A Modern Approach to Sexually Transmitted Infections
Seema Menon, MD
Assistant Professor
Department of OBGYN
Medical College of Wisconsin

Objectives
- Present trends in sexually transmitted infection prevalence
- Review the CDC 2010 Sexually Transmitted Disease Guidelines pertaining to common sexually transmitted infections
- Discuss reduction strategies

Genital Herpes—Initial Visits to Physicians’ Offices, United States, 1966–2011

NOTE: The relative standard errors for genital herpes estimates of more than 100,000 range from 18% to 30%.

Genital Herpes

- Chronic life-long virus
  - HSV-1
  - HSV-2
- Majority of transmission occurs by asymptomatic or unaware persons
- Transmission occurs by direct contact with the virus between mucosal surfaces or small cracks in the skin

Genital Herpes-Diagnosis

- Clinical diagnosis is insensitive; laboratory testing should be done
- Cell culture and PCR are preferred method to test.
  - Cell culture can have low sensitivity (recurrent lesions)
  - PCR assay higher sensitivity

Genital Herpes-Diagnosis

- Type specific antibody testing is available
  - Antibodies to HSV 1 and 2 develop during the first several weeks of infection
  - Persist indefinitely
- 50 million people are infected with HSV-2 in the US
  - 50%-80% have antibodies to HSV (I or II)
Genital Herpes

- Helpful If:
  - HSV culture/PCR testing of the lesion is neg
  - HSV diagnosis was by clinical criteria
  - Partner has HSV.

HSV Treatment

<table>
<thead>
<tr>
<th>Primary Lesions</th>
<th>Recurrent Lesions</th>
<th>Severe Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-10 days</td>
<td>Start within 1 day of onset or during the prodrome that precedes outbreaks</td>
<td>Disseminated disease: pneumonitis, hepatitis, meningoencephalitis</td>
</tr>
<tr>
<td>Acyclovir 400 mg po tid</td>
<td>Acyclovir 400mg tid, 800 mg tid x 5d</td>
<td>IV acyclovir (5-10 mg/kg q 8 hours) until clinically improved PO antiviral therapy for total of ten days</td>
</tr>
<tr>
<td>Acyclovir 200 mg 5x/day</td>
<td>Acyclovir 800 mg bid x 5 days</td>
<td></td>
</tr>
<tr>
<td>Famciclovir 250 mg po tid</td>
<td>Famciclovir 125 mg bid x 5d</td>
<td></td>
</tr>
<tr>
<td>Valacyclovir 1 gm po bid</td>
<td>Famciclovir 1000 mg bid x 1d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Famciclovir 500 mg x 1, then 250 mg bid x 2 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Valacyclovir 500 mg bid.x3d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Valacyclovir 1000 mg qd x 5d</td>
<td></td>
</tr>
</tbody>
</table>

HSV: Special Considerations

- Suppressive therapy reduces outbreak frequency by 70-80% in those with frequent outbreaks
  - Acyclovir 400 mg bid
  - Famciclovir 250mg bid
  - Valcyclovir 1 gm qd or 500 mg qd
NOTE: In 2011, 2,154 (68.5%) of 3,142 counties in the United States reported no cases of primary and secondary syphilis.
Syphilis

- Transmitted mainly by genital contact but can primarily involve oropharynx, rectum, conjunctiva, blood
- Also can have transplacental infections
- Can penetrate intact mucosa

Syphilis

<table>
<thead>
<tr>
<th>Primary</th>
<th>Secondary</th>
<th>Tertiary</th>
<th>Neurosyphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHANCRE- painless ulcerating lesion, hard CHANCRE</td>
<td>CONDYLOMA LATA --gray or white erosive lesions, 6-8 weeks after chancre</td>
<td>No genital lesions</td>
<td>No genital lesion</td>
</tr>
<tr>
<td>Pelvic lymphadenopathy 10-90 days after initial transmission</td>
<td>Systemic symptoms, rash on palms and soles,</td>
<td>Cardiac lesions</td>
<td>Cranial nerve dysfunction, meningitis, stroke, acute or chronic altered mental state, auditory or ophthalmic abnormalities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bone lesions (gumma)</td>
<td></td>
</tr>
</tbody>
</table>

