Gonococcal and Chlamydial Infections and Associated Syndromes
October 2012

Gonorrhea
Gonorrhea – Epidemiology

- Incidence geographically variable
  - Highest in South, Lower in West
  - Ever-increasing rates among MSM
- Peak incidence
  - Men – 20-24 years
  - Women – 15-19 years
- High rates
  - Black, Hispanic, & Native Americans
- Many Risk Factors
  - Multiple* or new sex partners
  - Lack of barrier precautions
  - Young age
  - Urban residence
  - Exchange of sex for drugs/money
  - Core population

* Defined as > 1 in a six-month period
US GC Rates by Sex – 1990-2010

GC Rates by State – US and Outlying Areas – 2010

NOTE: The total rate of GC for the US & Outlying Areas (Guam, PR, VI) was 99.6 per 100,000 population.
GC – Epidemiology

- Gram negative intracellular diplococcus known as *Neisseria gonorrhoeae*
- Attaches to non-ciliated columnar epithelial cells
- Detected by visualization (Gram’s Stain), growth (culture), or detection of bacterial products (EIA, NAATs, etc)
- Antimicrobial resistance possible – plasmid or chromosomal
  
  *Currently this is a critical problem with GC – more to follow*

GC – Transmission

- Efficiently transmitted by
  - Male to female via semen
  - Female to male urethra
  - Rectal intercourse
  - Fellatio (pharyngeal infection)
  - Perinatal transmission (mother to infant)
- GC is associated with increased transmission of & susceptibility to HIV infection
  
  *One of the more likely HIV facilitators, due to the inflammatory response to this infection*
Males – GC Urethritis

• Incubation
  • Typically 3-7 days but asymptomatic infection may occur (10%)

• Symptoms
  • Dysuria & purulent or mucopurulent discharge

• Signs
  • Purulent yellowish discharge is classic but it could be mucoid or mucopurulent

Note the erythema of the glans & foreskin secondary to the irritation due to the discharge

Females – GC Cervicitis

• Incubation
  • Unknown but S/S generally develop by 10 days

• Symptoms
  • Present in 50% of cases & they are non-specific, including vaginal discharge, dysuria, cervical bleeding

• Signs
  • Exam is highly variable (normal to frank purulent discharge)

Classic GC mucopurulent cervical discharge – pathognomonic – but not commonly seen
Gonococcal Pharyngitis

- Incubation
  - Unknown
- Symptoms
  - Rarely present but may include non-exudative pharyngitis, cervical adenitis

* May be only site of infection & is more difficult to eradicate with Rx – mounting evidence that treating pharyngeal GC is increasingly challenging

October 2012 Issue of Rolling Stone has article on GC

Oral Sex Is No Longer Safe Sex

October 24, 2012

“The list of things we’ve had to learn to live without – polar ice caps, Bengal tigers, jobs that pay a living wage, the White Stripes – grows longer every day. But now things are really getting out of hand: According to the New England Journal of Medicine…”

Read more
http://www.rollingstone.com/search?q=gonorrhea#ixzz2A8WuiH96
GC – Other Sites
Complications and Other Syndromes

• PID
• Epididymitis
• Anorectal disease
• Genital abscesses
  • Classically Bartholin’s or Skene’s Glands
• Eye disease
• Disseminated Gonococcal Infection (DGI)

Bartholin’s Gland Abscess

• This large abscess is intact – it could rupture spontaneously or would likely require an I & D
  • Some use a Word Catheter as a drain after performing an I & D
  • A GC culture should be done
Bartholin’s Gland Abscess

- This abscess is draining purulent discharge – which should be cultured for GC
- Some abscesses rupture spontaneously & others require I & D

Gonococcal Ophthalmia – Adult

- Incubation
  - 3-19 days – often there could be a Hx of urethral Sx (males) within the past 1-3 weeks; often transmitted by auto-inoculation

- Symptoms
  - Profuse purulent discharge with severe inflammation

- Signs
  - Discharge, injection of conjunctiva, lid swelling, & occasionally periorbital erythema
  - Characterized by rapid onset; preseptal cellulitis & corneal involvement do occur – though quite rare
Disseminated Gonococcal Infection

- DGI is usually related to 0.5-3% untreated mucosal GC
- DGI is a Dermatitis-Arthritis Syndrome
  - Tender, necrotic pustules (variable)
  - Asymmetrical Arthritis
  - Tenosynovitis
- Risk of Endocarditis or meningitis exists

Joint Involvement in DGI

- A hot, swollen, painful, & exquisitely tender joint is often the 1st indication of DGI
  - It is important that a case that presents without Hx of trauma or other known cause should be tested for GC (culture)
  - Emergency Department &/or Orthopedic surgeons are often the providers who see this patient first & unfortunately they do not always collect a GC culture
DGI – Skin Lesions

