STI & PrEP Updates

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STI & PrEP Updates

Marshal Miller, MD, AAHIVS
Sunny Lai, MD, MPH
April 29, 2020
Lecture Objectives

• Apply key findings from the DISCOVER trial to PrEP clinical decision-making
• Understand the gaps in PrEP research for cisgender women and adolescents
• Understand the use of on-demand pre-exposure prophylaxis
• Review Current treatment recs and emerging data on Gonococcal and Chlamydial infection
• Discuss diagnostic and management options for non-gonococcal urethritis
Case 1: Switching to Descovy for PrEP?

• 20-year-old man presents for his three-month PrEP visit.
• He has been seeing a lot of lawsuit ads on TV that Truvada is dangerous.
• He heard that Descovy is now an option.
• He asks for your opinion about switching to Descovy.
• How would you advise him?
**PrEP Timeline**

- **2012**: FDA approved Truvada for HIV pre-exposure prophylaxis for adults at risk for acquiring HIV
- **2018**: Truvada was approved for adolescents weighing at least 35 kg
- **2019**: USPSTF made a level A recommendation to offer PrEP to persons at high risk of HIV acquisition
- **2019**: FDA approved Gilead’s Descovy for PrEP for MSM and TGW, not for cis women who engage in receptive vaginal sex

## Truvada vs. Descovy

<table>
<thead>
<tr>
<th>Name</th>
<th>Tenofovir</th>
<th>Emtricitabine</th>
<th>Renal Function</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Truvada</td>
<td>Tenofovir disoproxil fumarate (TDF) 300 mg</td>
<td>Emtricitabine (FTC), 200 mg</td>
<td>Not recommended if CrCl &lt;60 mL/min</td>
<td>MSM TGW Heterosexual PWID</td>
</tr>
<tr>
<td>Descovy</td>
<td>Tenofovir alafenamide (TAF) 25 mg</td>
<td>Emtricitabine (FTC), 200 mg</td>
<td>Not recommended if CrCl &lt;30 mL/min</td>
<td>MSM TGW</td>
</tr>
</tbody>
</table>
## Prescribing PrEP

<table>
<thead>
<tr>
<th>Gay, Bisexual, and other Men who have Sex with Men, and Transgender Women</th>
<th>Heterosexual Men and Women</th>
<th>People who inject drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sexual partner with HIV</td>
<td>• Sexual partner with HIV</td>
<td>• HIV-positive injecting partner</td>
</tr>
<tr>
<td>• Recent bacterial STD</td>
<td>• Recent bacterial STD</td>
<td>• Sharing injection equipment</td>
</tr>
<tr>
<td>• High number of sex partners</td>
<td>• High number of sex partners</td>
<td>• High risk sexual behavior</td>
</tr>
<tr>
<td>• History of inconsistent or no condom use</td>
<td>• History of inconsistent or no condom use</td>
<td></td>
</tr>
<tr>
<td>• Commercial sex work</td>
<td>• Commercial sex work</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Lives in high prevalence area or network</td>
<td></td>
</tr>
</tbody>
</table>

Descovy and Truvada: approved for adolescents (>35 kg)
Truvada is safe in use in pregnancy and breastfeeding
## PrEP Labs and Monitoring

<table>
<thead>
<tr>
<th>Lab Screening and Visits</th>
<th>Initial visit</th>
<th>Month 1 (optional)</th>
<th>Every 3 months</th>
<th>At least every 6 months</th>
<th>At least every 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV test (ideally 4\textsuperscript{th} gen HIV ag/ab)</strong></td>
<td>HIV test (ideally 4\textsuperscript{th} gen HIV ag/ab)</td>
<td>Pregnancy test</td>
<td>HIV testing, assess s/sx of acute HIV</td>
<td>CrCl</td>
<td>Evaluate need to continue PrEP</td>
</tr>
<tr>
<td><strong>Cr</strong></td>
<td>Cr</td>
<td>GC/CT (site-specific)</td>
<td>Repeat pregnancy test for women who may become pregnant</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HbsAb/Ag</strong></td>
<td>HbsAb/Ag</td>
<td>Syphilis</td>
<td>STI testing</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HAV Ab</strong></td>
<td>HAV Ab</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HCV Ab</strong></td>
<td>HCV Ab</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Offer HAV, HBV and HPV immunization as indicated**
Time to steady state levels of TFV-DP:

Maximum intracellular concentrations of TFV-DP are reached in:
- Blood after 20 days of daily oral dosing
- Rectal tissue after 7 days of daily oral dosing
- Cervico-vaginal tissues at 20 days of daily oral dosing

CDC 2017
Side effects

### SHORT TERM

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Drug (%)</th>
<th>PBO (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>diarrhea</td>
<td>7%</td>
<td>8%</td>
</tr>
<tr>
<td>abdominal pain</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>back pain</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>headache</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>depression</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>anxiety</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>weight loss</td>
<td>3%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Early side effects were mild, usually resolved within first month.
Side effects may be due to non-adherence.

