Learning Objectives
At the end of this presentation, the participant will be able to:
1. List and recognize congenital and structural vulvar abnormalities
2. Distinguish various infectious conditions from follicular to deep tissue infections
3. Outline evaluation strategies to diagnose etiologies of infections and dermatologic abnormalities in external genitalia
4. Explain treatment options and patient counselling needed for infectious, dermatologic and neoplastic conditions of vulva

Congenital and Structural Problems
- Imperforate hymen/absent vagina
- Fused labia
- Urethral problems: caruncle, polyp
- Ambiguous genitalia
- Clitoromegaly
- Gartner’s duct cyst
- Inclusion cyst
Nelson: Vulvar Disease and Dermatological Conditions

Acrochordia (skin tags).
Female Circumcision/ Female Genital Mutilation

- WHO estimates:
  - Between 100 and 140 million women and girls have undergone FC/FGM
  - As many as two million suffer life-threatening injuries as a result
  - Each year another 3 million girls at risk\(^1\)
- Others live in Asia, the Middle East and immigrant communities around the world
- In US 228,000 women and girls living with or at risk for FGC\(^2\)


Female Genital Cutting: 4 Categories

- Type 1: Clitoridectomy
- Type 2: Partial or total removal of clitoris and labia minora
  * With or without excision of labia majora
- Type III: Infibulation: Cutting and aposing the labia to create covering that restricts introitus
- Type IV: Adds other alterations to genitals: piercing, pricking or cauterization
Considerations in OB/GYN

- Skill needed during pelvic exam
  - Pediatric speculum
  - Rectal exam for bimanual
- Awareness of role in problems of:
  - UTIs, dysmenorrhea, dyspareunia, infertility
- Delivery plans
  - Episiotomy desired “cut up”
  - Repair after delivery (re-infibulation)
- Requests for procedure for daughter
- Requests for reversals

Infectious Lesions/Cutaneous Changes: Red Lesions

- Candida vulvitis
- Herpes vulvitis
- Molluscum contagiosum
- Bartholin’s abscess/ vulvar abscess
- Impetigo
- Syphilis
- Lymphogranuloma venereum
- Chancroid
- Granuloma inguinale
- Paget’s disease of the vulva
- Hidradenitis suppurativa
- Vestibulitis
- Pemphigus
- Crohn’s disease
- Behcet’s syndrome
- Psoriasis
- Eczema
- Contact dermatitis
Bacterial Infections

- Follicular infections
- Glandular infections
- Epithelial infections
- Deep tissue infections

Follicular Infections

- **Etiology:** Generally staphylococcal organism produces infection by entering the opening of a hair follicle
- **Predisposing conditions:** Obesity, perspiration, malnutrition, DM, seborrhea, poor hygiene, insects, shaving (?)
- Range folliculitis, furuncles, carbuncles, pilonidal cysts

Folliculitis

- **Presentation:** Superficial infection
  - Limited to upper portion of pilosebaceous duct or deep involving entire follicle and sebaceous glands
  - Yellow-white, pinhead sized pustule typically penetrated by a hair
- **Treatment**
  - Erythromycin-containing antibiotic cream or lotion with
  - Germicidal soaps

Pubic Folliculitis


Furuncles

- **Appearance:** Acute inflammation of hair bulb with a tendency to form abscess around a central plug. Initial folliculitis infection spreads into perifollicular tissue and produces cellulitis. Often drain spontaneously and heal
- **Stages:** Hard, tender, erythematous nodule. Small pustule forms at apex. Ruptures and drains bloody, purulent matter
- **Treatment:** Hot packs to accelerate pointing, then incision and drainage. Systemic antibiotics used to reduce recurrence
Furuncle of the Genitals

Koting GW. Practical Dermatology of the Genital Region. W.B. Saunders, 1980

Carbuncles

- Appearance:
  - Multiple furuncles Intercommunicate
  - Multiple areas of drainage to the skin
  - Overlying skin thick and resistant to rupture
  - Can develop into necrotizing fascitis
- Treatment: Systemic antibiotics against staph, strep and anaerobes
  - Consider MRSA

Glandular Infections

- Acne
- Hidradenitis suppurativa
- Bartholin’s duct abscesses
- Infection of Skene’s glands

Acne

- Process: Sebaceous ducts become blocked with comedo (blackhead) formation
  - Gland distends and ruptures into dermis, exciting inflammatory response – pustules, cysts and nodules
- Risk factors: Androgen induces, estrogen protects. Worse with menses
- Presentation: Small nodules in inner aspects of labia minora; diffuse not solitary like epidermal cysts

Fox-Fordyce Disease

- Fox-Fordyce disease: rare inflammatory disorder that affects apocrine sweat glands
  - Axilla, anogenital, periaureolar, lips, umbilicus, sternum, perineum, upper medial thighs
- Symptoms: intense pruritus worsens with stress, excitement, exercise, hot weather, emotional crises, sex,
Fox-Fordyce Disease

- Affects women > men
  - Develops after puberty
  - Worsens premenstrually
  - Resolves during pregnancy and postmenopausally
- No laboratory abnormalities
- Obstruction of apocrine duct by hyperkeratotic plug
  - Duct ruptures, initiates inflammatory response

Fox-Fordyce Disease

- Appearance:
  - Lesions equidistant, smooth, uniform, firm, folliculocentric papules
  - Color: flesh-colored to red-brown to yellow

Fox-Fordyce Disease

- Treatments:
  - Difficult
  - Topical and interlesional glucocorticoids
    - First line
    - Use limited by atrophy
  - Others: Topical and systemic retinoids, topical clindamycin, topical pimecrolimus cream, benzoyl peroxide, oral contraceptives
  - Mechanical destruction or removal of apocrine glands

Hidradenitis Suppurativa

Foundation Definition

- “Hidradenitis Suppurativa 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 axillary, inguinal and anogenital regions”

Hidradenitis Suppurativa

- Prevalence:
  - 1-4/100 in general population
  - Usually underreported
- Risk factors:
  - Smoking (OR = 12.55)
  - Obesity: relative risk increased
  - By each 1.12/unit of BMI

Hidradenitis Suppurativa

- Etiology:
  - Hyperkeratosis of follicular epithelium
  - Occludes apocrine glands
  - Deficient innate immunity in the skin
  - Many markers downregulated
  - Immunosuppressive cytokine IL-10
  - Hormonal flares


Hidradenitis Suppurativa: Diagnostic Criteria

- Typical lesions:
  - Deep-seated painful nodules
  - Early lesions: blind boils
  - Secondary lesions: abscesses, draining sinuses, bridged scars, open "tombstone" comedos
  - Typical topography
    - Axillae, groin, perineal, perianal areas
    - Buttocks, infra and inter-mammary folds
  - Chronicity and recurrences


Hidradenitis Suppurativa (HS): Early Lesions

- Isolated lesions mistaken for boils or abscesses
  - Shape of HS nodule is round, not pointed and has no central necrosis
  - May not be visible because so deep
  - Very painful
  - Prodrome (burning, stinging, pain, pruritus, heat, sweating) 12-48 before nodule
  - May stay, regress or evolve into abscess


Hidradenitis Suppurativa: Complementary Testing

- Fissures or pustules
  - Do fungal or bacterial culture testing
  - PCR for HSV or varicella


Acute Superficial Abscess

Hidradenitis Suppurativa in a 25-Year-Old Woman

Sinus Tract Along Genitocrural Fold

Hidradenitis Suppurativa

More Extensive Axillary Involvement with Apocrine Acne


Hidradenitis Suppurativa


Multiple Hypertrophic Ropelike Scars

Hidradenitis Suppurative: Differential Diagnosis

- Crohns disease
- Pilonidal sinus
- Furunculosis
- Granuloma inguinale

Hidradenitis Suppurativa

- Treatment depends on stage, frequency of flares and patient’s goals.