Syphilis - Natural History

- Not necessarily progressive
- Neurosyphilis can occur at any stage
- Secondary syphilis can reappear over the first four years repeatedly
- Disease can become latent at any stage
Syphilis - Natural History

- Latent Syphilis
  - Early Latent disease within one year of acquisition
  - Late latent disease more than one year of acquisition
  - Latent syphilis of unknown duration

Syphilis - Diagnosis

- Darkfield examination detects T. Pallidum
  - Exudate
  - Tissue
- PCR testing for T. Pallidum is limited

Syphilis - Diagnosis

- Serology Tests
  - Nontreponemal VDRL and RPR (antibody titers)
    - Normalize after treatment
  - Treponemal FTA-ABS, and TP-PA (positive/negative)
    - Remains positive in majority of people
  - Treponemal screening tests
    - Can differentiate between new and old infections
    - Still relies on confirmatory nontreponemal test and possibly another treponemal test
Syphilis- Treatment

- Treatment relies on parental Penicillin (PCN) G
  - Combining different PCN preparations is not effective (benzathine-procaine penicillin)
  - Treatment is determined by stage

Syphilis Treatment

<table>
<thead>
<tr>
<th>Stage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary, Secondary and Early Latent Stage</td>
<td>Benzathine PCN G 2.4 million units IM x 1 dose</td>
</tr>
<tr>
<td>Late Latent Syphilis, unknown duration, and Tertiary stage</td>
<td>Benzathine PCN G 2.4 million units IM x 3 doses, 1 week intervals</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>Aqueous crystalline PCN G 18-24 units q day (3-4 million units IV q 4 hours x 10 days-14 days) OR Procaine PCN 2.4 million units q day plus probenecid 500 mg qid x 10-14 days</td>
</tr>
</tbody>
</table>

Syphilis-Follow Up

- Nontreponemal testing should be done at 6,12, 24 months
- CSF evaluation if titers increase by fourfold, don’t decreased by fourfold after 12-14 months of therapy, or signs/symptoms of syphilis develop
Syphilis—Special Considerations

- PCN allergy: doxycycline 100 mg bid or tetracycline 500 mg qid x 28 days
- Pregnant patient with PCN allergy should be desensitized and treated with PCN G
- HIV positive patients have the same recommendations of therapy
  - Follow up serology at 3, 6, 9, 12, 24 months

Chlamydia—Rates by Sex, United States, 1991–2011

Chlamydia—Rates by Age and Sex, United States, 2011
Chlamydial Infections

- Most frequently reported infectious disease in the US
- Significant reproductive sequelae
- Symptoms can include
  - purulent or mucoid discharge,
  - post coital bleeding
  - vaginitis

Chlamydial Infections

- Asymptomatic infection is common
  - Screen sexually active women 25 years of age and younger*
  - Screen older women with new partner or multiple partners
Chlamydial Infections

- Multiple laboratory techniques that can detect C. Trachomatis (CT)
  - Culture
  - Direct immunofluorescence
  - EIA
  - Nucleic acid hybridization tests
  - NAAT

Chlamydial Infections Diagnosis

<table>
<thead>
<tr>
<th>Urine specimen</th>
<th>Endocervical swab</th>
<th>Vaginal Swab</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT clean catch</td>
<td>Requires a speculum examination</td>
<td>Self collection is acceptable</td>
</tr>
<tr>
<td>Only NAAT is FDA approved</td>
<td>All testing techniques are acceptable</td>
<td>Only NAAT is approved</td>
</tr>
<tr>
<td></td>
<td>NAAT has the greatest sensitivity</td>
<td></td>
</tr>
</tbody>
</table>

