Gonorrhea and Chlamydia Update: Treat and screen in 2017

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Disclosures

• None

• Non-FDA labeled uses of diagnostic tests:
  – NG/CT nucleic acid tests at extragenital sites
Objectives

• Describe trends in gonorrhea (NG) and chlamydia (CT) incidence in the U.S. in the past decade

• State the CDC’s first-line treatment regimens for gonorrhea and chlamydia

• Describe how often NG and CT are asymptomatic at the urethral, rectal, and oral sites

• Name 4 risk factors that should prompt q3-6 month gonorrhea and chlamydia screening
Chlamydia — Rates of Reported Cases by Sex, United States, 2000–2015

Rate (per 100,000 population)

NOTE: Data collection for chlamydia began in 1984 and chlamydia was made nationally notifiable in 1995; however, chlamydia was not reportable in all 50 states and the District of Columbia until 2000. Refer to the National Notifiable Disease Surveillance System (NNDSS) website for more information: https://wwwn.cdc.gov/nndss/conditions/chlamydia-trachomatis-infection/.
Gonorrhea — Rates of Reported Cases by Race/Ethnicity, United States, 2011–2015

Rate (per 100,000 population)

* AI/AN = American Indians/Alaska Natives; NHOPI = Native Hawaiian/Other Pacific Islanders.

NOTE: Includes 45 states reporting race/ethnicity data in Office of Management and Budget compliant formats during 2011–2015
Chlamydia — Rates of Reported Cases by Race/Ethnicity, United States, 2011–2015

Rate (per 100,000 population)

- **Blacks**
- **American Indians/Alaska Natives**
- **Hispanics**
- **Whites**
- **Multirace**
- **Native Hawaiian/Other Pacific Islanders**
- **Asians**

**Year**

2011 2012 2013 2014 2015

**NOTE:** Includes 45 states reporting race/ethnicity data in Office of Management and Budget compliant formats during 2011–2015.
“Total combined cases of chlamydia, gonorrhea, and syphilis reported in 2015 reached the highest number ever…”

* CDC 2015 STD Surveillance Report

<table>
<thead>
<tr>
<th></th>
<th>Cases, 2015</th>
<th>Increase vs. 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia*</td>
<td>1,526,658</td>
<td>6%</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>395,216</td>
<td>13%</td>
</tr>
<tr>
<td>Syphilis (P&amp;S)</td>
<td>23,872</td>
<td>19%</td>
</tr>
</tbody>
</table>

* Most frequently reported infectious disease in U.S.

Case A: 41 y.o. male routine follow-up

- HIV+  CD4 657 / RNA <20, rATV / TDF/FTC
- Suppressed >10 years
- Second visit with me
- Worried about syphilis
  - Three episodes before, including CNS
  - Crack and crystal meth binges
  - Multiple anonymous partners
  - Never had NG or CT, 3 previous urine NAT’s
  - No prior extragenital screening
- Exam unremarkable
- A test was performed...
Case A: 41 y.o. male routine follow-up

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  - No prior extragenital screening
- Exam unremarkable
- Oral NG/CT NAT: POS NG
Case B: 45 y.o. male with 4 weeks rectal bleeding

- **CC:** Slight bloody discharge several times daily
  - Tenesmus; no diarrhea
  - No lightheadedness or pain
  - Similar episode 3 years ago
    - Saw GI doctor, “possible IBD”
    - Rectal steroid didn’t help, eventually resolved

- **PMH:** highly-resistant HIV currently off therapy

- **Social:** UAI w/ ~2-3 partners monthly

- Mild rectal tenderness, no blood, no ulcers

- **Test Performed...**
Case B: 45 y.o. male with 4 weeks rectal bleeding

- **CC:** Slight bloody discharge several times daily
  - Tenesmus; no diarrhea
  - No lightheadedness or pain
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- **PMH:** highly-resistant HIV currently off therapy

- **Social:** UAI w/ ~2-3 partners monthly

- **Rectal NG/CT NAT:** Pos CT
Gonorrhea — Proportion of STD Clinic Patients Testing Positive* by Age Group, Sex, and Sexual Behavior, STD Surveillance Network (SSuN), 2015

* Results based on data obtained from patients (n=124,441) attending SSuN STD clinics in 2015 in all SSuN jurisdictions, excluding Minnesota.

† MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.
Chlamydia — Proportion of STD Clinic Patients Testing Positive* by Age Group, Sex, and Sexual Behavior, STD Surveillance Network (SSuN), 2015

* Results based on data obtained from patients (n=125,238) attending SSuN STD clinics in 2015 in all SSuN jurisdictions, excluding Minnesota.
† MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.
Poll Question #1

Case A: 41 y.o. male routine follow-up
Oral NG/CT NAT: POS NG
Which of the following is CDC-recommended?