Hidradenitis Suppurativa: Ineffective Therapies

- Topical antibiotics and antiseptics
- Oral isotretinoin
- Colchicine (anti-inflammatory drug)


Hidradenitis Suppurativa

Acute Treatments: Fluctuant Abscess

- Medical therapy generally ineffective
- Incision and drainage previously advocated
- Packing was used if cavity very deep
  - Concave, narrow incision or incomplete evacuation
- Minimize packing changes
  - Extremely painful to patient

Hidradenitis Suppurative

Acute Treatments: Prevent Abscess

- Combination antibiotics + intralesional corticosteroids
  - Amoxicillin + clavulanic acid
    - Loading dose 3g/70kg within 1 hour of prodrome
    - Divided doses for several days
  - Intralesional triamcinolone (Kenalog) 10mg/ml
- High dose systemic steroids
  - In lieu of antibiotics
  - In addition to antibiotics

Hidradenitis Suppurative

Chronic Conditions

- Severely affected individuals with high level inflammation, pain and discharge
  - 10 weeks treatment course
    - Clindamycin 300mg BID
    - Rifampicin 600mg daily
  - Remission for 1 year possible
- Less severely affected women
  - 10 weeks treatment course
    - Tetracycline 250mg QID or doxycycline 100mg BID to prevent new abscesses
  - Substitute metronidazole in case of foul order

Hidradenitis Suppurative

Long Term Therapy

- Antiandrogens
  - Birth control pills (DRSP, CPA)
  - Finasteride
  - Spirolactone
- Anti-TNFα (used when antibiotics fail)
  - Infliximab
  - Etanercept
  - Adalimumab
- Botulinum toxin injections
Hidradenitis Suppurative: Surgeries
- Local excision and primary closure
  - Helpful for early stage disease with sinuses
  - Not helpful with many burrowing abscess
- Exteriorization and deroofing tracts
- Radical excision and healing with secondary intention or graft
  - Intraoperative mapping of sinus tracts with methylene blue essential
  - Remove all apocrine gland-bearing skin
  - Recurrence rate 30%
- Laser excision (CO₂ or YAG)

Crohn’s Disease of the Vulva
- Crohn’s disease is chronic granulomatous inflammatory bowel disease
  - May involve anus and perianal region
  - May co-exist with hidradenitis suppurative
  - May be clinically indistinguishable
  - Presence of granulomas in dermis away from area of acute inflammation
  - Consider Crohn or sarcoidosis
- Always perform digital exam of anus and rectum to R/O anal fistula

Crohn’s Disease
- Perianal cutaneous disease often develops usually as direct extension of rectal Crohn’s disease
  - Edematous skin tags
  - Fissures: linear “knifelike”
  - Abscess formation and fistula formation
  - Ulceration – deep in skin folds
- Edema ± granulomatous change on biopsies

Crohn Disease: Differential Diagnosis
- Melkersson – Rosenthal disease
- Hidradenitis suppurativa
- Granuloma inguinale
- Behçet
- HSV
- Ulcerative carcinoma
- Chancroid

Crohn Disease: Management
- Control associated bowel disease
- Intrallesional triamcinolone 10 mg/ml – solid lesions
- Incise and drain fluctuant lesions (aspirate?)
- Consider oral prednisone or TNFα inhibitors
- Observe for future squamous cell carcinoma
Bartholin’s Duct Abscesses

- **Etiology:** Infection in the ductal system (often GC, CT) can occlude duct. Spreads to surrounding tissue in labia majora and minora
- **Diagnosis:** Test for STDs
- **Treatment:** Incise at level of hymen, break up loculations, and place Word catheter for 6 weeks of drainage. Generally, no need to culture purulent material. May need marsupialization for recurrent lesion

Infection of Skene’s Glands

- **Etiology**
  - Younger women with GC or CT
  - Older women have GC or CT or chronic infection with non STD organisms
- **Treatment:** Sometimes surgery need for drainage

Epithelial Infections

- Involve keratinized epithelium not skin adnexa
- Impetigo contagiosa
- Ecthyma

Impetigo Contagiosa

- **Etiology:** Contagious disease caused by staphylococci and/or streptococci. May follow skin disruption from insect bite. Autoinoculation usually causes multiple lesions
- **Appearance:** Vesiculopustular lesions, which easily rupture and leave ulcers. Heals well. No significant lymphadenopathy
- **Treatments:** Local measures, including removal of crust with soap and water, boric acid, H₂O₂ soaks with frequent application of topical antibiotic for 7-10 days

Bacterial Impetigo of the Perineum

Ecthyma

- **Appearance**: Pustular infection similar to impetigo, but involves full thickness of epidermis and superficial layer of corneum "deep impetigo". More frequently involves lower portions of legs, buttocks and vulva. More likely to scar
- **Treatment**: Systemic antibiotics

Deep Tissue Infections

- Erysipelas
- Cellulitis
- Abscesses (relatively uncommon)
- Necrotizing fascitis
- Scrofuloderma (vulvar tuberculosis)
- Trichomycosis

Erysipelas

- **Etiology**: Rapidly spreading, interstitial infection of skin caused by B-hemolytic streptococcal infection in superficial lymphatics. Rare in vulva
- **Presentation**: Generally presents with constitutional symptoms (high fever, chills, headaches)
- **Appearance**: Flaming red, sharply demarcated lesion, edematous for 4-5 days, then becomes diffuse with irregular target-like border. May become gangrenous

Cellulitis

- **Definition**: Inflammation of interstitial cellular tissue especially subcutaneous tissue
- **Risks**: Often follows surgical repair; episiotomy, punch biopsy or local skin abrasion
- **Management**: Must R/O necrotizing fascitis, gangrene
- **Treatment**: Systemic antibiotics and local measures needed

Abscesses

- Relatively uncommon
- **Risks**: Diabetes, trauma, previous impetigo
- **Appearance**:
  - Usually involve labia majora
    - May spread to mons
  - Single lesions surrounded by edema, induration, erythema
Abscesses: Management

- Mark edge to rule out expanding lesion, i.e., necrotizing fascitis
- Hot packs, drainage (I&D or ultrasound-guided aspiration)
- Systemic antibiotics (anaerobic + aerobic coverage)
- Special case: Periclitoral abscesses (pilonidal abscess) require surgical excision deep to origin

Necrotizing Fascitis

- **Definition:** Rare, rapidly progressive condition – polymicrobial anaerobic infection of superficial fascia and subcutaneous tissue. Spread is unlimited and rapid
- **Presentation:** Erythema, edema, gas bubbles seen on x-rays. Skin necrosis only in 50% of cases ± crepitus, anesthesia due to nerve destruction, ulcers, bulla
- **Risks:** DM, peripheral vascular disease, immunosuppression, obesity, malnutrition, candidal infection

Fungal Infections: Tinea Infections

- **Description:** Usually begin as inflammatory blistering or pustules, which spread concentrically. Center dries, becomes scaly and periphery expands with blisters
- **Conditions:**
  - Candidiasis
  - Tinea cruris (jock itch)
  - Tinea versicolor (pityriasis versicolor)
  - Erythrasma

Candida Vulvitis
**Nelson: Vulvar Disease and Dermatological Conditions**

Microscopic Appearance of:

- **C. Albicans**
- **C. glabrata**
- **C. tropicalis**

**Candida Vaginitis**

- Albicans
- Tropicalis
- Glabrata
- Krausei
- Parapsilosis

\[15\%\]

- Non-albicans increasing

**Diagnosis of VVC**

- Symptoms
  - External dysuria
  - Vulvar pruritus, pain, swelling, redness
- Signs
  - Vulvar edema, fissures, excoriation
  - Thick, curdy vaginal discharge
- Lab tests
  - Yeast or pseudohyphae on wet prep or Gram stain
  - Culture or other test positive
Diagnosis of VVC

- Wet mount suspended in saline or with 10% KOH
- Should be performed in all women with signs or symptoms
- Culture for candida should be considered if microscopic studies negative
- Treat empirically if unable to culture for yeast
- Note: do not screen or treat women without signs or symptoms
- 10-20% of women harbor yeast in vagina

Correlation of Correct Self-Diagnosis of Vulvovaginal Candidiasis

<table>
<thead>
<tr>
<th>Variable (mean number)</th>
<th>Correct</th>
<th>Incorrect</th>
<th>P</th>
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<tbody>
<tr>
<td>Lifetime VC infections</td>
<td>6.5</td>
<td>17.8</td>
<td>0.01</td>
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<tr>
<td>Clinician-diagnosed VC in past year</td>
<td>1.6</td>
<td>1.5</td>
<td>0.68</td>
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<tr>
<td>VC infections in past year</td>
<td>2.1</td>
<td>2.2</td>
<td>0.31</td>
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<tr>
<td>Prior clinically diagnosed VC</td>
<td>4.0</td>
<td>9.9</td>
<td>0.02</td>
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<tr>
<td>Clinicians recommended OTC products in past year</td>
<td>1.2</td>
<td>1.4</td>
<td>0.36</td>
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<tr>
<td>Self-treatment of VC in past year</td>
<td>2.1</td>
<td>2.1</td>
<td>0.69</td>
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<tr>
<td>OTC product cured VC</td>
<td>2.9</td>
<td>1.4</td>
<td>0.08</td>
</tr>
</tbody>
</table>