DGI – Tenosynovitis
GC – Methods of Detection

- Gram’s Stain
  - Sensitivity – 95% male urethral smear
  - Sensitivity – 50% cervical smear
- Culture (Gold Standard) – allows for susceptibility testing
- Non-Amplified Assays
  - DNA probe – GenProbe™
  - EIA
- Amplification Assays (NAATs)
  - Polymerase chain reaction (PCR) – Roche Amplicor™ Transcription-mediated amplification (TMA) – Gen-Probe Aptima®
  - Strand displacement amplification (SDA) – Becton-Dickinson BD ProbeTec ET™

GC – Gram Stain of Male Urethral Discharge

- Note the intracellular Gram Negative diplococci
- Also, note the numerous pmns
GC – Gram Stain of Cervical Discharge

- This is a particularly clear stain showing Gram Negative intracellular diplococci (also some extracellular)
  - Note how the cervical stain has many organisms & other cells (e.g., an epithelial cell) as compared to the male urethra
  - A cervical Gram Stain is not sensitive, though it is specific

GC/CT – and – HIV

- Increased risk of PID/acute salpingitis
- Increased risk of tubo-ovarian abscess
- PID presents with lower WBC count
- Immunosuppressed HIV-infected women with PID – inpatient Rx with optimal anaerobic coverage
- Severely immunocompromised patients are at risk for
  - GC proctitis
  - Rectal abscess
  - Sepsis
Antimicrobial Susceptibility of *N. gonorrhoeae*

- Fluoroquinolone resistance is widely disseminated throughout the US & the world
- Approximately 25% of isolates are resistant to penicillin or tetracycline or both
- Approximately 0.5% of isolates show decreased susceptibility to azithromycin
- Sporadic cases of decreased susceptibility to ceftriaxone & cefixime have been reported recently

Gonococcal Isolate Surveillance Project (GISP) – % of *N gonorrhoeae* Isolates with Resistance or Intermediate Resistance to Ciprofloxacin – 1990-2010

NOTE: Resistant isolates have ciprofloxacin minimum inhibitory concentrations (MICs) >1 µg/ml; those with intermediate resistance have ciprofloxacin MICs of 0.125–0.5 µg/ml; susceptibility to ciprofloxacin was first measured in GISP in 1990
GISP Data – Proportion of Isolates with Elevated Cefixime MICs (≥ 0.25 μg/ml) – US – 2000-10

- Percentage of isolates: 1.4% (n = 77)
- Trend: *p < 0.05

GISP – Proportion of Isolates with Elevated Ceftriaxone MICs (≥ 0.125 μg/ml) – US – 2000-10

- Percentage of isolates: 0.3% (n = 19)
- Trend: *p < 0.05
inserted new slide
fve0, 8/19/2011
Updated CDC Recommendations
Issued August 11, 2012

For uncomplicated GC infections of the cervix, urethra, & rectum

<table>
<thead>
<tr>
<th>Recommended regimen</th>
<th>Alternative regimen If Ceftriaxone unavailable</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ceftriaxone 250 mg IM x one +</td>
<td>• Cefixime 400 mg PO x one +</td>
</tr>
<tr>
<td>• Azithromycin 1 gm PO x one OR Doxycycline 100 mg PO BID x 7 days *</td>
<td>• Azithromycin 1 gm PO x one OR Doxycycline 100 mg PO BID x 7 days * +</td>
</tr>
<tr>
<td></td>
<td>➢ Test-of-cure (TOC) in 1 week *</td>
</tr>
</tbody>
</table>

* Because of the high prevalence of Tetracycline resistance among GISP isolates, particularly those with elevated Cefixime MICs, use of Azithromycin as 2nd antimicrobial is preferred.

* Every effort should be made to use gonorrhea culture for TOC.

If Rx Failure is suspected/confirmed – contact an ID Specialist & notify the DoH
Updated CDC Recommendations
Issued August 11, 2012

For uncomplicated GC infections of the cervix, urethra, & rectum

If Severe Cephalosporin Allergy

- Azithromycin 2 gm PO x one
  + 
  ✓ TOC in 1 week

✓ Every effort should be made to use gonorrhea culture for TOC.

If Rx Failure is suspected/confirmed – contact an ID Specialist & notify the DoH

For uncomplicated GC infections of the pharynx

Recommended regimen | Alternative regimen
---------------------|---------------------
- Ceftriaxone 250 mg IM x one
  +
- Azithromycin 1 gm PO x one OR
  Doxycycline 100 mg PO BID x 7 days

If Severe Cephalosporin Allergy

- Azithromycin 2 gm PO x one
  +
  ✓ TOC in 1 week

✓ Because of the high prevalence of Tetracycline resistance among GISP isolates, particularly those with elevated Cefixime MICs, use of Azithromycin as 2nd antimicrobial is preferred.

