Sexually Transmitted Diseases

Family Medicine Board Review Course
July 2011

Ronald H. Goldschmidt, MD

Reference

Centers for Disease Control and Prevention

Guidelines for Treatment of Sexually Transmitted Diseases 2010

Available at www.cdc.gov and other sites

Syphilis: Screening (USPSFT)

All persons at increased risk
All pregnant women

Recommends against routine screening of persons not at increased risk

Syphilis: Screening

Non-treponemal tests
RPR
VDRL

Treponemal tests
FTA-ABS
TPPA
EIA /CIA *(chemiluminescent immunoassay)
*Reverse sequencing
Early Syphilis: Primary

- Chancre
  - painless
  - develops 3 wks post exposure
  - lymphadenopathy
  - resolves 3-12 wks

Early Syphilis: Secondary

Rash
Develops 2-6 wks after chancre appears; resolves in 2-10 wks
+/- mucous membrane involvement
+/- systemic & flu-like sx

Early Syphilis: Early Latent

Asymptomatic
Serologic evidence of syphilis
History establishing date of infection within the last 1 year

Early Syphilis

<table>
<thead>
<tr>
<th></th>
<th>+ VDRL or RPR</th>
<th>+ FTA or TPPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary syphilis</td>
<td>78 – 86 %</td>
<td>75 – 85 %</td>
</tr>
<tr>
<td>Secondary syphilis</td>
<td>97 – 100 %</td>
<td>97 – 100 %</td>
</tr>
<tr>
<td>Early latent</td>
<td>95 – 98 %</td>
<td>97 – 100 %</td>
</tr>
</tbody>
</table>

EIA/CIA – Unk.
Early Syphilis

Benzathine penicillin G 2.4 mU IM once

For penicillin-allergic patients:
Doxycycline 100 mg po bid or
TCN 500 mg po qid for 2 weeks
(Erythromycin, Ceftriaxone)

Syphilis

Jarish-Herxheimer Reaction

Release of endotoxin within 2 hours of destruction of treponemes
Fever, chills, myalgia, headache, tachycardia, tachypnea, vasodilation with hypotension
Peak at 7 hours, resolves in 12-24 hours
Rx: ASA
Document on chart (and educate patient) that it is not penicillin allergy

Syphilis of More Than 1 Year’s Duration

+ VDRL or RPR
+ FTA or TPPA

Late Latent Syphilis
75% 97-100%

Asymptomatic, positive VDRL/RPR for indeterminate duration or more than 1 year’s duration.
Syphilis of More Than 1 Year's Duration

Tertiary Syphilis
Cardiovascular
  Aortic aneurisms
  Aortic insufficiency
Gummas
  Locally destructive lesions of skin, soft tissues, bones, internal organs.
Neurologic abnormalities
  Tabes dorsalis
  General paresis

Syphilis of More Than 1 Year's Duration

Benzathine penicillin G 2.4 mil U IM once a week for 3 successive weeks
For penicillin-allergic patients:
  Doxycycline 100 mg po bid or TCN 500 mg po qid for 4 weeks
HIV + patients and patients with neurological symptoms with latent syphilis should have CSF examination to rule out neurosyphilis

Neurosyphilis
(Meningitis, Cranial Nerve Involvement, etc.)

Presentation can be similar to meningitis, encephalitis, or stroke
Can occur as early as the time of the secondary rash, or decades later

All HIV+ persons with positive syphilis serologies should have CSF examination (USPHS)

Neurosyphilis: CSF Examination

CSF Serology
  VDRL/RPR positivity usually indicates neurosyphilis
  Negative VDRL/RPR in 1/4 of patients with neurosyphilis
  FTA false positives occur

Spinal fluid activity suggestive of meningeal irritation:
  Total protein > 40 mg/uL
  WBC > 5/µL

Neurosyphilis can occur without elevated protein or cell count
Neurosyphilis

Aqueous crystalline penicillin G 18-24 mil U IV daily (3-4 mil U q 4 h) for 10-14 days followed by Benzathine penicillin G 2.4 mil U IM once.

or

Procaine penicillin G 2.4 mil U IM daily, plus probenecid 500 mg po qid, both for 10-14 days followed by Benzathine penicillin G 2.4 mil U IM once.