### LONG TERM

- Those in iPrEx who took Truvada generally showed 1–2% bone loss within first few months. Bone loss also seen in those on placebo.
- People with existing kidney dysfunction (<60 ml/min eCrCl) should probably not start Truvada.
- People on Truvada who show abnormal kidney function test results may want to stop Truvada.
- iPrEx participants who experienced kidney dysfunction saw kidney health return to normal after stopping.
- To prevent kidney damage, kidney function tests are done every 6 months.

Image credit: Please PrEP Me Navigator Manual
Metabolism of TDF vs. TAF

Image Credit: University of Washington, National HIV Curriculum

TDF 300 mg

TAF 25 mg

TDF → TDF → TFV → TFV

TAF → TAF → TAF

Cathepsin A

TFV-MP

TFV-DP
Safety Profiles of TDF vs. TAF (Studies in PLWH)

TDF

- Renal Toxicity: ↑ Prox. Tubule Dysfunction, GFR, Cr\textsuperscript{1-3}
- Bone Toxicity: ↓ BMD\textsuperscript{2,3}
- ↔ Weight\textsuperscript{4}, ↔/↑ Lipids\textsuperscript{3}

TAF

- More favorable renal and bone profile\textsuperscript{1-3}
- ↑ Weight\textsuperscript{4}
- ↑ TC, LDL, HDL; ↔ TC:HDL\textsuperscript{3}

\textsuperscript{1} Gupta et al. AIDS. 2019
\textsuperscript{2} Grant, P and Cotter, A. Curr Opin HIV AIDS. 2016; \textsuperscript{3} Wang et al. Medicine. 2016; \textsuperscript{4} Sax et al. Clin Infect Dis. 2019
What’s the safety data in people on PrEP?

Pilkington et al. *J Virus Erad*. 2018

Grade 1 Cr: 1.1-1.3x upper limit of normal

Grade 2 Cr: 1.1-1.8x upper limit of normal
DISCOVER: Study Design

• International, randomized, double-blind, active-controlled non-inferiority phase III trial

HIV and HBV-negative cis-MSM and transgender women at high risk of HIV* with eGFR ≥ 60 mL/min; previous PrEP use permitted (N = 5387)

- FTC/TAF 200/25 mg + FTC/TDF Placebo QD (n = 2694)
- FTC/TDF 200/300 mg + FTC/TAF Placebo QD (n = 2693)

• Prevention services (eg, risk reduction, condoms/lubricant) and adherence counseling provided at entry and every 12 wks

• Endpoints of current analysis: HIV incidence and safety, including renal AEs and biomarkers, bone fractures, BMD, and metabolic parameters at Wk 96

## DISCOVER: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FTC/TAF (n = 2694)</th>
<th>FTC/TDF (n = 2693)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, yrs (range)</td>
<td>34 (18-76)</td>
<td>34 (18-72)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ White</td>
<td>2264 (84)</td>
<td>2247 (84)</td>
</tr>
<tr>
<td>▪ Black</td>
<td>240 (9)</td>
<td>234 (9)</td>
</tr>
<tr>
<td>▪ Asian</td>
<td>113 (4)</td>
<td>120 (5)</td>
</tr>
<tr>
<td>Hispanic/Latinx ethnicity, n (%)</td>
<td>635 (24)</td>
<td>683 (25)</td>
</tr>
<tr>
<td>Transgender woman, n (%)</td>
<td>45 (2)</td>
<td>29 (1)</td>
</tr>
<tr>
<td>HIV risk factors, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Condomless receptive anal sex with ≥ 2 partners in past 12 wks</td>
<td>1616 (62)</td>
<td>1569 (60)</td>
</tr>
<tr>
<td>▪ Rectal gonorrhea in past 24 wks</td>
<td>274 (10)</td>
<td>262 (10)</td>
</tr>
<tr>
<td>▪ Rectal chlamydia in past 24 wks</td>
<td>342 (13)</td>
<td>333 (12)</td>
</tr>
<tr>
<td>▪ Syphilis in past 24 wks</td>
<td>230 (9)</td>
<td>263 (10)</td>
</tr>
<tr>
<td>▪ Recreational drug use in past 12 wks</td>
<td>1785 (67)</td>
<td>1786 (67)</td>
</tr>
<tr>
<td>▪ Binge drinking (≥ 6 drinks on ≥ 1 occasion; ≥ 1 time/mo)</td>
<td>618 (23)</td>
<td>599 (22)</td>
</tr>
<tr>
<td>Taking FTC/TDF for PrEP at baseline, n (%)</td>
<td>465 (17)</td>
<td>440 (16)</td>
</tr>
</tbody>
</table>

