CLINICAL PERSPECTIVES ON GYNECOLOGIC INFECTIONS

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CERVICITIS

Must distinguish from physiologic ectopy of columnar epithelial cells common in young women

CLINICAL PRESENTATION

- Red edematous cervix w purulent, often blood-streaked d/c
- Cervical motion tenderness
- Mucopurulent cervicitis insensitive predictor GC/chlamydia
  - Low positive predictive value
  - 20% have persistent/recurrent mucopus 3 months after treatment
    Not explained by relapse/reinfection
  - May be related to cervical ectopy/inflammation
    From columnar cell contact with vaginal environment

ETIOLOGY

STD (GC, chlamydia, herpesvirus)
- Herpesvirus: ulcers on cervix during primary Ix
- Chlamydia: yellow mucopurulent endocervical secretions and 10 WBC/hpf
- GC: yellow purulent discharge w WBC

TRAUMA: tears during delivery or TOP

OTHER: see ‘Diagnosis’

DIAGNOSIS:
- Inflammation frequently noted on pap smear
- Wet mount and cultures
- R/O non-infectious etiologies
  - Allergy, vaginal atrophy, trauma
  - OCs may cause transformation zone to fall on ectocervix -> inflammation

TREATMENT:
- Specific to etiology of inflammation
- Presumptive antibiotic treatment not indicated unless high prevalence of GC or Chlamydia in population

VAGINITIS

- Most common reason for patients to visit OB/GYN (10 million pts/year in US)
- Three primary infections in order of prevalence
  - Bacterial vaginosis
  - Candidiasis
  - Trichomonas
BACTERIAL VAGINOSIS

- Not sexually transmitted but intercourse can exacerbate (semen has alkaline pH)
- Most commonly occurring vaginitis
- Results from imbalance in normal vaginal flora
  - Normal lactobacilli overgrown by a variety of anaerobic organisms
  - Anaerobic are normally present only in small amounts
- Common pathogens:
  - Gardnerella vaginalis, Mobiluncus sp, bacteroids (non-fragilis), Peptococcus sp,
  - Mycoplasma hominis
- Can be associated w complications and unfavorable outcomes in pregnancy

CLINICAL PRESENTATION:

- Copious homogenous white/grey vaginal discharge adherent to vaginal walls
- Discharge appears as though “milk was poured into vagina”
- Characteristic “fishy” or foul odor often worsened with intercourse; positive “whiff test” (amines)
- No obvious vulvitis or vaginitis
- Non-inflammatory hence WBCs not present in discharge
- pH > 4.5 (5.0-5.5)
- Characteristic findings on wet mount
  - Clue cells (see below); no WBCs
  - Decreased lactobacillus
  - Increased numbers of abnormal organisms: long rods (Mobiluncus); coccobacillus

DIAGNOSIS

- Clue cells on wet mount
  - Epithelial cells characteristically covered with adherent coccoid bacteria
  - Adherent to such extent that cell borders are obscured.
- Positive “whiff test” (fishy odor when d/c mixed w KOH - due to liberation of amines)
- Vaginal cultures not useful in diagnosis
- Occasionally noted on pap smear but not reliable means of diagnosis

Microscopic view of a clue cell, an epithelial cell coated with bacteria, indicates BV.
**TREATMENT**

- **Metronidazole (Flagyl) 500 mg PO bid x 7 days**
  - Product labeling gives dose as q 6h but CDC guidelines recommend bid dosing
  - 2 gm PO single dose not as effective as 5-7 d course
- **Metronidazole gel (MetroGel):**
  - One applicator intravaginally qd to bid x 5 d
  - No disulfiram-like reaction; no systemic side effects
  - Effectiveness comparable to PO but more costly
- **Metronidazole extended release (Flagyl ER) - 750 mg PO qd x 7d (1 hr ac or 2h pc)**

Treatment of mail sexual partner not indicated unless balanitis is present

Metronidazole is pregnancy category B *

* Traditionally metronidazole was felt to be contraindicated during first trimester but this precaution is no longer considered necessary

- Clindamycin (Cleocin) 300 mg PO bid x 7d
- Clindamycin 2% vaginal cream (Cleocin vaginal cream) 5 gms intravaginally HS x 7d *
- Cleocin Vaginal Ovules - 1 suppository vaginally preferably HS x 3d*

**PRECAUTIONS WITH CLEOCIN**

* - Mineral oil in the product may weaken latex or rubber products (condom, diaphragm) if used within 72 hours of using topical products
- Do not engage in vaginal intercourse or use other vaginal products such as tampons or douches during the treatment period with topical products
- Consider diagnosis or pseudomembranous colitis if patient presents with diarrhea

**DIFFERENTIAL DIAGNOSIS OF VAGINAL INFECTIONS**

<table>
<thead>
<tr>
<th></th>
<th>NONE</th>
<th>BACTERIAL VAGINOSIS</th>
<th>TRICHOMONAS VAGINITIS</th>
<th>CANDIDA ALBICANS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VAGINAL PH</strong></td>
<td>3.8-4.2</td>
<td>&gt; 4.5</td>
<td>&gt; 4.5</td>
<td>&lt; 4.5 (usually)</td>
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<tr>
<td><strong>DISCHARGE</strong></td>
<td>White, clear, flocculent</td>
<td>Thin, homogenous, white, gray, adherent, often increased</td>
<td>Yellow-green, frothy, adherent, increased</td>
<td>White, curdy, ‘cottage cheese-like’, sometimes increased</td>
</tr>
<tr>
<td><strong>AMINE ODOR (KOH whiff test)</strong></td>
<td>Absent</td>
<td>Present (fishy)</td>
<td>May be present (fishy)</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>MAIN PATIENT COMPLAINTS</strong></td>
<td>None</td>
<td>Discharge, bad odor (often increased after intercourse), possible itching</td>
<td>Frothy discharge, bad odor, vulvar pruritus, dysuria.</td>
<td>Itching/burning discharge</td>
</tr>
<tr>
<td><strong>MICROSCOPIC</strong></td>
<td>Lactobacilli, epithelial cells</td>
<td>Clue cells with adherent coccoide (coagate) bacteria, no WBCs</td>
<td>Trichomonads, WBCs &gt; 10/hpf</td>
<td>Budding yeast, hyphae, pseudohyphae (w KOH prep)</td>
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</table>
CANDIDA VULVOVAGINITIS

- Results from infection with *Candidiasis Albicans*
budding yeast-like organism which can infect skin and mucosa of mouth, intestine and genital tract
- Particularly susceptible patients
  - Young infants, *pregnant females*
  - Both male and female *diabetics* (balanitis common in male diabetics)
  - Patients w prosthetic heart valves, patients on broad spectrum antibiotics
  - Immunocompromised patients; heat, moisture, occlusive clothing contribute
- Immunocompromised patients
  - Dissemination via blood stream may be life threatening
  - Oral or genital candidiasis may be first opportunistic infection in HIV+ patients

CLINICAL PRESENTATION

- Vaginal (or penile) candidiasis accompanied by local *irritationitching and burning*
- Genitalia can become quite reddened and edematous
- **Characteristic curdy white discharge** (odorless)
- pH < 4.5; whiff test is negative (no amine odor on mixing w KOH)

DIAGNOSIS

- Wet mount: budding yeast, hyphae, pseudohyphae w KOH
- Culture (discharge); can identified species

