CDC 2015 STD Treatment Guidelines: Update for IHS Providers

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Disclosure Information

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I have no financial relationships to disclose
Overview

- CDC Treatment Guidelines development
- STD Management Highlights
  - Diagnostics for GC/CT
  - Gonorrhea treatment options
  - Antibiotic resistance: Gonorrhea
  - Chlamydia Treatment
  - Urethritis: *Mycoplasma genitalium*
  - Syphilis: Late latent dosing
  - HSV: Diagnostics
  - Vaginitis: Trichomonas
Evidence-based on principal outcomes of STD therapy
Recommended regimens preferred over alternative regimens
Alphabetized unless there is a priority of choice
Reviewed April 2013; available June 2015
Pocket guides, teaching slides, charts
http://www.cdc.gov/std/tg2015/
Diagnostics for GC/CT
Swabs vs. Urine for Women

CDC RECOMMENDS:
• Nucleic acid amplification tests are the recommended method
• A self- or clinician-collected vaginal swab is the recommended sample type.
• A first catch urine specimen is acceptable but might detect 10% fewer infections when compared with vaginal and endocervical swab samples.

CDC. MMWR 2014 / 63(RR02);1-19
Recommendations for the Laboratory-Based Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* — 2014

**Major conclusions**

NAATs recommended for detection of genital tract infections in men and women – with and without symptoms

**Optimal specimen types are:**
- First catch **urine** for men
- Self collected **vaginal** swabs from women

NAATs **recommended for**: detection of **rectal** and **oropharyngeal** infections
- not FDA-approved for rectal or pharyngeal specimens but remain the preferred testing method over culture
Case Scenario

22 year old female
Asymptomatic, no prior STDs
STD Screening
NAAT testing for GC/CT

GC positive
CT negative
Audience Poll
What is recommended regimen to treat Gonorrhea?

1. Cefixime 400 mg PO + azithromycin 1 g PO
2. Azithromycin 2 gm PO
3. Ceftriaxone 250 mg IM + azithromycin 1 g PO
4. Ceftriaxone 250 mg IM + doxycycline 100 BID x 7d
Gonorrhea Dual Therapy
Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose

PLUS*

Azithromycin 1 g orally

or

Doxycycline 100 mg BID x 7 days*

* Regardless of CT test result

New in 2015: Move doxycycline from recommended to alternative drug for co-treatment due to high level of tetracycline resistance (23.7% in 2013) among GC isolates

CDC 2015 STD Treatment Guidelines
What does dual therapy mean?

• Ceftriaxone and azithromycin administered on the same day
• Preferably simultaneously and under direct observation
Gonorrhea Treatment Alternatives
Anogenital Infections

ALTERNATIVE CEPHALOSPORINS:

- Cefixime 400 mg orally once

**PLUS**

- Dual treatment with azithromycin 1 g plus doxycycline 100 mg BID x 7 days, regardless of CT

IN CASE OF SEVERE ALLERGY:

- Azithromycin 2 g orally once

2015 Revisions:
Gentamicin 240 mg IM or 5mg/kg IM + azithromycin 2g PO
OR
Gemifloxacin 320 mg orally + azithromycin 2g PO

CDC 2015 STD Treatment Guidelines
Alternative Urogenital GC Regimens

- NIH-sponsored non-comparative randomized trial in adults with urethral or cervical GC
  - gentamicin (240mg IM) + azithromycin 2 gm PO, or
  - gemifloxacin 320 mg PO + azithromycin 2 gm PO

Per-protocol efficacy:
- gent + AZ=100% (202/202)
- gemi + AZ=99.5% (198/199)

- Nausea was common (27% and 37%), vomiting also occurred (7% and 5%), additional 3-7% vomited <1hr after administration

Kirkcaldy et al. CID 2014.
Pharyngeal gonorrhea should **not** be treated with oral cephalosporins

- Cefixime 400mg PO provides lower bactericidal levels compared to ceftriaxone 250mg IM
- Time above the MIC is not as prolonged
- Efficacy is reduced

- **Test of Cure (TOC)** for patients with pharyngeal GC treated with an alternative regimen
  - 14 days after tx, culture or NAAT

*CDC 2015 STD Treatment Guidelines*
Neisseria gonorrhoeae causes gonorrhea, a sexually transmitted disease that can result in discharge and inflammation at the urethra, cervix, pharynx, or rectum.