A. Ceftriaxone 250mg IM one time dose
B. Cefixime 400mg PO one time dose
C. Azithromycin 1000mg PO one time dose
D. Ceftriaxone 250mg IM PLUS azithromycin 1000mg, one time doses
E. Cefixime 400mg IM PLUS azithromycin 1000mg, one time doses
NG Treatment

• Ceftriaxone 250mg IM + Azithromycin 1g PO

• Alternatives:
  – Cefixime 400mg PO x1 + azithro 1g PO (only if ceftriaxone is not available)
  – Doxycycline 100mg PO BID x 7 days (as the 2nd agent, if azithromycin allergic)

• Test of cure (NAT or culture) at 14 days if treating pharyngeal NG with alternative regimen (need culture if 2nd NAT pos)

Remember to re-screen at 3 months after treating
Beta-lactam allergy

• Assess allergy
  – If IgE-mediated or life-threatening PCN reaction (anaphylaxis, Stevens Johnson, TEN), then avoid CTX, even though cross-reaction < 2.5%
  – Other PCN reactions, proceed with cephalosporin

• Cephalosporin allergy (or life-threatening PCN)
  – Consult ID
  – Gemifloxacin 320mg PO plus Azithro 2000mg PO
  – Gentamicin 240mg IM plus Azithro 2000mg PO
Cefixime in Toronto 2010-2011

• Toronto STD Clinic routine practice
  – Cefixime 400mg PO, directly observed
  – Request test of cure (with culture) for all

• 133 patients returned for TOC
  – 13 positive with molecularly identical organism
  – 9 explicitly denied interval sex

• Failure rate: 9 of 133 (7%)
  – 4 of 76 urethral (5%)
  – 3 of 39 rectal (8%)
  – 2 of 7 pharyngeal (29%)

• Failure by cefixime MIC
  < 0.12 µg/mL 2%
  ≥ 0.12 25%

JAMA 2013;309:163
Relentless NG resistance

Unemo & Shafer, Clin Microbiol Rev. 2014: 587
Untreatable NG?

Plasmid-mediated TET resistance.
Chromosomal TET and PEN resistance

Cefixime, CRO clinical failures
FQ resist., US; CRO resist., Japan
High-level AZM resist., Europe
AZM resist., Latin Amer
Cefixime resist., Japan
FQ failures, Asia

Ceftriaxone (CRO)
• Highest sustained blood levels
• Highest efficacy in clinical trials, esp. at oral site

CRO + AZM failure, UK
*NEJM* 2016: 2504

What’s in our back pockets?

• Beta-lactam allergy regimens
  – Gemifloxicin 320mg PO plus Azithro 2000mg PO
  – Gentamicin 240mg IM plus Azithro 2000mg PO

• Investigational
  – Solithromycin (fluoroketolide, macrolide family): Phase 3
  – ETX0914 (spiropyrimidinetrione) gyrase/topoisomerase inhibitor: Phase 2, NCT02257918
  – GSK2140944, Gepotidacin (triazaacenaphthylene) gyrase/topoisomerase inhibitor: Phase 2, NCT02294682

Poll Question #2

Case B: 45 y.o. male with 4 weeks rectal bleeding

Rectal NG/CT NAT:  Pos CT

What is the CDC-recommended management?

A. Azithromycin 500mg PO now and 250mg PO daily for 4 more days

B. Azithromycin 1000mg PO now

C. Doxycycline 100mg PO twice daily for 7 days

D. Doxycycline 100mg PO twice daily for 21 days
CT Treatment

- **Azithromycin 1gm PO, or**
- **Doxycycline 100mg PO BID X 7 days**
- **Alternatives:**
  - Erythromycin base 500mg PO QID x 7 days
  - Erythromycin ethylsuccinate 800mg PO QID x 7d
  - Levofloxacin 500mg PO qday x 7 days
  - Ofloxacin 300mg PO BID x 7 days

*Remember to re-screen at 3 months after treating*
Lymphogranuloma Venereum (LGV)

- C. trachomatis serovars L1, L2, L3
- **Common presentations**
  - Genital: tender, unilateral lymphadenopathy; self-limited lesion at inoculation site
  - Rectal (MSM): proctocolitis (discharge, pain, tenesmus); +/- fever
- **Diagnosis**
  - Presumptive
  - Confirmation via PCR (poorly available, weeks); serology (weeks)
- **Recommended**: Doxycycline PO BID x 21 days
- **Alternative**:
  - Erythromycin base 500mg PO four times daily x 21 days
  - Azithromycin, levofloxacin, and ofloxacin not well-studied

*Remember to re-screen at 3 months after treating*
Case B: 45 y.o. male with 4 weeks rectal bleeding

