2020 Ryan White HIV/AIDS Program CLINICAL CONFERENCE

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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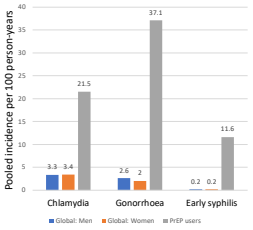
One million new curable STI infections per day, globally

- Each year there are an 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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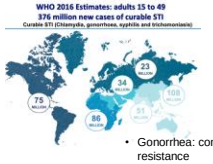
Rowley, Bull WHO 2019; Ong, JAMA Network Open, 2019

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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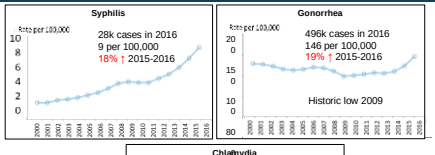
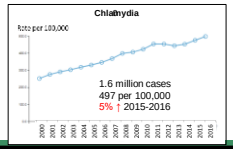
http://www.cdc.gov/std; Pathela *Sex Transm Dis* 2019; WHO; Oliver *Clin Infect Dis* 2018; Braun DL *Clin Infect Dis* 2018

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





CDC, STD Surveillance, 2016

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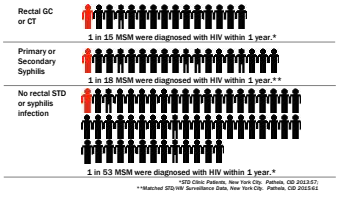
Why should we care?

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



*STD Clinic Patients, New York City. Pathela, CID 2013;57.
**Matched STD/HIV Surveillance Data, New York City. Pathela, CID 2015;61

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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

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

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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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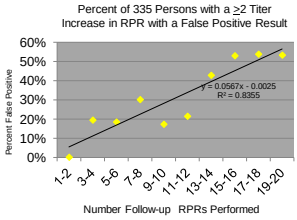
Increased Frequency of Syphilis Testing

- Among HIV- persons, 28% of 1° syphilis & 44% of 2° 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



Source: Romanoski B. Ann Int Med 1991;114:1005. Avoundjian, T. PHSKC (unpublished)

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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

MMWR Morbidity and Mortality Weekly Report

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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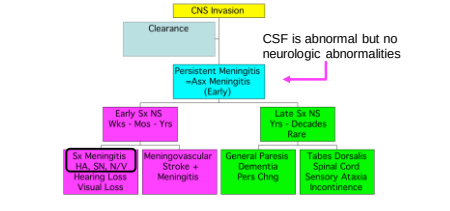
Natural history of CNS syphilis



Screen, rapidly evaluate & treat complicated syphilis

- Complicated Syphilis (3.5% of all syphilis)
  - Neurosyphilis (asymptomatic or symptomatic)
  - Otosyphilis
  - 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
- Otosyphilis is a clinical diagnosis – cannot be ruled out

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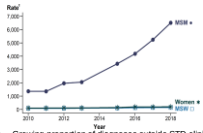
What is old with a new twist: Gonorrhea

- 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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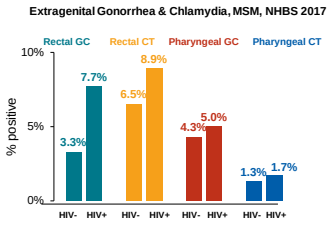
Extragenital GC & CT infections are common



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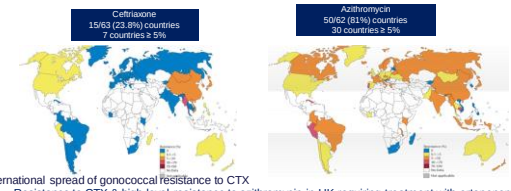
Decreased susceptibility to ceftriaxone & azithromycin in *GC*,



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 gonorrhea in UK, January 2019

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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, zolifodacin

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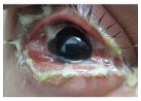
Case 3

- 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 gonorrheae
- 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) Azithomycin 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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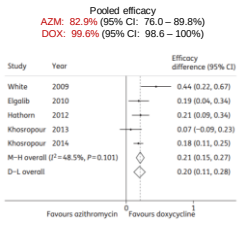
Treatment of Rectal Chlamydia: Data Favors Doxycycline

- 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



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

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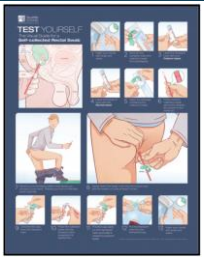
Multisite Screening in MSM and TGW

- 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



Self-testing is acceptable & sensitive

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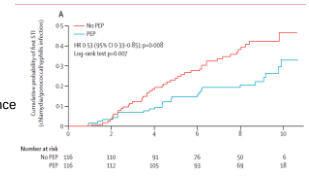
Beyond testing and treating: Doxy PEP as a future intervention???

- 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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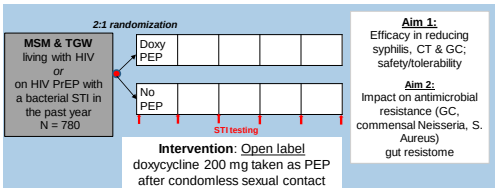
Stay tuned: Ongoing doxy PEP Study in SF & Seattle



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

Petousis-Harris, Lancet 2017

RESOURCES

stdccn.org

www.std.uw.edu

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

Acknowledgments

Matthew Golden

Julie Dombrowski

Jeanne Marrazzo

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Question-and-Answer Session