensitive and are increasingly used in many settings
Viral culture isolates should be typed to determine which type of HSV is causing the infection.
The use of cytologic detection of cellular changes of HSV infection is an insensitive and nonspecific method of diagnosis, both for genital lesions (i.e., Tzanck preparation) and for cervical Pap smears and therefore should not be relied upon.

Type-Specific Serologic Tests
Both laboratory-based assays and point-of-care tests that provide results for HSV-2 antibodies from capillary blood or serum during a clinic visit are available. The sensitivities of these glycoprotein G type-specific tests for the detection of HSV-2 antibody vary from 80%–98%, and false-negative results might be more frequent at early stages of infection. The specificities of these assays are ≥96%. False-positive results can occur, especially in patients with a low likelihood of HSV infection. Repeat or confirmatory testing might be indicated in some settings, especially if recent acquisition of genital herpes is suspected.

IgM testing for HSV is not useful

Since nearly all HSV-2 infections are sexually acquired, the presence of type-specific HSV-2 antibody implies anogenital infection. The presence of HSV-1 antibody alone is more difficult to interpret. Most persons with HSV-1 antibody have oral HSV infection acquired during childhood, which might be asymptomatic. However, acquisition of genital HSV-1 appears to be increasing, and genital HSV-1 also can be asymptomatic. Lack of symptoms in an HSV-1 seropositive person does not distinguish anogenital from orolabial or cutaneous infection, and regardless of site of infection, these persons remain at risk for acquiring HSV-2.

Type-specific HSV serologic assays might be useful in the following scenarios: 1) recurrent genital symptoms or atypical symptoms with negative HSV cultures; 2) a clinical diagnosis of genital herpes without laboratory confirmation; or 3) a partner with genital herpes. HSV serologic testing should be considered for persons presenting for an STD evaluation (especially for those persons with multiple sex partners), persons with HIV infection, and MSM at increased risk for HIV acquisition.

Differential diagnosis:
   Syphilis, chancroid, aphthous ulcers, Herpes zoster, HIV
Note – patients with HIV can have vulvar ulcers. 60% are due to aphthous ulcers alone. The other 40% are due to HSV. Always look for multiple or atypical infections in these patients.

Non-specific treatment for pain, discomfort etc. R/O other STD’s

Treatments for the relief of discomfort
The following non-specific treatments can alleviate the pain and discomfort of genital sores.
• SALT BATHS (1 teaspoon of salt in 600 ml of water or a handful in a shallow bath) can be used to wash, soothe and dry the sores.
• PAIN RELIEVERS
• LOOSE UNDERCLOTHES, preferably cotton (not nylon), can help minimize discomfort and allow healing.
  For anyone experiencing extreme pain when urinating, the process can be less painful when done in a cool bath. Encourage plenty of fluids to dilute the urine.

NEW CDC STD TREATMENT GUIDELINES WERE RELEASED IN 2015


First Clinical Episode of Genital Herpes

The initial genital herpes episode can last for more than 20 days. Symptoms include tingling, itching, burning or pain. Patients may experience a range of generalized symptoms, such as fever, aches and pains, swollen lymph nodes, as well as specific vulvar symptoms. For others, the initial infection can be mild with minimal symptoms. They may be totally unaware that they have had a herpes outbreak. The severity of symptoms for genital herpes varies in the population. The initial episode can be so mild as to pass unnoticed and a first recurrence may take place many years after the first infection.

Many patients with primary herpes present with mild clinical manifestations but later develop severe or prolonged symptoms. Newly acquired genital herpes can cause a prolonged clinical illness with severe genital ulcerations and neurologic involvement. Even persons with first-episode herpes who have mild clinical manifestations initially can develop severe or prolonged symptoms. Therefore, all patients with first episodes of genital herpes should receive antiviral therapy.

First Clinical Episode of Genital Herpes Recommended Regimens

Recommended Regimens*

- Acyclovir 400 mg orally three times a day for 7–10 days
  OR
- Acyclovir 200 mg orally five times a day for 7–10 days
  OR
- Valacyclovir 1 g orally twice a day for 7–10 days
  OR
- Famciclovir 250 mg orally three times a day for 7–10 days

NOTE: Treatment may be extended if healing is incomplete after 10 days of therapy.
Recurrent Episodes of HSV Disease Most patients with symptomatic, first-episode genital HSV-2 infection subsequently experience recurrent episodes of genital lesions; recurrences are much less frequent following initial genital HSV-1 infection. Antiviral therapy for recurrent genital herpes can be administered either continuously as suppressive therapy to reduce the frequency of recurrences or episodically, to ameliorate or shorten the duration of lesions.

Suppressive Therapy for Recurrent Genital Herpes

Suppressive therapy reduces the frequency of genital herpes recurrences by 70% to 80% among patients who have frequent recurrences. Safety and efficacy have been documented among patients receiving daily therapy with acyclovir for as long as 6 years and with valacyclovir or famciclovir for 1 year.

Recommended Regimens for Continuous Suppressive Therapy

**Recommended Regimens**

- Acyclovir 400 mg orally twice a day
  OR
- Valacyclovir 500 mg orally once a day*
  OR
- Valacyclovir 1 g orally once a day
  OR
- Famiciclovir 250 mg orally twice a day

*Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in persons who have very frequent recurrences (i.e., ≥10 episodes per year).

Episodic Therapy for Recurrent Genital Herpes Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset, or during the prodrome that precedes some outbreaks. The patient should be provided with a supply of drug or a prescription for the medication with instructions to self-initiate treatment immediately when symptoms begin. There is a new single-day famciclovir tablet for episodic treatment for recurrent genital herpes. 75% of all patients healed within 5.4 days. One in 4 patients had their outbreak stopped. (Data on file, Novartis Pharmaceuticals Corporation.) (Whitley R. Diaz-Mitoma F. Hamed K. Single-day famciclovir therapy for recurrent genital herpes. Current Medical Research & Opinion. 22(7):1307-10, 2006 Jul.) (Aoki FY. Tyring S. Diaz-Mitoma F. Gross G. Gao J. Hamed K. Single-day, patient-initiated famciclovir therapy for recurrent genital herpes: a randomized, double blind, placebo-controlled trial. [erratum appears in Clin Infect Dis. 2006 Feb 15;42(4):588 Clinical...
Patients should take two 500 mg famciclovir tablets at the first sign or symptom and take two tablets about 12 hours later.

### Episodic Therapy for Recurrent Genital Herpes Recommended Regimens

#### Recommended Regimens

- Acyclovir 400 mg orally three times a day for 5 days
  
  OR

- Acyclovir 800 mg orally twice a day for 5 days
  
  OR

- Acyclovir 800 mg orally three times a day for 2 days
  
  OR

- Valacyclovir 500 mg orally twice a day for 3 days
  
  OR

- Valacyclovir 1 g orally once a day for 5 days
  
  OR

- Fampciclovir 125 mg orally twice daily for 5 days
  
  OR

- Fampciclovir 1 gram orally twice daily for 1 day

  OR

- Fampciclovir 500 mg once, followed by 250 mg twice daily for 2 days

Few comparative studies of valacyclovir or famciclovir with acyclovir have been conducted. The results of these studies suggest that valacyclovir and famciclovir are comparable to acyclovir in clinical outcome. Ease of administration and cost also are important considerations for prolonged treatment.

### Severe Disease

Intravenous acyclovir therapy should be provided for patients who have severe disease or complications that necessitate hospitalization, such as disseminated infection, pneumonitis, hepatitis, or complications of the central nervous system (e.g., meningitis or encephalitis).

### Treatment of herpes in patients with HIV

#### Recommended Regimens for Daily Suppressive Therapy in Persons with HIV
• Acyclovir 400–800 mg orally twice to three times a day
  OR
• Valacyclovir 500 mg orally twice a day
  OR
• Famciclovir 500 mg orally twice a day

**Recommended Regimens for Episodic Infection in Persons with HIV**

• Acyclovir 400 mg orally three times a day for 5–10 days
  OR
• Valacyclovir 1 g orally twice a day for 5–10 days
  OR
• Famciclovir 500 mg orally twice a day for 5–10 days

**Resources for Herpes**

- American Social Health Association  www.ashastd.org  (patient information)
- International Herpes Alliance  www.herpesalliance.com
- International Herpes Management Forum  www.ihmf.org (geared to health care providers)

**Molluscum contagiosum**

Molluscum contagiosum is caused by a DNA poxvirus. The disease is more prevalent in children (lesions involve the face, trunk and extremities). Adults tend to have lesions most often near the genital areas. The incidence of molluscum has increased over the last 30 years. There are four main subtypes of molluscum contagiosum virus (MCV), MCV I, MCV II, MCV III and MCV IV. The disease is transmitted by direct skin contact. It presents clinically with a papular eruption of multiple umbilicated lesions. The central depression contains a white waxy curd-like core. The size of the papule ranges from 2-6 mm. The clinical appearance of molluscum contagiosum is the general diagnostic method, though it can be examined histologically (curetted or biopsied lesion). Large brick shaped inclusion bodies are seen. In-situ hybridization for MCV DNA has also been performed.

**Treatment of molluscum contagiosum**

Molluscum contagiosum is a self-limited disease, which will generally resolve in immunocompetent hosts. However, the time to resolution can be quite long. Treatment of molluscum contagiosum is advisable in healthy individuals to prevent autoinoculation or transmission.

**Common treatments for molluscum**
Cryosurgery (liquid nitrogen, dry ice)
Evisceration (scalpel, IV needle)
Curettage
Tape stripping
Podofilox
Imiquimod 5% cream
TCA

Condyloma accuminata
Genital warts are caused by the human papillomavirus (HPV), of which more than 200 subtypes exist, over 30 that are found on the genital area. The diagnosis is usually based on clinical appearance. They are soft in texture, nonpigmented and usually asymptomatic. At times they cause itching, bleeding and occasionally pain. They may involve the anus too. Of genital warts, 90% are caused by HPV 6 or 11.

Numerous treatments exist (2015 CDC STD Treatment Guidelines).