Tinea Cruris (Jock Itch)

- Fungal infection of genitocrural areas
- Etiology: Fungus does not invade living tissue; limited to Stratum Corneum of epidermis
- Appearance: Starts as small erythematous, scaly patch with crusting or scab formation. Spreads peripherally and coalesces. Well circumscribed, sharply defined, raised erythematous margins usually found in the upper parts of inner thighs but may spread to vulva. Color: Normal to slightly pigmented to fiery red

Tinea Cruris induces inflammation at the Advancing Edge of the Lesion (Edge Activity)


Tinea Cruris

Tinea Cruris (Jock Itch)

- **Presentation:** Intense pruritus
- **Diagnosis:** Hyphae of fungus on marginal scraping suspended in 10% KOH; only has hyphae without spores. Culture on Sabouraud’s medium
- **Treatments:** Miconazole nitrate, clotrimazole cream, Ketoconazole cream BID x 2-3 weeks

Tinea Versicolor (Pityriasis Versicolor)

- **Etiology:** Most common fungal infection; focuses in most superficial layers; caused by Pityrosporum ovale
- **Appearance:** Lesions multiple and round or discoid. Fine scales. Yellow, reddish or brown appearing. Edges not raised. Looks like erythrasma

Tinea (Pityriasis) Versicolor

- **Presentation:** Mild pruritus
- **Diagnosis:** Scrapings KOH 10% reveal hyphae short, rodlike and angular with groups of grapelike spores
- **Treatment:** Topical imidazole most effective, Ketoconazole 2% BID x 4 weeks

Erythrasma

- **Definition:** Superficial skin infection more common in men than women in tropical climates. Caused by Corynebacterium minutissimum (short GPR)
- **Distribution:** Penetrates upper half thickness of stratum corneum in intertriginous sites – groin, toe webs, axilla, submammary
- **Presentation:** Macular, well defined, confluent lesion, which is dark red or brown, partly visible in daylight. Edges not raised and have no vesicles. Lesion scaly when scratched
Erythrasma

- **Diagnosis:** Wood’s light in darkened room; coral red or pink fluorescence due to Coproporphyrin, which is a water soluble porphyrin (won’t fluoresce after washing)
- **Treatments:**
  - Topical antibiotics: 2% clindamycin or 2% miconazole
  - Erythromycin 250 mg QID X 7 days with scrubbing BID with antibacterial soap

Zoonotic Infections

- Pediculosis pubis (crab louse)
- Scabies of the vulva
- Eutrombicula alfreddugesi (chiggers)
- Leishmaniasis: Flagellated protozoa. Cutaneous leishmaniasis
- Cimex lectularius (bedbugs)
- Fleas and ticks

Pediculosis Pubis (Crab Louse)

- **Description:** Wingless insect 1.5 mm long grey or brownish. Bite skin of hair base on vulva and live on blood. Must feed continuously. Nits deposited on base of hair. Distance from skin surface is measure of duration of infection
- **Transmission:** Spread by sexual contact
- **Distribution:** Live in hair on pubis, perianal, perineal, eyelashes, eyebrows, axillary, anal, body hair

Pediculosis Pubis: Recommended Treatment Options

<table>
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<tr>
<th>Regimens</th>
<th>Dosage</th>
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<tr>
<td>Either Permethrin 1% cream</td>
<td>Apply to affected areas for 10 minutes, then wash off</td>
</tr>
<tr>
<td>or Pyrethrins with piperonyl butoxide</td>
<td>Apply to affected area for 10 minutes, then wash off</td>
</tr>
</tbody>
</table>

- Bedding and clothing should be decontaminated

Pediculosis Pubic

- Widespread resistance is reportedly increasing to permethrin
- Alternative responses:
  - Malathion 0.5% lotion applied for 8-12 hours than washed off
  - Ivermectin 250mcg/kg orally now and in 2 weeks

**CDC. Sexually transmitted diseases treatment guidelines 2010**
Scabies Of The Vulva

- **Etiology:** Sarcoptes scabiei (itch mites)
- **Presentation:** Vulvar infection, usually part of a widespread disease; seen in finger webs
- **Clinical course:** Female buries into epidermis, deposits ova and feces. Minute papula or vesicles form. Pruritus everywhere; worse in warm bed. No nits

Scabies

- **Diagnosis:** Unroof barrow to see organism microscopically
- **Treatment:** Permethrin creat 5% to all areas of body from deck down and washed off in 8-14 hours OR
- **Ivermectin 200mcg/kg orally, repeated in 2 weeks**

Eutrombicula Alfreddugesi (Chiggers)

- **Etiology:** 6 legged, barely visible mite
- **Habitat:** Southern US in summer, berry picking, grassy lawns and Bermuda grass pastures
- **Presentation:** Intense pruritus from bite; small erythematous pustule

Leishmaniasis

- Flagellated protozoa
- Cutaneous leishmaniasis
- Endemic in countries in Eastern Mediterranean, Asia, Minor, India
- Transmitted by sand flies

Cimex Lectularius (Bedbugs)

- **Etiology:** Wingless, blood sucking insect, 5 mm long
- **Habitat:** Beds, upholstered furniture, behind wallpaper, in cracks of woodwork
  - At night, come out and bite humans
- **Lesions:** Wheal, papule, blister in groups or straight line
Parasitic Infections

- Schistosomiasis (Bilharziasis)
- Enterobius vermicularis (Pinworm or thread worm)

Schistosomiasis (Bilharziasis): Risks

- Results from swimming in lakes in endemic areas contaminated with cercariae from aquatic snails

Schistosomiasis: Etiology

- Free swimming cercariae penetrate human skin. Mature in liver. Flukes mate and the females pass into pelvic veins and lay eggs, which penetrate rectum and bladder and are excreted. They hatch miracidia ingested by small host and reestablish cycle
- Some eggs migrate thru pelvic vessels to adjacent subcutaneous tissue to cause chronic granulomatous changes that look like condyloma acuminata in perineum, groin and external genitalia

Schistosomiasis: Papillomatous Lesion of the Cervix and Vaginal Vault


Enterobius Vermicularis (Pinworm Or Thread Worm)

- Habitat: Live in large bowel. Lay eggs in skin surrounding anus. Ova shed and ingested by another or larvae hatch and re-enter anal canal. Worms 3-14 mm long
- Diagnosis: Apply adhesive tape to perianal area in morning to catch small worms
- Treatment: Mebendazole 100 mg PO single dose. All family members need treatment

Ulcerative Diseases

- Aphthous ulceration
- Herpes simplex virus
- Herpes Zoster (shingles)
- Molluscum contagiosum (pox virus)
- Syphilis
- Lymphogranuloma venereum
- Chancroid
- Granuloma inguinale (donovanosis)
Aphthous Ulcers

- Aphthous ulcers ("canker sores")
  - Common in oral cavity; rarer in genitilia
- Categories
  - Minor (< 1 cm, heal-without scaring)
  - Major (≥ 1 cm, may heal with scarring)
  - Herpetiform (10 or more, very small clustered)
  - "Complex aphthosis" (recurrent oral and genital)

- Primary:
  - Idiopathic
  - Usually in girls and women < 25 years
- Secondary:
  - Associated with other medical conditions:
    - Behçet disease
    - IBS
    - HIV/AIDS
    - SLE
    - MAGIC (mouth and genital ulcers with inflamed cartilage)
    - PFAPA (periodic fever, aphthae, pharyngitis and adenitis)

Aphthous Ulcers: Clinical Presentation

- Symptoms:
  - Extremely painful
- Prodrome:
  - Possible low-grade fever, malaise, GI symptoms, respiratory symptoms
- Recurrence rates:
  - About one third

- Usually also oral ulcers (history)
- Location: primarily vestibule
  - Outer labia minora, perineum, labia majora, vaginal introitus. ?Intravaginal?
- Size:
  - Diameter: ≤ 2 cm
  - Depth ≤ 1 cm
- Appearance:
  - Majority ≥ 2 ulcers, often confluent
  - Base: bright red or covered with grey, necrosis or heme-colored scab

