Learning Objectives

After attending this presentation, learners will be able to:

▫ Describe current epidemiology of important sexually transmitted diseases in HIV-infected patients, especially syphilis, gonorrhea and chlamydia
▫ Know recommended indications for and approach to screening for asymptomatic sexually transmitted infections in HIV-infected patients
▫ Recognize common clinical syndromes associated with sexually transmitted pathogens in HIV-infected patients

Why Discuss STIs in the Era of PrEP and U=U?

“…mantras like “Getting to Zero”…will never be achieved without addressing the potentiating role of STI in the global HIV pandemic, in addition to responding to other drivers of HIV spread, including economic and gender inequality, and other human rights challenges.”

HIV and sexually transmitted infections: responding to the “newest normal”

Kenneth M Mayer, PhD and Henry de Inock
HIV incidence and predictors of incident HIV among men who have sex with men attending a sexual health clinic in Melbourne, Australia. Retrospective cohort study of 5256 MSM attending Melbourne Sexual Health Centre 2007–2013 with at least two HIV tests within 12 months of each other: 81 incident HIV infections.

- Inconsistent condom use during anal sex
- IDU
- PEP use
- Any STI diagnosis in last 12 months

ARS Question #1

- What percentage of new HIV infections in men who have sex with men are estimated to be attributable to gonorrhea and chlamydia infection?
  A. None
  B. <2%
  C. 5%
  D. 10%
  E. 25%
The U.S. Syphilis Epidemic: 2017-18

- Primary/Secondary Syphilis in Men
  - 85% of cases
  - 46% in MSM
  - 40% in HIV

- Primary/Secondary & Congenital Syphilis in Women
  - 50% of cases without prenatal care
  - Strong links to meth, heroin

Defining the STI Crisis: WHO & CDC Reports

- Gonorrhea: continued antimicrobial resistance; extragenital infection
- Chlamydia: treatment challenges with rectal infections; reappearance of LGV proctitis
- Syphilis: ocular disease; congenital cases

The U.S. Syphilis Epidemic: 2017-18

- 85% of cases
- 46% in MSM
- 40% in HIV

- Primary/Secondary: 156% increase compared to 2013
- Congenital syphilis: 154% increase

Approximately 10% of HIV infections among MSM are attributable to gonorrhea/chlamydia infection

Effect of Relative Risk for HIV Acquisition on HIV Incidence:
A Modeling Analysis Among MSM

<table>
<thead>
<tr>
<th>RR of HIV Acquisition by Anatomic Site</th>
<th>HIV Incidence Rate (per 100 PYAR)*</th>
<th>PAR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal</td>
<td>1.98 (1.78, 2.21)</td>
<td>1.57</td>
</tr>
<tr>
<td>Oral</td>
<td>1.38 (1.25, 1.52)</td>
<td>1.21</td>
</tr>
<tr>
<td>Anogenital</td>
<td>1.39 (1.26, 1.53)</td>
<td>1.25</td>
</tr>
<tr>
<td>Intrauterine</td>
<td>1.34 (1.21, 1.49)</td>
<td>1.19</td>
</tr>
<tr>
<td>Genital</td>
<td>1.31 (1.18, 1.46)</td>
<td>1.16</td>
</tr>
<tr>
<td>Anogenital</td>
<td>1.32 (1.19, 1.47)</td>
<td>1.17</td>
</tr>
</tbody>
</table>

Effect of Relative Risk for HIV Acquisition on HIV Incidence:
A Modeling Analysis Among MSM

Source: Peterman 2018 Sex Transm Dis; 45(9S):S65

Approximately 10% of HIV infections among MSM are attributable to gonorrhea/chlamydia infection
• Similar increases in incidence
• Antimicrobial resistance
• Challenge of extragenital infections
• Low efficacy of all but CTX at pharynx
• Limited options for alternative antibiotic regimens

ARS Question #2

• According to the CDC’s Gonococcal Isolate Surveillance Program, what percent of gonorrhea isolates from men who have sex with women were resistant to ciprofloxacin in 2016?
A. None
B. <2%
C. 11%
D. 24%
E. 40%

International spread of gonococcal resistance to CTX
• Resistance to CTX plus high-level resistance to azithromycin in UK requiring treatment with ertapenem (2018)
• Contacts in South East Asia
• Two new cases of resistant gonorrhea in UK, January 2019
CDC STD Treatment Guidelines, 2015
Gonorrhea Dual Therapy
Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose

Azithromycin 1 g orally (preferred)
or Doxycycline 100 mg BID x 7 days

PLUS*
• Regardless of CT test result

CDC 2015 STD Treatment Guidelines
www.cdc.gov/std/treatment

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CDC STD Treatment Guidelines, 2020?
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Uncomplicated Genital, Rectal, or Pharyngeal Infections

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Meager evidence base to address the role of pharyngeal infection:
• Contribution of commensal Neisseria spp to resistance
• PK / PD of antibiotics
• Natural history of infection
• Resolution without antibiotics
• Duration of infectivity
• Bacterial shedding in oral secretions

NIH Workshop February 2019

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A multicentre double-blind randomized controlled trial evaluating the efficacy of daily use of antibacterial mouthwash against oropharyngeal gonorrhoea among men who have sex with men: the OMEGA (Oral Mouthwash use to Eradicate Gonorrhoea) study protocol

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“Where are we now?”
Novel Antimicrobials Under Study for Gonorrhea

- **Zoliflodacin (AZ D0914)**
  - Spiropyrimidinetrione (topoisomerase inhibitor)
  - Activity at rectum; limited at pharynx
  - Activity vs. C. trachomatis, M. genitalium
  - Phase II trial completed (Taylor SA NEJM 2018)

- **Gapolitacin (BTZ116576)**
  - Triazacacenaphthyne (topoisomerase inhibitor)
  - High efficacy potential – 3 separate ribosomal targets
  - Phase II trial completed (Taylor SA CID 2018)

- **Solithromycin**
  - Fluoroketolide; inhibits protein synthesis
  - Initial Ph 3 trial did not show non-inferiority to standard-of-care; no resistance but given structural similarity to telithromycin, strains with high-level azithromycin resistance are concern (Hook EW CID 2015)

- **Delafloxacin**
  - Ineffective as single-dose therapy (Hook Sex Transm Dis 2019)

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So what do we do while we wait for a vaccine?

Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomized substudy of the ANRS 12163 trial

- Time to first chlamydia and syphilis with On-Demand PEP With Doxycycline for MSM

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On-Demand PEP (Doxycycline 100 mg) (Effective in the seronegative, up to 10 days)

No PEP

- Time to First Chlamydia (FT)
- Time to First Syphilis (FT)
- Time to First Gonorrhea (FT)

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New York, New York, September 12, 2019
Conclusions

- Doxy-PEP reduced overall incidence of bacterial STI by 47% in MSM on PrEP (8.7 months of follow-up)
- No effect on gonorrhea, but strong reduction in chlamydia and syphilis
- Analysis of antibiotic resistance still pending
- Long-term benefit & harms not yet known
- No data in reproductive age women
- At least two clinical trials in MSM planned (www.clinicaltrials.gov) & one in young women in South Africa

Slide of Lymphogranuloma Venereum Cases Among Men Who Have Sex with Men—Michigan, August 2015–April 2016

- 38 cases reported to CDC
- All HIV+ MSM
- Median CD4 463
- Suspect in severe or persistent proctitis, especially with lymphadenopathy
- Treat with doxycycline 100 mg bid x 3 weeks
- Report to local health department
Download the CDC STD treatment guidelines app …

Question-and-Answer