Sexually Transmitted Infection Prevention and Treatment

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Disclosures

I have no financial disclosures.
Learning objectives

1. Describe the epidemiology of syphilis, chlamydia, gonorrhea, and other STIs among LGBTQ+ populations
2. Summarize optimal screening strategies for STIs.
3. Outline approaches to STI control that can be integrated into primary care.
Caveats

- Many (most?) LGBTQ+ people do not face a high risk of STIs.
- Clinical care must be individualized, not based on group risk.
- Data about STIs among cisgender WSW and transgender/gender non-conforming people are limited.
- Terms that describe identity and behavior are imperfect and change over time.
The rate of chlamydia diagnosis is increasing.

Sexually Transmitted Disease Surveillance 2017, CDC
Proportion of STI clinic patients testing positive for chlamydia

Sexually Transmitted Disease Surveillance 2017, CDC
The rate of gonorrhea diagnosis is increasing.
MSM face an increasing disparity in the rate of gonorrhea.

Sexually Transmitted Disease Surveillance 2017, CDC
Antimicrobial resistance in gonorrhea is increasing.
Neisseria gonorrhoeae — Percentage of Urethral Isolates with Elevated Azithromycin Minimum Inhibitory Concentrations (MICs) (≥2.0 µg/ml) and Elevated Ceftriaxone MICs (≥0.125 µg/ml) by Reported Sex of Sex Partners, Gonococcal Isolate Surveillance Project (GISP), 2011–2017

A. Azithromycin

B. Ceftriaxone

* No cases of elevated ceftriaxone MICs were reported among MSM in 2017.

ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.
The rate of syphilis diagnosis is increasing.
A majority of new syphilis infections occur in MSM.

Sexually Transmitted Disease Surveillance 2017, CDC
Some transgender people face a high burden of STIs.

- **United States systematic review:**
  - STI lifetime prevalence = 21.1%, greater in MTF than FTM people

- **Prospective study of 230 MTF people New York City:**
  - Syphilis incidence 3.6% per year
  - Gonorrhea incidence 4.2% per year
  - Chlamydia incidence 4.5% per year

- **Retrospective study of 145 young people in Boston:**
  - Prevalence of syphilis 2.8%
  - Prevalence of gonorrhea and chlamydia 2.1% each

STIs are more than the “big three.”

- Lymphogranuloma venereum (De Baetselier I, BMC Infect Dis, 2018)
- Antibiotic-resistant *Shigella* species (Mook P, Emerg Infect Dis, 2016)
- Meningococcus (Folaranmi TA, Clin Infec Dis, 2017)
- Hepatitis C (Price JC, J Infect Dis, 2018)
- Zika (Rosenberg ES, J Infect Dis, 2018)
Mycoplasma genitalium

- First identified in men with non-gonococcal urethritis (NGU) in 1980
- Major cause of NGU; more common than gonorrhea but less common than chlamydia
- Diagnosed by nucleic acid detection; culture challenging
- Treatment can be difficult:
  - Intrinsically resistant to beta-lactams
  - Doxycycline ineffective
  - Azithromycin increasingly ineffective
  - Moxifloxacin usually effective

Workowski KA, Bolan G. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(3).
Bacterial vaginosis is more common among WSW than other women.

- Among WSW, risk of BV is increased by:
  - Greater number of sexual partners (recent and lifetime)
  - BV in a partner
- Female partners often share identical Lactobacillus strains.
- Routine BV screening is not recommended for WSW.
- Empiric treatment for female partners of patients with BV is not formally recommended.

Prevalence of human papillomavirus (HPV) DNA in the anal canals of HIV-negative men who have sex with men (MSM), by age group and by cancer-associated risk type. High-risk (HR) types include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 73; low-risk types include 6, 11, 53-56, 66, Pap 15S, and Pap 291.
Reprinted with permission from The University of Chicago Press.22
Herpes simplex virus

- HSV-2 not clearly more common among MSM than other men in the United States.
- Anogenital herpes is often due to HSV-1 among MSM.
- HSV-1 and HSV-2 are becoming less common in the United States.