Chlamydial Infections-Diagnostic Considerations

- Liquid-based cytology
  - Some NAATs have been FDA cleared
  - Sensitivity of this specimen may be lower than endocervical specimen
- Rectal and oropharyngeal infections
  - Most tests are not FDA cleared for this
  - NAAT testing appears to be the most sensitive

References: 2
Chlamydial Infections
Treatment

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin 1 gram po x 1</td>
<td>Erythromycin base 500 mg qid x 7 days OR</td>
</tr>
<tr>
<td>OR Doxycycline 100 mg po x 1</td>
<td>Erythromycin ethylsuccinate 800 mg po qid x 7 days OR</td>
</tr>
</tbody>
</table>

Chlamydial Infections—Treatment Consideration

- Abstain from sex for seven days
- Test of cure is not recommended
  - Retesting should occur 3 months after treatment
  - More than 3 weeks should pass before retesting
- Sex partners should be treated
- Treatment is same for HIV+ patients

Gonorrhea—Rates by Sex, United States, 1991–2011
Gonococcal Infections: Sequelae

- Associated with upper genital tract infections
- Disseminated disease results from bacteremia (DGI)
  - Petechial or pustular lesions, arthritis, asymmetric arthralgia, tenosynovitis.
  - Perihepatitis (occasional)
  - Endocarditis, meningitis (rare)
- Requires hospitalization
Gonococcal Infections

- **Screening**
  - Widespread screening is not recommended
  - Screening women under age 25 is the primary focus

Gonococcal Infections

- **Diagnostic tests**
  - Culture
  - Nucleic acid hybridization tests
  - NAAT
  - Gram stain

- **Suitable specimens**
  - Urine
  - Endocervical swabs
  - Vaginal swabs

### Gonococcal Infection-Diagnosis

<table>
<thead>
<tr>
<th>Urine Specimen</th>
<th>Endocervical swab</th>
<th>Vaginal Swab</th>
<th>Gram Stain</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT clean catch</td>
<td>Requires a speculum examination</td>
<td>Self collection is acceptable</td>
<td>High specificity Low sensitivity</td>
</tr>
<tr>
<td>Only NAAT is FDA approved</td>
<td>All testing techniques are acceptable</td>
<td>Only NAAT is approved</td>
<td>Only appropriate for SYMPTOMATIC men</td>
</tr>
</tbody>
</table>
Gonococcal Infections- Diagnostic Considerations

- Not all NAATs are the same
- Non-genital site infection
  - No FDA cleared test
  - NAATS appear to be the most sensitive

Gonococcal Infections- Treatment

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone 250 mg IM x 1</td>
<td>Cefpodoxime 400 mg po x 1</td>
</tr>
<tr>
<td>OR</td>
<td>OR</td>
</tr>
<tr>
<td>Cefixime 400 mg po x 1 OR</td>
<td>Cefuroxime axetil 1 gm po x 1 OR</td>
</tr>
<tr>
<td>Single dose injectable cephalosporin</td>
<td>Azithromycin 2 gm po x 1 OR</td>
</tr>
<tr>
<td>PLUS</td>
<td>OR</td>
</tr>
<tr>
<td>Azithromycin 1 gm po x 1</td>
<td>Spectinomycin</td>
</tr>
<tr>
<td>1 or Doxycycline 100mg po bid</td>
<td></td>
</tr>
</tbody>
</table>

Gonococcal Infection- Treatment Consideration

- First generation cephalosporin allergy in 5-10% of patients with PCN allergy
  - Contraindicated in those with a severe reaction
    - Anaphylaxis
    - Stevens Johnson syndrome
    - Toxic epidermal necrolysis
  - Azithromycin 2 gm
    - Uncomplicated infection
    - Resistance to macrolides is emerging
Gonococcal Infections-Follow Up
- Routine test of cure is not recommended
- Retested in 3 months
- Treatment failure
  - Culture with antimicrobial susceptibility testing
  - Retreat with at least 250 mg IM ceftriaxone
  - Ensure partner treatment
  - Report to local health department (CDC)
  - ID specialist consultation