TREATMENT

- *Fluconazole (Diflucan)* 150 mg PO single dose
- Intravaginal cream or suppository (see Vaginal Preps)
- Recurrent vulvovaginitis: ketoconazole (Nizoral) 100 mg qd for up to 6 months

**ALTERNATIVE:** Mycostatin (Nystatin) intravaginal tabs

VAGINAL PREPS FOR CANDIDIASIS

- *Butoconazole (Femstat 3 - OTC)* - 1 applicator hs x 3d - How Supplied: prefilled applicator (5 gm)
- *Clotrimazole (Gyn-Lotrimin - OTC)*
  - 1% vaginal cream (Gyn-Lotrimin): 1 applicator hs x 7 d
  - 100 mg vaginal suppository (Gyn-Lotrimin Vaginal Suppository) 1 hs x 7 d
  - 200 mg vaginal suppository (Gyn-Lotrimin 3 vaginal suppository) 1 HS x3d
  - Gyn-Lotrimin 3 combo: 3 200 mg vaginal suppository; 1% top cream*
  - Gyn-Lotrimin combo: 7 100 mg vaginal suppository; 1% top cream*

* Apply cream 1-2 x per day pm x 7d plus suppository: 1 HS x 3d or 7d
How Supplied:
   - Combo: suppository w applicator plus 7 gm cream
   - Suppositories: with applicator
   - Cream (45 gm) with applicator

- **Clotrimazole (Mycelex-G - RX/OTC)**

   - 1% vaginal cream: (Mycelex-G) 1 applicator hs x 7-14 days (RX)
   - 500 mg vaginal tab plus 1% cream (Mycelex Twin Pak) (RX)
     1 vaginal tab HS x 1 dose plus cream bid x 1 wk
   - 1% vaginal cream (Mycelex 7) 1 applicator vaginally HS x 7d (OTC)
   - 100 mg vaginal inserts (Mycelex 7 Vaginal Inserts) (OTC) - 1 insert vaginally HS x 7d
   - 100 mg vaginal tabs/1% top cream (Mycelex 7 Combo Pack) OTC
     1 insert vaginally HS x 7 d plus 1% cream 1-2x d pm 7d

   How Supplied:
   - 1% cream (Mycelex-G) (RX) 45g, 90g w applicator
   - 500 mg tabs (Mycelex-G Vaginal Tablets) (RX) 1 w applicator
   - 500 mg tab/1% cream (Mycelex Twin Pak) (RX): 1 500 mg tab w applicator and 7 gm cr
   - 1% cream (Mycelex-7) (OTC): 45 g w applicator
   - 100 mg vaginal inserts (Mycelex 7)(OTC) 7 ins w applicator
   - 100 mg vaginal tab/1% cream (Mycelex 7 Combo Pak (OTC): 7 inserts w applicator + 7 gms cream

- **Miconazole (Monistat 3 - OTC/RX)**

   - 200 mg vaginal suppository (Monistat 3): 1 hs x3d (RX)
   - 100 mg vaginal suppository (Monistat 7 Vaginal Suppository) 1 hs x7d (OTC)
   - 2% cream (Monistat 7 Vaginal Cream) 1 applicator hs x7d (OTC)
   - 100 mg vaginal suppository; 2% top cream (Monistat 7 Combo Pak) (OTC)
     1 suppository hs x 7d; apply cream bid prn x7d

   How supplied:
   - Monistat 2% cream: 7 prefilled applicators (5 gm) ; cream (45 gm) w applicators
   - 3 Combo Pak: 3 suppository w applicator plus 9 gm cream
   - 7 Combo Pak: 7 suppository w applicator plus 9 gm cream
   - Monistat 3 Vaginal Supp: 3 suppositories: with applicators
   - Monistat 7 Vaginal Supp: 7 suppositories with applicators

- **Terconazole (Terazol - RX)**

   - 80 mg vaginal suppository (Terazol 3 Supp): 1 hs x3d
   - 0.8% vaginal cream: (Terazol 3): 1 applicator HS x3d
   - 0.4% vaginal cream (Terazol 7): 1 applicator HS x 7d

   How supplied: cream (20 gm), suppositories w applicators

- **Tioconazole (Monistat-1; Vagistat-1 - OTC)**

   - 6.5% vaginal ointment: 1 applicator HS x 7d - How Supplied: 1 prefilled applicators (300 mg)
   - Complete relief may take up to 7 days
ADDITIONAL NOTES FOR CANDIDA

3. Fluconazole: 95% asymptomatic in 2 weeks, 75% at 4 weeks; GI S/E 15%; Resistance reported
4. Boric acid intravaginally has been used
5. Oral drugs decrease rectal Candida thus may decrease relapses
6. Vaginal preps with 85-95% cure rates
7. Avoid intercourse for 3-4 days after treatment.

TRICHOMONIASIS VAGINITIS

- STD caused by Trichomonas vaginalis (protozoan)

CLINICAL PRESENTATION

- Female
  - Acute occurring vulvovaginitis
  - Extremely irritant, foul-smelling vaginal d/c
  - D/c profuse, often frothy/yellow-green d/c
  - pH discharge > 4.5
  - “Strawberry” cervix (red macular lesions on cervix)
  - diffuse vaginal erythema
  - Symptoms subside but carrier state ensues
- Male: Recurrent urethritis and prostatitis

DIAGNOSIS

- Trichomonads seen on wet mount
  - Vaginal, prostatic urethral secretions
  - Motile, oval shaped w flagella
  - WBCs > 10/hpf
- May see trichomonads in urinary sediment

TREATMENT

- Metronidazole (Flagyl) 2 gms as single dose
  - Metronidazole gel (MetroGel) is not recommended for trichomonas
  - Contraindicated in first trimester of pregnancy
  - Disulfiram -like reactions; NO ETOH

- Pregnancy:
  - Clotrimazole (Gyn-Lotrimin vaginal suppositories)
    100 mg vaginal tabs hs x 2w
  - Clotrimazole cures 20%; decreases symptoms in others
  - Treat after pregnancy with metronidazole
ADDITIONAL NOTES:
- Must treat both partners
- Repeated failure: metronidazole 2 gms PO qd x 5 d
- Resistance rare but does occur - Metronidazole susceptibility testing can be arranged with CDC

GENITAL WARTS AND CERVICAL HPV

- STDs caused by the human papilloma viruses (HPV)
- DNA viruses
- 46 types of HPV: different stains assoc w diff diseases
- Affects genitalia and perianal region
  - Men: corona and frenum of the penis
  - Women: labial folds of vulva, lower third of vagina and on cervix
- Incubation period from contact to lesions 2-3 months
- Warts usually multiple and often grow together
  - Warts vary greatly in appearance
  - Sessile, filiform or hyperplastic forms

- Condylomata acuminata: confluent warts - Often involve whole perineum and anal region
- Rate of spread increased in immunocompromised patients

HPV causative factor in cervical neoplasia
- Premalignant changes in cervical epithelium -> may progress to invasive cervical CA
- Certain strains associated with cervical neoplasm
  - HPV 16, 18, 31,33, 35 associated with 90% of cervical dysplasia/CA of cervix
  - HPV 16 and 18 has a 1:30 lifetime risk of CA
  - Causes epithelial changes to penis, vulva, anus but significance is less clear.
- Cervical HPV
  - Almost always asymptomatic (acetowhite to epithelium may reveal presence)
  - More common than clinically apparent genital warts
  - Frequent coexistence: genital warts, cervical HPV
  - Characteristic premalignant changes on Pap smear