**Resistance of Concern**

*N. gonorrhoeae* is showing resistance to antibiotics usually used to treat it. These drugs include:

- cefixime (an oral cephalosporin)
- ceftriaxone (an injectable cephalosporin)
- azithromycin
- tetracycline

**Public Health Threat**

Gonorrhea is the second most commonly reported notifiable infection in the United States and is easily transmitted. It causes severe reproductive complications and disproportionately affects sexual, racial, and ethnic minorities. Gonorrhea control relies on prompt identification and treatment of infected persons and their sex partners. Because some drugs are less effective in treating gonorrhea, CDC recently updated its treatment guidelines to slow the emergence of drug resistance. CDC now recommends only ceftriaxone plus either azithromycin or doxycycline as first-line treatment for gonorrhea. The emergence of cephalosporin resistance, especially ceftriaxone resistance, would greatly limit treatment options and could cripple gonorrhea control efforts.

In 2011, 321,849 cases of gonorrhea were reported to CDC, but CDC estimates that more than 800,000 cases occur annually in the United States.

<table>
<thead>
<tr>
<th></th>
<th>Percentage</th>
<th>Estimated number of cases</th>
</tr>
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<tbody>
<tr>
<td>Gonorrhea</td>
<td>100%</td>
<td>820,000</td>
</tr>
<tr>
<td>Resistance to any antibiotic</td>
<td>30%</td>
<td>246,000</td>
</tr>
<tr>
<td>Reduced susceptibility to cefixime</td>
<td>&lt;1%</td>
<td>11,480</td>
</tr>
<tr>
<td>Reduced susceptibility to ceftriaxone</td>
<td>&lt;1%</td>
<td>3,280</td>
</tr>
<tr>
<td>Reduced susceptibility to azithromycin</td>
<td>&lt;1%</td>
<td>2,460</td>
</tr>
<tr>
<td>Resistance to tetracycline</td>
<td>23%</td>
<td>188,600</td>
</tr>
</tbody>
</table>

Source: The Gonococcal Isolate Surveillance Project (GISP)—5,000 isolates tested for susceptibility in 2011.

For more information about data methods and references, please see technical appendix.
Neisseria gonorrhoeae — Percentage of Isolates with Elevated Ceftriaxone Minimum Inhibitory Concentrations (MICs) (≥0.125 μg/ml), Gonococcal Isolate Surveillance Project (GISP), 2006–2013
Suspected GC Treatment Failure: First Consider Reinfection*

**TEST:** with culture and NAAT. If GC culture not available on-site, call local health department.

**REPEAT TREATMENT:** Gemifloxacin 320 mg + AZ 2g OR gentamicin 240 mg IM + AZ 2g. (If re-infection suspected see below)

**REPORT:** To your local health department within 24 hours

**TREAT PARTNERS:** Treat all partners in last 60 days with same antibiotic regimen as patient

**TEST OF CURE (TOC):** TOC 7-14 days with culture and NAAT

*When reinfection suspected:*

→ If initial RX was Ceftriaxone 250 IM/Azithro 1gm Retreat with Same regimen

→ If initial RX was Cefixime/Azithro Retreat with Ceftriaxone 250 IM plus Azithromycin 2 gm po

*CDC 2015 STD Treatment Guidelines*
Chlamydia Treatment
Adolescents and Adults

**Recommended regimens (non-pregnant):**
- Azithromycin 1 g orally in a single dose
- Doxycycline 100 mg orally twice daily for 7 days

*Doxycycline delayed-release 200 mg tablet QD x 7 d added as alternative regimen*

**Recommended regimens (pregnant***):**
- Azithromycin 1 g orally in a single dose
- **Amoxicillin 500 mg orally TID x 7 days**

*Amoxicillin 500 TID moved to alternative for pregnant women*

* Test of cure at 3-4 weeks only in pregnancy

*CDC 2015 STD Treatment Guidelines*
Rectal Chlamydia: Treatment

• **Azithromycin < Doxycycline**
  – Data from one nongonococcal urethritis trial and several rectal infection studies
  – Meta analysis
    • **Pooled cure rates: doxy 97.5%, azithro94.4%**

• **Doxycycline marginally more effective than azithromycin for rectal CT infection**

• **More research needed (RCT)**

• **No change in CDC 2015 RX recommendations**

Hathorn et al STI 2012, Kong et al. CID 2014
Case Scenario: Persistent Urethral Discharge

- 20 Year old Male complaint of persistent dysuria & urethral discharge.
  - Seen 1 week ago and treated for urethritis (Ceftriaxone 250 IM plus Azithromycin 1 gm PO)
  - States the discharge never really went away. No sexual exposures in past week (h/o female partners)
  - GC/CT NAAT both negative from prior visit
- Urethral discharge confirmed on exam today
Audience Poll
How would you treat his persistent urethritis?