Pelvic Inflammatory Disease
- Spectrum of inflammatory disorders of the upper female genital tract
  - Endometritis, salpingitis, TOA, pelvic peritonitis
- GC/CT ascending infections
  - Microorganisms of the vagina
  - Enteric gram negative rods
  - CMV
  - M. Hominis, U.urealyticum, M. genitalium

Pelvic Inflammatory Disease-Diagnosis
- Most specific criteria for diagnosing PID:
  - Endometrial biopsy
  - TVUS or MRI showing Tubo-ovarian abscess (TOA), thickened fluid filled tubes, or tubal hyperemia (doppler flow)
  - Laparoscopic abnormalities consistent with PID
Pelvic Inflammatory Disease - Diagnosis

- Pressure to make this diagnosis without specific testing
  - Early diagnosis
  - Often goes unrecognized
  - Low threshold for diagnosis
- Clinical diagnosis is imprecise
  - PPV value depends on the epidemiologic characteristics of the population

Pelvic Inflammatory Disease - Diagnosis

- Treatment for PID should be initiated in sexually active young or high risk women with
  - Pelvic pain/lower abdominal pain
  - Other causes for pain have been ruled out
  - At least ONE of the following is present
    - Cervical motion tenderness
    - Uterine tenderness
    - Adnexal tenderness

Pelvic Inflammatory Disease - Diagnosis

- Additional criteria to enhance the specificity of the minimum criteria:
  - Temperature >101°F
  - Cervical/vaginal mucopurulent discharge
  - Increase WBCs in vaginal secretions
  - Increased ESR
  - Increased C-reactive protein
  - Documented GC/CT infection*
Pelvic Inflammatory Disease - Diagnosis

- Signs of lower genital tract inflammation + one of the three minimal criteria increases the specificity of the diagnosis.

Pelvic Inflammatory Disease - Treatment Principles

- Treatment should be broad spectrum
  - GC/CT coverage even if testing is negative
  - Parenteral and Oral regimens

- Outpatient therapy in mild or moderate infection
- Hospitalization required if:
  - Surgical emergency can not be excluded
  - Pregnancy
  - No response to oral antibiotics
  - Unable to follow outpatient regimen
  - Severe illness including nausea, vomiting, or high fever
  - TOA
## Pelvic Inflammatory Disease - Treatment

<table>
<thead>
<tr>
<th>Parenteral Treatment</th>
<th>Recommended Therapy</th>
<th>Alternative Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cefotetan 2 gm IV q 12 hours or Cefoxitin 2 gm IV q 6 hours PLUS Doxycycline 100 mg IV or po every 12 hours OR Clindamycin 900 mg IV q 8 hours PLUS Gentamycin 2 mg/kg IV or IM x 1, then 1.5 mg/kg q 8 hours</td>
<td>Ampicillin/sulbactam 3 gm IV q 6 hours PLUS Doxycycline 100 mg po/IV q 12 hours</td>
</tr>
</tbody>
</table>

**Parenteral Therapy until 24 hours from clinical improvement**

**Followed by doxycycline 100 mg po bid or clindamycin 450 mg qid for total of 14 days**

<table>
<thead>
<tr>
<th>Oral Treatment</th>
<th>Recommended Therapy</th>
<th>Alternative Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ceftriaxone 250 mg IM x 1 PLUS Doxycycline 100 mg po bid x 14 days OR Cefoxitin 2 gm IM with Probenecid 1 gm IM x 1 PLUS Doxycycline 100 mg po bid x 14 days OR Parenteral third generation cephalosporin PLUS Doxycycline 100 mg po bid x 14 days</td>
<td>Limited</td>
</tr>
</tbody>
</table>
Pelvic Inflammatory Disease - Treatment
- Metronidazole can be added to all of the oral regimens
  - Improve anaerobic coverage
  - Treat bacterial vaginosis
- Quinolone-resistant N. Gonorrhoeae
  - Levofloxacin or Ofloxacin + Metronidazole
    - Low risk of GC (individual and community)
    - Sensitivity data
    - Add Azithromycin 2 gm if resistant or unknown