- Asymptomatic penile HPV: reservoir of infection - Dx via acetowhite application to epithelium
- Natural history of HPV infection
  - Warts
    - May persist, recur after treatment or regress spontaneously
    - Rarely: undergo malignant transformation (rare)
  - Cervical HPV similar spectrum but malignant transformation is common

- HPV often found in vulvar, vaginal, penile CA both CIN and invasive carcinoma of genital tract
- Some labs now offering to hold specimens for abnormal paps with Thin-Prep for purposes of subsequent HPV testing (saves patient fee of second office visit)

Digene Hybrid Capture II HPV ® test approved.
- DNA-based technology to detect HPV in cervical samples with equivocal paps
  - 10X more sensitive vs 1st generation assay to detect high-risk 13 high-risk HPV types.
- May prove more helpful than pap in identifying women at high risk for CA
Available from Digene Corp Beltsville, MD - www.digene.com

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CLINICAL MANIFESTATIONS:

- **Condylomata acuminata** (papillomatous raised lesions)
  - Flesh colored papillomatous, pedunculated, sessile
  - Single lesions 1-4 mm wide and 2-15 mm high -> coalesce to form multiple papules
  - Multiple papules become confluent, plaque-like, or multi-lobulated masses
    (May become so large as to cause deformity of normal structures - giant Condylomata of Buscke and Lowenstein)

- **Condylomata plana** (flat warts)
  - Appear on vulva or penis as flesh-colored or hypopigmented
  - Nearly invisible flat papules; **subclinical form of infection**
  - **Aceto-whiting** (3-5% acetic acid) enhances visualization of lesions
  - Hand lens or colposcope enhances visualization - aceto-whitening is **nonspecific**

- **Vaginal warts**: less common than cervical or vulvar
  - Bowenoid papulosis
    - Flat multicentric papules; erythematous, *hyperpigmented* or flesh-colored
    - Histologically resemble CIS but usually benign
    - Can be interspersed within condylomata acuminata

- **Cervical HPV** (variable presentation)
  - Invisible "flat condylomata" (subclinical)*
  - Spiked exophilic or florid papillomata
  - Cervicography: screening tool as adjunct to Pap
    - Cervix is photograph through special lens for subsequent viewing/interpretation
  - * most common form; may be invisible w/o aceto-whitening and/or colposcopy

DIAGNOSIS:

- Primarily via characteristic clinical appearance/location
- Can confirm with histology/cytology; serology not useful
- DNA testing available; FDA-approved in 2000

- DIFFERENTIAL DIAGNOSIS

  - **Condylomata lata** (syphilis)
    - More moist, may be ulcerated
    - Spirochetes on dark-field exam, positive serology
  - **Molluscum contagiosum**

  - **Seborrheic keratosis** (benign)
    - Brown/black hyperpigmented flat broad papules with waxy texture
    - Minute puncta on surface
- Other non-HPV lesions
  - Skin tags (acrochordons)
  - Pearly penile papules
  - Bowen’s disease of vulva
    - Flat velvety grey-white plaque with well-defined borders and slight ulceration
  - Erythema
- Biopsy lesion for positive ID or strain identification
- Annual pap smear: HPV changes or dysplasia often apparent

TREATMENT:

- **Imiquimod (Aldara) 5% cream top: immune response modifier** - Preferred treatment
  - Apply thin layer to warts/rub in; wash w soap/H2O after 6-8 h
  - Frequency: hs, tiw; max 16 weeks.
  - If local reaction: suspend therapy until reaction subsides.
  - Clearance rates 50% vs 11% for controls
  - Local reactions: mild erythema (60%), erosion (30%)

- **Podophyllin 25% in tincture of benzoin (Podocon-25)**
  - Apply (by provider) weekly x 4-6 wks - wash after 1-4 hrs
  - If no improvement after 4 treatment use alternative RX

- **Podophyllin 5% solution** - Podofilox (Condilox)
  - Apply with cotton swab bid x 3 days followed by 4-6 days w/o treatment
  - Repeat cycle 4-6x prn

Notes on podophyllin
- Local reactions in 50%: pain, burning, inflammation
- No systemic effects
- Efficacy: 74% vs 8% (placebo) - Recurrences: 55% vs 100% (placebo)
- Warts recur wi 1 month w either agent in 1/3 patients
- Results of pap smear should be available prior to RX
- **Avoid in pregnant women** (Pregnancy Cat C)
- Do not use on bleeding lesion

- **Trichloroacetic acid (TCA) (Tri-Chlor, Tri-Verszone)** - less commonly used
  - 50-90% solution carefully applied w Q-tip or wooden applicator
  - Avoid surrounding skin
  - Can apply Vaseline to skin around lesion prior to application
  - **Pain** (significant) can be lessened by application of sodium bicarbonate paste applied immediately after treatment.
  - Apply weekly prn x 3; can use with pregnancy
OTHER TREATMENT OPTIONS

- Surgical removal
- Extensive warts may require CO2 laser under local or general anesthesia
- Electrocautery
- Cryotherapy with liquid nitrogen
- Interferon: very expensive and no more effective than other therapies
  - Alpha 2b (Intron-a), Alfa-n3 (Alferon N)
  - 1 million units (0.1 ml) into lesion tiw x 3 weeks
  - Painful; dilute to 10 million units in 1 ml; other concentrations are hypertonic
  - Use when other RX fails esp in AIDS

ADDITIONAL NOTES
2. Recurrences common after all treatments

GENITAL HERPES

- Common, painful disease; potentially serious consequences
- Viral etiology: human herpesviruses
- Genital herpes caused by herpes simplex virus (HSV)
- Two types of herpes simplex exist: HSV type 1; HSV type 2
  - Six (6) know Human herpesviruses exist
    - *Herpes simplex 1* (HSV-1): Skin/mucosal vesicles and ulcers especially oral
    - *Herpes simplex 2* (HSV-2): Skin/mucosal vesicles and ulcers especially genital
    - *Varicella-zoster virus* (VZV -Chickenpox, shingles
    - *Epstein-Barr virus* (EBV): Infectious mono, Burkitt’s lymphoma
    - *Cytomegalovirus* (CMV) Serious disease in immunosuppressed patients + congenital infection
    - *Human herpesvirus-6* (HHV-6) - Roseola infantum

- HSV-1 and HSV-2 can cause either oral or genital lesions
  - HSV-1 more commonly causes orolabial herpes and herpes keratitis
  - HSV-2 more commonly causes genital lesions

- Viral shedding occurs from affected skin or mucous membranes
  - *Asymptomatic patients can shed virus* -> *Reservoir of Infection*

- Several types of specific humoral antibodies are produced - serotyping is possible
  - Antibodies attenuate disease severity
  - Recurrences less severe

- Sequence of infection:
  - Virus enters epidermal cells thru mucosal surface
  - Destroys affected epithelial cells
  - Travels to peripheral sensory or autonomic nerve endings
  - Ascents to the *dorsal root ganglia* where it becomes latent
- Subsequent **viral reactivation occurs**
  Virus descends along involved nerve root back to or close to original site of infection of skin or membrane