Aphthous Ulcers: Clinical Presentation

- Clinical presentation
  - No labs or biopsy findings diagnostic
  - Except to rule out other causes
- Differential diagnoses:
  - HSV – lesions usually much more superficial
  - Behçet's – very similar to secondary aphthous ulcers
  - Ulcers can precede precipitating disease
Aphthous Ulcers: Pathophysiology

- Several inciting events:
  - Viral infection, Crohn's, trauma, stress
- Influx of inflammatory cells
  - Elaboration of inflammatory cytokines
  - Interleukin 2, tumor necrosis factor alpha
- Vascular destruction
- Localized tissue necrosis
- Ulcer formation

Aphthous Ulcers: Diagnosis Summary

- Occur primarily in girls and young women
- Several, punched out, really painful ulcers
- Flu-like prodrome may precede or accompany ulcers
- Arcuate when ulcers become confluent
- R/O HSV, syphilis, chancroid
- Look for associated disease: Behçet and IBS

Aphthous Ulcers: Management

- Topical lidocaine ointment
- Silver nitrate sticks
- ? Topical steroids
- Intraleisional injections:
  - Triamcinolone 10 mg/ml
  - Prednisone 10 mg dose daily 7-10 days
  - NSAIDs with doxycycline 100 mg BID
  - Pentoxifylline 400 mg PD BID
  - * Colchicine 0.6 mg PD BID-TID and/or
  - * Dapsone 100-150 mg/day

Behçet Disease

- Aphthous ulcer oral and genital and uveitis
  - Multisystem disease involving
    - Skin, joints, cardiovascular system, CNS, GI
  - More prevalent Mediterranean, Middle East, Japan
  - Criteria for diagnosis: controversial
  - More painful, larger and more frequent recurrences than complex aphthous ulcer
  - Additional drugs:
    - Azathioprine, cyclophosphamide, cyclosporin, methotrexate, TNFα inhibitors:
      - Etanercept, infliximab

Herpes Zoster (Shingles): Definition

- Vesiculo-ulcerative lesions due to reactivation of varicella
- Virus localizes in dorsal root ganglion migrates along peripheral nerve to skin

Herpes Zoster: Presentation

- Low grade fever, malaise and severe neuritic pain
- Clusters of discreet vesicles on erythematous base
- Lymphatic enlargement and tenderness in regional nodes
- Vesicular lesions may coalesce into maculopapular lesion varying in diameter from millimeters to centimeters
- Lesions may rupture, leaving deep ulceration and suppuration
- Persists 3-4 weeks
- Lesions do not cross midline
Genital Herpes

Zoster

Koting GW. Practical Dermatology of the Genital Region. W.B. Saunders, 1980

Herpes Zoster (Shingles)

- May be warning of neoplastic process
- Treatment: Acyclovir

Herpes Simplex Virus

- **Definition:** Infection results from inoculation with virus (HSV-1 or HSV-2) through mucous membranes
- **Incidence:** 1.6 million new cases annually in US
- **Prevalence:** 45 million individuals infected
- **Epidemiology:** Prevalence of disease not well known because HSV is not a reportable disease. Antibody studies positive in 60% of all US adults; 90% of inner city adults positive

Herpes Simplex Virus: Microbiology

- HSV-1 usually "above the waist"; HSV-2 usually "below the waist"
- Virus invades cells. Body fluids infectious. Fomites also have role in spread
- Long-term ganglion nerve root sequestration

Herpes Simplex Virus: Types of Infections

- **Primary:** Infection in patient without previous infection anywhere
- **Non-primary:** Lesion at a new site
- **Recurrent:** Lesion at site previously affected

Herpes Simplex Virus: Primary Infection

- Incubation time is 3-7 days
- Involvement of several sites common with painful lesion(s) – vesicular to ulcerative
- **Associated symptoms:** Vaginal or urethral discharge, inguinal adenopathy, dysuria. 40% of patients get fever, malaise, myalgia
- **Duration until healing complete:** 3-4 weeks (viral shedding 1-2 weeks)
- **Complications:** Viral meningitis (4-8%), HSV encephalitis, hypotonic bladder, constipation
- AIDS retards healing process
Herpes Simplex Virus: Recurrent Infection

- Reactivation of latent virus along single ganglion
- Prodrome of tingling or aching several hours or days before outbreak
- Infection lasts 5-10 days. Viral shedding 3-6 days
- Relationship to menstrual cycle. Role of arginine in initiating recurrence

Herpes Genitalis

- HSV-2 recurrence on average 49 days after primary infection
  - Median number of recurrences 4.5 per year
  - 14% women; 26% of men have > 10 outbreaks/year
- Viral shedding 5-32% of days (median)
  - 40% of days subclinical

HSV Infection

- At least 50 million in the US infected HSV 2
- Increasing proportion of anogenital herpetic infections due to HSV-1 in young women and MSM
- Most HSV-2 infected people are underdiagnosed
  - Most have unrecognized (atypical) presentation but intermittently shed virus

CDC. Sexually Transmitted Diseases Treatment Guidelines 2010

HSV Diagnosis

- Cell culture and PER preferred HSV test
  - Viral culture sensitivity low
  - Swab base of freshly ruptured vesicle
  - 77% positive primary infection
  - 47% positive in recurrences
  - PCR preferred for CNS tests
  - Pap and Tzanck unreliable

CDC. Sexually Transmitted Diseases Treatment Guidelines 2010

HSV Serologic Tests

- Must use HSV specific glycoprotein C2
  - Sensitivity 80 - 90%
  - False negative in early infection

CDC. Sexually Transmitted Diseases Treatment Guidelines 2010

HSV Serology Testing

- Indicated:
  - Recurrent symptoms with negative HSV culture
  - Clinical diagnosis of genital herpes without laboratory confirmation
  - Partner with HSV
- Consider for:
  - Patient with STD
  - HIV infection
  - MSM


<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of genital lesion/symptom</td>
<td>Available</td>
</tr>
<tr>
<td>Culture negative recurrent lesion</td>
<td>Helpful</td>
</tr>
<tr>
<td>Hx of herpes without lesions to culture</td>
<td>Helpful</td>
</tr>
<tr>
<td>Suspected 1st herpes &gt; 6 weeks ago without lesions to culture</td>
<td>Helpful</td>
</tr>
<tr>
<td>Screening of HIV infected patients</td>
<td>Generally offer</td>
</tr>
</tbody>
</table>

Oral Treatment of Genital Herpes Recurrent Infection
- Acyclovir 400 mg TID X 5 days
- Acyclovir 800 mg BID X 5 days
- Acyclovir 800 mg TID X 2 days
- Famciclovir 125 mg BID X 5 days
- Famciclovir 1000 mg once
- Famciclovir 500 mg once, then 250 mg BID 2 days
- Valacyclovir 500 mg BID X 3 days
- Valacyclovir 1g daily X 5 days

Oral Treatment of Genital Herpes Suppressive Regimen
- Acyclovir 400 mg BID
- Famciclovir 250 mg BID
  - Less effective in preventing viral shedding
- Valacyclovir 500 mg daily
  - Less effective with ≥ 10 episodes/year
- Valacyclovir 1g daily

HSV-2 Suppressive Treatment
- 20% of US adults have serological evidence of HSV-2 infection
- 1,484 discordant heterosexual, monogamous couples in relationship for 2 years
  - Valacyclovir 500 mg daily vs placebo
- 8 month follow-up
  - Partner new onset HSV-2: Treated Control 1.9% 3.6%


Candidates for Suppressive Therapy: Good Candidate
- Patient’s partner is uninfected
- Patient has multiple partners
- Patient has painful recurrences
- Patient has frequent recurrences
- Patient is depressed or anxious about herpes outbreaks
- Patient wants to avoid as many outbreaks as possible
- Patient can pay for therapy or qualifies for financial assistance
- Patient or partner has HIV

CDC. Sexually Transmitted Diseases Treatment Guidelines 2010

Oral Treatment of Genital Herpes Recurrent Infection
- Acyclovir 400mg TID X 5 days
- Acyclovir 800mg BID X 5 days
- Acyclovir 800mg TID X 2 days
- Famciclovir 125mg BID X 5 days
- Famciclovir 1000mg once
- Famciclovir 500mg once then 250mg BID 2 days
- Valacyclovir 500mg BID X 3 days
- Valacyclovir 1g daily X 5 days