Pelvic Inflammatory Disease
- Patients should improve within 3 days of therapy
  - Hospitalization
  - More testing
  - Surgical intervention

Pelvic Inflammatory Disease - Follow Up
- Patients treated with oral regimen should be re-evaluated within three days
- Documented GC/CT infection
  - Re-test 3-6 months after treatment
- Abstain from sex until treatment is complete and no symptoms
- Empiric sex partner treatment
- Offer HIV testing
- IUD can remain in place
Genital Warts—Initial Visits to Physicians’ Offices, United States, 1966–2011

Visits in thousand

Year

NOTE: The relative standard errors for genital warts estimates of more than 100,000 range from 18% to 30%.


Human Papilloma Virus

- 100 different types
  - 40 types affect the genital tract
  - Nononcogenic cause genital warts and respiratory papillomatosis
  - 50% of sexually active people will be infected at least once
    - Vaginal and anal sex, also oral sex
    - Condoms are not fully protective
    - Difficult to identify how/when HPV was acquired

Human Papilloma Virus-Genital Warts

- 90% are caused by HPV 6 or 11
- Asymptomatic
- Flat, papular, or pedunculated lesions on the mucosa
  - Around the introitus most commonly
Human Papilloma Virus-
Testing
- Nucleic acid testing is available for women at least 30 years of age undergoing cervical cancer screening
- General STI testing is not advised

Human Papilloma Virus-
Genital Warts
- Diagnosis - clinical
  - Biopsy
    - Uncertain appearance
    - Therapy is not working
    - Worsens during therapy
    - Atypical appearance
    - Compromised immunity
    - Pigmented warts
  - DNA testing of lesions not appropriate
  - Acetic acid application not specific

Human Papilloma Virus-
Genital Wart Treatment
- Improve symptoms and remove warts
  - May reduce HPV viral DNA
- No superior regimen
  - Resources
  - Patient preference
  - Provider experience
  - Wart characteristics
- Some lesions may spontaneously resolve
Human Papilloma Virus-
Genital Wart Treatment

- Patient’s immunity plays a role in treatment response
- May take up to 3 months of therapy
- Persistent changes in pigmentation
- Develop scaring
- Rarely, can develop chronic pain syndrome
- Limited number of systemic effects from podophyllin and interferon therapy

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Patient Applied</th>
<th>Provider Applied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Podoflox 0.5% solution or gel bid x 3 days, 4 days off-4 cycles</td>
<td>Cryotherapy with liquid nitrogen or cryoprobe 1-2 weeks OR Podophyllin resin 10%-25% in a compound tincture of benzoin weekly OR Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80%-90% OR surgical removal</td>
<td></td>
</tr>
<tr>
<td>Imiquimod 5% cream qhs x 3 nights a week, 16 weeks OR Sinecatechins 15% ointment tid, 16 weeks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Genital Wart Treatment

<table>
<thead>
<tr>
<th>Cervical Warts</th>
<th>Vaginal Warts</th>
<th>Urethral meatus Warts</th>
<th>Anal Warts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td>Cryotherapy with liquid nitrogen OR TCA or BCA</td>
<td>Cryotherapy with liquid nitrogen OR Podophyllin 10-25% in a compound tincture of benzoin</td>
<td>Cryotherapy with liquid nitrogen OR TCA or BCA OR Surgical removal</td>
</tr>
</tbody>
</table>
Genital Warts - Treatment Considerations

- Commonly recur 3 months after treatment
- Unknown how long a person is contagious after treatment
- Unknown if informing subsequent sex partners of previous infection is beneficial
- Pap testing recommendations remain the same

STD Rates, Milwaukee, 2006:
2nd highest of 50 big cities in the U.S.