- **Transmission**
  - Contact w open vesicles
  - **Shedding of virus in asymptomatic** persons

- Clinical manifestations: 4 stages of genital herpes
  - **First episode primary** (most severe)
  - **First episode non-primary** (more severe than recurrent)
  - **Recurrent** (higher rate for HSV-2) less severe
  - **Asymptomatic**: shed at genital sites in absence of s/s

- Incubation period 2-12 days
- Morphology of lesions (process takes 15-20 days)
  - **Painful, grouped, discrete vesicles** appear.
  - **Vesicles** usually evolve into pustules which then erode, creating an ulcer
  - Remaining grayish plaques **crust before healing**

- Infectivity
  - **Lesions shed infectious** viral particles at least 10-12 d
  - New lesions appear until 10th day

- Clinical presentation of lesions
  - **MEN:**
  - Common: glans penis, coronal sulcus, urethra, shaft of penis or perianal region.
  - Less frequently: scrotum, thighs, mons, buttocks
  - **WOMEN:**
  - Common: introitus and urethral meatus, labia
  - Less frequently: perineal, perianal, thighs buttocks
  - Cervicitis is common: 70-90% of women with 1st episode
    - Less frequent with recurrent episodes
    - Cervix may appear normal or red/friable/ulcers

- Genitourinary symptoms (Primary)
  - Dysuria, vaginal discharge, urethral discharge, inguinal adenopathy
  - **Pain** for at least 1 week, sometimes 2 weeks

- Systemic manifestations (Primary)
  - H/A, fever, **malaise, myalgia** - more common women
  - Pharyngitis, ascetic meningitis, transverse myelitis, radiculitis
  - Stiff neck, H/A, photophobia 3-12 days after genital lesions
  - Neurologic complications 13-35% patients
  - Rare serious neurologic sequelae (encephalitis)

- Extragenital autoinoculation - **herpetic whitlow**
  - More common in women; lesions extremely painful
  - Fingers most common site
ANTI-HERPES THERAPY

Acyclovir (Zovirax)
Famciclovir (Famvir)
Valacyclovir (Valtrex)

- **Immunosuppression causes severe manifestations (HIV+ patients)**
- **Recurrent episodes genital lesions are usually less severe**
  - Run gamut from asymptomatic/mild to severe pain
  - Most persons have 5-8 recurrences per year
  - “**Trigger factors**: stress, fatigue, menses
  - Prodromes w/o lesions occur in 50% patients

- **Genital herpes and pregnancy**
  - Transmission to fetus during parturition; rarely in utero
  - Primary maternal infection: 50% transmission rate
  - Recurrent maternal infection: 8% transmission rate
  - Maternal HSV antibodies transferred to fetus thus prevent or attenuate infection
  - **Cesarian section** if primary or recurrent lesion present in labor
  - **Neonatal herpes high mortality/morbidity (3-30 days)**
    - Mucocutaneous disease, visceral illness or both
    - Visceral involves CNS: high morbidity/mortality

**DIAGNOSIS**

- Classic presentation of **painful group vesicles with erythematous base**
- **Serology** specific for HSV-1 or HSV-2:
  - Less useful clinically to establish current infections
  - Serology remains positive; HSV-1 oral labial lesions very common -> positive serology

**DIFFERENTIAL DIAGNOSIS**

- **Chancroid** most closely resembles (multiple painful lesions)
- **Syphilitic chancre** usually solitary and painless
- **Traumatic** genital lesions painful but not usually grouped

- **Contact dermatitis** can resemble herpetic lesions
  - Vesicles, crusting, erosion 2 weeks after exposure
  - R/O herpes w Tzanck smear and viral culture

- **Viral culture; serology**
  - **Tzanck smear**: herpetic lesions; not specific but sensitive (positive with other viral infections)
    - Scrape edge of “unroofed” lesion with sterile swab/scalpel and fix in 95% ETOH
    - Stain with Bouin’s solution -> characteristic changes on microscopy

**TREATMENT**

- **Genital Primary** (immunocompetent)
  - Acyclovir (Zovirax) 400 PO tid x 10 d *
  - Famciclovir (Famvir) 250 PO tid x 5-10 d **
  - Valacyclovir (Valtrex) 1000 mg PO bid x 10d

- **Genital - Recurrent** (immunocompetent)
  - Acyclovir 400 mg PO tid x 5d
  - Famciclovir (Famvir) 125 mg PO bid x 5d
  - Valacyclovir (Valtrex) 500 mg PO bid x 5d
- **Genital - Chronic Suppression**
  - Acyclovir (Zovirax) 400 mg PO bid
  - Famciclovir (Famvir) 250 mg PO bid
  - Valacyclovir (Valtrex) 500 mg qd

  * FDA approved dose is 200 mg PO 5x/day x 10 days
  ** Not FDA approved for this indication

**Topical preparations considered of little therapeutic value** in treatment of genital lesions

**GONORRHEA**

- Sexually transmitted
- **Cause:** *Neisseria gonorrhea* (*gonococcus*): gram negative diplococci
- Neonatal transmission via birth canal

**MALES:** (can be asymptomatic - reservoirs for transmission*)
- **Purulent urethral discharge and dysuria**
- Discharge demonstrated via "milking" urethra
- Occasional: epididymitis and inflammation of regional lymph nodes; meatalis
- Rare: penile edema, abscess of Cowper’s or Tyson’s glands, seminal vesiculitis
- Proctitis common in homosexual males (occasionally asymptomatic)
  Erythematous mucosa; *profuse purulent exudate*, tenesmus, bloody stool

* Approximately ½ men whose sexual partners have PID are asymptomatic for GC

**FEMALES:**

- Many females are asymptomatic
- Endocervical infection most common type GC in women *
- Dysuria and vaginal discharge indicates cervicitis
- Infection may spread to Bartholin’s glands (abscess)
- **PID:** one of most common causes
  - Endometritis, salpingitis, tuboovarian abscess, pelvic peritonitis
  - **Ectopic pregnancy, infertility.**

* GC cervicitis w mucoid d/c and marked cervical erythema/edema may be indistinguishable clinically from chlamydial cervicitis

- **Disseminated Gonococcal Infection** (DGI) via blood
  - Fever, **skin rash, painful septic arthritis** (esp knee)
  - Bacteremia, tenosynovitis, endocarditis, meningitis
  - Skin Rash: macular, erythematous, pustular, necrotic, hemorrhagic
- Buccal and pharyngeal lesions with oral sex: pharyngitis, erythema, asymptomatic

- **Ophthalmia neonatorum**
  - Purulent conjunctivitis follows 2-5 days after birth in infected infant,
  - May be associated w septicemia
  - Conjunctivitis adults: copious purulent discharge
    Keratitis, corneal ulceration, perforation, lens extrusion/opacification, **blindness**
DIAGNOSIS:

- Microscopy, culture (pus): Urethra, cervix, rectum, mouth, conjunctiva (neonate)
- Nucleic acid amplification ((PCR/LCR) becoming available

TREATMENT: always treat for both GC and Chlamydia

- 50% of patients have concomitant C. Trachomatis - treat for both!
- Penicillin G resistance is 16%
- Ciprofloxacin 500 x1 and Azithromycin 1 gm x1 is a common outpatient regimen

GONOCOCCUS (genital)

