Sexually Transmitted Diseases

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STDs....

- Gonorrhea
- Syphilis
- Chlamydia
- PID
- Genital Herpes
- HPV (genital warts)
- Trichomoniasis
General Approach

1. Clinical Presentation
2. Lab Test Meaning
3. Treatment Regimens
4. Monitoring Parameters
STD Approach

1. Clinical Presentation
   • Male vs. Female

2. Diagnosis
   • Bugs

3. Treatment Regimens

4. Monitoring Parameters
Gonorrhea — Rates: United States, 1941–2006 and the Healthy People 2010 target

Note: The Healthy People 2010 target for gonorrhea is 19.0 cases per 100,000 population.
Gonorrhea

Males
- Urethritis (2-8 days post exposure)
- Urinary symptoms
- Discharge (1-2 days later)

Females
- Urethritis (within 10 days post exposure)
- Nonspecific symptoms (UTI-like, discharge)
- Majority asymptomatic/minimal
  - PID
- Disseminated (DGI)
Neisseria gonorrhoeae

• Gram Stain
  – Gram (-) diplococci (kidney bean shape)
  – Sensitive and Specific in male urethritis

• Cultures
  – Necessary in females
  – Necessary: rectal, pharyngeal
Gonorrhea

• Single dose treatment
  – Ceftriaxone 125 mg IM x 1
  – Ciprofloxacin 500 mg po x 1
  – Other FQ’s

• Know local resistance

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Figure 11. Drugs used to treat gonorrhea in GISP participants, 1988–2004

Note: For 2004, “Other” includes no therapy (1.6%), azithromycin 2 g (0.3%), levofloxacin (0.2%), and other less frequently used drugs.
Gonococcal Isolate Surveillance Project (GISP) — Penicillin, tetracycline, and ciprofloxacin resistance among GISP isolates, 2006

Note: PenR=penicillinase producing *N. gonorrhoeae* and chromosomally mediated penicillin-resistant *N. gonorrhoeae*; TetR=chromosomally and plasmid mediated tetracycline-resistant *N. gonorrhoeae*; QRNG=ciprofloxacin resistant *N. gonorrhoeae*. 
Gonococcal Isolate Surveillance Project (GISP) —
Percent of *Neisseria gonorrhoeae* isolates with resistance or intermediate resistance to ciprofloxacin, 1990–2006

Note: Resistant isolates have ciprofloxacin MICs $\geq 1 \, \mu g/ml$. Isolates with intermediate resistance have ciprofloxacin MICs of 0.125 - 0.5 $\mu g/ml$. Susceptibility to ciprofloxacin was first measured in GISP in 1990.
Gonococcal Isolate Surveillance Project (GISP) — Percent of *Neisseria gonorrhoeae* isolates with resistance to ciprofloxacin by sexual behavior, 2001–2006

- **Heterosexual men**
- **Men who have sex with men (MSM)**

### Graph Details
- **Y-axis:** Percent Ciprofloxacin Resistant
- **X-axis:** Years 2001–2006
Gonococcal Isolate Surveillance Project (GISP) — Prevalence of ciprofloxacin resistant *Neisseria gonorrhoeae* by GISP site, 2003-2006

Note: Not all clinics participated in GISP for the last 4 years. Clinics include: ALB=Albuquerque, NM; ATL=Atlanta, GA; BAL=Baltimore, MD; BHM=Birmingham, AL; CHI=Chicago, IL; CIN=Cincinnati, OH; CLE=Cleveland, OH; DAL=Dallas, TX; DEN=Denver, CO; DTR=Detroit, MI; HON=Honolulu, HI; LAX=Los Angeles, CA; LBC=Long Beach, CA; LVG=Las Vegas, NV; MIA=Miami, FL; MIN=Minneapolis, MN; GRB=Greensboro, NC; NOR=New Orleans, LA; NYC=New York City, NY; OKC=Oklahoma City, OK; ORA=Orange County, CA; PHI=Philadelphia, PA; PHX=Phoenix, AZ; POR=Portland, OR; SDG=San Diego, CA; SEA=Seattle, WA; SFO=San Francisco, CA; and TRP=Tripler Army Medical Center, HI.
Gonorrhea