Rectal NG/CT NAT: Pos CT

LGV molecular serotyping: positive (C. Gaydos)
Practical Scenarios

• **Empiric treatment**
  – Urethritis (assuming no POC NG testing): NG therapy
  – Cervicitis: CT therapy + consider NG therapy

• **Post-treatment abstinence:** 7 days

• **Managing sex partners**
  – All sex partners in past 60 days (eval, dx, tx)
  – If no sex in >60 days, then most recent partner
  – **Expeditied partner therapy (EPT) rec’d where legal**
    • Heterosexual, provide written educational materials
    • Cefixime 400mg + Azithro 1000mg for NG; Azithro 1000mg for CT
    • [www.cdc.gov/std/ept](http://www.cdc.gov/std/ept)
Percent asymptomatic NG and CT

## CDC Screening Guidelines for Sexually Active Persons

<table>
<thead>
<tr>
<th></th>
<th>Syphilis</th>
<th>NG/CT</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td>Pregnancy</td>
<td>&lt;25: annual</td>
<td>13-64 (opt-out)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥25: consider*</td>
<td>If other STI</td>
</tr>
<tr>
<td><strong>MSW</strong></td>
<td></td>
<td>Consider CT*</td>
<td>13-64 (opt-out)</td>
</tr>
<tr>
<td><strong>MSM</strong></td>
<td>≥ annual**</td>
<td>≥ annual** at sites of contact (urethra, rectum, pharynx) regardless of condoms</td>
<td>≥ annual if new partner(s) since last test</td>
</tr>
<tr>
<td><strong>HIV+</strong></td>
<td>≥ annual**</td>
<td>≥ annual**</td>
<td></td>
</tr>
</tbody>
</table>

* New or multiple partners, anonymous partners, transactional sex, history of or partners with STI’s, illicit drug use, high local incidence

** q3-6 months *based on risk factors above*

# Point prevalence of asymptomatic STI’s among PLWH

<table>
<thead>
<tr>
<th>Study Description</th>
<th>NG</th>
<th>CT</th>
<th>Early Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analysis, 37 studies worldwide, 2011</td>
<td>9.5%</td>
<td>5%</td>
<td>9.5%</td>
</tr>
<tr>
<td>UCSF HIV clinic, 2003*</td>
<td>6.7%</td>
<td>8.3%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Los Angeles 2 HIV clinics, MSM, 2004-2005*</td>
<td>5.7%</td>
<td>6.3%</td>
<td>3%</td>
</tr>
<tr>
<td>Amsterdam HIV clinic, 2007-2008*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>5.2%</td>
<td>8.6%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Women &amp; MSW</td>
<td>0</td>
<td>1.2%</td>
<td>0.4%</td>
</tr>
<tr>
<td>London HIV clinic, 2009-2010*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>9.4%</td>
<td>14.1%</td>
<td></td>
</tr>
<tr>
<td>Women &amp; MSW</td>
<td>0</td>
<td>1.8%</td>
<td></td>
</tr>
<tr>
<td>US Military Men (79% MSM), 2010-2011*</td>
<td>8.0%</td>
<td>20.5%</td>
<td></td>
</tr>
</tbody>
</table>

* Consecutive, asymptomatic, offered testing at all relevant body sites

References:
- Sex Trans Inf 2011:183, AIDS Pat Care STD 2005:495,
Go forth and screen!

“Don’t hold your breath. I screen for NG/CT but never get any positives.”
- Senior faculty member
Case detection was flat in our clinic

Sex Trans Inf 2011:469
Similarly flat case detection in Ontario 2008-2011 despite increase in testing from 15% to 27%

*Sex Trans Inf* 2014:608
Why no increase in NG/CT case detection?

• Limited observation and type II error?
• Declining NG/CT prevalence in Baltimore – No¹
• Really not more than 0.5 – 1.0% point prevalence?
• Infections concentrated among a minority with frequent repeat infections?
• Not testing the right body sites?
  – What about oral and rectal screening?
  – Only 2% of MSM tested at ≥ 1 extragenital site annually
  – No increase over time (OR per year 0.99 [0.88, 1.12])

¹CDC, Sexually Transmitted Disease Surveillance, 2007
# Distribution of NG/CT by body site

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Genital</th>
<th>Rectal</th>
<th>Oral*</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCSF HIV clinic, 2003</td>
<td>12%</td>
<td>48%</td>
<td>40%</td>
</tr>
<tr>
<td>Los Angeles 2 HIV clinics, MSM, 2004-2005</td>
<td>21%</td>
<td>52%</td>
<td>27%</td>
</tr>
<tr>
<td>Amsterdam HIV clinic, 2007-2008 MSM</td>
<td>12%</td>
<td>76%</td>
<td>17%</td>
</tr>
<tr>
<td>London HIV clinic, 2009-2010 MSM</td>
<td>18%</td>
<td>58%</td>
<td>24%</td>
</tr>
<tr>
<td>US Military Men (79% MSM), 2010-2011</td>
<td>5%</td>
<td>80%</td>
<td>40%</td>
</tr>
</tbody>
</table>

Consecutive, asymptomatic, offered testing at all relevant body sites
Can exceed 100% because of multiple sites positive simultaneously
* Some studies only assessed oral NG

And, < 10% simultaneous positivity...