1. Ceftriaxone 250 mg plus azithromycin 1gm orally
2. Doxycycline 100 mg orally BID for 7 days
3. Metronidazole 2 gm orally
4. Moxifloxacin 400 mg orally QD for 7 days plus metronidazole 2 gm orally once
Emerging Issues: Mycoplasma genitalium

- Sexually transmitted pathogen
  - Urethritis: studies support association
    - Etiology in ~30% persistent urethritis
  - Cervicitis and PID (data suggestive)
- FDA approved test not commercially available
  - Some centers have done CLIA validation
- Azithromycin superior to doxycycline for M. genitalium urethritis
  - 82% vs 39% (older studies)
    - (*AZ efficacy may be declining for M. genitalium)
- Moxifloxacin effective for M. genitalium

*Manhart et al, CID 2013
CDC 2015 STD Treatment Guidelines
Persistent NGU Treatment

If azithromycin NOT given for 1st episode:
  - Azithromycin 1 g orally in a single dose
    PLUS
  - Metronidazole 2 g orally in a single dose OR
  - Tinidazole 2 g orally in a single dose

If azithromycin given for 1st episode:
  - Moxifloxacin 400 mg orally qd x 7d
    PLUS
  - Metronidazole 2 g orally in a single dose OR
  - Tinidazole 2 g orally in a single dose

Urology referral if symptoms persist

CDC 2015 STD Treatment Guidelines
Syphilis Treatment: No changes

Primary, Secondary & Early Latent:

- Benzathine penicillin G 2.4 million units IM in a single dose

Late Latent and Unknown Duration:

- Benzathine Penicillin G 7.2 million units total, given as 3 doses of 2.4 million units each at 1 week intervals

Neurosyphilis:

- Aqueous Crystalline Penicillin G 18-24 million units IV daily administered as 3-4 million IV q 4 hr for 10 -14 d

*Only one dose of PCN Is recommended for early syphilis in HIV-infected persons, extra doses not needed*

*Always order an RPR on the day of treatment!

CDC 2015 STD Treatment Guidelines
Maximum time between doses when treating late latent syphilis?

- Clinical experience suggests 10-14 days ok for non-pregnant adults
  - <9 days is best based on limited pharmacologic data
- In pregnancy, must adhere to strict 7 days between doses
  - 40% of pregnant women are below treponemicidal levels after 9 days
- Missed dose: entire series must be restarted
Genital Herpes

HSV-1 infection - increasing proportion of anogenital herpes in young women and MSM

Diagnosis
- HSV NAAT (PCR) or viral culture are preferred for diagnosis of genital ulcers
- HerpeSelect HSV-2 ELISA might be falsely positive at low index values (1.1-3.5); should be confirmed with WB or Biokit
- HerpeSelect HSV-1 ELISA is insensitive for HSV-1 Ab

IgM testing not useful - may detect recurrence

Treatment: No changes
Trichomonas

- Prevalence estimates ~3.7 million
- Screening recommended
  - HIV+ women (at least annually)
- Consider screening
  - High prevalence settings (STD clinics, corrections) or at high risk of infection
- Retesting recommended within 3 months after treatment for women
  - (insufficient data to recommend for men)
- Diagnostics: Limitations of wet mount microscopy
  - Sensitivity low ~51%-65%, declines if delay in microscopy
New testing algorithm:
Wet mount first, if negative then NAAT (NAAT FDA approved for women)
STD Clinical Consultation Network (STDCCN)

Provides STD clinical consultation services within 1-3 business days, depending on urgency, to healthcare providers nationally.

Your consultation request is linked to your regional PTC’s expert faculty.

We are just a click away!

www.STDCCN.org
Additional Resources for Clinicians

- CDC 2015 STD Treatment Guidelines
  - [CDC STD Treatment Guidelines free App available for Apple](http://www.cdc.gov/std/tg2015/)

- National Network of STD/HIV Prevention Training Centers
  - [http://nnptc.org/](http://nnptc.org/)

- CAPrevention Training Center
  - [www.stdhivtraining.org](http://www.stdhivtraining.org)