- Ceftriaxone (Rocephin) 125 IM x1
- Norfloxacin (Noroxin) 800 mg PO x1
- Cefixime (Suprax) 400 mg PO x1 (not for pharyngitis)
- Cefpodoxime (Vantin) 200 mg PO x1
- Ciprofloxacin (Cipro) 500 mg PO x1
- Ofloxacin (Floxin) 400 mg PO x1 no activity vs incubating syphilis
- Spectinomycin (Trobicin) 2 gm IM x 1

C. TRACHOMATIS

- Doxycycline 100 bid x 7 (tetracycline250 qid x 7d)
- Azithromycin (Zithromax) 1 gm x 1 dose**
- Erythromycin base 500 PO qid x 7d
- Ofloxacin (Floxin) 300 mg PO q 12h x 7d
** 2 gms is effective vs both GC and Chlamydia but side effects significant at this dosing

DISSEMINATED GONOCOCCAL INFECTION (dermatitis, arthritis)

- Ceftriaxone (Rocephin) 1 gm IV or IM qd
- Cefotaxime (Claforan) 1 gm q 8 hrs IV
- Ceftizoxime (Cefizox) 1 GM Q 8 hrs IV
- Spectinomycin 2 gm q 12 IM

Treatment for 24 hrs after symptoms decrease. Reliable patients may be discharged 24 hours after symptoms resolve to complete 7 days treatment with cefixime (Suprax) 400 mg BID. Consider concomitant treatment for C trachomatis urethritis

SUPPURATIVE GONOCOCCAL CONJUNCTIVITIS (adult)

- Ceftriaxone (Rocephin) 125 mg IM/IV x 1 dose
CHLAMYDIA TRACHOMATIS

- Sexually transmitted - caused by bacterium C. trachomatis
- One of most frequently occurring causes of STDs
- Commonly coexists with gonorrhea
- Bacterium which grow only in intracellular environment of parasitized hosts; 1/8 size of E.coli
- Non-specific (non-gonococcal) urethritis

- C Trachomatis diseases
  - Genitourinary disease (STD) - serotypes B, D-K
  - Lymphogranuloma venereum (LVG): serotypes L1, L2, L3 rare in US (mainly tropics)
  - Endemic trachoma depending on serotype of organism - Serotype A, B, Ba, C
    - Not an STD
    - Common cause of blindness in developing countries

- Other common chlamydia: C. psittaci, C. TWAR

- Perinatal transmission Infections - exposure to infected birth canal
  - Most common is a self-limited purulent conjunctivitis
  - Lasts several weeks following birth (10-30%)
  - Distinctive neonatal pneumonitis develops in <10% wks to months after birth
    - Afebrile, dry cough
    - Most common cause of infant pneumonitis in first 6 months

- Major role in tubal infertility
  - Conjunctival infection - STD and nonsexual transmission
  - Ophthalmologic issues
    - Endemic C. trachomatis: one of most common causes of third-world blindness
    - STD transmission with genital-ocular autoinoculation
      - Usually self-limited with no significant sequelae
  - Incubation period 5-10 days
  - Urethral or vaginal discharge; severe dysuria
    - Mucopurulent discharge; tends to me more watery than gonorrhea
    - Must exclude GC by culture
  - Complications: cervicitis, salpingitis, urethral stricture
  - Other non-specific urethritis organisms: Mycoplasma hominis - Ureaplasma urealyticum

CLINICAL PRESENTATION

MALES: 25% are asymptomatic
  - Urethral inflammation where no GC identified
  - Urethral discharge, dysuria, pruritus of urethra
  - Epididymitis (rare)
  - Rectal infection results in severe proctocolitis

FEMALES: Up to 75% of women are asymptomatic
  - Cervicitis/urethritis usually non-specific
    - Dysuria, vaginal pruritus
    - Mucopurulent cervical d/c and/or friable cervix
  - Endocervical canal samples can be purulent
  - Isolated from urethra and bladder of women with dysuria
- **“Acute urethral syndrome”** - Dysuria-abacteriuric pyuria in sexually active women

- Salpingitis: major cause of infertility
  - Non specific signs and symptoms
  - Fever, lower abdominal pain, prostration, tenderness of uterus and adnexa

- Severe inflammation fallopian tubes/peritoneum (PID)
- Fitz-Hugh-Curtis syndrome (perihepatitis)
  - Pain tenderness in upper right quadrant (URQ )
  - Occasional hepatic friction rub from hepatic capsular adhesions (from peritoneal inflammation)

**BOTH MALES AND FEMALES**

- Reiter’s Syndrome (reactive arthropathy):
  Urethritis, arthritis, conjunctivitis, dermatitis
- Post infectious arthropathy (chlamydial particles in joint aspirates)
- Follicular conjunctivitis (usually self-limiting) - STD-mediated autoinoculated

**PERINATAL INFECTIONS (via infected birth canal)**

- Purulent conjunctivitis most common (10-30%); normally self-limiting
  - Occurs within several weeks birth
- Distinctive pneumonitis (10%)
  - Most common cause of infant pneumonitis in 1st 6 mo
  - Occurs several weeks to months post delivery
  - Notable lack of fever; hacking, non-productive cough

**DIAGNOSIS**

- Uncomplicated cases produce few diagnostic symptoms and signs
- Leukocytic urethral discharge and excluding GC
- Culture is difficult and unreliable
- Lack of specific clinical criteria mandates laboratory diagnosis in almost all cases
  - PCR (polymerase chain reaction) of voided urine (male/female)
    Sensitive and specific: otherwise use culture or antigen
  - Antigen detection testing (enzyme immunoassay, DFA testing)
  - Cell culture (preferred method) - requires special collection swabs and transport media
  - Serology available not always positive
    - IgM seen in first episode
    - IgG persists for years
- Gram stain (intracellular gm (-) diplococci (sensitive for diagnosing GC)
  - Negative gram stain can exclude GC
  - Cannot exclude co-morbid chlamydia
- Pap smear (intact chlamydial inclusions)
  Insensitive and non-specific; may alert to culture
- Nucleic acid probes (less sensitive than culture but can screen)
TREATMENT

Normally treated concurrently with CG  (See Gonorrhea: Treatment)

NON SPECIFIC URETHRITIS (NSU)*, CERVICITIS

- Doxycycline 100 bid x 7
- Azithromycin (Zithromax) 1 gm x 1 dose
- Erythromycin base 500 PO qid x 7d
- Ofloxacin (Floxin) 300 mg PO q 12h x 7d

CERVICITIS: MUCOPURULENT: - Treat as for gonorrhea
PROSTATITIS: Treat as for gonorrhea then follow-on RX for NSU or ofloxacin

ADDITIONAL NOTES

1. Pregnancy: Erythromycin base 500 mg PO qid x 7d or Amoxicillin 500 mg PO tid x 7d
   - Alternative is Erythromycin base 250 qid x14d or azithromycin (Zithromax) 1 gm PO x1
   - No doxycycline or fluoroquinolones in pregnancy

2*. Non-gonococcal or post gonococcal urethritis:
   - Chlamydia 50% or Mycoplasma hominis (see Genital Mycoplasmas)
   - Other etiologies: ureaplasma, trichomonas, herpes simplex virus, M. genitalium.