## Prevalence of extragenital sexual behaviors

### ORAL SEX

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Insert</td>
<td>Recep</td>
</tr>
<tr>
<td>Lifetime</td>
<td>77%</td>
<td>79%</td>
</tr>
<tr>
<td>Last sex</td>
<td>27%</td>
<td>28%</td>
</tr>
</tbody>
</table>

### ANAL SEX

- Young MSM: 50%
- Young heterosexual men and women: 14-49%
- Among women, ~25% of cases extragenital

AIDS 1999:1525, AIDS Pt Care STDs 1999:717, Sex Trans Dis 2011:783*
NATs not FDA-approved for extragenital, but they are standard of care

### Sensitivity / Specificity for Culture and 2 Commercial NATs

<table>
<thead>
<tr>
<th></th>
<th>Rectal NG</th>
<th>Rectal CT</th>
<th>Oral NG</th>
<th>Oral CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture¹</td>
<td>49/100</td>
<td>35/100</td>
<td>55/100</td>
<td>67/100</td>
</tr>
<tr>
<td>Culture², ³</td>
<td>67/100</td>
<td>36/98</td>
<td>50/99</td>
<td></td>
</tr>
<tr>
<td>Strand Displacement Amplification¹</td>
<td>89/100</td>
<td>89/100</td>
<td>88/99</td>
<td>86/100</td>
</tr>
<tr>
<td>Strand Displacement Amplification², ³</td>
<td>97/99</td>
<td>92/96</td>
<td>93/96</td>
<td></td>
</tr>
<tr>
<td>Transcription-Mediated Amplif. ¹</td>
<td>93/100</td>
<td>93/100</td>
<td>88/98</td>
<td>100/100</td>
</tr>
<tr>
<td>Transcription-Mediated Amplif. ², ³</td>
<td>100/98</td>
<td>100/96</td>
<td>84/99</td>
<td></td>
</tr>
</tbody>
</table>

### Clinical Laboratory Improvement Amendments (CLIA) Certification
- Quality performance demonstration pursued by individual labs
- National labs including Quest, LabCorp

**Self-testing for NG/CT**

*Self-performed swabs (rectal, vaginal, and oral) well-accepted or preferred and highly concordant with provider*

Testing rates 12 months before/after implementation self-testing for MSM (N=1500) at Seattle’s Madison HIV Clinic

- NG/CT test positivity unchanged yielding 25-75% increases in case detection at each body site
- 92% rated “good” or “very good”
Patient resources

Poster at Madison Clinic, Seattle
JAIDS 2016;72:e26-e31

YouTube Video Anal Pap Self Collection
https://www.youtube.com/watch?v=ytOTNi8yVOC

Credit to Medical College of Wisconsin
Does broader NG/CT screening yield increased NG/CT case detection?  
(HIV Research Network, 2017)

- Case detection significantly increased in all groups.
- Reached only 25% extragenital among MSM.
Recap

• Combined NG, CT, and syphilis at highest levels ever
• Minorities / youth have highest incidence, though incidence remains high among older MSM
• NG treatment
  – CTX *plus* Azithro or Doxy
  – Resistance is growing!
• CT treatment
  – Azithro *OR* Doxy
  – Consider LGV in some scenarios
• Vast majority of NG and CT is asymptomatic
• Screening must include *all relevant body sites*, use NAT’s
• Remember risk factors for more frequent screening
STD Treatment Guidelines Apps

STD Tx Guidelines

Recommended Regimen

Ceftriaxone 250 mg IM in a single dose
PLUS
Azithromycin 1g orally in a single dose

Alternative Regimen

If ceftriaxone is not available
Cefixime 400 mg orally in a single oral dose
PLUS
Azithromycin 1 g orally in a single dose

Available on iTunes & Google Play

STD Clinical Toolbox

Available on iTunes

STD Treatment Guidelines, wall charts, pocket guides, and the full MMWR article at:  www.cdc.gov/std/tg2015
The NNPTC provides:

• Clinical training
• STD clinical consultations
• Resources and tools for STD treatment

Visit: www.nnptc.org
THANK YOU!

Questions?