Recommended Regimens for External Anogenital Warts (i.e., penis, groin, scrotum, vulva, perineum, external anus, and perianus*)

**Patient-Applied:**

- Imiquimod 3.75% or 5% cream†
  OR
- Podofilox 0.5% solution or gel
  OR
- Sinecatechins 15% ointment†

**Provider–Administered:**

- Cryotherapy with liquid nitrogen or cryoprobe
  OR
- Surgical removal either by tangential scissor excision, tangential shave excision, curettage, laser, or electrosurgery
  OR
- Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90% solution

*Many persons with external anal warts also have intra-anal warts. Thus, persons with external anal warts might benefit from an inspection of the anal canal by digital examination, standard anoscopy, or high-resolution anoscopy.
\textbf{Vulvar Neoplasia  
Benign Cysts and Tumors}

<table>
<thead>
<tr>
<th>Mucous cyst</th>
<th>Lipoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skene’s Duct Cyst</td>
<td>Fibroma</td>
</tr>
<tr>
<td>Cyst of canal of Nuck (hydrocele)</td>
<td>Syringoma</td>
</tr>
<tr>
<td>Bartholin’s duct cyst</td>
<td>Granular cell tumor</td>
</tr>
<tr>
<td>Epidermal inclusion cyst</td>
<td>Neurofibroma</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>Angiokeratoma</td>
</tr>
<tr>
<td>Ectopic breast</td>
<td>Aggressive Angiomyxoma</td>
</tr>
<tr>
<td>Hidradenoma</td>
<td>Leiomyoma</td>
</tr>
<tr>
<td>Varicose veins</td>
<td></td>
</tr>
</tbody>
</table>

\textbf{Syringomas}

Syringomas are often associated with itching. There are a number of treatment options for itchy syringomas:

1. Atropine 1\% aqueous solution (5 mL bottle) Apply 2-4 drops at a time (20 drops to 1 ml so that would last about 3 weeks).
2. Destruction which can either be electrodessication or laser CO laser destruction.
3. Tretinoin can be given as a 0.025 or 0.05\% cream but it can be a bit irritating. Oral isotretinoin or Accutane has been reported to be helpful.
4. Steroids topically with antihistamines have been used but notoriously give poor results.
5. Tranilast (brand name Rizaben) is an anti allergenic drug used in Asia for bronchial asthma. It has been reported to be helpful. It seems to block macrophages. The dosage is 300 mg po daily (in a report out of Japan).
6. Topical glycopyrrolate 0.1% in a compounded topical cream has been used. This stops sweating and has been helpful in patients that sweat a great deal in the vulva area and that potentially might be helpful. It is used daily.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>VIN I</td>
<td>Flat condyloma or HPV effect</td>
<td>LSIL (VIN1)</td>
</tr>
<tr>
<td>VIN II</td>
<td>VIN, usual type; (bowenoid, basaloid, mixed)</td>
<td>HSIL (VIN2; VIN3)</td>
</tr>
<tr>
<td>VIN III</td>
<td>VIN, differentiated type</td>
<td></td>
</tr>
</tbody>
</table>

**Intraepithelial Neoplasia**

**VIN TERMINOLOGY**

**SQUAMOUS VIN TERMINOLOGY (ISSVD 2004)**

VIN, usual type
- VIN, warty type

VIN, differentiated type
- VIN, differentiated type

2. Nonsquamous type
- Paget’s disease
- Melanoma in Situ

**2012 Lower Anogenital Squamous Terminology (LAST) Project**

New terminology regarding the histopathologic nomenclature system that reflects current knowledge of HPV biology, optimally uses available biomarkers, and facilitates clear communication across different medical specialties was developed in 2012. The Lower Anogenital Squamous Terminology (LAST) Project was cosponsored by the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology met and published the terminology to use across all lower genital tract sites, including the vulva. A two tiered nomenclature was recommend, consisting of LSIL and HSIL. However, this does not generally refer to VIN differentiated (most often non HPV related), which must be considered, especially in patients with lichen sclerosus.

Before 1970, VIN was found most often in women in the fifth or sixth decade of life; currently about half of the patients are less than 40 years old. VIN in young women is frequently in multiple locations and is associated with HPV. Currently, approximately 80% of patients with VIN are HPV positive. Patients may be asymptomatic or complain of pruritus or burning. Treatment: Biopsy before any therapeutic trial is initiated.

- Smoking cessation may be necessary for the methods below to succeed
- Wide local excision in hair bearing tissue is recommended
1. Local: Scalpel  
a. Standard procedure: an inked margin around the lesion is made providing gross clearance (0.5 cm to 1 cm) at resection. The depth of resection is to the subcutaneous fat but not deeper. Closure depends on the size of resection but is often by primary approximation. Smaller resections may not require closure and larger lesions may require local advancement skin flaps or grafts.

Special points: Vulvar skin thickness varies considerably by location. Particular care must be taken in the clitoral, urethral, anal and labia minora locations as the squamous epithelium is very thin. Resections in this area don’t require deep dissection and every effort should be made to minimize trauma.

2. CO2 laser - in non-hair bearing areas  
Confidence that no invasive disease exists is important to patient selection.

3. LEEP: difficult to control depth of dissection

4. Medical
   - Imiquimod (Aldara®) has reported to be effective for VIN 3 (same dosage as for condyloma)(Off label use)

It is important to screen these patients with Anal Pap smears. Use a moistened Dacron swab or Cytobrush. Insert into the canal approximately 5-6 cm above the anal verge to the rectum. Rotate, applying pressure to the walls of the canal while removing the sampling device.

**Anal Cytology**

Place the cytology sampling device (Dacron swab or Cytobrush moistened with water) into the anal canal until resistance is met (approximately 4 cm)  
Rotate/apply pressure to walls of canal while removing sampling device  
slowly (count to 10) Place in liquid media.  
Notify Pathology (Cytology) Department before you start these, so that they are prepared for them. HPV testing is not required on these specimens.

**Anal colposcopy**

After the cytology has been obtained, place an anoscope (use a clear plastic anoscope) with a small amount of lubricant into the anus. Then place an opened 4 x 4 soaked in 3 to 5% acetic acid over a cotton swab through the anoscope. Remove the anoscope, leaving in the 4 x 4 and cotton swab. Place a 4 x 4 with 3 to 5% acetic acid around the outer anus. Leave these on for about 3 minutes. Then, remove the 4 x 4’s and cotton swab and reinsert a lubricated anoscope. The anus is visualized sequentially, with a colposcope, keeping in mind the location of the dentate line.

**Paget’s Disease of the Vulva**

Primary extramammary Paget’s Disease – an epidermotropic carcinoma arising within the epidermis or epidermal appendages (may arise in Toker cells) – no underlying carcinoma (most common)

Secondary extramammary Paget’s disease – is a visceral carcinoma (anorectal, bladder or urethra) that is epidermotropic to the skin.
Clinical Presentation:

Itching “rash” on perineum with eczematous, soft velvety papules slowly growing into crusty scaly plaques that do not respond to topical steroid.

Paget's disease of the skin is generally confined to the integument along the mid line. It occurs most commonly on the nipple and areola, where its presence signifies an underlying adenocarcinoma of the breast. Extramammary lesions have been described in the genital, perianal, and axillary regions as well as the ear canal, all of which contain abundant apocrine glands.

Vulvar Paget's disease appears as a red velvety area with white islands of hyperkeratosis and at times may be pinkish and eczematoid. It primarily occurs on the labia majora. Pruritus is present in over half of the patients. The mean age for Paget’s disease of the vulva is 65 years. Almost all of the patients are Caucasian.

Signs

- Red and white vulva - ulceration and hyperkeratosis
- Well demarcated
- Eczematoid

Symptoms

- Pruritus in over 50%
- Soreness
- Bleeding or discharge

When present on the vulva, it is most commonly an intraepithelial disease that tends to recur locally and has a minimal propensity to invade. Usually it is a slowly progressive, indolent, superficial process. It is rarely associated with an underlying skin appendage carcinoma such as a primary carcinoma of the rectum, urethra, or bladder.

Only about 25% of vulvar Extramammary Paget’s are associated with an underlying adenocarcinoma of an adnexal tissue or a Bartholin gland. Less commonly it is associated with a distant carcinoma of breast, GI, GU or the genital tract. Perianal Extramammary Paget’s is associated with underlying colorectal adenocarcinoma in 80% of cases. In view of the possible coexistence of sweat gland carcinoma of the vulva or another adjacent internal carcinoma, the overall prognosis for Paget's disease is less favorable than for VIN III. Clinical diagnosis based on gross appearance may be erroneous. Biopsy confirmation of the diagnosis is mandatory. Large, irregular Paget's cells containing clear, vacuolated pale cytoplasm are seen on histologic evaluation. Nuclei are vesicular. Mitotic figures are uncommon. Paget cells are most numerous in the tips and sides of the rete pegs and deep in the epithelium. They may be scattered throughout the outer keratinized layer. Paget cells, as well as the cells and secretions of normal eccrine and apocrine glands are rich in CEA.

Markers

The immunoprofile of vulvar Paget's disease includes cells that are typically positive for cytokeratin 7, keratin CAM5.2, EMA, CEA and GCDFP; mucin stains are also positive in a subset of the neoplastic cells (less cost).

Work up to detect associated adenocarcinoma (location dependent)

- H+P
- Pap
- Mammogram
- Hemoccult
- Cystoscopy
- Flex sigmoidoscopy vs BE vs colonoscopy
Treatment
Paget’s disease of the vulva is generally treated with a wide local excision of the circumscribed lesions. It is important to remove the full thickness of the skin to the subcutaneous fat to be certain that all of the skin adnexal structures are excised. Even if resection margins are free of Paget's disease at the time of surgical excision, local recurrence remains a major risk. Laser therapy has been used on Paget’s disease (particularly recurrent Paget’s). On rare occasions, radiation therapy has been used to treat Paget’s disease. 5% imiquimod cream 1 to 5 times a week (frequency of application depends on tolerance) has been used for superficial involvement and when surgery would be poorly tolerated. Duration of treatment depends on response and this can be months.

Atypical junctional melanocytic hyperplasia
This is a preinvasive condition. If margins are not clear, a repeat resection should be performed.

Melanoma in situ
Clear margins should be obtained.

Malignant Tumors/Vulvar Cancer
Vulvar Cancer
Most vulvar cancers are found in patients age 60 to 70 years. The risk for vulvar cancer continues to increase with age. The diagnosis is often delayed (mean = 1 year). It is usually unifocal. Most vulvar cancers are squamous cell carcinomas.
Squamous carcinoma –87%
Melanoma-6%
Bartholin's Adenocarcinoma-4%
Basal Cell carcinoma <2%
Sarcoma <2%

Incidence and Mortality
Vulvar cancer accounts for about 5% of cancers of the female genital system in the United States.

Estimated new cases and deaths from vulvar cancer in the United States in 2015:

- New cases: 5,150.
- Deaths: 1,080.

The vulva is the area immediately external to the vagina, including the mons pubis, labia, clitoris, Bartholin glands, and perineum. The labia majora are the most common site of vulvar carcinoma involvement and account for about 50% of cases. The labia minora account for 15% to 20% of vulvar carcinoma cases. The clitoris and Bartholin glands are less frequently involved. Lesions are multifocal in about 5% of cases. About 90% of vulvar carcinomas are squamous cell cancers. This evidence summary covers squamous cell cancers and vulvar intraepithelial neoplasias (VIN), some of which are thought to be precursors to invasive squamous cell cancers.
Prognosis

Survival is dependent on the pathologic status of the inguinal nodes and whether spread to adjacent structures has occurred. The size of the primary tumor is less important in defining prognosis. In patients with operable disease without nodal involvement, the overall survival (OS) rate is 90%; however, in patients with nodal involvement, the 5-year OS rate is approximately 50% to 60%.