Oral Treatment of Genital Herpes Simplex Virus (HSV) Infections Primarily Infant

<table>
<thead>
<tr>
<th>1st episode (x 7-10 days)</th>
<th>Acyclovir 400 mg t.i.d. or 200 mg 5 times daily</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Famciclovir 250 mg t.i.d. X 7-10 days</td>
</tr>
<tr>
<td></td>
<td>Valacyclovir 1g b.i.d. X 7 days</td>
</tr>
</tbody>
</table>

CDC. Sexually transmitted diseases treatment guidelines 2010


Anita L. Nelson, MD - 04/17/14 14:35
VD 2014-04-22 Nurses Assoc. Montana
Syphilis

- Heterosexual rates highest in South:
  - 53% of all US cases in 16 states
- 1° and 2° syphilis rates 42x higher in black women than among white women
- Rates among MSM increasing in many cities in US and Canada¹
  - King County Washington 2001 rates 1° and 2° syphilis:
    - MSM 141/100,000
    - MSM HIV+ 683/100,000
    - Heterosexuals < 1/100,000

Primary, Secondary or Early Latent Syphilis: Treatment Options

- **Recommended regimen:**
  - Benzathine penicillin G 2.4 million U IM once
- **Alternative regimens for penicillin-allergic patients:**
  - Pregnant women and noncompliant patients
  - Desensitize and treat with penicillin
  - Jarisch-Herxheimer reaction may impact fetus
- **Doxycycline 100 mg orally b.i.d. x 14 days or**
- **Tetracycline 500 mg orally q.i.d. x 14 days**

Late Latent, Latent of Unknown Duration, or Tertiary Syphilis: Treatment Options

- **Recommended regimen:**
  - Benzathine penicillin G 2.4 million U IM weekly x 3 weeks
- **Alternative regimens for penicillin-allergic patients:**
  - Desensitize pregnant women and treat with penicillin
  - **Doxycycline 100 mg orally b.i.d. x 28 days or**
  - **Tetracycline 500 mg orally q.i.d. x 28 days**

Penicillin Oral Desensitization

- For patients with a positive skin test
- Dilute each dose in about 30 mL of water
- Desensitize in hospital because serious IgE-mediated allergic reactions, although unlikely, can occur
- After desensitization, maintain penicillin therapy continuously until complete
Lymphogranuloma Venereum (LGV)

Clinical Manifestations
- Serotype L1, L2, L3
- Relatively rare in women (1:5)
- Infection of vulva, urethra, rectum or cervix
- Primary infection is a shallow painless ulcer
- Secondary infections 1-4 weeks later – painful adenopathy in inguinal and perianal areas
- Untreated lesions become bulbous ("groove sign")

Diagnosis
- Clinical diagnosis based on appearance, epistemology and exclusion of other causes
- Support by test for C. trachomatis
  - Use lesum swabs or bubo aspirate
  - Culture, nucleic acid detection or direct immunofluorescent
  - Other emergency
    - NAATS for rectal swab
    - PCR-based genotyping
  - Chlamydia serology (complement fixation titers > 1:64)

Clinical Aspects
- Caused by C trachomatis serovars L1, L2, or L3
- Initial manifestation: Self limited genital ulcer or papule at site of inoculation
- Presenting problem: Tender inguinal and/or femoral lymphadenopathy
  - If rectal involvement: proctocolitis
    - Mucoid, ± hemorrhagic discharge, anal pain, constipation, fever, tenesmus
  - Can lead to structures and fistulas
  - Superinfection common

Treatment Options
- Recommended regimen:
  - Doxycycline 100 mg orally b.i.d. x 21 days
- Alternative regimen:
  - Erythromycin base 500 mg orally q.i.d. x 21 days
- Buboes may require aspiration thru intact skin or I & D

CDC. Sexually transmitted diseases treatment guidelines 2010
Chancroid Clinical Presentation
- Incubation period 2-10 days
- Small papule with ring of erythema
- 2-3 days later: pustule, vesiculopustule or ulcer forms
- Classical appearance
  - Superficial ulcer with ragged edges, surrounding red halo
  - Base of ulcer covered with necrotic exudate
  - Very painful and tender, multiple ulcers from autoinoculation
- Bubo forms in 50% of cases 7-10 days after lesion appears
  - Acute, tender, inflamed inguinal adenopathy
  - If not treated, bubo will rupture, forming large ulcer

Chancroid Diagnosis
- Definitive diagnosis – culture of H. ducreyi
  - Not widely available
- PCR non FDA approved but
  - Some commercial labs offer
- Clinical diagnosis
  - Painful genital ulcer plus tender suppurative inguinal adenopathy
  - No evidence of syphilis
  - R/O HSV

Chancroid Treatment Options
- Azithromycin 1 gram orally once or
- Ceftriaxone 250 mg IM once or
- Ciprofloxacin* 500 mg orally b.i.d. x 3 days or
- Erythromycin base 500 mg orally TID x 7 days
- May need to drain abscesses

CDC. Sexually transmitted diseases treatment guidelines 2010
Granuloma Inguinale (Donovanosis)

- A rare disease in the US
- Chronic, ulcerative bacterial infection by GNR *Klebsiella granulomatis*
- Asymptomatic nodule ulcerates to slow growing beefy red ulcer that bleeds easily on contact. Ulcers coalesce. Destroys architecture. Lymphedema
- Diagnosis: Clinical. Donovan bodies “safety pin” formed in monos from biopsy of lesion edge

Granuloma Inguinale (Donovanosis) Treatment Options

- Recommended regimens (for at least 3 weeks): until all lesions heal
  - Doxycycline 100 mg orally b.i.d
  - Azithromycin 1 g orally weekly or
  - Ciprofloxacin 750 mg orally b.i.d. or
  - Erythromycin base 500 mg orally q.i.d. or
  - Trimethoprim-sulfamethoxazole double strength (800 mg/160 mg) tablet orally b.i.d.
- Alternative regimens (for at least 3 weeks):

Exophytic STDs

- Molluscum Contagiosum
- HPV

Molluscum Contagiosum (Pox Virus)

- Presentation: Lesions are 1-2mm diameter, clear vesicles smooth with central umbilication. Nodular lesions possible: Smooth and glistening but pedunculated
- Transmission: Sexually transmitted
  - Autoinoculation spreads locally
  - Imiquimod
  - TCA

Molluscum Contagiosum Lesions: Treatment Options

- Physician administered
  - Electrosurgery
  - Curettage
  - Cryosurgery
  - Trichloroacetic acid
  - Podophyllin
- Patient administered
  - Podofilox (podophyllotoxin)
  - Retinoic acid
  - Imiquimod cream (immune response modifiers)
Human Papilloma Virus (HPV)

- **Etiology:** HPV 6, 11 or others
- **Incidence:** 5.5 million new cases in US annually
- **Prevalence:** 20 million cases
- **Presentation:** Small warty growths. Soon surrounded by ring of similar lesions. May coalesce into large cauliflower-like masses with broad base
  - Variant: Verrucous carcinoma

Clinical Manifestations of Genital Warts

- **Distribution:** Found most commonly in vestibule and labial folds but also perianal, mons, vagina, cervix, mucosa of anus and lower half of rectal canal and urethra
- **Diagnosis:** Clinical. Biopsy reserved for large, unresponsive-to-therapy and unusual-appearing lesions
- **Treatment:** Destruction of wart: Podophyllin, trichloroacetic acid (TCA) or bichloracetic acid, imiquimod, cryotherapy, laser, LEEP
Condyloma Acuminata

- Most common on partially keratinized areas (fourchette, perianal area)
- Multiple projections merging to a single base
- Location of condyloma acuminata in women. Rochester study. (See table at right)

<table>
<thead>
<tr>
<th>Site</th>
<th>% of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vulva</td>
<td>66</td>
</tr>
<tr>
<td>Vagina</td>
<td>37</td>
</tr>
<tr>
<td>Perineum</td>
<td>29</td>
</tr>
<tr>
<td>Perianal area</td>
<td>23</td>
</tr>
<tr>
<td>Cervix</td>
<td>8</td>
</tr>
<tr>
<td>Urethra</td>
<td>4</td>
</tr>
</tbody>
</table>

