

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)

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Learning Objectives

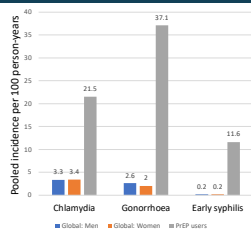
After attending this presentation, learners will be able to:

- Describe recent sexually transmitted infection (STI) trends
- Diagnose and treat syphilis, including complicated syphilis
- Screen for and treat extragenital gonorrhea and chlamydia

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One million new curable STI infections per day, globally

- Each year there are 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 DALY, esp. in women and infants in sub-Saharan Africa.
- High rates of STIs have been observed in individuals using PrEP.

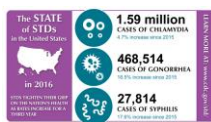


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Rowley, Bull WHO 2019; Ong, JAMA Network Open, 2019

STIs continue to increase globally

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

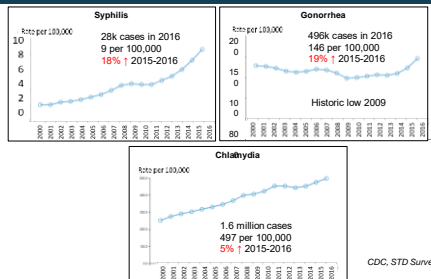


- Gonorrhea: continued antimicrobial resistance
- Syphilis: incidence above pre-AIDS era in MSM, spread into heterosexual networks
- Reappearance of classics: LGV proctitis

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<http://www.cdc.gov/std> Pathwell, Sex Transm Dis 2019; WHO, Obss Clin Infect Dis 2018; Braun DL, Clin Infect Dis 2018

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

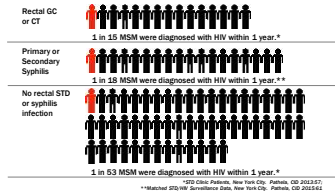


CDC, STD Surveillance, 2016

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Why should we care?

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



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Asymptomatic STDs also increase risk of HIV

Key Principle

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

The associated inflammation increases HIV acquisition risk

Symptomatic Vaginal Discharge Is a Poor Predictor of Sexually Transmitted Infections and Genital Tract Inflammation in High-Risk Women in South Africa

Katrina Wilson,^{1,2} Rosalind Nkomo,¹ Lisa Wilson,¹ Lindi Ndlovu,¹ Tinashe van Zyl,^{1,2} Cheryl Dube,¹ Jo Ann S. Passmore,^{1,2} Amanda L. Gail,¹ & William Dunn,¹ George Williams,^{1,2} Katherine Rasmussen,¹ Gerhard Walia,¹ and John S. Robert Kuhn^{1,2}

Inflammatory cytokine biomarkers of asymptomatic sexually transmitted infections and vaginal dysbiosis: a multicentre validation study

Lindt Mason,^{1,2} Shayan Rambaran,^{1,2} Jennifer Dene,^{1,2} Katie Larnard,¹ Smittee Dabbe,¹ Hayan Garmakhan,¹ Sharmeen Z. Joudaily,¹ Anna Lisa Williams,¹ Francesca Lotti,¹ Lou Van Damme,¹ Khusha Ahmed,¹ Tanya Crichton,¹ Sajid Akbarali,¹ Linda-Gail Bekker,^{1,2} Glenda Gray,^{1,2} Janan Dietrich,^{1,2} Heather Jansen,^{1,2} Jo Ann S. Passmore^{1,2}

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Rising STI rates:

A public health problem arising in part from public health successes



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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 5 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

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ARS Question 1: Case 1: Treatment

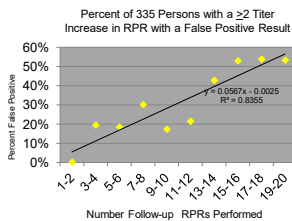
What would you do next?

- 1) Treat with benzathine PCN 2.4 million units IM x 1
- 2) Treat with benzathine PCN 2.4 million units IM weekly x 3 weeks
- 3) Call patient and ask about ocular/oto and neuro symptoms. If none, repeat lab test and treat if 1:32 or higher
- 4) Repeat RPR
- 5) Refer for lumbar puncture

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Increased Frequency of Syphilis Testing

- Among HIV- persons, 28% of 1st syphilis & 44% of 2nd cases remain RPR+ at 36 months
- Among 335 persons with syphilis, the positive predictive value of a 2-titer RPR increases was 73%
- **Implication:** 2-titer increases often need to be confirmed



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Source: Romanowski S. Ann. Int. Med. 1991;114:1005. Ausubel J. T. PHEAC (unpublished)