Risk Factors

Risk factors for lymph node metastasis include the following:

- Clinical node status.
- Age.
- Degree of differentiation.
- Tumor stage.
- Tumor thickness.
- Depth of stromal invasion.
- Presence of capillary-lymphatic space invasion.

Overall, about 30% of patients with operable disease have lymph nodal spread.

Other risk factors In many cases, the development of vulvar cancer is preceded by condyloma or squamous dysplasia. The prevailing evidence favors human papillomavirus (HPV) as a causative factor in many genital tract carcinomas. The HPV-related basaloid and warty types are associated with VIN. About 75% to 100% of basaloid and warty carcinomas harbor HPV infection. In addition to the much higher prevalence of HPV in these subtypes than in the keratinizing subtypes, the basaloid and warty subtypes also share many common risk factors with cervical cancers, including multiplicity of sex partners, early age at initiation of sexual intercourse, and history of abnormal Pap smears. HPV-associated VIN (termed usual-type VIN when high-grade 2 and 3) is most common in women younger than 50 years, whereas non-HPV VIN (termed differentiated-type VIN when high-grade 3) is most common in older women. The former lesion-type VIN grade 1 is no longer classified as a true VIN.

Histopathology The pattern of spread is influenced by the histology. Well-differentiated lesions tend to spread along the surface with minimal invasion, whereas anaplastic lesions are more likely to be deeply invasive. Spread beyond the vulva is either to adjacent organs such as the vagina, urethra, and anus, or via the lymphatics to the inguinal and femoral lymph nodes, followed by the deep pelvic nodes. Hematogenous spread appears to be uncommon.

Staging Information for Vulvar Cancer

- Definitions: FIGO The diagnosis of vulvar cancer is made by biopsy. The patient may be examined under anesthesia. Cystoscopy, proctoscopy, x-ray examination of the lungs, and intravenous urography (as needed), are used for staging purposes. Suspected bladder or rectal involvement must be confirmed by
biopsy. The staging system does not apply to malignant melanoma of the vulva, which is staged like melanoma of the skin.

**Definitions: FIGO**

The Fédération Internationale de Gynécologie et d’Obstétrique (FIGO) and the American Joint Committee on Cancer (AJCC) have designated staging to define vulvar cancer; the FIGO system is most commonly used.[1,2] Stage is based upon pathology staging at the time of surgery or prior to any radiation or chemotherapy, if they are the initial treatment modalities.[3]

**Table 1. Carcinoma of the Vulva**

*a*Adapted from FIGO Committee on Gynecologic Oncology.[2]

*b*The depth of invasion is defined as the measurement of the tumor from the epithelial-stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Tumor confined to the vulva.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Lesions ≤2 cm in size, confined to the vulva or perineum and with stromal invasion ≤1.0 mm*, no nodal metastasis.</td>
</tr>
<tr>
<td>IB</td>
<td>Lesions &gt;2 cm in size or with stromal invasion &gt;1.0 mm*, confined to the vulva or perineum, with negative nodes.</td>
</tr>
<tr>
<td>Stage II</td>
<td>Tumor of any size with extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus) with negative nodes.</td>
</tr>
<tr>
<td>Stage III</td>
<td>Tumor of any size with or without extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus) with positive inguino-femoral lymph nodes.</td>
</tr>
<tr>
<td>IIIA</td>
<td>(i) With 1 lymph node metastasis (≥5 mm), or</td>
</tr>
<tr>
<td></td>
<td>(ii) 1–2 lymph node metastasis(es) (&lt;5 mm).</td>
</tr>
<tr>
<td>IIIB</td>
<td>(i) With 2 or more lymph node metastases (≥5 mm), or</td>
</tr>
<tr>
<td></td>
<td>(ii) 3 or more lymph node metastases (&lt;5 mm).</td>
</tr>
<tr>
<td>IIIC</td>
<td>With positive nodes with extracapsular spread.</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Tumor invades other regional (2/3 upper urethra, 2/3 upper vagina), or distant structures.</td>
</tr>
</tbody>
</table>
Tumor invades any of the following:

(i) upper urethral and/or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or

(ii) fixed or ulcerated inguino-femoral lymph nodes.

Any distant metastasis including pelvic lymph nodes.

Grade is reported in registry systems. A two-, three-, or four-grade system may be used. If not specified, the following system is generally used:[1]

- GX: Grade cannot be assessed.
- G1: Well differentiated.
- G2: Moderately differentiated.
- G3: Poorly differentiated.
- G4: Undifferentiated.

Melanoma
Melanoma is the second most common invasive cancer occurring in the vulva, but its occurrence is rare. Melanoma probably arises from a lesion containing a junctional or compound nevus. Consider pigmented lesions on the vulva suspicious if they are blue-black in color, have a jagged or fuzzy border, are raised or ulcerated, or are larger than approximately 1 cm. Melanomas may be misdiagnosed as undifferentiated squamous carcinoma, particularly if they are amelanotic.

Approximately 3% of all melanomas are located in the genital tract. Melanoma of the vulva accounts for 5-7% of invasive vulvar cancers and has an estimated annual incident rate of 1 per 1,000,000 women. The disease can affect women of all ages (e.g., women aged 7-97 y in 1 study) but is more common in the older population, with almost half of the patients aged 70 years or older. More than 90% of melanomas occur in white women.

Clinical Appearance
Lesions suspicious for melanoma are often characterized by the ABCDs. They are asymmetrical (A), have irregular or scalloped border (B), often black in color (C) or variegated with shades of red, white, or blue, and may have a diameter (D) greater than 6 millimeters. Early signs include change in size, shape, and color of a lesion. Pruritus is an early symptom. Late signs and symptoms include bleeding, ulceration, pain, and tenderness. Vulvar melanoma is often detected later than cutaneous melanoma simply due to location, resulting in more advanced lesions at presentation with a poorer prognosis. Biopsy is indicated to make the diagnosis of melanoma. Several studies have documented that an incisional biopsy for melanoma does not increase the risk of tumor seeding, metastasis, or decrease survival. The biopsy should be interpreted by a pathologist with experience in the interpretation of pigmented lesions and melanoma. Two important factors in the cutaneous melanoma pathology report are tumor thickness measured in millimeters (Breslow depth) and ulceration status. Other potentially important factors include mitotic rate, microsatellitosis,
angiolympathic involvement, Clark level (anatomic measure of thickness), neurotropism, and extensive regression.

**Treatment**

A wide local excision with 1 to 2-cm margins appears to be adequate for most well-circumscribed lesions. Whether inguinal lymphadenectomy should be performed for this cancer is undecided at present. Obviously, if lymph nodes are involved, this finding is not only diagnostic but also prognostic. If lymph nodes are negative, the patient may be reassured. Lymph node involvement is directly related to the depth of invasion. If the disease is intraepithelial, the cure rate is close to 100% and is reported to be as high as 99% with invasion of 1.5 mm or less. The survival rate drops to 65-70% if the lesion invades 1.5-4 mm.

Medical management for metastatic disease continues to be experimental. If the melanoma recurs locally in the vulvar area, reexcision may be adequate therapy, with long-term survival.

**Summary**

An overview of the different types of vulvovaginal conditions has been given. Many vulvar conditions must be considered when a patient complains of discharge and itching. It is important to remember that

**If treatment is not working, reconsider the diagnosis.**
Prescriptions for Vulvar Disease

Pain Medications

**Xylocaine® (lidocaine)**
- 5% Xylocaine® (lidocaine) ointment
  sig: apply to vulva prn
  Disp: 35 grams

**Elavil® (amitriptyline)**
Start low and increase dose slowly.
Initial amitriptyline prescription:
- amitriptyline 10-25 mg
  - Sig: 1 po qhs x 1 week; If sx persist, 2 po qhs x 1 wk; if sx persist, 3 po qhs x 1 wk; if sx persist, 4 po qhs. Maintain nightly dose that relieves symptoms (Generally not to exceed 4 po qhs) Do not stop suddenly
- Start at 10 mg in patients age 60 or older; increase by 10 mg weekly

Future amitriptyline prescriptions
- Amitriptyline ___mg
  Sig: 1 po qhs (comes in 10 mg, 25 mg, 50 mg, 75 mg, 100 mg and 150 mg tablets)

**Neurontin®**
Neurontin® (gabapentin)
- Sig: 300 mg po qd x 3 days; if sx persist, 300 mg po bid x 3 days; if symptoms persist, 300 mg po tid. Stay on this dose for a month and increase gradually if needed.
- It comes in 100, 300, 400, 600 and 800 mg doses
- Do not exceed 2700 to 3600 mg total dose per day
- Do not give more than 1200 mg in a single dose

  Gabapentin ointment 3% or 6%
  Sig: apply to affected area bid-tid
  Disp: 3 month supply

**Pregabalin (Lyrica®)**
Lyrica® (pregabalin)
- 50 mg po qd x 4 days, if sx persist, 50 mg po bid x 4 days, if sx persist, 50 mg po tid
- Can gradually increase up to 100 mg po tid; doses up to 300 mg po bid have been used for pain control

**Topiramate (Topamax®)**
- 25 mg po qd 1 week; if sx persist 25 mg po bid x 1 week; if sx persist 25 mg po in am and 50 mg po in pm x 1 week; if sx persist, 50 mg po bid; Can gradually increase up to maximum of 100 mg po bid for pain control.
Blocks
Bupivacaine (0.25% or 0.5%) and Kenalog®
Draw up Kenalog® first (40 mg/mL) (can use up to 40 mg steroid in single dose per month) 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
Do not use high doses on thin skin.

Medications for localized pain or itching
Zonalon® (doxepin) 5% cream
Sig: apply to skin q d with gradual increase not to exceed qid
Disp: 30 g

Topical Elavil® (amitriptyline) 2% with Baclofen 2% in water washable base (WWB) - squirt ½ mL from syringe onto finger and apply to affected area qd to tid
Disp: 30 day supply

Gabapentin 6% with Ketamine 5% WWB – 30mL apply ½-1 mL to Vulvar Vestibule twice daily for pain

Amitriptyline 2% with Baclofen 2% WWB and Lidocaine 5% mg – 30mL Apply ½-1 mL to Vulvar Vestibule twice daily for pain

Estradiol 0.1mg with Lidocaine 5% ointment – Disp 30g Apply thin layer over Vulva twice daily for pain

Yeast medications
Fluconazole 150 mg
Sig: 1 po q 3 days x 3, then 1 po q week for up to 6 months (If using for longer than 6 months, check LFT’s) Do not use with active liver disease.

5 flucystosine 500 mg/5 grams compounded in a hydrophilic cream base
-Insert 5 gram applicator (500 mg of active drug) full of mixture per vagina qhs x 14 days

Boric acid- fill 0-gel capsule halfway (600 mg)
To treat active yeast infection - Insert per vagina nightly for 14 days
For prevention of yeast - Insert per vagina twice weekly. Keep out of reach of children. Warn patients not to receive oral sex while on the boric acid. There is an herbal product called Yeast Arrest. It contains 600 mg boric acid, Oregon Grape Root and Calendula flowers.