HPV Treatment Modalities

- Topical chemotherapy
  - Tincture of podophyllin
  - Trichloroacetic acid
  - Bichloracetic acid
  - Podofilox
- Intra-lesional: Interferon
- Surgical
  - Cryotherapy
  - Laser surgery
  - Electrocautery
- Note: these do not eradicate viral infection

HPV DNA in Biopsy Specimen

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Mid treatment</th>
<th>End of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imiquimod 5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* P < .05 by Wilcoxon Rank Sum test

Catechins for EGW Treatment

- Polyphenon E (Veregen) 15% ointment
  - 85% catechins
- Biological activities observed
  - Antiviral, immunostimulation, antitumor, antioxidative, antiangiogenic

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>15% Ointment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT complete clearance</td>
<td>41.5%</td>
<td>58.1%</td>
</tr>
<tr>
<td>&gt; 50% clearance</td>
<td>52.9%</td>
<td>77.3%</td>
</tr>
<tr>
<td>Median time (weeks)</td>
<td>16.7</td>
<td>16.1</td>
</tr>
</tbody>
</table>

Cutaneous Changes: Pigmented Lesions/Masses
- Nevus
- Lentigo
- Acanthosis nigricans
- Hyperplasia
- Endometriosis
- Choriocarcinoma
- Leiomyoma
- Vulvar dysplasia
- Vulvar intraepithelial neoplasia (VIN)
- Vulvar carcinoma

Vulva Lichen Sclerosis
- Prevalence: 13% of all vulvar disease
- Etiology unclear
  - Genetic component
  - Autoimmune process
- Symptoms:
  - Pruritus, irritation, burning, dyspareunia, tearing, no symptoms

Lichen Sclerosis
- Vulvar abnormality characterized by
  - Thinning of epithelium with loss of rete pegs
  - Loss of subcutaneous adnexal structures
  - Hyalinization of superficial dermis
  - Lymphocytic infiltrate below basement membrane
  - Intense pruritus in about 50%
- Treatment
  - Clobetasol 0.05% 2 times daily
  - Doxepin 10 mg orally nightly PRN pruritus

Vulva Lichen Sclerosis
- Porcelain white papules and plaque
  - With areas of ecchymosis or purpura
  - Fissures possible
- Skin appears thin, white with crinkling
  - “Cigarette paper” appearance on stretch
- Involvement of mucocutaneous junctions
  - Narrows introitus, anus
- Agglutination of labia minora
- Phimosis of clitoral hood
- Overall “figure of eight” distribution
- Vulva + perianal area

Possible Etiologies
- Epidermal atrophy and dermal fibrosis
- Autoimmune: activated T cells and # Langerhans cells.
- Metabolic: abnormal 5x-reductase activity
- Infections: Borrelia burgdorferi

Newer Treatment Ideas:

- **Vulvar Lichen Sclerosis**

  - Triamcinolone ointment 0.1% 1-2 times daily
  - Medium potency corticoid
  - May have fewer complications than clobetasol which include:
    - Burning, stinging, atrophy, cracking, fissuring, numbness of fingers, telangiectasia, Cushing syndrome
  - Few symptoms reported at baseline present after 6-10 weeks of treatment


Newer Treatment Ideas

- **Lichen Sclerosis**

  - Dermasilk Briefs: Adjunctive tool
  - Double-blind vs. cotton
  - Combined with Clobetasol 0.05% ointment + vitamin E moisturizer
  - Evaluated baseline, 1 month, 6 month


| LS Treatment: Clobetasol with Vitamin E Moisturizer and Dermasil vs. Cotton Briefs |
|---------------------------------|-----------------|-----------------|
|                                | DS   | Cotton |
| Number of subjects             | 21   | 21    |
| Symptoms                        |      |       |
| Complete response               | 1    | 0     |
| Good/partial response           | 20   | 17    |
| Poor response                   | 0    | 4     |
| Clinical signs                  |      |       |
| Complete response               | 2    | 0     |
| Good/partial response           | 19   | 12    |
| Poor response                   | 0    | 9     |

Vulvar Lichen Simplex Chronicus

- Chronic eczematous disease
- Characterized by scaling and lichenified plaque
- Intense and unrelenting itching
- May be localized variant of atopic dermatitis
  - 65-75% report such history
- End stage of irritating process due to
  - Environmental factors
  - Dermatologic disease (yeast, lichen sclerosus)


Vulvar Lichen Simplex Chronicus

- Chronic eczematous disease
- Characterized by scaling and lichenified plaque
- Intense and unrelenting itching
- May be localized variant of atopic dermatitis
  - 65-75% report such history
- End stage of irritating process due to
  - Environmental factors (heat, sweat . . .)
  - Dermatologic disease (yeast, lichen sclerosus)


Vulvar Lichen Simplex Chronicus

- Appearance
  - Skin thickened and leathery
  - Hyperpigmentation
  - Hypopigmentation
  - Erosions and ulcers
    - From chronic scratching
- Most commonly on vulva
- Extragenital lesions in over 10% of cases

Erosive Lichen Planus

- Inflammatory dermatosis: several clinical variations
  - Vulva and vagina
    - Erosion
    - Scarring, shortening and narrowing of vagina
    - Involution of labia minora
    - Phimosis of clitoral hood
    - Wickham striae
  - Oral lesions
    - Erythematous patches
    - Wickham striae – buccal mucosa and gingival border

Vulvar Lichen Planus

- Erosive form: most difficult to treat
  - Scarring and pain
  - Deep, painful, erythematous erosions in posterior vestibule and labia minor
    - Results in agglutination and labial resorption
  - Vaginal epithelium erythematous, eroded, acutely inflamed and denuded
    - Eroded, denuded areas adhere to form synechia
    - Obliterate vault


Lichen Planus: Vaginal

- Epithelium erythematous, eroded, acutely inflamed
  - Inflamed
  - Denuded
- Erosive patches friable
  - Overtime agglutinates
  - Obliterates vault
- Erosive lichen planus = desquamative inflammatory
  - Vaginitis when discharge inflammatory cells and immature parabasal/basal cells vaginal pH 5-6

Erosive Lichen Planus: Treatments

- May be associated with Group B Strep
  - Clindamycin 2% vaginal cream 2-3 weeks
- Cell mediated immune problem
  - Corticosteroid vaginal suppositories
  - Tacrolimus 0.1% ointment BID → QHS
    - 3 times weekly
  - A & D ointment to lesion
- Vaginal constriction
  - Dilate with vaginal dilators and estrogen cream or coitus 3 time a week

Squamous Hyperplasia

- Elongation and widening of rete ridges
- Hyperkeratosis of superficial layer
- Acanthosis and mild inflammation
- Treatment: mid-potency corticosteroid

VIN Overview

- Increasing common problem
  - VIN incidence: 1973-2000: 4-fold increase
  - 75% VIN in young women
  - Occult cancer found in 3% women undergoing VIN excision
  - 16% untreated VIN will progress to cancer
- Classification for VIN: 2 categories
- Clinician screening has kept cancer rate increases lower than increases seen in VIN

VIN Clinical Features

- Premenopausal:
  - Multifocal (associated with VAIN and CIN)
  - Multicentric (vulva, anus, clitoris)
- Postmenopausal:
  - Unifocal
  - Unicentric
- Lesions
  - Raised
  - White or brown
  - Sharp borders
  - May be keratinized
  - May only be seen after acetic acid
- Most common area:

VIN Appearances

- DDX: Hyperplasia, vitiligo, lichen sclerosis
- Hyperplastic lesions: faint, gray, diffuse, flat
- EGW: Exophytic with multiple projections from single base
- VIN: Raised, irregular in shape with sharp borders

Current ISSVD Terminology

- “VIN 1” no longer used
  - Self limited HPV infection not precursor for invasive cancer
  - Findings not reproducible
  - Generally reactive or HPV-related
  - VIN 1→3 does not progress along a continuum
  - VIN 2 and 3-no diagnostic distinction
  - Only high grade disease classified a VIN

1. ACOG Committee Opinion No. 509. 2011
VIN Types

- VIN, usual type
  - Progression HR-HPV to invasive squamous cell cancer unequivocally demonstrated
  - Especially in women > 30 or immunocompromised
  - Morphological subtypes: warty, basaloid, mixed
- VIN, differentiated type
  - Related to lichen sclerosis or squamous hyperplasia — more likely carcinoma
  - Older women, unifocal
- VIN, unclassified
  - Pagetoid type or not fitting into other 2 types