• Single dose treatment - usual
  – Ceftriaxone 125 mg IM x 1
  – Cefixime 400 mg PO x 1
• NEW – No FQ’s
• Know local resistance
Neisseria gonnorhoeae

- When not ruled out, always:

  **Treat for Chlamydia**

- 50% co-infection rate – treat both
- TREAT PARTNERS
- No routine follow-up

Note: As of January 2000, all 50 states and the District of Columbia had regulations requiring the reporting of chlamydia cases.
Chlamydia

- Males
  - Dysuria, frequency
  - Mucoid discharge (7-21 days exposure)
  - ¼ asymptomatic
- Females
  - Largely asymptomatic
  - PID
Chlamydia trachomatis

- Diagnosis
  - DFA and ELISA

- Treatment
  - Doxycycline 100 mg po BID x 7 days
    - Inexpensive, effective
  - Azithromycin 1 g po x 1
    - Expensive, convenient

Figure 12. Drugs used to treat Chlamydia trachomatis infection in GISP participants, 1992-2004

Note: For each year, “Other” accounted for only 0 – 0.9% of C. trachomatis treatment and erythromycin accounted for only 0.1 – 1.0% of C. trachomatis treatment.
Chlamydia trachomatis

• Diagnosis
  – DFA, ELISA, NAAT (Nucleic Acid Amplification Tests)

• Treatment
  – Doxycycline 100 mg po BID x 7 days
    • Inexpensive, effective
  – Azithromycin 1 g po x 1
    • Expensive, convenient
Chlamydia

- Pregnancy
  - Erythromycin base or ethyl succinate
- Follow-up not recommended

- TREAT PARTNERS

- TREAT FOR GONORRHEA
Cause of Death: Syphilis
Syphilis — Reported cases by stage of infection: United States, 1941–2006

Cases (in thousands)

- P&S
- Early Latent
- Total Syphilis

Year:
- 1941
- 1946
- 1951
- 1956
- 1961
- 1966
- 1971
- 1976
- 1981
- 1986
- 1991
- 1996
- 2001
- 2006
Treponema pallidum

Primary

– Chancre (usually appears ~3 weeks)
  • Painless, disappears 1-8 weeks w/o tx

Secondary

– Skin lesions (2-6 weeks after 1°)
  • Non-pruritic, disappears
    4-10 weeks w/o tx
Treponema pallidum

Latent

- Asymptomatic
- Early <1 yr, late >1 yr

Tertiary

- Neurologic, cardiac, systemic
  - 2-30 years later
  - 30%
Treponema pallidum

- Nontreponemal Tests (screen & follow-up)
  - VDRL (Venereal disease research lab)
  - RPR (Rapid plasma reagin card)

- Treponemal Tests (confirmatory)
  - Positive for life
  - FTA-abs (Fluorescent treponemal absorption)
  - MHA-TP (Micohemagglutination assay to T.pallidum)
Syphilis

Primary, Secondary, Early Latent
• 2.4 MU Benzathine Penicillin G IM x 1

Late Latent
• 2.4 MU Benzathine Pen G IM weekly x 3

Neurosyphilis
• Aqueous Pen G IV 2-4 MU q4h x 10-14d
Syphilis – Penicillin Allergy

Primary, Secondary, Early Latent
Doxycycline 100 mg twice daily x 14 days

Late Latent
Doxycycline or Tetracycline * 28 days

Neurosyphilis
• Ceftriaxone 2 gm daily IM/IV for 10-14 days
• Limited data
Treponema pallidum

- Jarisch-Herxheimer Reaction
  - Start 2-4°, peak 8°, gone 24°
- Follow-up
  - RPR or VDRL (non-treponemal)
  - 6 and 12 months
  - Also 24 months if latent
Genital Herpes

Visits (in thousands)

Note: The relative standard error for genital herpes estimates range from 20% to 30%.