If Rx Failure is suspected/confirmed – contact an ID Specialist & notify the DoH
GC Treatment – CDC Guidelines

- Still stress single dose, dispensed therapy
- Treat all patients with GC for co-existing/incubating CT infection regardless of CT test result
- Resistance on the rise – use increased dose of Ceftriaxone, i.e., the full 250 mg dose (Use the “Intern Rule”: 250 mg comes in the vial – use the whole vial!)
  - Oral cephalosporin is not an equivalent choice anymore
- Azithromycin another alternative agent for Rx

Special Considerations – Pregnancy

- Treat with recommended Cephalosporin-based combination therapy
- If Cephalosporin is not tolerated, treat with Azithromycin 2 g PO x 1
  - A TOC should be performed 1 week after treatment
- Pregnant women should not be treated with Quinolones or Tetracyclines; Spectinomycin is not commercially available
If Penicillin-Allergic *

- Azithromycin 2 g orally
  - Plus TOC in 1 week

* Desensitization is impractical in most settings

Treatment Follow-Up – Test of Cure

- A TOC is **not** considered necessary (nor recommended) as long as the CDC recommended Cephalosporin-based regimen is administered
- **A TOC is recommended if an alternative regimen is administered**
  - If symptoms persist, perform culture for *N gonorrhoeae*
    - Any gonococci isolated should be tested for antimicrobial susceptibility at site of exposure
  - Repeat testing in 3 months
GC Rx – DGI

Ceftriaxone 1g IV/IM q 24 hours – until improved x 2 d
~ or ~
Cefotaxime 1g IV q 8 hours
~ or ~
Ceftizoxime 1g IV q 8 hours

Followed by
Cefixime 400 mg PO BID – to finish 7 days
~ plus ~
Azithromycin 1 gm PO x 1
~ or ~
Doxycycline 100 mg PO BID x 7

GC – Test-of-Cure vs Re-Screening

• Test-of-Cure *
  • As noted – any time a non-recommended GC Rx is given, or if patient does not recover

• Re-screening *
  • 3-4 months post-Rx – or when they next present for care within next 12 months
  • Population statistics show that ~ 35% of persons Rx’d for GC will have infection again within 3-4 months
    • Thus re-screening might detect these re-infected persons

* If using NAAT – not before 3 weeks post-Rx
Chlamydia

Chlamydia trachomatis Incidence

- Estimated 3 million cases in US annually
- Most frequently reported STD in US
- Reported rates 3 times higher in females than in males
- Rule of thumb – 3 times more Chlamydia (CT) than GC in most communities
CT US Rates by Sex – 1990-2012

Rate (per 100,000 population)

- Men
- Women
- Total

Year

Rate
0 125 250 375 500 625 750

NOTE:
As of January 2000, all 50 states & Wash DC require the CT reporting CT

CT Rates by State – US and Outlying Areas – 2010

Rate per 100,000 population
- <300.0 (n = 10)
- 300.1–400.0 (n = 18)
- >400.0 (n = 26)

NOTE:
The total rate of CT – US & Outlying Areas (Guam, PR, VI) – was 422.6 per 100,000 population
US CT Rates – By Age and Sex – 2010

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–19</td>
<td>774.3</td>
<td>3,378.2</td>
</tr>
<tr>
<td>20–24</td>
<td>1,187.0</td>
<td>3,407.9</td>
</tr>
<tr>
<td>25–29</td>
<td>598.0</td>
<td></td>
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<tr>
<td>30–34</td>
<td>309.0</td>
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<tr>
<td>35–39</td>
<td>153.2</td>
<td></td>
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<tr>
<td>40–44</td>
<td>91.3</td>
<td></td>
</tr>
<tr>
<td>45–54</td>
<td>39.3</td>
<td></td>
</tr>
<tr>
<td>55–64</td>
<td>10.9</td>
<td></td>
</tr>
<tr>
<td>65+</td>
<td>2.8</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>233.7</td>
<td>610.6</td>
</tr>
</tbody>
</table>

US CT Rates – By Race/Ethnicity – 2001-10

- American Indians/Alaska Natives
- Asians/Pacific Islanders
- Blacks
- Hispanics
- Whites

Prevalence is an important contributing factor for disproportionately high rates of STDs.
US CT Cases – Reporting Source and Sex – 2001-10

- Non-STD Clinic, Men
- Non-STD Clinic, Women
- STD Clinic, Men
- STD Clinic, Women

CT – Risk Factors

- Adolescence
- New or multiple* sex partners
- History of STD infection
- Presence of another STD
- Oral contraceptive user
- Lack of barrier contraception