Xu F, Sex Transm Dis, 2010; Durukan D, Sex Transm Infect, 2018; McQuillan G, CDC, 2018
Why are STI diagnoses increasing?

**Increased detection**
- Affordable Care Act (2010, 2014)
- Extragenital gonorrhea and chlamydia testing

**Increased transmission**
- Smartphones and geosocial networking apps
- HIV treatment as prevention
- PrEP

Minority Stress Model (adapted from Meyer)

Environmental Circumstances

Minority Status

Minority Identity

General Stressors

Distal (External) Minority Stressors (e.g., stigma, discrimination, violence, abuse)

Proximal (Internal) Minority Stressors (e.g., internalization of negative societal attitudes, rejection sensitivity)

Resilience Development

Health Outcomes

Slide courtesy of Dr. Alex Keuroghlian
Condom use is falling among MSM.

Condomless anal sex at last sex among MSM is increasing.

Sexual histories should be routine and free of assumptions.
STI prevention for LGBTQ+ people

1. Addressing socioeconomic factors that increase vulnerability
2. Vaccines – HAV, HBV, HPV
3. Condoms and risk-reduction counseling
4. PrEP for those at risk for HIV
5. STI screening and treatment – interrupting transmission prevents future infections
What do we say about condoms in 2019?

- One item on a menu of options for HIV/STI prevention
- Condom counseling must adapt to the era of biobehavioral HIV prevention
- Advantages and disadvantages:
  - Protect against a wide range of STIs
  - Widely available; not a medical intervention
  - Use is apparent to partners
  - Efficacy is imperfect (as with all strategies); 70% effective at preventing HIV among MSM
  - Consistent condom use is rare
  - Some patients are unlikely to benefit from condoms (e.g., mutually monogamous serodifferent couple in which the partner living with HIV is virologically suppressed)

Smith DK, J Acquir Immune Defic Syndr, 2015
CDC’s screening recommendations for MSM

- HIV antibody/antigen assay
- Syphilis serology
- NAAT for *N. gonorrhoeae* and *C. trachomatis*
  - From the urethra/urine and rectum for both, if exposed
  - From the pharynx for *N. gonorrhoeae* only
- At least once: Hepatitis B surface antigen
- Yearly, if living with HIV: HCV antibody assays
Screening for transgender people and sexual minority women is based on risk assessment.

“Clinicians should assess STD- and HIV-related risks for their transgender patients **based on current anatomy and sexual behaviors**. Because of the diversity of transgender persons regarding surgical affirming procedures, hormone use, and their patterns of sexual behavior, providers must remain aware of symptoms consistent with common STDs and screen for asymptomatic STDs on the basis of behavioral history and sexual practices.”
Syphilis testing follows a “traditional” or “reverse” testing algorithm.
Causes of discordant syphilis test results in the “reverse” algorithm?

• Previously treated syphilis
• Old, untreated syphilis
• Very early syphilis (in a “window period” between treponemal antibody and RPR positivity, or the prozone phenomenon)

2015 Sexually Transmitted Disease Treatment Guidelines. CDC. Available at: www.cdc.gov/std/tg2015/default.htm
Jurado RL, Arch Intern Med, 1993
What we know about gonorrhea and chlamydia testing in cisgender people

**CIS WOMEN**

- NAATs are preferred.
- Sensitivity of first-catch urine is 10% less than a vaginal swab.
- A self-collected vaginal swab performs as well as a clinician-collected swab.
- Vaginal swabs perform as well as endocervical swabs.

**CIS MEN**

- NAATs are preferred.
- Sensitivity of first-catch urine is the same as a urethral swab.

Unanswered questions in STI screening for transgender people

• What is the risk of STIs in surgically-constructed vaginas and penises?
  • Vaginoplasty techniques may involve urethral or colorectal mucosa, which is presumably susceptible to infection.

• What is the optimal screening strategy for gonorrhea/chlamydia in the setting of genital reconstruction?
  • Urine NAAT versus vaginal/urethral NAAT in vaginoplasty/phalloplasty
  • Some experts consider urine NAAT preferred.

• Do STIs present differently in reconstructed tissue?
  • Case report of neovaginal gonorrhea presenting as coital bleeding

PrEP may be an STI control intervention among MSM.