Screening

Women ≤ 25 GC, Chlamydia (*CDC: risk based)
Women 26+ Risk-based
Women, pregnant GC, Chlamydia, syphilis, HSV, HIV
Men Risk-based
MSM GC & Chlamydia (urethral), syphilis, HIV
Men/Women HIV - All 13-64 (CDC)
HIV - Risk-based (USPSTF)

Retest women with GC, CT @ 3mos

Prevention of Chlamydial Disease

Screening:
Routine for all sexually active women <26 y.o.
All women at increased risk
Pregnant women

Abstain from sexual activity for 7 days following treatment
Partner notification with testing and/or treatment
Retest women after 3 months

• Incubation: 1 week - 1 month
Chlamydial Disease

**Males**
- Urethritis, Epididymitis/Orchitis, Reiter’s (approx 20% asymptomatic)

**Females**
- Mucopurulent Cervicitis
- Pelvic Inflammatory Disease (as many as 75% are asymptomatic)
- Infertility

**Both**
- Pharyngitis, Proctitis

**Diagnosis:**
- NAAT (Nucleic acid amplification test)
- Cultures

Chlamydial Disease

**Males**
- Urethritis, Epididymitis/Orchitis, Reiter’s (approx 20% asymptomatic)

**Females**
- Mucopurulent Cervicitis
- Pelvic Inflammatory Disease (as many as 75% are asymptomatic)
- Infertility

**Both**
- Pharyngitis, Proctitis

**Diagnosis:**
- NAAT (Nucleic acid amplification test)
- Cultures

Non-chlamydial /Non-gonococcal Urethritis

- *U. uralyticum*
- *M. genitalum*
- *T. vaginalis*
- HSV

Gonorrhea

**Males**
- Urethritis (males) - 5-10% asymptomatic
- Cervicitis - > 50% asymptomatic
- Proctitis - 50% asymptomatic
- Pharyngitis - 50% asymptomatic
- Epididymitis-orchitis (GC, chlamydia, or secondary to UTI)
- Disseminated
- Pelvic Inflammatory Disease

**Females**
- Mucopurulent Cervicitis
- Pelvic Inflammatory Disease (as many as 75% are asymptomatic)

**Diagnosis:**
- NAAT (Nucleic acid amplification test)
- Cultures

**Pregnancy:**
- Azithromycin, amoxicillin, erythromycin

**Treatment:**
- Azithromycin 1 g po once
- or
- Doxycycline 100 mg po bid for 7 days

**Alternatives:**
- Erythromycin, Ofloxacin, Levofloxacin

**Abstain from sexual activity for 7 days following treatment**
**Partner notification with testing and/or treatment**
**Retest women after 3 months**
**Uncomplicated Gonococcal Infections**

Ceftriaxone 250 mg IM once
or, if not an option:
Cefixime 400 mg po (when available)

Alternatives (second line):
Other single-dose cephalosporins: ceftizoxime, cefotaxime, cefoxitin plus probenecid, possibly cefpodoxime or cefuroxime.

followed by

Azithromycin 1 g po once or
Doxycycline 100 mg po bid for 7 days

*Note: If partner follow-up is unlikely, patient-delivered therapy is recommended.*

**Disseminated Gonococcal Disease**

Most (80%) have asymptomatic (cervical, rectal, or pharyngeal) infection prior to dissemination

**Arthritis - Dermatitis Syndrome**

Rash: discrete lesions
especially on hands and feet.
Migratory polyarthralgias of large joints
Tenosynovitis in 25%

Septic joint syndrome
Septic joint syndrome
Can be very destructive

43-5. *Tenosynovitis is part of the dermatitis-arthritis syndrome.*
Disseminated Gonococcal Disease

Patients with typical syndromes are considered to have disseminated GC, even without positive cultures of primary sites, blood, or disseminated lesions.

Rare: meningitis, endocarditis, peri-hepatitis.

Disseminated Gonococcal Disease

**Ceftriaxone** 1 g IV or IM once daily every 24 hours
Alternatives:
- Cefotaxime 1 g IV q 8 h
- Ceftizoxime 1 g IV q 8 h

Outpatient Completion of Treatment
Reliable patients with uncomplicated disease can be discharged 24-48 hours after improvement begins. Complete therapy with:
- Ceftriaxone IM or Cefixime 400 mg po bid

Treat for a total of 7 days
Treat for chlamydia/NGU

Pelvic Inflammatory Disease

Recurrent infections - 25% experience recurrence
Chronic pelvic pain - 15% of patients
Ectopic pregnancy - seven-fold increase
(10% of those who conceive)

Involuntary infertility – 20%
- 12% one episode
- 25% two episodes
- 50% three or more
Pelvic Inflammatory Disease

Pelvic pain occurs in virtually all patients.