3. Recurrent/persistent disease:
   - Metronidazole (Flagyl) 2.0 gm PO x1 or
   - Erythromycin base 500 mg PO qid x 7

4. Azithromycin 1.0 gm won’t cover for concomitant GC; 2 gms covers but increased side effects

GENITAL MYCOPLASMAS

- Ureaplasma urealyticum, Mycoplasma hominis, Mycoplasma genitalium

- Total of eight species of mycoplasma routinely found in genital tract
  - Non-pathogenic:  M. Fermentans, M. primatum, M. salivarium, Acholeplasma laidlawii, A.. oculi
  - Pathogenic:  Ureaplasma urealyticum, Mycoplasma hominis, Mycoplasma genitalium

- Smallest known free living organisms (1/8 size of E. coli) - virus are smaller
- Absence of cell wall is most distinguishing feature (results in beta-lactam resistance)
- Strictly extracellular ( Unlike chlamydia); attach to epithelial cells, rarely penetrate submucosa.
- M. hominis and U. urealyticum commonly colonize female lower genital tract without causing harm

- Neonates are transiently colonized
- Colonization increases after puberty with sexual activity
- Linked to the following:
  - Younger age, lower socioeconomic status, sexual activity
  - Multiple partners, black ethnicity, oral contraceptive use
- *M. hominis* and *U. urealyticum*: no evidence of causing disease in female lower genital tract
- *M. Hominis* linked with female upper genitourinary tract (PID); probably not *U. Urealyticum*
- *M. Hominis* proven cause of peripartum infections: most common cause of post partum fever
- *M. hominis* and *U. urealyticum* cause disease in the newborn
  - Congenital pneumonia
  - Newborn respiratory disease and sepsis

- **M. Hominis and U. Urealyticum** associated with disease states in males
  - *U. urealyticum* causes
    - Urethritis (non specific, non-chlamydial) in males
  - Possibly renal calculi
  - *M. hominis* causes pyelonephritis in males; no evidence for role in NSU
  - **Prostatitis**: ureaplasma isolated more frequently than with controls - possible role

- Septicemia and other extragenital infections occur
  Post partum fever, postabortal septicemia, newborn septicemia and respiratory distress, septicemia following renal transplantation, trauma, genitourinary manipulations. Also would infections, brain abscesses and osteomyelitis have been reported.

- Septic arthritis in immunocompromised patients

**DIAGNOSIS**

- Not visible on gram stain - very demanding requirements but can be cultured
- Serology
- Usually treated empirically; diagnostic cultures not usually ordered
- Sometimes discovered inadvertently in the course of culturing for other organisms

**TREATMENT**: treat as for Chlamydia urethritis/cervicitis

**NON SPECIFIC URETHRITIS (NSU)**, **CERVICITIS**

- Doxycycline 100 bid x 7
- Azithromycin (Zithromax) 1 gm x 1 dose
- Erythromycin base 500 PO qid x 7d
- Ofloxacin (Floxin) 300 mg PO q 12h x 7d

**CERVICITIS: MUCOPURULENT**: - Treat as for gonorrhea
**PROSTATITIS**: Treat as for gonorrhea then follow-on RX for NSU or ofloxacin

**ADDITIONAL NOTES**

1. Pregnancy: Erythromycin base 500 mg PO qid x 7d or Amoxicillin 500 mg PO tid x 7d
   - Alternative is Erythromycin base 250 qid x14d or azithromycin (Zithromax) 1 gm POx1
   - No doxycycline or fluoroquinolones in pregnancy
2. Non-gonococcal or post gonococcal urethritis:
   - Chlamydia 50% or *Mycoplasma hominis*
   - Other known etiologies: ureaplasma, trichomonas, herpes simplex virus, *Mycoplasma genitalium*.
PELVIC INFLAMMATORY DISEASE (PID)

- Sexual (GC or chlamydia) transmission is most common
- Non-sexual: infection with normal vaginal bacteria flora
  - Group B streptococci, *E. coli*, other enterobacteria, *G. Vaginalis, H influenzae*,
  - *Bacteroides* sp. *Peptococcus* sp. Genital mycoplasmas (?)
  - *Actinomyces israelii* (only w IUD)
- Sequence of extension:
  Agents ascend from endocervical canal thru endometrium to fallopian tubes and
  ultimately to pelvic peritoneum
- Results in endometritis, salpingitis and peritonitis
- Presentation: pelvic and **abdominal pain**, **fever**, chills and **cervical motion tenderness**
- Complications:
  - Tubo-ovarian abscesses, pelvic peritonitis (often mimicking appendicitis)
  - **Fitz-Hugh-Cutis syndrome** (inflammation of Glisson’s capsule of the liver)

**DIAGNOSIS:**

- Clinical diagnosis is imprecise
- Consider in women with lower abdominal pain, adnexal or midline tenderness
  (endometritis).
- Abnormally painful menses and metromenorrhagia are common
- Associated with use of **IUD**
- Laparoscopy best method of establishing dx may appear normal in early disease
- **DX:** ectopic pregnancy; appendicitis
- Endocervical cultures: *N. gonorrhea* and *C. Trachomatis*
- Chlamydial disease associated w high incidence of tubal scarring and **infertility**

**INDICATIONS TO HOSPITALIZE**

- Likely poor compliance as outpatient
- Pregnant
- Peritonitis
- Suspected pelvic abscess
- Temp > 38 C
- Laparoscopy needed to establish dx
- Failure to respond to outpatient treatment in 72 hrs
- Dx uncertain

**ADDITIONAL NOTES**

1. If hospitalization appropriate but pt will not comply, add metronidazole (Flagyl) 500 mg
   PO qid.
2. Majority of patients (94%) w tubo-ovarian abscess will respond to antibiotics and CT-
   directed needle biopsy drainage.
TREATMENT

OUTPATIENT TREATMENT FOR PID

Outpatient treatment is limited to patients with T < 38 C; WBC < 11,000/mm3; minimal evidence of peritonitis, active bowel sounds and able to tolerate oral nourishment and to infections with GC, chlamydia, bacteroides, enterobacteriaceae, streptococci

PO REGIMENS - any of the following (4)
- Ofloxacin (Floxin) 400 mg PO bid x14 d plus metronidazole 500 mg PO bid x14d
- Ceftriaxone (Rocephin) 250 IM x1 and doxycycline 100 mg PO bid x 14d

PARENTERAL REGIMENTS - any of the following (1)
- Cefotetan (Cefotan) 2 gms IV q 12h
- Cefoxitin (Mefoxin) 2 gms IV q 6h
- Doxycycline 100 mg IV/PO q 12h
- Clindamycin (Cleocin) 900 mg IV q 8h plus gentamicin (Garamycin) 2 mg/kg loading dose then 1.5 mg/kg q8 hrs

* Treat with one of above regimens until afebrile for 48 hours then switch to doxycycline 100 mg PO bid for total of 14d

INPATIENT TREATMENT FOR PID

- Cefoxitin (Mefoxin) 2.0 gm q6h IV plus doxycycline 100 mg IV/PO q 12 hours
- Cefotetan (Cefotan) 2.0 gm IV q 6h plus doxycycline 100 mg IV/PO q 12 hours
- Clindamycin (Cleocin) 600-900 mg q 8h IV plus gentamicin (Garamycin) mg/kg loading dose then 1.5 mg/kg q8h (2)