Gentian violet- 0.25% or 0.5% aqueous solution applied at home daily or it may be given in the office as a 1.0% solution (once weekly for up to three times). Warn patients that if they have oral sex, their partner’s teeth and lips could stain.

Medications for Lichen planus
Anusol HC suppository
1/2 of a 25 mg suppository per vagina bid x 2 months
Decrease to qd x 2 months
Maintenance therapy of 1 - 3 x per week

Hydrocortisone acetate 100 mg compounded suppository used QHS
Use for 2-4 weeks then use Mon Wed Fri for 2-4 weeks and change to milder
25 mg suppository as needed

Hydrocortisone acetate 10% compounded Vaginal cream used QHS –
4-5 gram q d (400 to 500 mg dose). For severe vaginal Lichen Planus
Use for 2-4 weeks then use Mon Wed Fri for 2-4 weeks and change to milder
25 mg suppository as needed

**Tacrolimus**

<table>
<thead>
<tr>
<th>For oral Lichen planus: Tacrolimus 0.1% in Orabase</th>
<th>For vaginal lichen planus Tacrolimus vaginal suppositories</th>
<th>For vulvar Lichen planus Tacrolimus 0.1% Ointment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sig: apply to mouth bid</td>
<td>Insert one supp per vagina (2 mg tacrolimus per 2 gm supp) qhs</td>
<td>Sig: apply to skin bid</td>
</tr>
<tr>
<td>Disp 50 g</td>
<td>Disp 50</td>
<td>Available in 30 or 60 gram tubes</td>
</tr>
</tbody>
</table>

**Folliculitis** (swab for culture to r/o MRSA)
- Emgel® 2% topical gel (erythromycin) or 1% clindamycin lotion
- Sig: apply to skin bid
- Available in 27 or 50 gram bottles

Other topical antibiotics include bacitracin, neomycin, mupirocin

**For fungal folliculitis**
- Topical clotrimazole, miconazole
- Oral terbinafine, itraconazole, griseofulvin

**Furunculosis- very responsive to antibiotics** (swab for culture to r/o MRSA)
- Topical antibiotics (bacitracin, neomycin, mupirocin)
- Oral antibiotics (dicloxacillin, cephalexin)
- Dial soap or Phisohex
- If wrinkled, I and D useful

**For Recurrent Impetigo Staphlococcus +/- Streptococcus**
- Take bacterial culture from site of infection, nose and gluteal cleft to find any hidden source of infection.
- Do bleach baths to reducing re-infection 2-3 times a week. Add one half cup of household bleach (125 mL) to a 10 inch (25 cm) deep tub of comfortably warm bath water. **Mix well.** Soak for 5-7 minutes, ensuring penetration of the solution into all cracks and genital / buttock / skin folds, using a plastic cup and bare hands to spread over all involved areas. For sitz bath mix 1 ¼ tsp bleach in 1 gallon of water. Treat with oral antibiotics as indicated by culture results.
- Use an antibiotic ointment (mupirocin ointment twice a day) bid for nose or gluteal cleft. If MRSA use retapamulin 1% ointment (Altabax) bid for 5 days.
Desquamative inflammatory vaginitis- A variety of regimens exist

- Clindamycin 2% cream 5(g)
  - Insert one applicator intravaginally qhs x 3 weeks
    - Longer suppression time may be required (consider 2 x per week x 2 months)
    vs.
  - Clindamycin 200 mg vaginal suppository qhs x 3 weeks
    - Longer suppression time may be required (consider 2 x per week x 2 months)

- Intravaginal hydrocortisone suppositories 25 mg intravaginal bid for 3 weeks (then consider 3 x per week x 2 months)
  Longer suppression may be required
  or
- Intravaginal hydrocortisone cream 300 to 500 mg intravaginal qhs for 3 weeks (then consider 2 x per week x 2 months for maintenance therapy)
  Longer suppression may be required

Combine clindamycin cream and hydrocortisone suppositories.
  1 applicatorful of 2% clindamycin cream and 25 mg hydrocortisone nightly x 14 or every other night x 14
  Longer suppression may be needed.

If above have failed:
Compound a high dose intravaginal corticosteroid and 2% clindamycin* (variety of regimens)
  Hydrocortisone 100 mg/gram in clindamycin in 2% base. Insert 3 to 5 gram (applicator full) (300 to 500 mg active drug) per vagina every other night x 14 doses. Consider taper.
  * This needs to be made at a compounding pharmacy.

Steroid medications

<table>
<thead>
<tr>
<th></th>
<th>Triamcinolone acetonide ointment 0.1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clobetasol propionate ointment (Temovate®) 0.05%</td>
<td>Sig: apply to vulva bid x 1 month, then qd x 2 months</td>
</tr>
<tr>
<td>Sig: apply to vulva bid x 1 month, then qd x 2 months</td>
<td>Disp: 30 g</td>
</tr>
<tr>
<td>Disp: 80 g</td>
<td>Consider decreasing gradually to Triamcinolone acetonide ointment 0.025% qd to bid</td>
</tr>
</tbody>
</table>

TOPICAL CORTICOSTEROIDS

Learn three to four ointments of different strengths, making appropriate selections as needed
  - Ointments are stronger than creams
  - Ointments stay on longer than creams (creams are diluted and washed away with body fluids)
  - Ointments are less irritating and have fewer allergens than other bases
Patients may find one base more irritating than another. Be flexible. Do not use steroids for dysesthetic vulvodynia - steroids work by reducing inflammation, not pain.

Note: **Topical steroids are not a cure.** Use the steroid potency that will do the job in the quickest period of time and then decrease to a lower potency. Either stop or maintain with the lowest potency or use intermittently as necessary.

Tips: When considering topical corticosteroids, especially the superpotent types, consider:
- There are more available than you need
- Use them in an educated way
- Limit the amount prescribed to 15g to 30 grams for high dose topical steroids
- Show the patient exactly how to use it – a tiny dab spread in a thin film just to the involved area is all that is necessary
- Vulvar mucous membrane (vulvar trigone and inner labia minora) is remarkably steroid resistant. The outside of the labia minora and the labiocrural fold and the thighs will thin easily and develop striae.
- When the patient improves, decrease the frequency of topical steroid or manage with a low potency product.
- Use under close supervision.
- At any suggestion of secondary yeast infection, add a topical or oral anti-fungal.

For example, for thick itchy dermatoses like lichen simplex chronicus – use name brand clobetasol or halobetasol 0.05% ointment bid for 1-2 weeks, once a week for 1-2 weeks and then M-W-F for 1-2 weeks and for long term maintenance either infrequent and intermittent usage each week of the same or switch to intermittent use of a mild ointment such as 1% -2.5% hydrocortisone in petrolatum or a 1% hydrocortisone / 1% pramoxine cream mix.

Effects of corticosteroids:
- Vasoconstriction – decrease erythema and swelling
- Decreasing fibroblastic proliferation thins out thickened dermal lesions
- Decreasing rapidly turning over keratinocytes thins out thickened epidermal lesions

Corticosteroid responsive vulvar dermatoses include:
- Thick and scaly (lichen sclerosus, lichen simplex chronicus, psoriasis, contact dermatitis)
- Blistering erosive disease
- Bullous diseases

Corticosteroid potency depends on:
- Cortisone molecule
- Partition co-efficient of steroid vehicle system
- Concentration of steroid in vehicle
- Application frequency and length of time used

**Caution:** steroids can be associated with irregular menses, increased BP, worsening of diabetes control, infection and glaucoma.
Table 1. Potency Ranking of Some Commonly Used Topical Corticosteroids