SOURCE: National Disease and Therapeutic Index (IMS Health)
Herpes Simplex Virus

HSV-1 – oropharyngeal
HSV-2 – genital

• Stages
  – Cutaneous infection
  – Nerve ganglia infected
  – Latent infection
  – Reactivation
  – Recurrent infection
Genital Herpes

• Primary Infection (50% asx)
  – Flu-like symptoms
  – Pustular/Ulcerative lesions * 2-3 wk
• First-episode Non-Primary (new site)
  – Mild symptoms
• Recurrent
  – Genital lesions
  – Shorter duration 8-12d
  – 50% patients with prodrome (tingling, itching)
Herpes Simplex Virus

• Diagnosis
  – Clinical appearance
  – Tissue culture
Anti-virals

Deoxyguanosine

Acyclovir
Anti-virals

• Viral thymidine kinase
  – Monophosphorylated
• Cellular enzymes
  – Triphosphorylated
• Two mechanisms
  • Competes w/ DNA polymerase
  • Terminates DNA chain
Anti-virals

• Acyclovir (PO & IV & topical)
  – Well tolerated PO
  – IV: nephrotox, neurotox

• Valacyclovir (PO)
  – Prodrug w/ better absorption (50%)

• Famciclovir (PO)
  – Prodrug of penciclovir
Genital Herpes

• Incurable, >45 million cases in U.S.
• First Episode: treat
  – Decrease viral shedding
  – Reduce symptoms
  – No effect on latency or recurrence
• 7-10 day treatment
  – Acyclovir 400 mg po TID
  – Famciclovir 250 mg TID, Valacyclovir 1 g BID
Genital Herpes

• Recurrence
  – Episodic (controversy to treat)
    • Reduce shedding 1 days
    • Speed lesion healing 1-2 days
  – Daily Suppressive
    • >6 outbreaks/year

Note: The relative standard error for genital warts estimates range from 20% to 40%.

SOURCE: National Disease and Therapeutic Index (IMS Health)
Genital Warts (HPV)

- Human Papillomavirus
- Condyloma acuminatum
  - Anogenital location
  - Hyperkeratotic
  - Millimeters to centimeters
  - 75% asymptomatic
  - Linked to cervical cancer
Human Papillomavirus

• Diagnosis
  – Physical Exam
  – Biopsy

• Treatment (10-20% spontaneous recovery)
  – Cosmetic
  – Local symptoms
  – Psychological impact
Genital Warts

• Provider applied
  – Cryotherapy (q1-2 wk)
  – Podophyllin 10-25% solution (qwk *6)
  – Acids (trichloroacetic, bichloroacetic)

• Patient applied
  – Podofilox 0.5% solution BID x 3 day cycle
  – Imiquimod 5% cream TIW
Human Papillomavirus

• Treatment response
  – Variable efficacy: 50-100%
  – NO EFFECT on cancer
HPV-associated Conditions
HPV types 16, 18, 6, 11

HPV 16, 18

- Cervical cancer 70%
- High/low grade cervical abnormalities 30-50%
- Anal, Vulvar, Vaginal, Penile
- Head and neck cancers

HPV 6, 11

- Low grade cervical abnormalities 10%
- Genital warts 90%

Clifford Cancer Epi Biomarkers Prev 2005; Gissman Proc Natl Acad Science 1983;
Kreimer Cancer Epidemiol Biomarkers Prev. 2005
Vaccine Efficacy
Gardasil (Merck)

• (2) Phase III placebo controlled efficacy studies
  – 3 doses: 0, 2, 6 months
  – Age 16 – 23
  – n = 5455 & 12,167
  – 2+ year follow-up
  – Per protocol seronegative day 1 & PCR(-) month 7
  – Measures of efficacy
    • CIN
    • AIS (adenocarcinoma \textit{in situ})
    • Genital warts
# Efficacy for Prevention of Clinical HPV Disease Due to HPV 6/11/16/18 among 16-26 year-old females

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Vaccine N</th>
<th>Vaccine Cases</th>
<th>Placebo N</th>
<th>Placebo Cases</th>
<th>Efficacy</th>
<th>(95% CI)</th>
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<tbody>
<tr>
<td>HPV 16/18 related CIN2/3 or AIS</td>
<td>8487</td>
<td>0</td>
<td>8460</td>
<td>53</td>
<td>100</td>
<td>(93,100)</td>
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<tr>
<td>HPV 6/11/16/18 related CIN</td>
<td>7858</td>
<td>4</td>
<td>7861</td>
<td>83</td>
<td>95</td>
<td>(87,99)</td>
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<tr>
<td>HPV 6/11/16/18 related genital warts</td>
<td>7897</td>
<td>1</td>
<td>7899</td>
<td>91</td>
<td>99</td>
<td>(94,100)</td>
</tr>
</tbody>
</table>