VIN, Usual Type Lesions

- Unifocal, multifocal
- Patches, erosions, plaques, papules and nodules
- Hyperkeratotic, verrucous, pigmented, white or red changes

VIN, Usual Type

- Histological types:
  - Warty (condylomatous – with koilocytosis and multi-nucleation)
  - Basaloid (flat surface – immature parabasal cells)
  - Differentiated (simplex type – basal or parabasal cells, keratin pearls)

VIN, Differentiated Type

- Usually in older women
- Associated with dermatologic conditions
  - Lichen sclerosis
- More likely to be associated with squamous cell carcinoma of vulva
- May be mistaken histologically for hyperplasia

VIN, Differentiated Type

- More likely to be unifocal
- Varied appearances:
  - Ulcer
  - Warty plaques
  - Hyperkeratotic plaques
- Always regarded as high-grade lesions
- Progresses to cancer in
  - 9% untreated women
  - 3% of treated women

EGW and VIN

<table>
<thead>
<tr>
<th></th>
<th>HIV Infected</th>
<th>HIV Not-Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2791</td>
<td>953</td>
</tr>
<tr>
<td>EGW prevalence</td>
<td>5.3%</td>
<td>1.9%</td>
</tr>
<tr>
<td>EGW cumulative</td>
<td>33.0%</td>
<td>9.0%</td>
</tr>
<tr>
<td>EGW regression</td>
<td>82.0%</td>
<td>95.0%</td>
</tr>
<tr>
<td>VIN 2</td>
<td>55 (2.0%)</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

EGW and VIN

HIV Infected vs Non-infected

13 year follow-up 4-6 month exams

### “Condyloma”
- Flat lesions with basal atypia and koilocytic changes
  - Previously “VIN1”
  - Treat as condyloma

---

### Tests for VIN
- **Biopsy:**
  - Needed for all pigmented lesions
  - Warty lesions > 2 cm and those unresponsive to treatment
- Colposcopy helpful to define extent of lesion
  - Use 3-5% acetic acid, but allow several minutes exposure before evaluating
  - Use lower magnification than used with cervix
- Toluidine blue rarely helpful, rarely used

---

### Selection of Biopsy Sites for VIN
- **Biopsy(ies) needed**
- Select most affected area
- If have options, select area with
  - Least vascularity
  - Least tension
  - Greatest distance from urethral meatus or anus

---

### Types of Biopsies
- **Punch biopsy**-most common
  - Obtain adequate specimen (~ 4mm)
  - No need to include healthy tissue
- **Shaving biopsy**-helpful with exophytic lesions
- **Excisional biopsy**
  - Tailor to size of lesion (wide local excision)
  - Use matching elliptical incisions, so defect will close most securely
Choice of VIN Therapies

- Individualize based on:
  - Clinical presentation
  - Extent of disease
  - Patient preference
  - Surgical excision – diagnostic advantage
  - Long term surveillance mandatory


Treatment of VIN

- Surgery is mainstay for managing VIN
- Surgical options:
  - Local excision(s)
    - Preferred if any suspicion of cancer
    - Acceptable in absence of suspicion
  - Local destruction
    - Laser ablation
    - LEEP
  - Partial/total superficial vulvectomy
    - +/- split thickness skin grafting

ACOG Committee Opinion No. 509. 2011

Surgical Options for VIN

- Clinical or pathological finding suggesting invasion
  - Wide local excision
    - 0.5-1.0 cm of disease-free margins needed
  - Confluent or multifocal lesions or immunocompromised
  - Skinning vulvectomy
  - Risk of recurrence still substantial

ACOG Committee Opinion No. 509. 2011

Laser Ablation for VIN

- Acceptable option when cancer is not suspected
  - Single lesion
  - Multifocal lesion
  - Confluent lesion
- Define area to be treated with colposcopy after acetic acid soaks
  - Margin of normal tissue must be treated
  - Risk of recurrence higher than with excision

ACOG Committee Opinion No. 509. 2011
Laser Ablation for VIN

- Power density (750-1250 W/cm³) to prevent deep coagulation injury
  - Use micromanipulation or hand held gauge
  - Must destroy cells through entire thickness of the epidermis (not just superficial)
  - In hair bearing areas, must ablate hair follicles (into sub Q by ≥ 3 mm)
  - Non-hair bearing area – go through dermis (≤ 2 mm)

Medical Therapy for VIN

- Topical imiquimod 5%; effective off-label
  - 3 applications per week for 12-20 weeks
  - Colposcopic assessment every 4-6 weeks to monitor response
  - Residual lesions should be surgically excised
  - Photo dynamic therapy – specialized equipment and training
  - Topical cidofovir cream or 5-fluorouracil cream
  - Fallen out of favor due to side effects

Medical Therapy: Imiquimod for VIN, Usual Type

- Several trials have established efficacy of medical therapies
  - 39 patients (36 VIN) daily imiquimod x 16 weeks vs historical surgical cohort
    - 21-complete response
    - 9-partial response
    - No progression
  - Follow-up for 16 months: 20.5% recurrence rate vs 53.3% recurrence rate in surgically treated controls


Medical Therapy: Imiquimod for VIN, Usual Type

- 50 patients with VIN with ≥ 1 year follow-up
  - Median follow-up was 43.5 months
    - Complete response: 56%
    - Partial response: 8%
  - Surgical excision: 77% complete response
  - Ablation: 21-33% complete response


Post-Treatment VIN Surveillance

- Recurrences 30-50% with all treatment
  - Rates higher when margins involved
  - Women should be considered at risk for VIN and vulvar cancer for rest of lives
  - Follow-up at 6 and 12 months following treatment
  - Annually thereafter

ACOG Committee Opinion No. 509. 2011

Response and Recurrence Rates Surgical Treatments VIN

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Complete Response</th>
<th>Partial Recurrence</th>
<th>No Recurrence</th>
<th>6 Month Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO₂ laser ablation</td>
<td>1</td>
<td>1 (72.7%)</td>
<td>1 (9.1%)</td>
<td>2 (18.2%)</td>
<td>0</td>
</tr>
<tr>
<td>CO₂ laser excision</td>
<td>9</td>
<td>7 (77.8%)</td>
<td>1 (11.1%)</td>
<td>1 (11.1%)</td>
<td>2 (28.5%)</td>
</tr>
<tr>
<td>Local surgical excision</td>
<td>7</td>
<td>4 (57.1%)</td>
<td>2 (28.6%)</td>
<td>1 (14.3%)</td>
<td>2 (50.0%)</td>
</tr>
</tbody>
</table>

Risk Factors for VIN Recurrence

- Immunosuppression
- Multifocal or multicentric disease
- Positive margins on biopsy
  - Most powerful predictor of both
    - Recurrence rate
    - Time to recurrence


Longer Term VIN Recommendations

- Long term follow-up mandatory
  - Recurrence rate
  - Time to recurrence


Conclusions and Recommendations: VIN

- Immunization with the quadrivalent HPV vaccine has been shown to decrease the risk of VIN and should be recommended for women in target populations.
- No screening strategies have been developed for the prevention of vulvar cancer through early detection of VIN.

ACOG Committee Opinion No. 509. 2011

Conclusions and Recommendations: VIN

- Diagnosis is limited to visual assessment. Biopsy is indicated for most pigmented vulvar lesions.
- Presumed genital warts should be biopsied in post-menopausal women and in women in whom topical treatments have failed.
- Treatment is indicated for all cases of VIN. Wide local excision is recommended when cancer is suspected, despite a biopsy diagnosis of only VIN, to identify occult invasion.

ACOG Committee Opinion No. 509. 2011

Conclusions and Recommendations: VIN

- When occult invasion is not a concern, VIN can be treated with excision, laser ablation, or topical imiquimod (off-label use).
- Women with VIN should be considered at risk of recurrent VIN and vulvar cancer throughout their lifetimes. After resolution, women should be monitored at 6 and 12 months and annually thereafter.

