Chlamydia and Gonorrhea on the Rise: Updated Guidelines

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Financial Relationships With Commercial Entities

Dr. Celum has served as a scientific advisor to Merck & Co, Inc. and Gilead Sciences, Inc. (Updated 07/16/20)

Learning Objectives

After attending this presentation, learners will be able to:

• Describe recent sexually transmitted infection (STI) trends
• Diagnose and treat syphilis, including complicated syphilis
• Screen for and treat extragenital gonorrhea and chlamydia
Each year there are an estimated 376 million new infections with one of four curable STIs: chlamydia, gonorrhoea, syphilis and trichomonas.

An estimated 92% of these infections occur in low and middle-income countries where access to effective screening and treatment is limited.

Untreated STIs are associated with significant health negative health and social outcomes. Overall, they result in a considerable number of DALYs, especially in women and infants in sub-Saharan Africa.

High rates of STIs have been observed in individuals using PrEP.

STIs continue to increase globally

Dramatic increases in bacterial STI incidence in era of effective HIV treatment & prevention

- Gonorrhoea: continued antimicrobial resistance
- Syphilis: incidence above pre-AIDS era in MSM, spread into heterosexual networks
- Reappearance of classics: LGV proctitis

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Bacterial STI Rates in U.S., 2000-2016

- Syphilis
- Gonorrhoea
- Chlamydia

http://www.cdc.gov/std; Pathela Sex Transm Dis 2019; WHO; Oliver Clin Infect Dis 2018; Braun DL Clin Infect Dis 2018
Why should we care?

- STDs cause morbidity, especially syphilis
- STDs increase risk of HIV acquisition


Asymptomatic STDs also increase risk of HIV

Key Principle

Most STI are asymptomatic, or are associated with non-specific symptoms, and do not prompt diagnostic testing. Yet...

The associated inflammation increases HIV acquisition risk.

Rising STI rates:

A public health problem arising in part from public health successes

![U=U logo]  
![PEP logo]
Case 1
One of your HIV patients comes to clinic for routine HIV follow-up. He is doing well and has been virally suppressed for 6 years. He lives with his longtime partner, with whom he does not use condoms, but uses condoms for anal sex with others. 4 sex partners in the last 3 months. He’s versatile. He denies any recent rash, urethral discharge or genital/anal or oral ulcer.
PMH: Two episodes of secondary syphilis - the last 24 months ago. RPR 1:128 at diagnosis >1:64>1:16>1:8>1:8>1:4 3 months ago.
PE: Unremarkable
Lab: RPR 1:16
Case 2
Pt is a 29 y.o. HIV+ man (CD4=219 VL=41K off ART) presents with loss of vision, which started about 3 months ago L>R. Progressive since then with floaters. Pt also c/o paresthesia of his feet and hands and sore joints. Reports having a rash on his torso about 8 months ago. 40lb weight loss, and bed bound for 8 weeks. Diarrhea. “Oh yeah, my husband has similar symptoms.”
PE: Cachexic man
Visual exam: Sees shapes and light only. Cannot count fingers. Unable to stand due to weakness. Ophtho exam – bilateral anterior uveitis – retinal detachments bilaterally LP - CSF:WBC 318 (38% PMN, 58% L, 12% M) VDRL 1:4 FTA - reactive

ARS Question 2: Case 2: Treatment
1) IV ceftriaxone 2 gm q 24 hrs
2) Procaine penicillin 2.4 mill U qd plus probenecid
3) IV Penicillin 20 mill U daily
4) Benzathine penicillin 2.4 mill U IM weekly x 3 weeks
5) Doxycycline 100 mg bid x 28 days

Natural history of CNS syphilis
Screen, rapidly evaluate & treat complicated syphilis

- Complicated Syphilis (3.5% of all syphilis)
  - Neurosyphilis (asymptomatic or symptomatic)
  - Oto syphilis
  - Ocular Syphilis

- Key Questions to ask:
  - Change in vision, floaters, flashing lights or photophobia?
  - Change in hearing?
  - New or changed tinnitus?
  - Difficulty walking?

Evaluation & treatment of complicated syphilis

Key Points:
- Lumbar puncture
  - Can be normal in ocular syphilis and oto syphilis
- If vision symptoms: urgent ophthalmologic eval
- If hearing symptoms: urgent audiologic eval
- Treatment
  - Do not delay treatment for evaluation
  - Give Bicillin if plan is uncertain at end of visit
- Normal LP + normal ophtho exam rules out ocular syphilis
- Oto syphilis is a clinical diagnosis – cannot be ruled out

What is old with a new twist: Gonorrhea

- Antibiotic resistance and treatment issues
- Diagnostic testing: urine-based NAAT work well, but do not identify antibiotic resistance
  - Obtain culture if suspicious
- Routine annual screening of sites exposed (urethra, pharynx, rectum); more if risky
- Re-testing after treatment

Gonorrhea Cases by MSM, MSW, and Women, STD Surveillance Network, 2010-2018

- Growing proportion of diagnoses outside STD clinics (eg from private providers)
Extragenital GC & CT infections are common

![Graph showing % positive HIV- and HIV+ for Rectal GC, Rectal CT, Pharyngeal GC, and Pharyngeal CT.]