ADDITIONAL NOTES RE: PID

1. Inpatient: Treat with one of above IV regimens until afebrile for 48 hours then switch to doxycycline 100 mg PO for total of 14d
2. Clindamycin IV effective vs C. trachomatis but effectiveness of PO clindamycin not determined.
3. IV azithromycin (Zithromax) is an alternative to IV doxycycline. Dosing: azithromycin 500 mg IV qd x2d then 250 mg PO qd for a total of 7d
SYPHILIS

- Sexually transmitted; also perinatal
- Causative agent: *Treponema pallidum* (a spirochete)
- Does not grow on culture; does not gram stain
- False positive serology with other treponemes
- Persons are *infective* during the primary and secondary stages
- Untreated syphilis is a *chronic disease* with manifestations in virtually every organ system
- "The Great Masquerader"
- Primary and secondary stages are transient events
- Latency phase (begins in first year after secondary phase)
- Divided into early and late phases - No s/s disease (diagnosed only via serology)

- Late stage (tertiary) - can occur *decades* after infection
  - Cardiovascular manifestations
  - Gummatous
  - Meningovascular (neural) manifestations

CLINICAL PRESENTATION

PRIMARY SYPHILIS

CHANCRE

- First clinical manifestation
- Appears 10-30 days (avg 3 weeks) after infection
- Occurs at site where treponemal invasion first occurred
- May occur on any skin or mucus membrane
- Usually *single, painless lesion* (unless superinfected)
- May be missed in occurs inaccessible region cervix, pharynx, rectum, etc.
- Untreated: persist 2-6 weeks; heal w/o scarring
- Occasional relapse of chancre at same spot
- Dark-field exam (+) for motile spirochetes
  - Difficult to demonstrate in late/healing lesion
  - Local medication/antibiotics - may not demonstrate
- Typical morphology: clean base, rolled edges

- Atypical appearance from bacterial/herpesvirus infection
  - Major confusion would be with chancroid, granuloma inguinale, or occasionally herpes
- Labia and fourchette most typical areas in women
- Perirectal area common with history of anal intercourse
- Exogenous sites: fingers, oral cavity

OTHER SIGNS OF PRIMARY SYPHILIS

- Adenopathy: ipsilateral inguinal, not tender or fluctuant
- No constitutional signs
SECONDARY SYPHILIS

- Onset 6 weeks to 6 months after infection
- Signs and symptoms last only few weeks - may relapse
- Primary chancre may still be present with secondary lesions
- Spirochetes enter bloodstream, disseminate to most tissues/organs

- **Nonspecific symptoms**: fever, malaise, headache, ST, arthralgia, anorexia
  - Other systemic signs:
    - Generalized adenopathy (½ patients)
    - Hepatomegaly, splenomegaly (occasional)
    - Leukocytosis, anemia, elevated ESR
    - Syphilitic hepatitis:
      - Mild derangement of liver enzymes
      - Markedly elevated alkaline phosphatase
    - Acute "viral type" meningitis may occur

**Syphilid (Rash)** occurs in 75% of patients - variable presentation
- Localized or generalized
- Symmetrical discrete erythematous brown or hyperpigmented macules
- Eruption begins on trunk
- Macules enlarge, become annular; no scaling/pruritus
- Macules become thickened + papular -> macular/papular rash
- Papular form more common -> dry, thin collarette of scale
- **Frequent involvement of palms and soles** distinguishes

**Condylomata lata** moist hypertrophic papular lesions
- Occurs in interdigital areas: genitals, gluteal folds
- May become hyperplastic, verrucous resembling *condylomata acuminata* (HPV)
- May occur in extragenital areas
- Covered w grayish exudate containing spirochetes (very infectious)

"**Split papules**":
- Another form papular syphilid
- Found in post-auricular areas, oral commissures

**Mucus patches**: common manifestation of secondary syphilis

Round, oval lesions appearing as grayish or denuded patches on buccal or labial mucosa, tongue, palate, tonsils

**Alopecia**: patchy thinning or more diffuse hair loss
  - Eyebrows, beard hair, other body hair
  - Regrows in both treated and untreated hair
LATENT SYPHILIS

- Period of quiescence after secondary stage
- No clinical manifestations
- Exposure history and positive serology only means of dx
- Early latency: 1st yr after history of secondary infection
  - Recurrence of 2nd stage may occur
  - Occasional transmission to partner
- Late latency: more than one year into latency
- Decreased risk transmission as progresses

LATE SYPHILIS (TERTIARY SYPHILIS) - can be decades

- **Cardiovascular Syphilis** (uncommon) 10% untreated cases
  - Aortic aneurism
  - Aortic valvular disease
- **Late Benign Syphilis - gummatas** (gummatous lesions)
  - Severe inflammatory response to treponemes
  - Microscopically lesions are granulomas
  - Extensive fibrosis; deep scarring
  - Treponemes difficult to detect in gummatas
  - Skin and bones most common sites (any organ)
  - Chronic, painless, slowly progressive lesions
  - Nodular, nodulo-ulcerative lesions (perforations)
  - Often initially misdiagnosed as carcinoma

- **Neurosyphilis**
  - *T pallidum* invades meninges and neural tissue
  - Spirochetes may be demonstrated in neural tissue
  - Extensive CNS sequelae (variable presentation)

CONGENITAL SYPHILIS

- Hematogenous infection of fetus in utero
- Clinically may resemble acquired secondary syphilids
- Affects bones, teeth, hearing, organ systems
- Characteristic clinical presentation
- **Early congenital**: manifests before age 2
  - Papulosquamous/bullous eruptions, condylomata lata, mucous patches
  - Inflammatory rhinitis (*snuffles*)
- **Late congenital**: manifests after age 2
  - Interstitial keratitis, mulberry (first) molars, pegged (Hutchinson’s) incisors
  - Saber shins, Charcot joints
DIAGNOSIS:
- Syphilids infinitely varied and mimic many common dermatosis
  Generalized scabies, pityriasis rosacea, tinea versicolor, guttate psoriasis, fixed drug eruptions, erythema multiforme
- Dark field microscopy:
  Collected directly from lesion scrapings, fluids, gyn sites, lymph node aspirates
- Direct immunofluorescent antibody (DFA-TP) - Serology
  - Indirect serology - many false (+); 28% early false (-)
    - Screening: VDRL, RPR
    - Confirming: FTA-ABS, FTA-ABS DS 98% sensitivity

TREATMENT

SYPHILIS - EARLY PRIMARY, SECONDARY, LATENT < 1 YEAR

**Benzathine Penicillin G (Bicillin CR)**
2.4 million u IM x 1

ALTERNATIVE CHOICES
- Doxycycline 100 mg PO bid x 28 days
- Tetracycline 250 mg PO qid x 28 days
- Ceftriaxone (Rocephin) 125 mg IM qd x 10 days
- Ceftriaxone (Rocephin) 250 mg IM q other day x 5 doses
- Ceftriaxone (Rocephin) 1000 mg IM q other day x 4 doses

ADDITIONAL NOTES
1. Every effort should be made to document penicillin allergy before choosing alternative choices (NEJM 326:1060, 1992)
2. All pts with early or congenital syphilis should have quantitative VDRL at 3,6,12, 24 months after treatment.
   - Primary or secondary syphilis: VDRL should decrease:
     - 2 tubes at 6 months, 3 tubes at 12 months
     - 4 tubes at 24 months
   - Early latent: VDRL should decrease 2 tubes at 12 months
3. Primary syphilis:
   - 50% will be RPR seronegative a 12 months
   - 24% negative FTA/ABS at 2-3 years
4. Retreat if
   - Clinical signs persist or recur
   - Sustain 4-fold increase in titre occurs
   - Initially high titre does not ↓ to < 1:8 at 1 yr
5. Good article: Guidelines (Syphilis) *Infectious Disease in Clinical Practice* 4:407, 1995