Combined rates* for chlamydia, gonorrhea and primary and secondary syphilis for the 50 largest metropolitan areas, 2006, CDC data

* Cases per 100,000 population.

Expedited Partner Therapy

- Late 1990s programs were developed to ensure partner treatment
- Expedited Partner Therapy (EPT) treats sex partners of patients with an STI diagnosis without examination
  - EPT increases the numbers of partners treated
  - EPT leads to lower rates of persistent or recurrent infection
Expedited Partner Therapy

- Can decrease reinfection rates compared to referral for examination
  - Reinfection from untreated partner contributes to high rates of GC/CT infection
- Costs from societal and health care perspective are lower than referral for care
- Insufficient data to support effectiveness for trichomoniasis or syphilis

Expedited Partner Therapy

- Notification and treatment of sex partners of patients with syphilis is responsibility of the public health department
  - Not feasible to include GC and CT in this program

Expedited Partner Therapy

- CDC has recommended EPT since 2006
  - Ideally, partner receives complete in person evaluation
  - Therapy is given if this is not possible
- Supported by
  - AMA
  - Society for Adolescent Health and Medicine
  - American Academy of Pediatrics
  - American Bar Association
  - ACOG
Expedited Partner Therapy

- ACOG recommendations
  - Heterosexual partners of female patients with GC or CT infection in past 2 months who are unable to seek care should receive EPT
  - Partners should be encouraged to seek medical evaluation
  - Should be compliant with CDC, local, and states guidelines
    - Abstinence from sex for 7 days
  - Index patient should be counseled
    - Written information should be provided to her partner(s)
    - Medication can be dispensed or a prescription written to her partner(s)
  - Mechanism in place for patient to report adverse events

Expedited Partner Therapy

- Use of EPT is governed by state, not national law

Expedited Partner Therapy

- 2009 Wisconsin Act 280 was signed into law
  - Enables physicians, physician assistants and certified advanced practice nurse practitioners to prescribe and dispense medication to partners of patients with GC, CT, and trichomoniasis
  - CDC cautions against widespread partner treatment in cases of trichomoniasis infections
Expedited Partner Therapy

- Wisconsin legislation protects health care professionals and pharmacists providing EPT from civil and professional liability, except for willful and wanton misconduct.

- Risk of adverse events are low
  - Minimized with written information on dosing instructions
  - Monitored expedited partner therapy programs
    - No drug-related adverse events
    - No lawsuits

- Guidance from Department of Health Services
  - First choice is to notify and refer partner for evaluation
  - Treatment according to CDC guidelines
  - All sex partners within 60 days of diagnosis or symptoms are allowed one EPT dose
  - Information material must be furnished
    - [http://dhs.wisconsin.gov/communicable/STD/EPT.htm](http://dhs.wisconsin.gov/communicable/STD/EPT.htm)
  - Retested at 3 months if GC or CT infection
  - Report the infection
    - Section for documenting that EPT given
Expedited Partner Therapy

- Prescription should be written in partner’s name and address
  - Can be replaced with “EXPEDITED PARTNER THERAPY” or “EPT”

Expedited Partner Therapy

- Treatment for CT
  - Follow CDC guidelines

Expedited Partner Therapy

- Gonococcal resistance
  - Early stages of resistance to oral cephalosporin
  - Oral Cefixime is no longer recommended as EPT for GC infection
    - Single dose ceftriaxone 250 mg IM x1 PLUS
    - Azithromycin 1 gm orally or doxycycline 100 mg po bid x 7 days
  - If clinical evaluation is impossible
    - Cefixime PLUS Azithromycin
    - Test of cure one week after therapy
REFERENCES

- http://www.cdc.gov/std/default.htm
- Golden MR, Estcourt CS. Barriers to the implementation of expedited partner therapy. Sex Transm Infect 2011; 87:437-438