On PrEP, reduce condom use by 40%

42% of gonorrhea and 40% of chlamydia infections prevented over 10 years

## SUMMARY OF THE 2015 CDC SEXUALLY TRANSMITTED DISEASE (STD) TREATMENT GUIDELINES

Massachusetts Department of Public Health (MDPH) – Division of STD Prevention (DSTD)

These guidelines for treatment of STDs reflect recommendations of the MDPH DSTD and of the CDC STD Treatment Guidelines. These guidelines focus on STDs encountered in outpatient settings and are not an exhaustive list of effective treatments. Please refer to the complete CDC document for more information or call the DSTD. Clinical and epidemiological services are available through the DSTD including staff to assist healthcare providers with confidential notification of sexual partners of patients with STDs and/or HIV infection. Please call the DSTD for assistance at (617) 983-6940.

### DISEASE

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>RECOMMENDED TREATMENT</th>
<th>ALTERNATIVES (use only if recommended regimens are contraindicated)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SYPHILIS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults Primary, Secondary or Early Latent (≤ 1 Year)</td>
<td>Benzathine penicillin G 2.4 million units IM once</td>
<td>(For penicillin-allergic; non-pregnant patients only): Doxycycline 100 mg orally 2 times a day for 14 days OR Tetracycline 500 mg orally 4 times a day for 14 days</td>
</tr>
<tr>
<td>Late Latent (&gt; 1 Year) or Latent of Unknown Duration</td>
<td>Benzathine penicillin G 2.4 million units IM for 3 doses at 1-week intervals (total 7.2 million units)</td>
<td>(For penicillin-allergic; non-pregnant patients only): Doxycycline 100 mg orally 2 times a day for 28 days OR Tetracycline 500 mg orally 4 times a day for 28 days</td>
</tr>
</tbody>
</table>

**All Suspected Syphilis Cases:** Call the STD Program at (617) 983-6940 for past tests and treatment.

**Neurosyphilis** (including Ocular Syphilis) | Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion for 10-14 days | Procaine penicillin G 2.4 million units IM once daily PLUS probenecid 500 mg orally 4 times a day, both for 10-14 days |

**Children Primary, Secondary or Early Latent (≤ 1 Year)** | Benzathine penicillin G 50,000 units/kg IM once, up to adult dose of 2.4 million units | No specific alternative regimens exist. |
| Late Latent (> 1 Year) or Latent of Unknown Duration | Benzathine penicillin G 50,000 units/kg IM (up to adult dose of 2.4 million units) for 3 doses at 1-week intervals (up to total adult dose of 7.2 million units) | |

**Congenital Syphilis** | See complete CDC guidelines. | |

**HIV Infection** | Same stage-specific recommendations as for HIV-negative persons. | |

**Pregnancy** | Penicillin is the only recommended treatment for syphilis during pregnancy. Women who are allergic should be desensitized and treated with penicillin. Treatment is the same as in non-pregnant patients for each stage of syphilis. | |

### GONOCOCCAL INFECTIONS

**Adults, Adolescents and Children >65 kg** (Pharyngeal, Urogenital, Rectal) | Ceftriaxone 250 mg IM once PLUS Azithromycin 1 g orally once | **Note:** Use of an alternative regimen for pharyngeal gonococcal infection should be followed by a test-of-cure 14 days after treatment. For urogenital or rectal infections ONLY, and ONLY if ceftriaxone is not available: Cefixime 400 mg orally once PLUS Azithromycin 1 g orally once OR in case of azithromycin allergy Doxycycline 100 mg orally 2 times a day for 7 days |

For azithromycin allergy: Cefixime 250 mg IM once PLUS Doxycycline 100 mg orally 2 times a day for 7 days |

For cephalosporin allergy or IgE-mediated penicillin allergy: Cefixime 400 mg orally once OR Gentamicin 240 mg IM once PLUS Azithromycin 2 g orally once |

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Point-of-care testing for STIs may decrease transmission but shortening duration of infectivity.