<table>
<thead>
<tr>
<th>Class</th>
<th>U.S. Brand Name</th>
<th>Generic name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Super-high Potency</td>
<td>Temovate® Cream, 0.05%</td>
<td>clobetasol propionate</td>
</tr>
<tr>
<td></td>
<td>Temovate® Ointment, 0.05%</td>
<td>clobetasol propionate</td>
</tr>
<tr>
<td></td>
<td>Temovate® E, 0.05%</td>
<td>clobetasol propionate</td>
</tr>
<tr>
<td></td>
<td>Diprolene® Cream, 0.05%</td>
<td>betamethasone dipropionate</td>
</tr>
<tr>
<td></td>
<td>Diprolene® Ointment, 0.05%</td>
<td>betamethasone dipropionate</td>
</tr>
<tr>
<td></td>
<td>Diprolene® AF Cream, 0.05%</td>
<td>betamethasone dipropionate</td>
</tr>
<tr>
<td></td>
<td>Psorcon® Ointment, 0.05%</td>
<td>diflorsone diacetate</td>
</tr>
<tr>
<td></td>
<td>Ultravate® Cream, 0.05%</td>
<td>halobetasol propionate</td>
</tr>
<tr>
<td></td>
<td>Ultravate® Ointment, 0.05%</td>
<td>halobetasol propionate</td>
</tr>
<tr>
<td></td>
<td>Cyclocort® Cream, 0.1%</td>
<td>Amcinonide</td>
</tr>
<tr>
<td></td>
<td>Cyclocort® Ointment, 0.1%</td>
<td>amcinonide</td>
</tr>
<tr>
<td></td>
<td>Diprosone® Ointment, 0.05%</td>
<td>betamethasone dipropionate</td>
</tr>
<tr>
<td></td>
<td>Florone® Ointment, 0.05%</td>
<td>diflorsone diacetate</td>
</tr>
<tr>
<td></td>
<td>Lidex® Cream, 0.05%</td>
<td>fluocinonide</td>
</tr>
<tr>
<td></td>
<td>Lidex® Ointment, 0.05%</td>
<td>fluocinonide</td>
</tr>
<tr>
<td></td>
<td>Lidex-E® Cream, 0.05%</td>
<td>fluocinonide</td>
</tr>
<tr>
<td></td>
<td>Maxiflor® Ointment, 0.05%</td>
<td>diflorsone diacetate</td>
</tr>
<tr>
<td></td>
<td>Maxivate®, Ointment 0.05%</td>
<td>betamethasone dipropionate</td>
</tr>
<tr>
<td></td>
<td>Topicort® Cream, 0.25%</td>
<td>desoximetasone</td>
</tr>
<tr>
<td></td>
<td>Topicort® Ointment, 0.25%</td>
<td>desoximetasone</td>
</tr>
<tr>
<td></td>
<td>Aristocort A® Cream 0.5%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Cutivate® Ointment, 0.05%</td>
<td>fluticasone propionate</td>
</tr>
<tr>
<td></td>
<td>Diprosone® Cream, 0.05%</td>
<td>betamethasone dipropionate</td>
</tr>
<tr>
<td></td>
<td>Elocon® Ointment, 0.1%</td>
<td>mometasone furoate</td>
</tr>
<tr>
<td></td>
<td>Florone® Cream, 0.05%</td>
<td>diflorsone diacetate</td>
</tr>
<tr>
<td></td>
<td>Maxiflor® Cream, 0.05%</td>
<td>diflorsone diacetate</td>
</tr>
<tr>
<td></td>
<td>Maxivate® Cream, 0.05%</td>
<td>betamethasone dipropionate</td>
</tr>
<tr>
<td></td>
<td>Valisone® Ointment, 0.1%</td>
<td>betamethasone valerate</td>
</tr>
<tr>
<td></td>
<td>Aristocort® Ointment, 0.1%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Cordran® Ointment, 0.05%</td>
<td>flurandrenolide</td>
</tr>
<tr>
<td></td>
<td>Elocon® Cream, 0.1%</td>
<td>mometasone furoate</td>
</tr>
<tr>
<td></td>
<td>Kenalog® Ointment, 0.1%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Synalar® Ointment, 0.025%</td>
<td>fluocinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Topicort LP® Cream, 0.05%</td>
<td>desoximetasone</td>
</tr>
<tr>
<td></td>
<td>Aristocort® Cream, 0.1%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Cordran® Cream, 0.05%</td>
<td>flurandrenolide</td>
</tr>
<tr>
<td></td>
<td>Cutivate® Cream, 0.05%</td>
<td>fluticasone propionate</td>
</tr>
<tr>
<td></td>
<td>Dermatop® Emollient cream, 0.05%</td>
<td>prednicarbate</td>
</tr>
<tr>
<td></td>
<td>Kenalog® Cream, 0.1%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Kenalog ointment, 0.025%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Locoid® Cream, 0.1%</td>
<td>hydrocortisone butyrate</td>
</tr>
<tr>
<td></td>
<td>Synalar® Cream, 0.025%</td>
<td>fluocinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Valisone® Cream, 0.1%</td>
<td>betamethasone valerate</td>
</tr>
<tr>
<td></td>
<td>Uticort® Cream 0.025%</td>
<td>betamethasone benzoate</td>
</tr>
<tr>
<td></td>
<td>Westcort® Cream, 0.2%</td>
<td>hydrocortisone valerate</td>
</tr>
<tr>
<td></td>
<td>Westcort® Ointment, 0.2%</td>
<td>hydrocortisone valerate</td>
</tr>
<tr>
<td></td>
<td>Aristocort® Ointment, 0.1%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Aclovate® Cream, 0.05%</td>
<td>flurandrenolide</td>
</tr>
<tr>
<td></td>
<td>Aclovate® Ointment, 0.05%</td>
<td>fluticasone propionate</td>
</tr>
<tr>
<td></td>
<td>Tridesilon® Cream, 0.05%</td>
<td>prednicarbate</td>
</tr>
<tr>
<td></td>
<td>Aclovate® Cream, 0.05%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Aclovate® Ointment, 0.05%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Tridesilon® Cream, 0.05%</td>
<td>triamcinolone acetonide</td>
</tr>
<tr>
<td></td>
<td>Numerous preparations exist</td>
<td>Dexamethasone, flumethalone, hydrocortisone</td>
</tr>
<tr>
<td>Low Potency</td>
<td></td>
<td>Methylprednisolone, prednisolone</td>
</tr>
</tbody>
</table>
ALTHERNATIVES TO CORTICOSTEROIDS
Alternative topicals to corticosteroids are the Calcineurin inhibitors
Calcineurin inhibitors:
- Pimecrolimus 1% cream (Elidel)
- Tacrolimus 0.03 and 0.1% ointment (Protopic) or compounded 0.1% vaginal cream
  or a 2g suppository.
These are non-steroidal
Does not cause atrophy
May sting or burn initially when used topically
Equivalent to mild to moderate topical steroids – Pimecrolimus to a mild
topical steroid and tacrolimus equivalent to a moderate to strong
topical steroid.
These are topical immunosuppressants usually for maintenance of
steroid responsive dermatoses
Note: there is a black box warning on these medications. This is because of reports of skin cancers and
lymphoma with systemic Calcineurin inhibitors used in organ transplant patients. This warning was also
imposed because of one manufacturer’s failure to conduct safety studies.
Note: Skin application results in minimal systemic exposure.
  Vaginal use can result in systemic absorption.
Side effects of Calcineurin inhibitors:
  Burn, sting
  Infection – worsening of HSV, HPV, tinea, molluscum contagiosum
Safety with regard to lichen sclerosus and squamous cell carcinoma? There are a
number of studies showing good results with this medication in
lichen sclerosus in adults and children. There are three reports of genital
squamous cell carcinoma
  with patients who have used tacrolimus and one with squamous cell
carcinoma on pimecrolimus.
Treatment of choice for lichen sclerosus is still superpotent topical steroids
For lichen planus that is difficult to treat with only partial control of topical steroids consider using
tacrolimus and pimecrolimus. The response reported is between 55 and 94%.
Summary of Calcineurin inhibitors:
  For lichen planus start with topical steroids and consider alternating with Calcineurin inhibitors.
  For lichen sclerosus with atrophy or reaction to topical steroids, consider usage, discuss the risks and
  follow carefully. No refills without follow-up vulvar exams.
  Consider for use in the following: vulvar dermatoses, psoriasis, Crohn’s, pemphigoid, etc.
Systemic corticosteroids can be useful at times. A full discussion is beyond this lecture.
IM triamcinolone acetonide (Kenalog 40) 1 mg per kg for an acute dermatosis (e.g. contact dermatitis or
severe lichen simplex chronicus). This can be repeated in 3-4 weeks once or twice to get a severe condition
under control. See appropriate monograph for all side effects of all corticosteroids and calcineurin
inhibitors.
  Caution in patients with diabetes- high dose steroids can interfere with their glucose control.
TO DO FOR ALL VULVAR RASHES
   Educate
   Support
   Stop: irritation, contact dermatitis, scratching
   Treat: infection – Candida, bacteria, atrophy, and inflammation
   Poor response: biopsy

CAUSES OF TREATMENT FAILURE
   Non-compliance
      Poor education
      Fear of topical steroids
      Limited mobility

INCORRECT DIAGNOSIS
   Associated problems
      LS plus SCC or contact dermatitis
      Scarring

MOST COMMON ASYMPTOMATIC VULVAR DISEASES
   Lichen sclerosus, Lichen planus, Malignancy – compounded by
      Ignorance
      Denial

CAUSES OF POOR COMPLIANCE
   Fear of steroids
   Vulvar ignorance
   Miscommunication
   Physical impairment
   Secondary gain – no sex
   Phobic about touching “down there”
List of Lubricants

This does not attempt to be a complete list, but rather describes commonly used lubricants. We do not officially recommend use of any one of these products, nor do we recommend any one product over any other products.

Slippery Stuff: a silken gel that does not leave a sticky residue. It is hygienic, water-based and water-soluble, odorless, long lasting and latex compatible.

Astroglide: A long lasting, light lubrication that is odorless and flavorless. It is water soluble. Many like it because it is a long lasting lubricant that does not become "stringy"

Femigel: Natural product from tea trees. For vaginal dryness.

Jo: water based, silicone based or a combination of both

K-Y Jelly: Generally considered an all-purpose lubricant that many people have found helpful with a "medium" degree of thickness. Some report it comes out too fast and gets "gummy."

Lubrin: A suppository. Many post-menopausal women find this a helpful lubricant because, since it is inserted into the vagina, it lasts longer. They indicate that it needs some time to melt inside the vagina because it is a suppository. For some women, they indicate that it is almost "too much" lubrication.

Moist Again Natural

Replens: A lubricant that is inserted by applicator into the vagina. It comes in a package of 12 single-use applications. This vaginal gel is considered to have medium thickness and properties similar to Ortho Personal Lubricant. Women note that, like Lubrin, it does not dissolve too quickly. Must be used several times weekly.


Surgilube: Many consider this to be thicker than K-Y Jelly

Albolene - Most drug stores sell it in the cosmetic section. Is actually intended to remove make up and provide moisture to the face.

Vitamin E oil: Available in health food stores, preferred by some women for natural, non-irritating qualities.

Vegetable oil (like olive oil) can also be used.

Egg whites have been used for lubrication.
Saliva has been used for lubrication

Pre-Seed is a vaginal lubricant that does not appear to cause significant damage to sperm

**Agents for sexual enhancement**

- **Viafem** – Aminophylline 30mg/mL 15mL Apply ½-1 mL to clitoris before intercourse
- Ergoloid Mesylates 0.5 mg/mL
- Nitroglycerine 1mg/mL
- L-Arginine 60mg/mL
- Pentoxyphylline 50mg/mL

- **Trimix FM** – Papaverine 30mg/mL 5mL Apply 0.5mL to clitoris one hour before intercourse
  - Phentolamine 1mg/mL
  - PGE₁ 20mcg/mL

- **Testosterone**  0.5mg/mL 30mL Apply 1/2mL to labia and 1/2mL to inner arm or Thigh q AM.
Recalcitrant and Recurrent Candidiasis and Bacterial Vaginosis

Vaginitis is a common problem seen daily in different care provider’s offices. It accounts for over 10,000,000 office visits each year. The most prevalent infections are bacterial vaginosis (50%), candidiasis (30%) and trichomoniasis (20%). Less common causes of vaginitis include, foreign body, desquamative inflammatory vaginitis, and streptococcal vaginitis (very uncommon). Other conditions that cause vaginitis symptoms include collagen vascular disease, Behçet’s syndrome, pemphigus and idiopathic conditions. The patient with chronic vaginitis is often frustrated, encounters difficulty in personal relationships, may suffer economic losses and at times, develops depression. A sense of hopelessness may exist.

NORMAL INHABITANTS OF THE LOWER GENITAL TRACT

<table>
<thead>
<tr>
<th>Lactobacillus</th>
<th>Klebsiella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corynebacterium</td>
<td>Prevotella</td>
</tr>
<tr>
<td>Diphtheroids</td>
<td>Peptostreptococcus</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>Eubacterium</td>
</tr>
<tr>
<td>Escherichia</td>
<td>Proteus enterobacteria</td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>Fusobacterium</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Morganella bacteroides</td>
</tr>
</tbody>
</table>

Pelvic examination

The pH of the vaginal discharge can easily and inexpensively be determined using pH strips. The pH paper should range from 3.5 to 7.0. The sample should be obtained approximately one third to midway down the lateral vaginal wall. It should not be contaminated with cervical mucous (pH=7.0). An aliquot of the diluted vaginal discharge should be examined microscopically (40x magnification). A drop or two of the discharge should be mixed with a drop of concentrated potassium hydroxide and whiffed to detect the presence of amines ("whiff test"). A positive test is detected by the presence of a fish-like odor which indicates the presence of bacterial vaginosis.
and/or anaerobes. The same specimen should be examined microscopically for the presence of fungal hyphae and/or budding yeast cells, which are resistant to alkali.

**Potential causes for elevated vaginal pH** include menses, heavy cervical mucus, semen, ruptured membranes, hypoestrogenism, trichomoniasis, bacterial vaginosis, foreign body with infection, Streptococcal vaginitis (group A) (rare), desquamative inflammatory vaginitis.