ACOG Committee Opinion No. 509. 2011

Vulvar Carcinoma Incidence

- 1.6/100,000 women annually
- 4,850 new cases in 2014
- 1,030 deaths in 2014
- 1% of all malignancies in women
- Most frequent in women 65-75 years old
- 15% of cases are ≤ 40 years old
- Rate increase 20% in last 30 years

### Vulvar Carcinoma: Risk Factors
- Increasing age
- Low SES
- Multiple partners (partners?)
- Non-Jewish women
- Vulvar dysplasia
- Previous abnormal Pap
- Longstanding condyloma
- Chronic dystrophy, especially with atypia
- Inflammatory disease, LGV, syphilis (more aggressive and in younger age)
- Laundry worker (toxins?)
- Coffee drinker
- Smoker
- Age, HPV infection and smoking increase risk
  - Cigarette smoking and genital warts (RR=35)
- Obesity may increase risk because of difficulty examining
- Frequent pap smears decrease risk via early detection

### Vulvar Carcinoma: Clinical Findings
- Raised lesion, ulcerated, pigmented or warty
- Most lesions on labia majora; then labia minora, perineal body, and perirectal region
- May be multifocal, but usually unifocal
- Advanced disease reflects methods of spread:
  - Local extension to vagina, urethra and anus
  - Lymphatic embolization to inguinal nodes (superficial, then deep femoral)
  - Hematogenous spread to lungs, liver and brain

### Vulvar Carcinoma Location: Usually Unifocal
- Labia majora 30%
- Labia minora 20%
- Vagina 20%
- Clitoris 15%
- Urethra 10%
- Anus 10%
- Posterior fourchette 10%
- Anterior commissure 10%

### Vulvar Carcinoma: Pathology
- Squamous 85%
- Melanoma 10%
- Adenocarcinoma 3%
- Sarcoma 2%
- Basal cell 1%
- Invasive Paget’s 1%
- Verrucous 1%

### Vulvar Carcinoma: Treatment
- Depends upon stage
- Surgery usually necessary
- Prognosis:
  - Stage I: 92% 5-year survival
  - Stage IV: 15% 5-year survival
- Potential role for chemotherapy
- Radiation therapy not helpful in most cases, secondary to severe radiation vulvitis
Melanoma of the Vulva and Vagina

- 3% of all melanoma
- Risk factors: Light pigmentation
- Symptoms: Usually asymptomatic.
  - May itch, bleed
- Location: Anywhere on genitalia
- Prognosis: Dependent on Clark’s staging
Nelson: Vulvar Disease and Dermatological Conditions

Vulvar Carcinoma: Preventive Early Detection Measures
- Advise smoking cessation
- Teach vulvar self examination
- Encourage STD risk reduction
- Thorough examination and biopsy persistent lesions
- Acetic acid enhancement tests
- No chemotherapeutic interventions available now
  - Future: HPV vaccination, retinoids for patients with VIN or genital warts and smoking

Tips To Improve Examination
- Careful exposure of all surfaces
- Use hand-held lens to magnify lesion
- Ask patient to check for changes with mirror
- Acetic acid enhancement
- Be aware of the potential for contamination

Diagnostic Tests for Evaluation of the Vulva

<table>
<thead>
<tr>
<th>Analysis of vaginal secretions</th>
<th>Wet mount, maturation index, pH paper, cytology, bacterial/fungal morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cultures</td>
<td>Fungal, HSV, consider self-culture instruction for “recurrent yeast”</td>
</tr>
<tr>
<td>Biopsy</td>
<td>Hematoxylin-eosin, direct immunofluorescence, special stains</td>
</tr>
<tr>
<td>Colposcopy</td>
<td>Acetic acid (3-5%), soak before colposcopy; perianal VIN should include anal colposcopy</td>
</tr>
</tbody>
</table>

Diagnostic Tests for Evaluation of the Vulva

- Pyridium test/methylene blue enema: For fistula diagnosis
- Imaging: Limited use of ultrasound, radiology and magnetic resonance imaging (MRI)
- Wood’s lamp: For cutaneous mycoses
- Cellophane tape test: For pinworm

External Genitalia Examination Special Tests for Vulva
- Candida: scrape edge for KOH
- Herpes: culture base of ulcer
- Syphilis: dark field prep
- Condyloma: clinical appearance and therapeutic response
- Any suspicious lesion(s): biopsy
Diagnostic Tests for Evaluation of the Vulva

<table>
<thead>
<tr>
<th>Tests</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital photography</td>
<td>Downloading capabilities to disk adequate for chart filing may be preferable</td>
</tr>
<tr>
<td>Sensory testing</td>
<td>Cotton tip sensory testing with pain scale</td>
</tr>
<tr>
<td>Blood tests</td>
<td>ssA Ab(+) or ssB Ab(+), HSV Ab, heterophile AB, HIV</td>
</tr>
</tbody>
</table>

*ssA = single-stranded anti-Ro; ssB = single stranded anti-La; HSV = herpes simplex virus; HIV = human immunodeficiency virus*

Vulvodynia

- **Prevalence**
  - 15.7% women lower genital tract discomfort for > 3 months

- **Etiology**
  - Unknown, probably multiple causes
  - Other explanations
    - Psychosexual dysfunction
    - Fungal or HPV infection


Vulvodynia – New Understanding

- Newer explanations
  - Neuropathic pain
    - Complex regional pain syndrome (old name – reflux sympathetic dystrophy)
    - Pudendal neuralgia
    - Increased inflammation (not infection)
  - Pelvic floor abnormalities
  - Trauma – prior laser therapy


NIH Conference: Vulvodynia

- Pain originating in pudendal nerve, levator ani nerve, pelvic nerves
- Cross sensitization and cross talk
- Abnormalities of sensation
- Genetic factors: pain-susceptibility gene
- Inflamnogenic products from fibroblasts
- Referred visceral pain
- Myofascial pain: women with trigger points

NIH Conference: Vulvodynia

- Patients do not have elevated incidence of sexual or physical abuse
- Co-morbid conditions occurring at higher incidence:
  - Interstitial cystitis, headaches, fibromyalgia, irritable bowel syndrome
- Depression commonly present, worsen symptoms
Evaluation of Patients With Vulvar Pain
- Examination of vulva for abnormal redness, erosions, crusting, ulceration, hypopigmentation
- Cotton swab test to identify areas of pain on pressure (e.g., vestibule)
- Sensory neurologic examination for allodynia and symmetrical sensation
- Examination for vaginal redness, erosions, pallor, dryness
- Biopsy of specific skin findings for evaluation by dermatologist


Vulvodynia: Differential Diagnosis
- Lichen planus
- Contact dermatitis
- Cicatricial pemphigoid
- Pemphigus vulgaris
- Atrophic vaginitis
- Desquamative inflammatory vaginitis
- Squamous hyperplasia


Nonspecific Activities for Managing Vulvodynia
- Validate symptoms, be supportive
- Treat any objective abnormalities
- Discontinue irritants (e.g., excessive washing, irritating lubricants, tight clothing, douching, nonessential medications, sanitary pads, hair dryers)
- Apply lubrication during sexual activity
  - Use water soluble or silicone preparations
- Apply Xylocaine 2% jelly or 5% ointment for pain 20 min before sexual activity


Nonspecific Activities for Managing Vulvodynia
- Apply cold compresses (e.g., crushed ice)
- Address and manage depression
- Offer education (including written material) for both patient and partner
- Refer patient for membership in National Vulvodynia Association
- Refer both patient and partner for sex therapy and counseling to help cope with symptoms


Dysesthetic Vulvodynia Treatment Options: Tricyclic Medications
- Amitriptyline (Elavil)
  - Dose ½ tablet 10 mg gradually increase max dose 150 mg
  - Distinguishing side effects: drowsiness
- Desipramine (Norpramine)
  - Same dosing schedule
  - Side effects: anxiety and tremulous
- Other side effects: dryness of mouth and eye, constipation, increased appetite and urinary retention


Oral Desipramine and Topical Lidocaine 5% 12-Week Trial
- Tampon-test pain score reduction
  - Placebo – placebo 33%
  - Placebo – lidocaine cream 20%
  - Desipramine – Placebo 24%
  - Desipramine – lidocaine cream 36%

Dysthetic Vulvodynia:
Other Therapies

- Inject trigger points with triamcinolone
- Estrogen application
- Topical capsaicin to deplete substance P (unpublished clinical trial)
- SSRI to treat neuropathic pain – sole agents or with tricyclic medications
- Lidocaine regularly applied to break pain cycle
- Imiquimod – suggested but no clinical evidence