* Defined as > 2 in a 6-month period
CT – Transmission

- Transmission is sexual ~ or ~ vertical
- Highly transmissible
- Incubation period 7-21 days
- Significant asymptomatic reservoir exists in the population
  - Prevalence is an important factor that drives this infection
- Re-infection is common

* Defined as > 2 in a 6-month period

CT – Microbiology

- Obligatory intracellular bacteria
- Infect columnar epithelial cells
- Survive by replication that results in the death of the cell
- Takes on two forms in its life cycle
  - Elementary body (EB)
  - Reticulate body (RB)
Chlamydiaceae Family
Species that Cause Disease in Humans

<table>
<thead>
<tr>
<th>Species (genus)</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C. trachomatis</em></td>
<td>• Conjunctivitis,</td>
</tr>
<tr>
<td>2 biovars, non-LGV</td>
<td>• Trachoma,</td>
</tr>
<tr>
<td>LGV</td>
<td>• Sexual Transmission: NGU, MPC, PID,</td>
</tr>
<tr>
<td></td>
<td>• Infant pneumonia</td>
</tr>
<tr>
<td></td>
<td>• LGV</td>
</tr>
<tr>
<td><em>C. pneumoniae</em></td>
<td>• Pharyngitis</td>
</tr>
<tr>
<td></td>
<td>• Bronchitis</td>
</tr>
<tr>
<td></td>
<td>• Pneumonia</td>
</tr>
<tr>
<td><em>C. psittaci</em></td>
<td>• Psittacosis</td>
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</tbody>
</table>
Clinical Syndromes Caused by *C. trachomatis*

<table>
<thead>
<tr>
<th></th>
<th>Local Infection</th>
<th>Complications</th>
<th>Sequelae</th>
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<tbody>
<tr>
<td><strong>Males</strong></td>
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<td></td>
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<tr>
<td></td>
<td>Conjunctivitis</td>
<td>Reiter’s Syndrome</td>
<td>Chronic Arthritis</td>
</tr>
<tr>
<td></td>
<td>Urethritis</td>
<td>Epididymitis</td>
<td>(rare)</td>
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<tr>
<td></td>
<td>Proctitis</td>
<td>Endometritis</td>
<td></td>
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<tr>
<td></td>
<td>Prostatitis (?)</td>
<td>Salpingitis</td>
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<td></td>
<td></td>
<td>Perihepatitis</td>
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<td>Reiter’s Syndrome</td>
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<td>Ectopic Pregnancy</td>
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<td>Infertility</td>
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<td>Chronic Pelvic Pain</td>
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<td>Chronic Arthritis</td>
<td>(rare)</td>
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<tr>
<td><strong>Females</strong></td>
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<tr>
<td></td>
<td>Conjunctivitis</td>
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<td>Urethritis</td>
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<td>Cervicitis</td>
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<td>(rare)</td>
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<tr>
<td><strong>Infants</strong></td>
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<td></td>
<td>Conjunctivitis</td>
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<td>Pneumonitis</td>
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<td>Pharyngitis</td>
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<td>Rhinitis</td>
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<td></td>
<td>Chronic Lung</td>
<td>Rare (if any)</td>
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<td></td>
<td></td>
<td>Disease (?)</td>
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CT – Urethritis

**Most Common Manifestation in Males**

- **Incubation**
  - Unknown – 5-10 days in symptomatic, but > 50% asymptomatic

- **Symptoms**
  - Urethral discharge, dysuria, meatal erythema

- **Signs**
  - None or clear, mucoid, or mucopurulent discharge
CT – Cervicitis

- Incubation
  - Unknown – with > 80% asymptomatic
- Symptoms
  - Non-specific – vaginal discharge or spotting, dyspareunia
- Signs
  - 30-50% with signs of MPC, including endocervical discharge, edematous cervical ectopy, cervical friability

CT – Cervical Infection

- A CT-infected cervix can look entirely normal – healthy, pink, with clear mucus
- Friability can be seen with CT
  - Defined in different ways, but usually as 1+, 2+, or 3+
  - Here, it is 3+
CT – Other Manifestations

- Females
  - Urethritis
    - Usually asymptomatic, frequently with cervicitis, may cause “sterile” pyuria
  - Pelvic Inflammatory Disease
  - Perihepatitis (Fitz-Hugh-Curtis)
    - May be due to GC (30%) or CT (70%)
    - Presents like PID plus RUQ pain/nausea/fever
- Males
  - Epididymitis
    - 70% of STD-associated epididymitis is due to CT