- Gastic acid 1.5-1.0
- Vinegar 2.9
- Orange juice 3.5
- Beer 4.5
- Vaginal fluid (reprod age) 4.5
- Milk 6.5
- Saliva 6.5-7.0
- Pure water 7.0
- Semen 7.2-8.0
- Blood 7.3-7.5
- Seawater 7.7-8.3
- Sodium bicarbonate 8.4
- Hand soap solution 9.0-10.0
- Bleach 12.5
Vulvovaginal Candidiasis (VVC)

The incidence of mycotic vulvovaginitis is rising dramatically in the United States. There are over 13 million cases of vulvovaginal candidiasis annually in the United States. Seventy-five percent of all women will have at least one episode of vulvovaginal candidiasis. About half of those infected experience more than one episode, and some patients suffer relapse and recurrence over a period of many years. Five percent of women with vulvovaginal candidiasis will develop recurrent episodes. Candida albicans most often causes infections in the United States. It is a dimorphic fungus that forms both spores and mycelia. It is followed in infection rate by C. glabrata and C. tropicalis. Over the past two decades, an increasing trend in the number of vaginal infections attributable to yeasts other than Candida albicans has emerged. If the common antifungal preparations used to treat yeast are ineffective, consideration should be given to culturing for a resistant strain of fungus. Recurrences are common. Predisposing factors include uncontrolled diabetes mellitus, steroid use, tight-fitting clothing/synthetic underwear, antibiotic use, increased frequency of coitus, "candy binges", and IUD use. Additionally, immune system alterations such as HIV/AIDS may be associated with a higher incidence and greater persistence of yeast infections. In patients with frequent yeast infections, consideration should be given to culturing specimens from sexual partners as well and giving appropriate antifungal therapy to them if positive cultures are obtained. Accurate diagnosis depends on culture techniques that will yield correct identification of the fungal pathogen(s).

Symptoms/Signs

The main symptoms and signs of candidiasis are discharge, itching, burning/irritation, erythema, edema and excoriation. Rarely is vulvar candidiasis seen without concomitant vaginal candidiasis. Not all patients have symptoms of yeast infection. The incidence of asymptomatic fungal carriage in the vagina is quoted as 8-12 percent.

Diagnosis

The acidity of vaginal secretions in candidiasis is usually within the pH range of 4.0-4.7. A wet mount preparation reveals spores of C. albicans which are uniform in size, isolated and almost always associated with hyphal-filaments. The spores of C. glabrata are of variable size (2-8 micrometers), spherical or ovoid, and usually smaller than a red cell. They are often grouped in clusters, although they may appear alone. Potassium hydroxide (10%-20%) preparation is often used to evaluate for yeast when they are not seen on saline prep. In this solution, pus cells and red blood cells dissolve. The branching, budding, and hyphal cell walls of C. albicans are easily visualized. Stained smears may also be used to diagnose Candida. Spores of Candida are strongly gram positive. The filaments are uniformly gram positive or have large gram positive granules.

Cultures should be obtained when symptoms are not explained on the wet prep or a patient presents with recurrent candidiasis. Some yeast forms may require as long as a month of incubation for detection (particularly with a small inoculum). Sabouraud’s dextrose agar on modified Sabouraud’s Difco mycobiotic media and Nickerson’s media are satisfactory for growing Candida in an incubator or at room temperature, although identification of the species is not permitted. The most reliable differentiation of the species is provided by sugar fermentation reactions.
**Treatments**  It is necessary to consider removal or improvement of predisposing factors in the treatment of candidiasis. Numerous antifungal preparations are available. If these are ineffective, then consideration should be given to culturing for a resistant strain of fungus. Such infections may require topical application of gentian violet solution or boric acid (per vagina) or amphotericin B (per vagina).

The ISSVD has recently developed an iphone app (YEAST) that addresses the diagnosis and treatment of simple and recurrent Candida infections. (See iphone app store or www.issvd.org)

**Risk Factors for Recurrent Vulvovaginal Candidiasis**

<table>
<thead>
<tr>
<th>Antibiotic use</th>
<th>Receptive oral genital sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen excess (OCP’s, hormone replacement, local estrogens)</td>
<td>Sponge for contraception</td>
</tr>
<tr>
<td>Immune suppression (Lupus, HIV, corticosteroids)</td>
<td>Glucose excess (uncontrolled diabetes; refined sugar excess)</td>
</tr>
<tr>
<td>IUD use</td>
<td>Vulvar dermatoses (lichen sclerosus, eczema, atopic dermatitis)</td>
</tr>
</tbody>
</table>


Complicated Vulvovaginal Candidiasis- culture to identify the species and treat with antifungal that that species generally responds to. Sensitivity testing is rarely needed.

Both oral and topical treatments may be utilized. Topical treatments (particularly the shorter duration treatments) may be irritating to the vulva and vagina. Oral treatments, while generally tolerated well, can have some adverse effects.

**Fluconazole: Adverse effects**

- Nausea and vomiting in 3-4% (long term therapy)
- LFT monitoring consideration secondary to hepatotoxicity

  >> chronic therapy  >> AIDS patients
Fluconazole: Drug-Drug Interaction

- Drug history important with long term/chronic fluconazole therapy
- Not as much of a clinical concern with single dose therapy

Drug interactions with long term fluconazole:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>warfarin (Coumadin®)</td>
<td>may increase PT</td>
</tr>
<tr>
<td>cimetidine (Tagamet®)</td>
<td>20% lower Fluconazole peak</td>
</tr>
<tr>
<td>oral contraceptives</td>
<td>decreased estradiol levels; no effect on break through bleeding, efficacy</td>
</tr>
<tr>
<td>phenytoin (Dilantin®)</td>
<td>increased phenytoin serum levels</td>
</tr>
<tr>
<td>rifampin levels</td>
<td>increased Fluconazole metabolism</td>
</tr>
<tr>
<td>cyclosporine</td>
<td>increased levels of cyclosporine</td>
</tr>
<tr>
<td>oral hypoglycemics</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>theophylline</td>
<td>increased theophylline levels</td>
</tr>
<tr>
<td>terfenadine</td>
<td>?cardiac arrhythmias</td>
</tr>
</tbody>
</table>

Ketoconazole

Ketoconazole traditionally has been used for long term therapy, however it is not routinely used today. Hepatotoxicity occurs and liver function tests need to be performed monthly.

Itraconazole

Itraconazole is used at times for vulvovaginal Candida treatment. Serious cardiac arrhythmias have occurred in patients taking oral azoles together with non-sedating antihistamines (e.g. astemizole and terfenadine).

For irritation of yeast (like a diaper rash), triamcinolone acetonide ointment 0.1 % plus Nystatin 100,000 units per gram to vulva bid x 14 days.
Bacterial vaginosis.

Various terms have existed throughout time for bacterial vaginosis. These include non-specific vaginitis, Hemophilus vaginitis, Corynebacterium vaginitis, Gardnerella vaginplus vaginitis, and anaerobic vaginosis. Bacterial vaginosis represents a complex change in vaginal flora. It is characterized by a reduction in the prevalence and concentration of hydrogen peroxide producing lactobacilli and an increase in the prevalence and concentration of Gardnerella vaginalis (found in 40% of women normally, found in 95% of women with bacterial vaginosis), mobiluncus species, Mycoplasma hominis, anaerobic gram negative rods belonging to the genera prevotella, porphyromonas, bacteroides, and peptostreptococcus species. Treatment of bacterial vaginosis (BV) is based on the understanding that it is not a disease but an unbalance of the vaginal ecosystem. This is an important concept because the imbalance is not due to a single bacterium or pathogen, but a disturbance in the ecosystem that allows the non-dominant symptom causing bacteria to become dominant.

The patient presents with a foul, "fishy" odor, more noticeable following intercourse and during menses. There is an increased or different vaginal discharge. Vulvar itching and/or irritation are present. The undergarments are stained at times.

Bacterial vaginosis may be diagnosed with other laboratory methods such as the use of DNA probes. These are expensive, but may be useful to practitioners unable to perform microscopy. Cultures have been used at times, but they are not useful since they are positive in 40-60% of asymptomatic females.

A new technique that includes nucleic acid probes for high concentrations of G. Vaginalis has become available (Affirm VPIII Microbial Identification Test).

Etiology of vaginal odor in BV

- anaerobic bacteria concentrations increase 100-1000x with BV
  - anaerobic metabolism produces amines (cadaverine, putrescine, trimethylamine)
  - alkalinity volatilizes amines causing the sharp odor associated with BV

Treatment (from 2015 CDC STD Treatment Guidelines)

Recommended Regimens
- **Metronidazole** 500 mg orally twice a day for 7 days
  
  OR

- **Metronidazole** gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days
  
  OR

- **Clindamycin** cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days

**Alternative Regimens**

- **Tinidazole** 2 g orally once daily for 2 days
  
  OR

- **Tinidazole** 1 g orally once daily for 5 days
  
  OR

- **Clindamycin** 300 mg orally twice daily for 7 days
  
  OR

- **Clindamycin** ovules 100 mg intravaginally once at bedtime for 3 days*

*Clindamycin ovules use an oleaginous base that might weaken latex or rubber products (e.g., condoms and vaginal contraceptive diaphragms). Use of such products within 72 hours following treatment with clindamycin ovules is not recommended.

**Treatment Guidelines for Recurrent/Resistant Bacterial Vaginosis**

- For women with multiple recurrences after completion of a recommended regimen, 0.75% metronidazole gel twice weekly for 4–6 months
- Limited data suggest that an oral nitroimidazole (metronidazole or tinidazole 500 mg twice daily for 7 days) followed by intravaginal boric acid 600 mg daily for 21 days and then suppressive 0.75% metronidazole gel twice weekly for 4–6 months for those women in remission may be an option
- Monthly oral metronidazole 2g administered with fluconazole 150 mg has also been evaluated as suppressive therapy-this regimen reduced the incidence of BV and promoted colonization with normal vaginal flora

Probiotics for bacterial vaginosis have been recommended. Studies are currently being performed to investigate their effectiveness.
Vulvodynia

Introduction

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

Historical Information on Vulvar Pain Terminology

Vulvar pain discussion first appeared in the literature in the late 1861 in an article by J. Marion Sims, MD. He describes a patient he saw in 1857 with vaginismus, but upon further analysis of her history, she appears to have vulvodynia. In 1874 Dr. T.G. Thomas described a patient with “excessive sensibility of the nerves supplying the mucous membrane of some portion of the vulva…” In 1889, A.J. C. Skene commented on a condition characterized by “a supersensitiveness of the vulva. When, however, the examining finger comes in contact with the hyperaesthetastic part, the patient complains of pain, which is sometimes so great as to cause her to cry out…..” In the same year, Kellogg wrote about a patient with “sensitive points about the mouth of the vagina”. The topic was not readdressed until 1928, when Howard Kelly mentioned “exquisitely sensitive deep red spots in the mucosa of the hymeneal ring are a fruitful source of dyspareunia”. In 1983, Friedrich reported on 13 patients with “vestibular adenitis”. The International Society for the Study of Vulvovaginal Disease (ISSVD) popularized a definition of vulvar pain in the 1980's (essential or dysesthetic vulvodynia) describing patients with a chronic discomfort, burning, stinging, irritation, and rawness of the vulva. In 1987, Friedrich developed the term “vulvar vestibulitis syndrome”. The terminology of vulvar pain continues to undergo change. The most recent terminology changes, developed by the ISSVD are described below.
### Table 1
PREVIOUS ISSVD TERMINOLOGY AND CLASSIFICATION FOR VULVAR PAIN

<table>
<thead>
<tr>
<th>Generalized Vulvar Dysesthesia</th>
<th>Provoked vulvar dysesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Santa Fe, New Mexico ISSVD World Congress</td>
<td>Portugal ISSVD World Congress</td>
</tr>
<tr>
<td>Vulvar Dysesthesia (1999)</td>
<td>(Of note: this is a provisional terminology system)</td>
</tr>
<tr>
<td>Vulvar Dysesthesia (2001)</td>
<td></td>
</tr>
</tbody>
</table>

Generalized Vulvar Dysesthesia

- Generalized
- Localized (vestibule, clitoris, other)

Localized Vulvar Dysesthesia.