SYPHILIS OF MORE THAN ONE YEAR DURATION
- Latent of indeterminate duration.
- Cardiovascular, late benign
**Benzathine Penicillin G** (Bicillin CR) - 2.4 million units IM q wk x 3 (7.2 total)

**ALTERNATIVE CHOICES**
- Doxycycline 100 mg PO bid x 28 d
- Tetracycline 500 mg PO qid x 28d

**ADDITIONAL NOTES RE SYPHILIS**

1. No published data on efficacy of alternatives
2. Value of routine lumbar puncture in asymptomatic late syphilis is questioned in US - treat all patients as primary
3. Indications for LP
   - Neurologic symptoms
   - Treatment failure
   - Serum non-treponemal antibody titre > 1:32
   - Other evidence of active syphilis (aortitis, gumma, iritis)
   - Non-penicillin RX
   - HIV +

**NEUROSYPHILIS**

- **Very difficult to treat** (23% failure rate)
- Includes ocular syphilis (retrobulbar neuritis)
- Follow sequential serum and CSF serology titers

**PRIMARY THERAPY:** *Penicillin G 2-4 million IV units q 4h x 10-14d*

**ALTERNATIVE CHOICES**
- Doxycycline 100 mg PO bid x 21d (for penicillin allergic)
- Procaine penicillin G 2.4 million units IM plus probenecid 1.0 gm PO qd x 10 days
- Ceftriaxone (Rocephin): 1 gm IV/IM x 14d

**ADDITIONAL NOTES:** 1. Good article - *Infectious Diseases in Clinical Practice* 5:33, 1996

**SYPHILIS IN PREGNANCY**

- Same as for stage in non-pregnant
- Some recommend Benzathine Penicillin G one week after initial doses esp for 3rd trimester or with secondary syphilis

**ADDITIONAL NOTES**

1. Skin test for penicillin allergy - desensitize prn (no good alt)
2. Monthly quantitative VDRL or equivalent - retreat if 4-old increase
3. *Doxycycline, tetracycline contraindicated*
4. Erythromycin not indicated due to high risk of failure to cure fetus
CONGENITAL SYPHILIS

- *Aqueous crystalline Penicillin G* (100,000 to 150,000 u/kg/d) - give 50,000 u q8h IV x14d

ALTERNATIVE CHOICE- Aqueous procaine penicillin G (50,000 u/kg/d) IM x 14d

ADDITIONAL NOTES

1. If more than 1 day missed, restart entire course
2. Ophthalmologic exam indicated if symptomatic

CHANCROID

- Sexually transmitted (STD)
- Painful genital ulceration followed by tender inguinal lymphadenopathy
- Cause *Haemophilus ducreyi* (gram negative)
- Rare in developed countries
- More common in men (under diagnosed in women?)
- Incubation 2-5 days
- Clinical presentation
  - First lesion is tender, painful macule which becomes pustular
  - On bursting, forms painful ulcer which has necrotic gray membrane.
- Lesion location (typically multiple ulcerating lesions)
  - Usually found on glans or shaft of penis, anus
  - Women: cervix, vagina, vulva or perianal region
  - Occasionally mouth and other skin surfaces
- Regional lymphadenopathy (buboes) invariable - May suppurate -> chronic fistula

DIAGNOSIS - Microscopy of exudate or pus

TREATMENT

- *Ceftriaxone (Rocephin)* 250 IM x 1 dose
- *Azithromycin (Zithromax)* 1 gm PO x 1 dose
- *Erythromycin base* 500 mg PO qid x 7 days
- Amoxicillin Clavulanate (Augmentin) 500/125 PO tid x 7 days (no data for 875/125)
- Ciprofloxacin (Cipro) 500 mg bid PO x 3 days

In HIV+ patients failures reported with single dose azithromycin

GRANULOMA INGUINALE

- Usually transmitted sexually
- Organism *Calymmatobacterium granulomatis*
- Found predominantly in Far East - Some cases reported in homosexuals in USA and Europe
- Clinical signs develop 1-10 weeks p exposure
- Indurated papule forms on penis, labia, anal margin
- Extranodal lesions common (face, lips, neck)
CLINICAL PRESENTATION

- Primary lesions tender; foul smelling discharge
- Ulcerated lesions deep; floor covered with thick, offensive, purulent discharge.
- Regional lymphadenopathy is usual
- Suppuration and secondary infection common
- Extensive scarring may occur w healing
- Often chronic w mutilating ulceration, chronic swelling and ultimately extensive scarring

DIAGNOSIS

- Finding typical 'Donovan' bodies in gm-stained exudate
- Must exclude other venereal diseases

TREATMENT

- Doxycycline 100 mg PO bid x 1-4 weeks
- Erythromycin base 500 PO qid x 7 days

- Clinical response usually seen in 1 week; treat until all lesions healed (up to 4 weeks).
- Treatment failures seen with doxycycline and TMP/SMX (Bactrim)

LYMPHOGRANULOMA VENEREUM

- Sexually transmitted
- Caused by strain of Chlamydia trachomatis
  - Different strain from that causing NSU, cervicitis/PID
  - Strain found in many tropical countries
  - Serovars L1, L2, L3

CLINICAL PRESENTATION

- Primary lesion appears within a few days of sexual contact
- Small indurated papule to genitalia, anus, mouth
- Papule heals rapidly w/o leaving a scar
- Lymph node enlargement develops in 2-8 weeks
- Nodes undergo suppuration; may discharge thru skin.
- Systemic signs: Fever, arthralgia, splenomegaly, generalized lymphadenopathy and meningism
- Healing may be associated with extensive scarring
- Local edema from lymphatic obstruction
- Strictures of vagina, urethra or rectum

DIAGNOSIS:

- Serology only (previously would view organism in lesions)
  biopsy is contraindicated due to sinus tract formation!
TREATMENT

- **Doxycycline 100 mg PO bid x 21 d**
- **Erythromycin 500 mg PO qid x 21 d**
- **Sulfamoxole (Gantrisin) 0.5 gm PO qid x 21 d**

Rectal infections may require re-treatment

**PTHIRUS PUBIS** (Crabs) - ectoparasite

- **Permethrin 5% (Elimite) - RX**
  
  Wash hair, apply lotion for 10 minutes, rinse; comb to remove nits; 2nd treatment in 7-10
to kill newly hatched lice. Wash clothing/bedding in hot water; preferable w bleach
- **Permethrin 1% (Nix) - OTC - same directions as above**

ALTERNATIVES:
- Less effective, more toxic - use only if treatment failure with permethrin
- **Lindane 1% (Kwell) - seizures can result from broad area coverage or ingestion**
- **Pyrethrin (Rid)**

**SCABIES:** (mites)

- **Permethrin 5% (Elimite):**
  
  - Massage into skin over entire body from chin to soles of feet
  - Wash off 8-14 hours later.
- One treatment usually sufficient; may repeat prn in 14 days.
- Wash clothing/bedding hot water/bleach.