CT – Other Manifestations

- Conjunctivitis
  - Auto-inoculation
  - Follicular conjunctivitis
  - Rarely purulent in adults
- Proctitis/Proctocolitis
- LGV (*Lymphogranuloma venereum*)
  - Caused by serovars L1-L3
  - Rare in the US
  - Presents with tender adenopathy that may suppurate & sometimes a painless ulcer (often not detected)
  - Recent outbreaks in MSM – presents like proctitis
LGV – Lymphadenopathy

These buboes have started to drain spontaneously

CT – Other Manifestations

• Reiter’s Syndrome
  • More common in males
  • Syndrome of conjunctivitis, urethritis, oligoarticular arthritis, & spondyloarthritis
  • May occur 3-6 weeks after infection
  • Associated with HLA-B27
CT – Methods of Detection

• Culture
• Non-Amplified Assays
  • Direct Fluorescent Antibody (DFA)
  • ELISA/EIA
  • DNA probe – GenProbe™
• Amplification Assays (NAATs)
  • Becton Dickinson BDProbeTec™
  • Gen-Probe AmpCT™, Aptima™
  • Roche AmpliCor™
• Serology

CT – Methods of Detection – Culture

• Historically the “gold standard”
• Variable sensitivity – 50-80%
• Depending on the laboratory – culture might be the only way to test for CT in non-genitourinary sites (e.g., eye, rectum)
• High specificity
• Used in legal investigations
• Not suitable for widespread screening
CT – Methods of Detection – **Nucleic Acid Amplification Tests**

- NAATs amplify & detect organism-specific genomic or plasmid DNA or RNA
- FDA cleared for urethral swabs from men/women, urine from men/women, and cervical & vaginal swabs
- Significantly more sensitive than other tests
- Downside is cost, possible false positives, no approval for non-genital sites
  - However, as noted – the FDA has approved NAATs for non-genitourinary sites, but specific lab competencies must be fulfilled

CT – Methods of Detection – **Serology**

- Rarely used for uncomplicated infections
  - The results difficult to interpret
- Criteria used in LGV diagnosis
  - Complement fixation titers > 1:64 suggestive
  - Complement fixation titers > 1:256 diagnostic
  - Complement fixation titers < 1:32 rule out
### Laboratory Diagnosis of CT

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture</td>
<td>52-92</td>
<td>99-100</td>
</tr>
<tr>
<td>Antigen detection ~ or ~ Nucleic Acid Hybrid</td>
<td>50-70</td>
<td>95-99</td>
</tr>
<tr>
<td>PCR (NAAT)</td>
<td>65-95</td>
<td>&gt; 99</td>
</tr>
<tr>
<td>LCR (NAAT)</td>
<td>85-95</td>
<td>&gt; 99</td>
</tr>
<tr>
<td>Serology</td>
<td>85-100</td>
<td>&lt; 65</td>
</tr>
</tbody>
</table>

### Rx of Uncomplicated CT Infection

- **Standard Rx**
  - Azithromycin 1 gm PO in a single dose
  - *or*
  - Doxycycline 100 mg PO BID for 7 days

- **Alternative Agents**
  - Erythromycin 500 mg PO QID for 7 days
  - Ofloxacin 300 mg PO BID for 7 days
  - Levofloxacin 500 mg PO QD for 7 days
Rx of CT Infection in Pregnancy

- Standard Rx
  - Azithromycin 1 gm PO as a single dose
    - or -
  - Amoxicillin 500mg TID PO for 7 days
- Alternative Agents
  - Erythromycin base 500 mg PO QID for 7 days
  - Erythromycin base 250 mg PO QID for 14 days
  - Erythromycin ethylsuccinate 800 mg PO QID for 7 days
  - Erythromycin ethylsuccinate 400 mg PO QID for 14 days

CT – Test-of-Cure vs Re-Screening

- Test-of-Cure *
  - Pregnancy
  - Therapeutic compliance is in question
- Re-screening *
  - 3-4 months post-Rx – or when they next present for care within next 12 months
  - Population statistics show that ~ 35% of persons Rx’d for CT will have infection again within 3-4 months
    - Thus re-screening might detect these re-infected persons

* If using NAAT – not before 3 weeks post-Rx
Rx of Lymphogranuloma Venereum (LGV)

• Recommended regimen
  Doxycycline 100 mg PO BID for 21 days

• Alternative regimen
  Erythromycin base 500 mg PO QID for 21 days
  ? Azithromycin 1 gm weekly x 3 doses

GC/CT – and – HIV

• Increased risk of PID/acute salpingitis
• Increased risk of tubo-ovarian abscess
• PID presents with lower WBC count
• Immunosuppressed HIV-infected women with PID – inpatient Rx with optimal anaerobic coverage
• Severely immunocompromised patients are at risk for
  • GC proctitis
  • Rectal abscess
  • Sepsis
Why Screen for Chlamydia?