- Vestibulodynia (formerly vulvar vestibulitis)
- Clitorodynia
- Other localized forms of vulvar dysesthesia

Spontaneous vulvar dysesthesia

- Generalized
- Localized (vestibule, clitoris, other)

Salvador, Brazil October 2003

**THE CURRENT TERMINOLOGY**  The 2003 ISSVD Terminology and Classification

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

A) Vulvar Pain Related to a Specific Disorder

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

B) Vulvodynia

1) Generalized
   a) Provoked (sexual, nonsexual, or both)
   b) Unprovoked
   c) Mixed (provoked and unprovoked)

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

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

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

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

<table>
<thead>
<tr>
<th>Disease</th>
<th>Disease</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Podophyllin overdose</td>
<td>Pemphigus</td>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>Condylux overdose</td>
<td>Pemphigoid</td>
<td>Bartholin’s abscess</td>
</tr>
<tr>
<td>Behcet’s disease</td>
<td>Atrophy</td>
<td>Trauma</td>
</tr>
<tr>
<td>Aphthous ulcers</td>
<td>Lichen sclerosus</td>
<td>Prolapsed urethra</td>
</tr>
<tr>
<td>Herpes (simplex and zoster)</td>
<td>Lichen planus</td>
<td>Vulvar intraepithelial neoplasia</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Sjorgen’s disease</td>
<td>Carcinoma</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>Contact dermatitis</td>
<td></td>
</tr>
<tr>
<td>Chancroid</td>
<td>Endometriosis</td>
<td></td>
</tr>
</tbody>
</table>
Etiologic theories on vulvodynia  The exact etiology of vulvodynia is unknown. There most likely is not one single etiology. Etiologic theories proposed include abnormalities of embryologic development, infection, inflammation, genetic/immune factors, and nerve pathways.

<table>
<thead>
<tr>
<th>Theory</th>
<th>Descriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryologic development</td>
<td>It has been noted that tissues from these two distinct anatomic sites have a common embryologic origin, and therefore are predisposed to similar pathologic responses when challenged. vii,viii</td>
</tr>
<tr>
<td>Infection</td>
<td>Candida infections in patients with vestibular pain have been studied.ix,x  The exact association is difficult to determine since many patients report candida infections without verified testing for yeast. Bazin et al. found little association of infection and pain on the vestibule.xi</td>
</tr>
<tr>
<td>Inflammation</td>
<td>“-itis” (as in vestibulitis) has been excluded from the recent ISSVD terminology since studies found a lack of association between excised tissue and inflammation. Bohm-Starke et al. found a low expression of the inflammatory markers cyclo oxygenase 2 and inducible nitric oxide synthase in the vestibular mucosa of women localized vestibular pain as well as in healthy control subjects.xii</td>
</tr>
<tr>
<td>Genetic/Immune Factors</td>
<td>Goetsch was one of the first researchers to question a genetic association of localized vulvar pain.xiii Fifteen percent of patients questioned over a 6 month period were found to have localized vestibular pain. Thirty-two percent had a female relative with dyspareunia or tampon intolerance, raising the issue of a genetic predisposition. Another genetic connection was found in a study evaluating gene coding for interleukin 1 receptor antagonist. xiv,xv,xvi,xvii</td>
</tr>
<tr>
<td>Neuropathways</td>
<td>Kermit Krantz examined the nerve characteristics of the vulva and vagina.xviii  The region of the hymeneal ring was richly supplied with free nerve endings. No corpuscular endings of any form were observed. Only free nerve endings were observed in the fossa navicularis. A sparsity of nerve endings occurred in the vagina as compared to the region of the fourchette, fossa navicularis and hymeneal ring. More recent studies have analyzed the nerve factors, thermoreceptors and nociceptors in women with vulvar pain.xix,xx</td>
</tr>
</tbody>
</table>
Vaginismus
It is important to evaluate for vaginismus in the patients with vulvodynia, particularly localized vulvodynia. It is an involuntary spasm of the pelvic floor muscles affecting the vaginal entranceway. It can make penetration painful or even impossible. One of the main causes is fear or anticipation of pain. When painful penetration has been experienced, this pain may be expected in further sexual intercourse attempts. The degree of vaginismus may then increase the amount of pain, and a vicious circle is established.

Treatment of localized vulvar pain (vestibulodynia)
Many treatment regimens exist for localized vulvodynia. Patients often combine a variety of the following regimens:

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

Other lubricant information
www.drugstore.com Search lubricants
Cool gel packs are helpful in some patients.

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

**Tricyclic antidepressants**

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

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

**Initial Amitriptyline prescription:**

Amitriptyline HCL  25 mg  
Sig:  1 po qhs x 1 week;  If sxs persist, 2 po qhs x 1 wk, if sxs persist, 3 po qhs x 1 wk; if sxs persist, 4 po qhs. Maintain nightly dose that relieves symptoms (Not to exceed 4 po qhs). Do not stop suddenly (i.e. wean)
Start at 5-10 mg in patients age 60 or older and increase by 10 mg weekly.
It is important to have patients avoid more than 1 drink of alcohol daily while on this medication.
Contraception should be utilized in the reproductive age population. For the elderly patient,
lower doses should be used or other medications considered.

**Other antidepressants**

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

**Anticonvulsants**

Gabapentin (Neurontin®) has been used to treat chronic pain conditions.\textsuperscript{xxii,xxiii} Gabapentin comes
in 100 mg, 300 mg, 400 mg, 600 mg and 800 mg tablet sizes. Generally it is started at 300 mg po
qd x 3 days, then 300 mg po bid x 3 days, then 300 mg po tid. It can gradually be increased to
3600 mg po total daily (usually in a tid regimen). No more than 1200 mg should be given in a
dose. Neurontin side effects include: somnolence, mental change, dizziness, weight gain.

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

*Lyrica*
-50 mg po qd x 4 days, if sxs persist, 50 mg po bid x 4 days, if sxs persist, 50 mg po tid
-Can gradually increase up to 100 mg po tid; some reports using 300 mg po bid exist (maximum).

*Topiramate (Topamax®)*
25 mg po qd 1 week; if sxs persist 25 mg po bid x 1 week; if sxs persist 25 mg po in am and 50
mg po in pm x 1 week; if sxs persist, 50 mg po bid; Can gradually increase up to maximum of 100 mg po
bid for pain control.
Biofeedback and physical therapy

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

Low oxalate diet with calcium citrate supplementation

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

Intralesional and trigger point injections:

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

**Acupuncture**

Very few studies have been done using acupuncture for vulvar pain. Three studies have evaluated acupuncture for vulvar pain therapy, with a variety of outcomes. xliii, xlv

**Hypnotherapy**

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

**Vestibulectomy  Surgical excision**

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

Physical examination

Cutaneous or mucosal surface disease present

- No
- Yes

Cotton swab test

Not tender; no area of vulva touched described as area of burning

Alternative diagnosis (incorrect belief that vulvodynia present)

Tender, or patient describes area touched as area of burning

Yeast culture

- Positive
- Negative

Antifungal therapy

- Inadequate relief

Adequate relief

No additional treatment; stop treatment when indicated

Good relief

1) Vulvar care measures
2) Topical medications
3) Oral medications
4) Injections
5) Biofeedback/Physical therapy (pelvic floor awareness)
6) Low oxalate diet Ca²⁺ citrate supplementation
7) Cognitive behavioral therapy; sexual counseling

Inadequate relief and pain localized to vestibule; patient desires additional treatment

Surgery (vestibulectomy)

New Research

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

Botox - Botulinum toxin type A is used as a treatment for many chronic pain disorders. Further studies are being performed.

Internet Addresses of Interest

<table>
<thead>
<tr>
<th>National Vulvodynia Association</th>
<th>International Society for the Study of Vulvovaginal Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong><a href="http://www.nva.org/">http://www.nva.org/</a></strong></td>
<td><strong><a href="http://www.issvd.org">www.issvd.org</a></strong></td>
</tr>
<tr>
<td><strong>Everything You Need to</strong></td>
<td><strong>The University of Michigan Center for Vulvar Diseases</strong></td>
</tr>
<tr>
<td><strong>Know About Vulvodynia</strong></td>
<td><strong><a href="http://obgyn.med.umich.edu/patient-care/womens-health-">http://obgyn.med.umich.edu/patient-care/womens-health-</a></strong></td>
</tr>
<tr>
<td>**<a href="http://learnpatient.nva.org**">http://learnpatient.nva.org**</a></td>
<td><strong>library/vulvar-diseases</strong></td>
</tr>
<tr>
<td>Physical Therapy</td>
<td></td>
</tr>
<tr>
<td><strong><a href="http://www.apta.org/">http://www.apta.org/</a></strong></td>
<td></td>
</tr>
<tr>
<td>Pudendal Nerve Information</td>
<td></td>
</tr>
<tr>
<td><strong><a href="http://www.pudendalnerve.com/">http://www.pudendalnerve.com/</a></strong></td>
<td></td>
</tr>
</tbody>
</table>
Prescriptions for Vulvar Pain
Pain Medications

Xylocaine
- 5% Xylocaine ointment
- sig: apply to vulva prn
- Disp: 35 grams

Amitriptyline
- Initial Amitriptyline prescription:
  - Amitriptyline HCL 10 mg
  - Sig: 1 po qhs x 1 week; If sx$s persist, 2 po qhs x 1 wk, if sx$s persist, 3 po qhs x 1 wk; if sx$s persist, 4 po qhs. Maintain nightly dose that relieves symptoms (Generally not to exceed 4 po qhs) Do not stop suddenly

You should start at 10 mg in patients age 60 or older; increase by 10 mg weekly, as above. In younger women, you can start at 25 mg po qhs, with 25 mg weekly increases if desired. More side effects may occur. Do not exceed 150 mg po qhs on either regimen. Do not stop suddenly.