Amsterdam STI clinic modelling study:
- 35% of MSM had sexual contexts in the time between testing and treatment (23% of whom had CAS)
- POC testing for all MSM anticipated to decrease gonorrhea prevalence by 11% over 5 years

Bartelsman M, Sex Transm Infect, 2017
What about anal cytology?

**YES**
- Anal cancer is HPV-associated and exhibits biology similar to that of cervical cancer
- Rates of anal cancer are high in MSM, especially in those with HIV
- Recommended for all HIV-infected MSM

**NO**
- As of yet, no randomized trials have been performed to assess the benefits of screening
- Whom to screen, how often, and when to start/stop screening are unclear

How to obtain anal cytology

• Place the patient in the lateral recumbent position.
• Insert a Dacron swab 5-6 cm into the anus.
• Apply lateral pressure and, while withdrawing the swab, rotate it.
• Submit the specimen as you would cervical cytology.

2. Image available from: www.hivandhepatitis.com
Hepatitis A
Hepatitis B
Human papillomavirus
(Meningococcus)

HPV Vaccine Expanded for People Ages 27 to 45

About 14 million women and men become infected with the human papillomavirus each year in the United States, according to the Centers for Disease Control and Prevention.

Keith Bedford/The Boston Globe, via Getty Images
Group B OMV meningococcal vaccine prevents gonorrhea infection.

- Mass vaccination against meningococcal group B infection in New Zealand from 2004-2008 (81% coverage of people < 20 years)
- Case control study of people ages 15-30 in sexual health clinics
  - Cases = Confirmed gonorrhea
  - Controls = Confirmed chlamydia
  - Exposure = Group B OMV meningococcal vaccination
- Vaccine effectiveness against gonorrhea = 31% (95% CI 21-39)

Doxycycline PEP prevents syphilis and chlamydia among MSM.

- 232 MSM in a trial of open-label, on-demand PrEP with TDF-FTC
- Randomized to doxycycline within 24 hours of sex or no PEP
- Doxycycline reduced chlamydia and syphilis infections but not gonorrhea

Molina JM, Lancet Infect Dis, 2018
PEP with doxycycline is generally well-tolerated.

<table>
<thead>
<tr>
<th></th>
<th>PEP (n=116)</th>
<th>No PEP (n=116)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Any adverse events</td>
<td>106 (91%)</td>
<td>104 (90%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Any serious adverse events</td>
<td>5 (4%)</td>
<td>10 (9%)</td>
<td>0.18</td>
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<tr>
<td>Any grade 3 or 4 events</td>
<td>4 (3%)</td>
<td>8 (9%)</td>
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<td>Treatment discontinuation because of adverse events</td>
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<tr>
<td>Gastrointestinal adverse events</td>
<td>62 (53%)</td>
<td>47 (41%)</td>
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<tr>
<td>Drug-related gastrointestinal adverse events</td>
<td>29 (25%)</td>
<td>16 (14%)</td>
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<tr>
<td>Nausea or vomiting</td>
<td>10 (9%)</td>
<td>3 (3%)</td>
<td>--</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>14 (12%)</td>
<td>5 (4%)</td>
<td>--</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>6 (5%)</td>
<td>9 (8%)</td>
<td>--</td>
</tr>
<tr>
<td>Other gastrointestinal disorders</td>
<td>5 (4%)</td>
<td>1 (1%)</td>
<td>--</td>
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</tbody>
</table>

Molina JM, Lancet Infect Dis, 2018
Single-Dose Zoliflodacin (ETX0914) for Treatment of Urogenital Gonorrhea

Stephanie N. Taylor, M.D., Jeanne Marrazzo, M.D., M.P.H.,
Byron E. Batteiger, M.D., Edward W. Hook, III, M.D., Arlene C. Seña, M.D., M.P.H.,
Jill Long, M.D., M.P.H., Michael R. Wierzbicki, Ph.D., Hannah Kwak, M.H.S.,
Shaconda M. Johnson, B.S.P.H., Kenneth Lawrence, Pharm.D.,
and John Mueller, Ph.D.
Recap

▪ Provide LGBTQ+-affirming care
▪ Make the sexual history part of routine care
▪ Screen frequently, if the history indicates the need
▪ Vaccinate
▪ Consider doxycycline for MSM who have a high risk of STIs