Integrated dataset; results in the per-protocol populations
Current Recommendations

• Females 11-12 years of age
  – as young as 9 years of age
• Catch-up recommended
  – 13-26 years of age
  – Ideally, before potential exposure to HPV
2nd HPV Vaccine – Cervarix (GSK)

- Bi-valent HPV vaccine (types 16 & 18)
- Omits genital warts types (unlike Gardasil)
- Proprietary adjuvant
  - Better / more durable response?
  - Head to head immunogenicity trial underway
- Approval
  - EU on 9/24/07
  - Submitted to FDA 03/07, early ’08?
Trichomonas vaginalis
Trichomoniasis and other vaginal infections in women — Initial visits to physicians’ offices: United States, 1966–2006

<table>
<thead>
<tr>
<th>Year</th>
<th>Trichomoniasis Visits (in thousands)</th>
<th>Other Vaginitis Visits (in thousands)</th>
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<tbody>
<tr>
<td>1966</td>
<td>900</td>
<td>1,800</td>
</tr>
<tr>
<td>1969</td>
<td>72</td>
<td>3,600</td>
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<td>2002</td>
<td>4,500</td>
</tr>
<tr>
<td>2005</td>
<td>2008</td>
<td>1,800</td>
</tr>
</tbody>
</table>

Note: The relative standard error for trichomoniasis estimates range from 16% to 30% and for other vaginitis estimates range from 9% to 13%.

SOURCE: National Disease and Therapeutic Index (IMS Health)
Trichomoniasis

- Females
  - 50% asymptomatic
  - Discharge, pruritis, dysuria

- Males
  - Asymptomatic
  - Self-limited
Trichomoniasis

• Treatment
  – Metronidazole 2 g po x 1
    • 500 mg BID x 7d (tolerability)
  – Tinidazole 2 g po x 1

• Follow-up
  – Repeat treatment if symptomatic
  – Treat partners (asx males)
Pelvic Inflammatory Disease

• PID includes:
  – Endometritis, salpingitis, pelvic peritonitis, tuboovarian abscess
• *N. gonorrhoeae, C. trachomatis*
  – 10-40% progression
• Anaerobes, Gram (-) rods, Streptococci
Pelvic inflammatory disease — Hospitalizations of women 15 to 44 years of age: United States, 1996–2005

Hospitalizations (in thousands)

Acute, Unspec.

Chronic

Note: The relative standard error for these estimates of the total number of acute unspecified PID cases ranges from 8% to 11%. The relative standard error for these estimates of the total number of chronic PID cases ranges from 11% to 18%. Data only available through 2005.

SOURCE: National Hospital Discharge Survey (National Center for Health Statistics, CDC)
Pelvic inflammatory disease — Initial visits to physicians’ offices by women 15 to 44 years of age: United States, 1997–2006

Note: The relative standard error for these estimates ranges from 19% to 30%.

SOURCE: National Disease and Therapeutic Index (IMS Health)
Pelvic Inflammatory Disease

↑ Ectopic pregnancy risk
  Once – 13% infertile
  Twice – 12-35% infertile
  Three or more – 50-75% infertile
PID - diagnosis

• Lower quadrant tenderness, adnexal tenderness, cervical motion tenderness

• Also:
  – Tmax 38.3°C
  – Cervical discharge
  – Elevated ESR, or CRP
  – *N. gonorrhoeae, C. trachomatis*
PID – 14 day therapy

- Parenteral
  - Cefotetan 2 g IV q12h or Cefoxitin 2 g IV q6h
    PLUS: Doxycycline 100 mg po/IV q12h
  - Clindamycin 600 mg IV q8h
    PLUS: Gentamicin 1.5 mg/kg IV q8h
- Oral Conversion (at 24h / clinical improvement)
  - Doxycycline or Clindamycin
PID – 14 day therapy

• Initial Parenteral/Oral
  
  **Ceftriaxone** 250 mg IM x 1  
  PLUS  
  **Doxycycline** 100 mg PO BID x 14 days  
  WITH OR WITHOUT  
  **Metronidazole** 500 mg PO BID x 14 days

• Re-evaluate at 72 hours
PID

- Always evaluate for STD
- TREAT PARTNERS if isolated