- Screening can reduce the incidence of PID by more than 50%
- Most infections are asymptomatic
- Screening decreases the prevalence of infection in the population
- Screening reduces the transmission of disease

CT – Screening Recommendations
Non-pregnant Women

- Sexually active women age ≤ 25 years should be screened annually *(HEDIS recommendations ≤ 24 yr)*
- Women >25 years old should be screened if risk factors are present
- Repeat screening of women 3-4 months post-Rx for CT infection, especially adolescents
- Repeat screening of all women treated for CT when they next present for care
**Screening Recommendations**

**Pregnant Women**

- Screen all pregnant women at the first prenatal visit
- Pregnant women aged < 25 years & those at increased risk for CT should be screened again in the 3rd trimester

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**Partner Management**

- Sex partners should be evaluated, tested, & treated if they had sexual contact with the patient during the 60 days preceding the onset of symptoms or diagnosis of GC or CT
- The most recent sex partner should be evaluated & treated even if the time of the last sexual contact was > 60 days before symptom onset or diagnosis
- **DoH Partner Services** – Disease Investigation Specialists (DIS) – can be extremely helpful
  - To find & bring in patients that have been lost to follow-up
  - To find partner(s) & get them into care for screening & Rx
Expedited Partner Therapy for CT and GC

- Delivery of antibiotic therapy by index (original) patient – either by prescription or medication
- Male partners – inform female partners about still seeking care for assessment of possible PID
- Partners of patients with GC should receive CT co-Rx
- Not routinely recommended for MSM due to co- morbidities (other STDs, HIV)
- Recommended by CDC * since 2006 – what about your state?


EPT Studies

- Schillinger et al. (STD (2003), 30)
  - 20% reduction in CT re-infection among women (P = 0.102)
- Golden et al. (NEJM (2005), 352)
  - 73% reduction in GC re-infection among men & women (P < 0.01)
  - 17% reduction in CT re-infection (P = 0.17)
- Kissinger et al. (Clin Inf Dis (2005), 41)
  - 46% reduction in GC &/or CT infection among men with urethritis (P<0.001)
Patient Education and Counseling

- Nature of infection
  - Asymptomatic
  - Risks of complications

- Transmission issues
  - Increased risk of HIV acquisition
  - Need to have partner treated
  - Need to complete therapy before sexual activity

- Risk Reduction Strategies
  - Safer sex, mutual monogamy with an uninfected partner, abstinence
  - Develop individualized plans – does patient believe that s/he is at risk/vulnerable?
  - Moreover – does the patient see a need to change behaviors?
  - Need for repeat screening

DoH Reporting – Which STDs?

- GC & CT are reportable STD in all states & jurisdictions (also syphilis)
- Report cases to the local or state STD program
- The Health Department uses reported info to assure Rx of the index case & contacting sexual partners for screening & treatment (for the health of the public)
  - Partner Services
Females and STDs

Syndromes

STDs & Women

- Disproportionately affect women
- More easily infected – biological bias for infection acquisition – compared to males (consider the anatomy)
- More likely to develop complications
- Perinatal & neonatal complications
- Teenagers biologically most vulnerable – due to “immature” cervix (i.e., presence of ectopy)
CDC’s Strategic Common Element in Maternal Child Health

STDs

- HIV Transmission
- Adverse Pregnancy Outcomes
- Impaired Fertility
- Reproductive Tract Neoplasias

Female STD Syndromes

Cervicitis
Cervicitis

• Common STD syndrome
  • S & S previously discussed
• Not as well-studied as male counterpart – urethritis
  • **Significantly under-diagnosed**
    • This is associated with potential complications & long-term sequelae
• Can lead to PID/infertility

Cervicitis – Etiology

• Known Causes
  • GC 5-10%
  • CT 30-40%
  • HSV
• Unknown Causes
  • 50-70%
  • **Mycoplasmas** (increasingly implicated – see STD Rx Guidelines for discussion & references), Streptococci, or simply inflammation
Cervicitis – Some Specifics re Chlamydia

- Women infected with CT more than once are at higher risk of developing PID
- Reinfection rates have a 3 times greater prevalence than from primary screening
- Recommendation to re-screen all women with CT (& GC) – as previously noted – 3-4 months after Rx
  - Based on population-based statistics, ~35% of those with CT &/or GC become re-infected within 3-4 months
- Re-screening is a critical tool for infertility prevention, particularly in young women

Female STD Syndromes

Pelvic Inflammatory Disease
PID’s Pathway of Ascendant Infection

- Peritonitis
- Salpingitis /oophoritis /tubo-ovarian abscess
- Endometritis
- Cervicitis