Pain is often bilateral, as pus passes out of fallopian tubes and creates bilateral pelvic peritonitis.

Atypical PID can present with bleeding or dyspareunia.

Pelvic Inflammatory Disease

Physical Findings

Abdominal, cervical and/or adnexal tenderness - almost 100% of patients.

Vaginal or cervical discharge - less than 1/2 of patients with gonococcal PID.

Fever greater than 38.3 C (101 F) - only about 1/3 of patients.

Pelvic mass (tuboovarian abscess) may be present.

Pelvic Inflammatory Disease

Laboratory Findings

WBC, sedimentation rate, C-reactive protein - can be elevated; normal does not exclude PID.

Pregnancy test - to rule out ectopic pregnancy.

Ultrasound - can confirm presence of fluid-filled tubes, free fluid, or pelvic abscess.

Laparoscopy - cannot detect endometritis nor subtle tubal inflammation.

Pelvic Inflammatory Disease

Minimum Criteria for Clinical Diagnosis of PID

- Uterine/adnexal tenderness (or mass)
- Cervical motion tenderness

Additional Criteria that Support Diagnosis of PID

- T > 101 F (38.3 C)
- Mucopurulent discharge
- WBCs on saline microscopy
- Elevated sedimentation rate or C-reactive protein
- Lab evidence of N. gonorrhoeae or C. trachomatis
Pelvic Inflammatory Disease

- *N. gonorrhoeae*
- *C. trachomatis*
- *U. urealyticum, M. hominis, and M. genitalum*
- *G. Vaginalis*
- *E. coli, other GNRS, H. influenza*
- Other aerobes and anaerobes

Hospitalization for PID

- Serious peritonitis
- Diagnosis is uncertain, including:
  - need to exclude surgical emergencies
  - adnexal mass (TOA)
- Lack of patient adherence
- Adolescents
- Outpatient treatment failure
- Pregnant patients
- Nausea and vomiting
- HIV-infection

PID: Inpatient Treatment

**Cefotetan** 2 g IV q 12 h
**or**
Cefoxitin 2 g IV q 6 h
PLUS
Doxycycline 100 mg IV or po q 12 h

(Continue for 24+ hr after patient improves)

FOLLOWED BY
Doxycycline 100 mg po bid to complete 14 d therapy.
Add clindamycin or metronidazole if TOA suspected.

**Gentamicin** 2.0 mg/kg IV, followed by 1.5 mg/kg IV q 8 h
(Continue for 24+ hr after patient improves)
Followed by
Doxycycline 100 mg po bid to complete 14 d therapy
Alternative to doxycycline, especially if TOA present: Clindamycin
**P I D: Ambulatory Treatment**

Ceftriaxone 250 mg IM once
(or ceftizoxime or cefotaxime)

or

Cefoxitin 2 g IM plus probenecid 1 g po

Plus

Doxycycline 100 mg po bid for 14 days
with or without

Metronidazole 500 mg po bid for 14 days

---

**Genital Herpes Simplex**

- Spontaneous Abortion
- Premature birth
- Low birthweight

- Perinatal transmission 30-50% when acquired near delivery
- Perinatal transmission 1% when acquired at other times

- Asymptomatic shedding approximately 1%
- Asymptomatic shedding HIV+ = 10%

---

**Genital HSV: Primary Episode**

- Incubation: 2 - 10 days; lasts 2 - 4 wks
- Fever, malaise, lymphadenopathy
- Dx: Cell culture or PCR

- Acyclovir 400 mg po tid or 200 mg po 5x/daily or
- Famciclovir 250 mg po tid or
- Valacyclovir 1 g po bid
  all for 7-10 days or until clinical resolution

- When initiated within 1 wk of onset of symptoms or lesions:
  symptoms, viral shedding & healing time reduced by 5-10 d

---

**Genital HSV: Recurrent Episodes**

- Acyclovir 400-800 mg po tid x 5d
- Acyclovir 800 mg po tid x 2d
- Famciclovir 1 gm bid x 5d
- Famciclovir 1 gm bid x 1d
- Famciclovir 500 mg x 1, 250 mg po bid x 2d

  Must begin within 1 d of lesion onset (or prodrome)
  Shortens viral shedding, symptoms and
decreases new lesions