Future Amitriptyline prescriptions
- Amitriptyline HCL ____mg
- Sig: i po qhs (comes in 10 mg, 25 mg, 50 mg, 75 mg, 100 mg and 150 mg tablets)

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

Cymbalta® (duloxetine)
- Cymbalta 30 mg
  - Sig: 1 po q am x 1 week. If sx$s persist, 2 po q am. (If the patient is depressed, it is better to increase after one week to a bid dose such as 30 mg po bid).
  - (also comes in 20 mg; can start at this dose if desired)

Neurontin
- Neurontin® (gabapentin)
  - Sig: 300 mg po qd x 3 days; if sx$s persist, 300 mg po bid x 3 days; if symptoms persist, 300 mg po tid. Stay on this dose for a month and increase gradually, by 300 mg weekly, if needed.
  - It comes in 100, 300, 400, 600 and 800 mg doses
  - Do not exceed 2700 to 3600 mg total dose per day. Do not give more than 1200 mg in a single dose. Do not stop suddenly, wean when stopping.
Gabapentin ointment 3% or 6%
Sig: apply to affected area bid-tid
Disp: 3 month supply

**Lyrica**
- 50 mg po qd x 4 days, if sxns persist, 50 mg po bid x 4 days, if sxns persist, 50 mg po tid
- Can gradually increase up to 100 mg po tid (Some report utilizing up to a maximum of 300 mg po bid). Do not stop suddenly. Wean when stopping.

Paper regarding the use of lamotrigine for vulvodynia.

**Topiramate (Topamax®)**
- 25 mg po qd 1 week; if sxns persist 25 mg po bid x 1 week; if sxns persist 25 mg po in am and 50 mg po in pm x 1 week; if sxns persist, 50 mg po bid; Can gradually increase up to maximum of 100 mg po bid for pain control.

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

**Medications for localized pain or itching**
- Zonalon® (Doxepin) 5% cream
  Sig: apply to skin q.d with gradual increase not to exceed qid
  Disp: 30 gms

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

**Vaginal pain**
- Intravaginal valium Start at 5 mg per vagina qhs. If symptoms persist, gradually increase by 5 mg qhs, not to exceed 20 mg per vagina qhs.

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

**Self-help books**
Sex Matters for Women
A Complete Guide to Taking Care of Your Sexual Self

Sallie Foley,
Sally A. Kope, and Dennis P. Sugrue

A Woman’s Guide to Confronting, Diagnosing, and Treating Sexual Pain
Healing Painful Sex

CONDITIONS COVERED INCLUDE:
vulvodynia and clitorodynia
pelvic floor dysfunction
pelvic nerve pain
orthopedic pain
painful bladder syndrome
endometriosis
and many others

DEBORAH COADY, MD
& NANCY FISH, MSW, MPH
Self-help Website Information

www.nva.org
I Have Vulvodynia-What Do I Need to Know

Vulvodynia, Pregnancy and Childbirth

My Partner Has Vulvodynia-What Do I Need to Know

http://www.uofmhealth.org/medical-services/sexual-health
References

General


**Nonneoplastic Epithelial Conditions/Lichen sclerosus/Pruritus**


Fite C, Plantier F, Dupin N, Avril MF, Moyal-Barracco M. Vulvar verruciform xanthoma: Ten cases associated with lichen sclerosus, lichen planus, or other conditions. Archives of Dermatology. 2011;147(9):1087-92.


van de Nieuwenhof HP, Bulten J, Hollema H, Dommerholt RG, Massuger LF, van der Zee AG, et al. Differentiated vulvar intraepithelial neoplasia is often found in lesions, previously diagnosed as lichen sclerosus, which have progressed to vulvar squamous cell carcinoma. Modern Pathology : An Official Journal of the United States and Canadian Academy of Pathology, Inc 2011;24(2):297-305.


**Lichen Planus**


Fite C, Plantier F, Dupin N, Avril MF, Moyal-Barracco M. Vulvar verruciform xanthoma: Ten cases associated with lichen sclerosus, lichen planus, or other conditions. Archives of Dermatology 2011;147(9):1087-92.


99


**Crohn’s Disease References**


Hanauer SB. **Updating the approach to Crohn's disease.** Hospital Practice (Office Edition). 1999;34:77-8, 81-3, 87-93; discussion 94.


**Hidradenitis Suppurativa**

Argenta PA; Lindsay R; Aldridge RB; Siddiqui N; Burton K; Telfer JR. Vulvar reconstruction using the "lotus petal" fascio-cutaneous flap. Gynecologic Oncology. 131(3):726-9, 2013 Dec.


Deckers IE, Prens EP. An Update on Medical Treatment Options for Hidradenitis Suppurativa. Drugs. 2016 Feb;76(2):215-29


Martin-Ezquerra G; Masferrer E; Masferrer-Niubo M; Ferran M; Sanchez-Regana M; Collgros H; Bordas X; Notario J; Alsina M; Gil I; Izquierdo N; Aparicio G; Mollet J; Garcia-Patos V; Pujol RM. Use of biological treatments in patients with hidradenitis suppurativa. Journal of the European Academy of Dermatology & Venereology. 29(1):56-60, 2015 Jan.


Ring HC; Riis Mikkelsen P; Miller IM; Jenssen H; Fuursted K; Saunte DM; Jemec GB. The bacteriology of hidradenitis suppurativa: a systematic review. Experimental Dermatology. 24(10):727-31, 2015 Oct.


Yadav S; Singh S; Edakkanambeth Varayil J; Harmsen WS; Zinsmeister AR; Tremaine WJ; Davis MD; Wetter DA; Colombel JF; Loftus EV Jr. Hidradenitis Suppurativa in Patients With Inflammatory Bowel Disease: A Population-Based Cohort Study in Olmsted County, Minnesota. Clinical Gastroenterology & Hepatology. 14(1):65-70, 2016 Jan.

Zouboulis CC; Desai N; Emtestam L; Hunger RE; Ioannides D; Juhasz I; Lapins J; Matusiak L; Prens EP; Revuz J; Schneider-Burrus S; Szepietowski JC; van der Zee HH; Jemec GB. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. Journal of the European Academy of Dermatology & Venereology. 29(4):619-44, 2015 Apr.

Contact Dermatitis

O'Gorman SM, Torgerson RR. Allergic contact dermatitis of the vulva. Dermatitis. 2013 Mar-Apr;24(2):64-72

**Lymphedema**


**Ulcers (including aphthous ulcers)**


**Behçet’s Disease**


**Vaginitis and Infectious Diseases**

**General**


2015 CDC STD Treatment Guidelines http


Sheeley A. Sorting out common causes of abnormal vaginal discharge. JAAPA. 2004;17(10):15-6, 18-20, 22.


Bacterial Vaginosis

Bacterial Vaginosis References


Hay P. How important are the newly described bacteria in bacterial vaginosis?. Sexually Transmitted Infections. 2009;85(4):240-1.


Larsson PG, Stray-Pedersen B, Ryttig KR, Larsen S. Human lactobacilli as supplementation of clindamycin to patients with bacterial vaginosis reduce the recurrence rate; a 6-month, double-blind, randomized, placebo-controlled study. BMC Women's Health. 8:3, 2008.


Marcone V, Calzolari E., Bertini M. Effectiveness of vaginal administration of Lactobacillus rhamnosus following conventional metronidazole therapy: how to lower the rate of bacterial vaginosis recurrences. New Microbiologica. 2008;31(3):429-33.


Sobel JD. http://www.uptodate.com/contents/bacterial-vaginosis?source=search_result&search=bacterial+vaginosis&selectedTitle=1%7E70


Sobel JD. http://www.uptodate.com/contents/bacterial-vaginosis

UK national guideline for the management of bacterial vaginosis 2012


**Trichomonas**


Candidiasis


Sobel, JD. http://www.uptodate.com/contents/candida-vulvovaginitis?source=search_result&search=candida&selectedTitle=2%7E150


Urnsak M, Ilkit M, Evruke C, Urnsak I. Clinical and mycological efficacy of single-day oral treatment with itraconazole (400 mg) in acute vulvovaginal candidosis. Mycoses 2004;47:422-7. (200 mg po bid x 1 day was the dose utilized)


**Desquamative Inflammatory Vaginitis**


**Atrophic Vaginitis**


**Herpes**


Molluscum contagiosum


Pruritus ani


Vulvodynia

2015 CONSENSUS TERMINOLOGY AND CLASSIFICATION OF PERSISTENT VULVAR PAIN is now available on the ISSVD website http://issvd.org/resources/terminology/


Bachmann G; Brown C; Foster DC. Toward a better understanding of the relationship between vulvodynia and chronic stressors. Journal of Women's Health. 2014;23(8):634-5.


Kroll R, Archer DF, Lin Y, Sniukiene V, Liu JH. A randomized, multicenter, double-blind study to evaluate the safety and efficacy of estradiol vaginal cream 0.003% in postmenopausal women with dyspareunia as the most bothersome symptom. Menopause 2018;25:133-8.

Lamvu G, Nguyen RH; Burrows LJ; Rapkin A; Witzeman K; Marvel RP; Hutchins D; Witkin SS; Veasley C; Fillingim R; Zolnoun D. The Evidence-based Vulvodynia Assessment Project. A National Registry for the Study of Vulvodynia. Journal of Reproductive Medicine. 2015;60(5-6):223-35.


Morrisey D, El-Khawand D, Ginzburg N, Wehbe S, O'Hare P, Whitmore, K. Botulinum Toxin A Injections into Pelvic Floor Muscles under Electromyographic Guidance for Women with Refractory High-Tone Pelvic Floor Dysfunction: A 6-Month Prospective Pilot Study. Female Pelvic Medicine and Reconstructive Surgery 2015; 21 ( 5 ) 277 - 82.


Rosen NO; Bergeron S; Sadikaj G; Glowacka M; Baxter ML; Delisle I. Relationship satisfaction moderates the associations between male partner responses and depression in women with vulvodynia: a dyadic daily experience study. Pain. 2014;155(7):1374-83.


Swanson CL; Rueter JA; Olson JE; Weaver AL; Stanhope CR. Localized provoked vestibulodynia:. outcomes after modified vestibulectomy. *Journal of Reproductive Medicine. 2014;59(3-4):121-6.*


**Persistent Genital Arousal Disorder**


**Langerhan’s Cell Histiocytosis**


**Preinvasive and Invasive Diseases of the Vulva**


cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. BMJ. 2010;341:c3493.


www.cdc.gov/cancer/knowledge/ Vaginal and Vulvar cancers Inside Knowledge


2015 CDC STD Treatment Guidelines

Plastic Surgery

Lymphangioma Circumscriptum


Other Articles of Interest

Hamilton BK, Goje O, Savani BN, Majhail NS, Stratton P. Clinical management of genital chronic GvHD. Bone Marrow Transplant 2017;52:803-10.


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


xxxii http://www.vulvarpainfoundation.org/Low_oxalate_treatment.htm