Pelvic Inflammatory Disease

- Acute First Episode
  - Considered to be due to STD etiology (GC or CT) unless recent surgery, abortion (spontaneous or therapeutic), or instrumentation
- Acute Recurrent
- Chronic
Fallopian Tube Tissue – Normal and Infected

Sequelae of Untreated GC & CT in Women

Untreated Chlamydia
20-40%

Untreated Gonorrhea
10-40%

Infertility
20%

Ectopic Pregnancy
9%

Recurrent PID
23%

Chronic Pelvic Pain
18%
PID – Classification

- Subclinical silent 60%
- Mild to moderate symptoms 36%
- Severe symptoms 4%
- Overt 40%

PID – Etiology

STD Etiology
- *Neisseria gonorrhea*
- *Chlamydia trachomatis*
- *Mycoplasma hominis* (not considered to be true STD)
- ? *Mycoplasma genitalium*?

Opportunistic Contributors
- Group B Streptococcus
- Peptostreptococci
- *Escherichia coli*
- *Bacteroides* – several different Sp
- *Clostridium* Sp
PID – **Symptoms**

- Abdominal pain – may be described or identified as “cramps” or “worse than usual” menstrual “cramps”
- May be abnormal vaginal discharge, including spotting
- Sometimes women c/o vague urinary symptoms (lower abdominal pain that changes before/during urination)
- Dyspareunia (most likely due to moving the cervix during intercourse)

PID – **Clinical Criteria**

- Lower abdominal tenderness – during abdominal exam
- Tenderness – during bimanual exam
  - Uterus, tubes, &/or ovaries
- Possibly cervical motion tenderness (CMT)
- Possibly, mucopurulent cervical discharge
  - Elevated temperature (> 101 F), leukocytosis, elevated Sed Rate or C-reactive protein are not necessary for the clinical diagnosis – nor is laboratory documentation of GC &/or Chlamydia
**PID – Minimum Clinical Criteria**

- Uterine &/or adnexal tenderness *or* cervical motion tenderness (CMT) – often called a Positive Chandelier Sign; CMT is
  - Patient has pain when the cervix is moved during bimanual examination
- Absence of other causes of pelvic inflammation, specifically
  - Ectopic or other abnormal pregnancy, appendicitis, ovarian cyst – *be sure to R/O pregnancy!*

**PID – Differential Diagnosis**

- Mittelschmerz (ovulation related)
- Ovarian Cyst
- Acute Appendicitis
- Ectopic Pregnancy
- Ruptured, Bleeding, Torsion of Ovary
- Pelvic Endometriosis
- Inflammatory Bowel Disease (mesenteric lymphadenitis, regional ileitis, enteritis)
- Urinary Tract Infection
- Renal/Ureteral Stones

*These are 3 conditions are life-threatening – be sure to R/O (testing/imaging)*
**Outpatient PID Treatment Regimens**

- Ceftriaxone 250 mg IM in a single dose
  - or -
- Cefoxitin 2g IM in a single dose & Probenecid 1gm PO
  - plus -
- Doxycycline 100 mg PO BID for 14 days
  - with or without -
- Metronidazole 500 mg PO BID x 14 days

**No need to remove IUD unless recently inserted**

*Based on 2010 CDC Rx Guidelines*

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**Outpatient PID Rx Regimen Alternatives**

- Azithromycin 2 gm PO x 1 dose
  - plus -
- Levofloxacin* 500 mg PO QD x 14 days
  - or -
- Levofloxacin 500* mg PO QD x 14 days
  - with or without -
- Metronidazole 500 mg PO BID x 14 days

- If risk of GC low or if rates of quinolone resistance in GC is low

*Based on 2010 CDC Rx Guidelines*
PID – Pregnancy – This is Rare

- PID in pregnancy is rare because of local cervical immunity during pregnancy, but it does happen occasionally
  - Should be diagnosed with help of obstetrical provider (including probably ultra-sound, blood work, others)
- Pregnancy & PID – from to CDC Guidelines
  - “Because of the high risk for maternal morbidity and preterm delivery, pregnant women who have suspected PID should be hospitalized and treated with parenteral antibiotics.” (p 67)

Males and STDs

Syndromes
Urethritis – Gonococcal

- Bacterial, curable
  - *Except now increasingly challenging to cure* (as noted)
- Common male STD syndrome
  - S & S previously discussed
- Responsible for about 10-15% of all urethritis, depending on location
  - Check the epidemiology of the geographical area in which you work

Urethritis – Non-Gonococcal

- Very Common STD syndrome
  - Much more common than GC Urethritis
- NGU is typically bacterial – so curable
  - Though there is known viral cause as well as unknown causes – see next slide
- Incidence is stable – however, since it is not reportable – tracking this is through research & sentinel screening sites
  - There is one exception – if CT test is positive – then the infection (not the syndrome) gets reported
NGU – Etiology