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



Morbidity and Mortality Weekly Report
Volume 162, No. 44, October 26, 2015

Notes from the Field

A Cluster of Ocular Syphilis Cases — Seattle, Washington, and San Francisco, California, 2014–2015

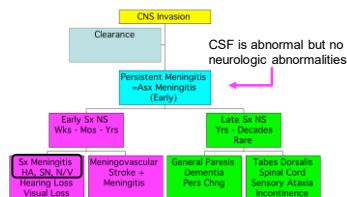
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ARS Question 2: Case 2: Treatment

- 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

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Natural history of CNS syphilis



Screen, rapidly evaluate & treat complicated syphilis

- Complicated Syphilis (3.5% of all syphilis)
 - Neurosyphilis (asymptomatic or symptomatic)
 - Ootosyphilis
 - Ocular Syphilis
- Key Questions to ask:
 - Change in vision, floaters, flashing lights or photophobia?
 - Change in hearing?
 - New or changed tinnitus?
 - Difficulty walking?

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Evaluation & treatment of complicated syphilis

Key Points:

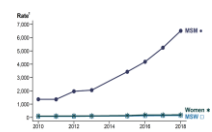
- Lumbar puncture
 - Can be normal in ocular syphilis and otosyphilis
- If vision symptoms: urgent ophthalmologic eval
- If hearing symptoms: urgent audiologic eval
- Treatment
 - Do not delay treatment for evaluation
 - Give Bicillin if plan is uncertain at end of visit
- Normal LP + normal ophtho exam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

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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

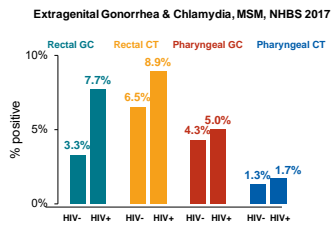


- Growing proportion of diagnoses outside STD clinics (eg from private providers)



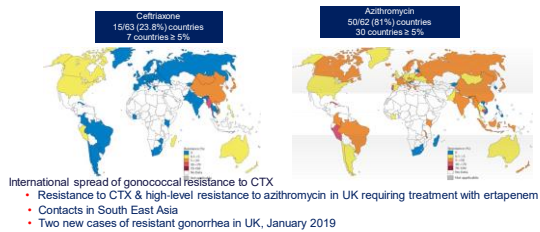
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Extragenital GC & CT infections are common



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Decreased susceptibility to ceftriaxone & azithromycin in GC,



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WHO, GASP 2016

Gonorrhea – Treatment Issues

- European countries use higher doses of ceftriaxone (eg 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, zolifadacin

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Case 3

- 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 gonorrhea*
- Source: blood, pharyngeal, urine, and rectal culture negative
- Treatment?



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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

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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?

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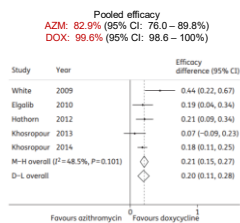
ARS Question 4: Case 4 Treatment

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

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Treatment of Rectal Chlamydia: Data Favors Doxycycline

- Guidelines: azithromycin x 1 or 7 days of doxycycline
- Clinicians prefer azithromycin
- Retrospective studies suggest that 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



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Khoorpoor C et al STD 2014; Kong FY et al J Antimicrob Chemother 2015

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



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Self-testing is acceptable & sensitive

Summary of STIs: Diagnosis and management

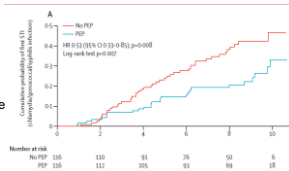
- Ask patients with syphilis about photophobia, vision loss, or gait incoordination & hearing loss
- Gonorrhea – may soon drop azithro and increase the dose of Ceftriaxone
- Rectal chlamydia – Doxy not azithro
- NGU and Chlamydia – Doxy not azithro
- Higher risk MSM
 - Quarterly HIV/STI testing
 - PrEP

Self-testing: Make it easy!

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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



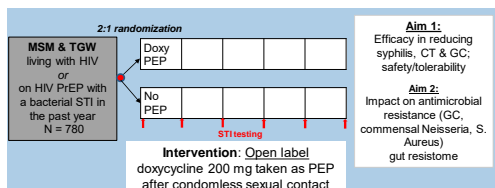
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Questions after doxyPEP results from IPERGAY

- 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

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Stay tuned: Ongoing doxy PEP Study in SF & Seattle



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DOXYPEP

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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Petousis-Harris, Lancet 2017

RESOURCES



stdccn.org



www.std.uw.edu

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

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Acknowledgments

Matthew Golden

Julie Dombrowski

Jeanne Marrazzo

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2020 Ryan White
HIV/AIDS Program
CLINICAL CONFERENCE

Question-and-Answer Session