<table>
<thead>
<tr>
<th>Location</th>
<th>HIV-</th>
<th>HIV+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal GC</td>
<td>3.3%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Rectal CT</td>
<td>6.5%</td>
<td>8.9%</td>
</tr>
<tr>
<td>Pharyngeal GC</td>
<td>4.0%</td>
<td>12.0%</td>
</tr>
<tr>
<td>Pharyngeal CT</td>
<td>1.3%</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

Decreased susceptibility to ceftriaxone & azithromycin in GC,

- **Ceftriaxone**
  - International spread of gonococcal resistance to CTX
  - Resistance to CTX & high-level resistance to azithromycin in UK requiring treatment with ertapenem
  - Contacts in South East Asia
  - Two new cases of resistant gonorrhoea in UK, January 2019

- **Azithromycin**
  - WHO, GASP 2016

Gonorrhea – Treatment Issues

- European countries use higher doses of ceftriaxone (e.g., 500 mg instead of 250 mg)
  - Stay tuned for 2020 CDC STD treatment guidelines
- Limited options in cephalosporin-allergic patients
  - Spectinomycin is no longer manufactured
  - CDC recommends desensitization
- Azithromycin requires 2 grams; GI tolerance issues
  - Resistance to azithro is increasing and treatment failures have been seen
- If fluoroquinolones are the only option, obtain culture if possible prior to treatment to document sensitivity
  - If not possible, obtain test-of-cure
- GC drug pipeline: Solithromycin, zoliflodacin
• 45 yo HIV+ MSM with congenital cataracts presents with discharge, pain and decreased acuity in left eye
• Denies sexual activity other than deep kissing
• External eye culture positive for Neisseria gonorrhoeae
• Source: blood, pharyngeal, urine, and rectal culture negative
• Treatment?

Case 3

ARS Question 3: Case 3 Treatment

Treat with?
1) Ceftriaxone 125 mg IM
2) Ceftriaxone 250 mg IM
3) Azithromycin 2 gm PO
4) Ceftriaxone 1 gm IV

Case 4

An asymptomatic HIV+ patient you see in clinic tests positive for rectal chlamydial infection.

His other GC/CT tests are negative. He is RPR negative.

How do you treat him?
ARS Question 4: Case 4 Treatment

1) Doxycycline 100mg po bid x 7 days
2) Azithromycin 1g once
3) Azithromycin 2g once
4) Ceftriaxone 250mg IM plus Azithromycin 1g once

Treatment of Rectal Chlamydia: Data Favors Doxycycline

- Guidelines: azithromycin x 1 or 7 days of doxycycline
- Clinicians prefer azithromycin
- Retrospective studies suggest doxycycline is more effective than azithromycin
- Ongoing phase IV double-blind, placebo-controlled RCT of doxycycline vs. azithromycin for treatment of rectal CT in MSM

Multisite Screening in MSM and TGW

- Sexually active MSM and transgender or non-binary persons who have sex with men
- Rectal or pharyngeal exposure in past year
- Screen at least annually, or
- Screen Q3 months if any of the following:
  - Bacterial STD in the past year
  - Methamphetamine or popper use in past year
  - ≥10 sex partners (oral or anal) in the past year
  - Condomless anal intercourse with an HIV serodiscordant partner in the past year
  - Taking PrEP

Pooled efficacy
- AZM: 82.9% (95% CI: 76.0–89.8%)
- DOX: 99.6% (95% CI: 98.6–100%)

Guidelines: azithromycin x 1 or 7 days of doxycycline

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Multisite Screening in MSM and TGW

Self-testing is acceptable & sensitive
Summary of STIs: Diagnosis and management

- Ask patients with syphilis about photophobia, vision loss, or gait incoordination & hearing loss
- Gonorrhea – may soon drop azithro and increase the dose of Ceftriaxone
- Rectal chlamydia – Doxy not azithro
- NGU and Chlamydia – Doxy not azithro
- Higher risk MSM
  - Quarterly HIV/STI testing
  - PrEP

Beyond testing and treating:
Doxy PEP as a future intervention???

- RCT in open label extension of IPERGAY PrEP study
- Doxy 200mg x1 within 72 hours after sex
- 70% reduction in CT & syphilis
- No reduction in GC
- 70% TCN resistance in GC in France
- Median 7 pills/month (IQR: 3-15)
- No risk compensation

Questions after doxyPEP results from IPERGAY

- Will doxy PEP work …?
  - In MSM & TGW living with HIV, given potentially different adherence, efficacy and effect on antimicrobial resistance
  - In persons taking daily PrEP when they are on 2 different dosing strategies with daily HIV PrEP and event-driven STI PEP?
  - In younger, more heterogeneous populations?
  - Have partial efficacy against GC when TCN resistance is lower?
- Will intermittent doxycycline increase antimicrobial resistance?
  - STIs (GC, CT, syphilis)
  - Sources of transferable resistance (Neisseria spp.)
  - S. aureus (since doxycycline is sometimes used for MRSA)
  - Impact on gut microbiome
Stay tuned: Ongoing doxy PEP Study in SF & Seattle

### 2:1 Randomization

<table>
<thead>
<tr>
<th>MSM &amp; TGW living with HIV or on HIV PrEP with a bacterial STI in the past year</th>
<th>N = 780</th>
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<tbody>
<tr>
<td>PEP</td>
<td>No PEP</td>
</tr>
<tr>
<td>Interventions</td>
<td></td>
</tr>
<tr>
<td>Open label doxycycline 200 mg taken as PEP after condomless sexual contact</td>
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</tbody>
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### Aim 1:
- Efficacy in reducing syphilis, CT & GC; safety/tolerability

### Aim 2:
- Impact on antimicrobial resistance (GC, commensal Neisseria, S. Aureus) gut resistome

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**Meningococcal vaccine and GC?**

- Men-ACWY currently recommended in persons living with HIV & consideration for MSM without HIV
- 30% reduction of GC with New Zealand meningococcal B vaccine (retrospective analysis)
- Prospective trial planned with Bexsero; has additional outer membrane proteins with high homology with GC

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**RESOURCES**

- stdccn.org
- www.std.uw.edu

Download CDC STD treatment guidelines app; new guidelines in 2020!
### Acknowledgments

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