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Cause</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>~ 35%</td>
<td>Chlamydia trachomatis</td>
<td>Males &lt; 35 years</td>
</tr>
<tr>
<td>~ 30%</td>
<td>Ureaplasma urealyticum (a Mycoplasma)</td>
<td>In all males</td>
</tr>
<tr>
<td>Unknown</td>
<td>Mycoplasma genitalium</td>
<td>Likely a major etiologic organism</td>
</tr>
<tr>
<td>Up to 10%</td>
<td>Herpes simplex Virus (HSV)</td>
<td>In some studies</td>
</tr>
<tr>
<td>&lt; 5%</td>
<td>&lt; 5% Trichomonas – Rare</td>
<td>Trich does not stay in urethra – so probably less (&lt;2%)</td>
</tr>
<tr>
<td>Up to 10%</td>
<td>Inflammation from unknown causes</td>
<td></td>
</tr>
</tbody>
</table>

NGU – Signs

- Urethral erythema (seen here)
- Urethral discharge
  - Mucoid (seen here)
  - Purulent (next slide)
- Discharge is spontaneous or may only be seen with stripping
- Often no clinical signs
NGU – Chlamydia
Urethral Discharge – If has Any

- Purulent Discharge
- Eryhematous Meatus

GC Urethritis ~ and ~ NGU – Symptoms

- Urethral Sx can vary from mild to severe – NGU is typically milder while GC is more symptomatic
  - Burning – can be mild to severe (GC likely more so)
  - Irritation – sometimes described as “itching” or “tingling” (vague Sx are usually associated with NGU)
- GC Sx can appear within 48 hours of infection – NGU causes usually appear after several days to ~ 2 weeks
- Urethral discharge by patient history
- **NGU often has no Sx**
  - This is another reason to conduct routine screening
NGU – Diagnostic Criteria

Must Meet criteria either 1 or 2 & 3

1. Laboratory evidence of > 4 pmns /oil immersion field (1000X) in a urethral Gram Stain
2. Clinical sign of abnormal urethral discharge with erythema on examination
3. Exclusion of gonorrhea (i.e., Gram negative intracellular diplococci)

Male STD Syndromes

Epididymitis
Epididymitis – Recall the Male Anatomy

- Closed & protective
  - Deeper structures are protected – unlike the “open system” of the female reproductive system
  - Epididymitis is the male counterpoint of PID – however – it is much less common due to the male anatomy as it is more “closed”

Epididymitis

- Complication of GC, Ct, or any other NGU
- May result in infertility
- **Less common than PID – but a counterpart for the male** (as noted)
- For men < 35 years – etiology is STD unless proven otherwise
Epididymitis – Signs and Symptoms

**Signs**
- Tenderness (can be exquisite) & swelling (subtle to severe) of anterior/posterior lobe of epididymis – in one or both epididymides
  - With severe swelling – it can be difficult to distinguish scrotal contents
- May have clinical/laboratory evidence of urethritis
- Need to rule out other causes, especially testicular torsion

**Symptoms**
- Pain in scrotum – mild to severe – usually described by patient as pain in testicle(s)
- Scrotal swelling
- Recent history of urethral burning/discharge
  - Not always a symptom

Epididymitis
Epididymitis – Diagnostic Criteria

Must meet criteria 1 & either 2 or 3

1. Clinical Sx of pain or Sign of tenderness of at least one epididymis (but could be bilateral)
2. Acute epididymitis in heterosexual men < 35 yr of age is usually
   • Frequently associated with urethritis (> 4 pmns/oil immersion field (1000X) on Gram-stained urethral smear
   • Absence of underlying genitourinary pathology
   • Absence of Gram-negative rods on Gram-stained urine

Continued...

Epididymitis – Clinical Criteria (continued)

3. Acute epididymitis in heterosexual men > 35 years usually not associated with GC &/or CT
   • Infrequently associated with urethritis
   • Commonly associated with underlying genitourinary pathology (including prostate enlargement, “plumbing problems”)
   • Presence of Gram-negative rods on Gram-stained urine (epididymitis in men > 35 is often due to normal flora organisms)
   • Evaluation for underlying urinary trace disease/problem may be indicated
Epididymitis – **Treatment**

- Etiology most likely STD
  
  Ceftriaxone 250 mg IM
  
  ~ **plus** ~
  
  Doxycycline 100 mg PO BID x 10 days

- Etiology most likely enteric or Ceftriaxone-allergic patients (*& with negative GC test results*)
  
  Ofloxacin 300 BID x 10 days
  
  ~ **or** ~
  
  Levofloxacin 500 mg QD x 10 days