  Can be reserved for patients with severe sx.
Genital Herpes Simplex: Suppression

Acyclovir 400 mg po bid, Famciclovir 250 mg po bid, Valacyclovir 500 mg po qd or 1g po qd

Significantly decreases (70-80%) frequency & duration of recurrent episodes in patients with six or more recurrences/year.
Can discontinue after 1yr to assess recurrence rate.
Markedly decreased shedding
Decreased transmission

Genital Ulcerative Disease: Chancroid

<table>
<thead>
<tr>
<th>CAUSE</th>
<th>CHARACTERISTIC</th>
<th>ADENOPATHY</th>
<th>DIAGNOSIS</th>
<th>TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chancroid</td>
<td>H. ducreyi</td>
<td>Deep, Indurated, painful</td>
<td>1/3 - 2/3 of cases Tender</td>
<td>Azithromycin Ceftriaxone Ciprofloxacin Erythromycin</td>
</tr>
</tbody>
</table>

Genital Ulcerative Disease: Lymphogranuloma venereum

<table>
<thead>
<tr>
<th>CAUSE</th>
<th>CHARACTERISTIC</th>
<th>ADENOPATHY</th>
<th>DIAGNOSIS</th>
<th>TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphogranuloma venereum C. trachomatis</td>
<td>Small papules, Painless, ulcerated nodules, Usually disappear by time of lymphadenopathy</td>
<td>Bubo tender, Systemic sx, hemorrhagic proctocolitis</td>
<td>Clinical presentation +/-Serology+complement fixation</td>
<td>Doxycycline Erythromycin 3 weeks</td>
</tr>
</tbody>
</table>

Genital Ulcerative Disease: Granuloma inguinale

<table>
<thead>
<tr>
<th>CAUSE</th>
<th>CHARACTERISTIC</th>
<th>ADENOPATHY</th>
<th>DIAGNOSIS</th>
<th>TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granuloma inguinale C. granulomatis</td>
<td>Highly vascular, red, irregular, may bleed on contact, Granulomatous, painless</td>
<td>Pseudobuboes</td>
<td>Donovan bodies in histiocytes India &amp; Southern Africa Rare in US.</td>
<td>Doxycycline, Alt: TMP/SMX Ciprofloxacin Erythromycin</td>
</tr>
</tbody>
</table>
Acute HIV Syndrome: 1-8 weeks

- Fever: 96%
- Rash: 70%
- Sore Throat: 70%
- Adenopathy: 74%
- Myalgias: 54%
- Headache: 32%
- Diarrhea, N-V, malaise, thrush, hepatosplenomegaly, neuro sx (meningitis/neuropathy, facial palsy)
- Oral/Genital Ulcers -- Specific

Counseling and Testing

Emphasis on testing as routine part of medical care
- ‘Opt out’ vs. ‘Opt in’
- Rec: Universal ‘opt-out’ screening for all 13 – 64 y.o. (CDC)*
- Rec: Risk-based testing (USPSTF and AAFP)
- Decrease perinatal transmission
- Recommend ‘opt-out’ for all

Screening: Rapid tests or ELISA or IFA
- Confirmatory: Western Blot
Natural History of HIV Infection

Healthcare worker needlestick from HIV+ source

What's the transmission risk?

A- 0.3 %
B- 1.3 %
C- 3.0 %
D- 9.0 %
E- 13.0%
Exposures in the Occupational Setting

Needlestick—0.3 percent (3/1000)

Risk Stratification
- Deep injury
- Visible blood
- Device used in artery or vein
- Advanced disease

Treatment (PEP) reduced transmission 80%
Begin ASAP
PEP usually not initiated after 72 hrs
ARVs for 28 days
- tenofovir/emtricitabine or zidovudine/lamivudine +/- lopinavir/ritonavir

Other regimens for exposures from source patients with documented or possible ARV drug resistance

Exposures in the Non-occupational Setting

Sexual and injection drug use
Treatment well tolerated and might be effective
Begin ASAP
PEP usually not initiated after 72 hrs
ARVs for 28 days
- tenofovir/emtricitabine or zidovudine/lamivudine +/- lopinavir/ritonavir

Other regimens for exposures from source patients with documented or possible ARV drug resistance

Preventing Perinatal (Vertical) Transmission

Diagnose HIV infection in pregnancy
- prenatal testing
- rapid testing in labor
ARVs in 3rd trimester, L&D, newborn
Consideration of C-section
Most successful when mother’s HIV viral load is well controlled before delivery
Routine Health Care for Adults with HIV:
Routine Labs

Markers of HIV Disease Progression q 3-4 mo.
- CD4+ (T-helper lymphocyte count)
- Viral load (HIV RNA)
- CBC + Platelets
- Serum chemistries
- Syphilis, hepatitis serologies
- Cryptococcal antigen
- Toxoplasmosis titre
- Urinalysis
- Lipid profile
- Resistance test prior to treatment

Other Health Care Maintenance

Immunizations:
- All standard immunizations except live virus vaccines (OPV, smallpox, live influenza) can be given in patients or families with HIV positive person
- Measles (MMR) and varicella OK if not severely immunocompromised

Pap smear: 6 mos x 2; 12 mos
PPD (5 mm) - Anergy testing not recommended: assess risk
CXR – only if clinically indicated

Indications for Antiretroviral Therapy

CD4 <350 : should be given
CD4+ 350-500 cells/uL: recommended
- data stronger for < 350 than 350-500
CD4+ >500 (divided panel opinion)
- Symptomatic disease and AIDS-defined illnesses
- HIV nephropathy
- Pregnancy
- Hepatitis B when HBV treatment is indicated
- Decision must be individualized

Combination ARV Therapy

Reverse transcriptase inhibitors
Non-nucleoside reverse transcriptase inhibitors
Protease inhibitors
Integrase inhibitors
Fusion inhibitors
Others
Preferred regimens most commonly used

Tenofovir/emtricitabine
   plus
   Efavirenz (NNRTI) or darunavir (PI, boosted) or atazanavir (PI, boosted) or raltegravir (integrase inhibitor)
   - OR -
   Zidovudine/lamivudine plus lopinavir/ritonavir

Indications of response to ARVs

Viral load decrease
CD4+ count increase
Some VL decrease within 1-2 months
CD4+ increase within 2-4 months
Ideal: undetectable by 4-6 months

Treatment failure

Adherence problems
Drug interactions
   - among ARVs
   - rifampin and other anti-tuberculosis drugs
   - simvastatin and lovastatin
Resistance
   - de novo
   - during treatment
   - off treatment
Genotypic, phenotypic resistance testing while taking ARVs

Changing Therapy

Viral load increase, CD4+ decrease, progressive disease
Genotypic (+/- phenotypic) resistance test while taking ARVs
Change 2 or more drugs (usually)
Complications of ARV therapy

Lipodystrophy, lipid abnormalities - NRTIs
Lactic acidosis – nNRTIs and PIs
Glucose intolerance - PIs

Activation or reactivation of disease
(immune reconstitution syndromes)

Prophylaxis against OIs
( Opportunistic Infections)

Pneumocystis jiroveci < 200 CD4+
Toxoplasma gondii < 100 CD4+
M. avium complex (MAI) < 50 CD4+
M. tuberculosis Any CD4+

Discontinuation of prophylaxis
with effective ARV therapy

Pneumocystis jiroveci >200 for >3 months
Toxoplasma gondii >100 for > 3 months
M. avium complex (MAC) >100 for > 3 months
( primary prophylaxis)
>100 for > 6 months
following 12 months of acute therapy
( secondary prophylaxis)

Candidal infections

Oral, vaginal infections
Esophageal candidiasis
Systemic candidal infections
Acute PCP

Trimethoprim-Sulfamethoxazole (Septra, Bactrim)
15 mg TMP/75 mg SMX per kg daily given in 3 - 4 doses po or as 1 - 2 hour IV infusion
for patients with PaO₂ ≤ 70 add:
Methylprednisolone (IV) 40 mg bid for 5 days followed by 40 mg q d for 5 days followed by 20 mg q d for 11 days (can also be tapered to zero over last 11 days)

Cotton wool spots
CMV retinitis

CNS Toxoplasmosis
- Focal findings
- Seizures
- Cognitive difficulties
- Treatment:
  - Pyrimethamine plus sulfadiazine
Cryptococcal Meningitis

- Headache
- Cognitive difficulties
- Confusion
- +/- Stiff neck
- Fever

Sources of Information

Guidelines
www.aidsinfo.nih.gov
www.cdc.gov
www.nccc.ucsf.edu

General info, links to guidelines & other Websites
www.hivinsite.ucsf.edu
www.hopkins-aids.edu
www.ama-assn.org/special/hiv