FTC/TAF is non-inferior to FTC/TDF

- Noninferiority of FTC/TAF vs FTC/TDF for HIV prevention at Wk 96 established
  - Upper bound of 95% CI of incidence rate ratio < 1.62

<table>
<thead>
<tr>
<th>HIV Incidence</th>
<th>FTC/TAF (n = 2670)</th>
<th>FTC/TDF (n = 2655)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current analysis at Wk 96†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV infections, n</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>PY of follow-up</td>
<td>5029</td>
<td>5052</td>
</tr>
<tr>
<td>HIV incidence/100 PY</td>
<td>0.16</td>
<td>0.30</td>
</tr>
<tr>
<td>Incidence rate ratio for FTC/TAF vs FTC/TDF (95% CI)</td>
<td>0.54 (0.23-1.26)</td>
<td></td>
</tr>
</tbody>
</table>
DISCOVER: Safety Data Through Wk 96

- Both regimens well tolerated with low rates of discontinuation for AEs (1% to 2%)
- FTC/TAF associated with statistically significantly more favorable renal and bone safety outcomes vs FTC/TDF
  - More favorable eGFR_{CG} changes in overall population, participants aged ≥ 50 yrs, and participants with BL CrCl 60 to ≤ 90 mL/min (P < .001 for PrEP regimen comparison in each group)
    - FTC/TAF: -0.6 mL/min vs. FTC/TDF: -4.1 mL/min
  - More favorable spine and hip BMD changes through Wk 96 (P < .001)
    - FTC/TAF: Spine (+1.0%), Hip (+0.6%) vs. FTC/TDF: Spine (-1.4%), Hip (-1.0%)
### DISCOVER: Metabolic Parameters at Wk 96

<table>
<thead>
<tr>
<th>Median Change From BL at Wk 96</th>
<th>FTC/TAF</th>
<th>FTC/TDF</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>-3</td>
<td>-14</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>-2</td>
<td>-7</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>-1</td>
<td>-4</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>+3</td>
<td>-4</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>+2</td>
<td>+2</td>
<td>.63</td>
</tr>
<tr>
<td>Total cholesterol:HDL ratio</td>
<td>+0.1</td>
<td>0</td>
<td>.18</td>
</tr>
<tr>
<td>Median body weight, kg</td>
<td>+1.7</td>
<td>+0.5</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

- Wk 96 median BMI: 25.9 with FTC/TAF vs 25.4 with FTC/TDF (P < .001)
  - BL BMI 25.3 in both arms
Messaging:
- Descovy is an alternative, non-inferior, safe and effective daily oral PrEP option for men who have sex with men and transgender women who have sex with men.
- It is not superior nor a “better PrEP.”
- Can be considered in people who are at risk for renal impairment and osteoporosis, older age.
The importance of including cisgender women in research

- Unknown relative importance of serum vs. tissue drug levels to provide protection against HIV
- Increased risk of HIV acquisition per sex act in late pregnancy and postpartum
- There is no established safety database for TAF/FTC in pregnancy
- Concerns for increased weight gain in women on TAF.

CDC, 2018; UNAIDS. Fact Sheet—Global AIDS Update 2019 Published July 2019.; Thomsen et al. CROI 2018.
The importance of prescribing PrEP to cisgender women

- Globally, more than 48% of new HIV infections are among cis women.
- Cis-gender women make up 1 in 5 new HIV infections in the United States, yet fewer than 1 in 10 are on PrEP.
- Women-controlled option
Adolescents and PrEP

• 2018, FDA approved TDF/FTC (Truvada) use for adolescents weighing >35 kg (77 lbs) for pre-exposure prophylaxis

• Unique aspects of providing PrEP among adolescents:

> Provider may provide service to minor without parental or guardian consent

https://www.cdc.gov/hiv/policies/law/states/minors.html
HHS launched this program in December 2019 as part of the government’s “End the HIV Epidemic” initiative.
Case 2: On-Demand PrEP

- 36-year-old man presents for STI screening
- MSM
- He only has sex once a month, usually planned
- Is interested in pre-exposure prophylaxis, but does not want to take a daily medication
- What do you recommend?
What do you recommend?

a) No PrEP
b) Daily TDF/FTC
c) On-demand TDF/FTC
d) Daily TAF/FTC
e) On-demand TAF/FTC
On-Demand PrEP (TDF/FTC; Truvada)

• Other terms: “non-daily PrEP,” ”event-driven PrEP,” or “2-1-1 PrEP”

• Off-label use
  • Recommended as an alternative to daily PrEP by International Antiviral Society-USA and European AIDS Clinical Society for men who have sex with men
  • Not yet recommended in the 2017/2018 CDC PrEP Guidelines

Saag et al. JAMA. 2018; https://eacs.sanfordguide.com/art/pre-exposure-prophylaxis; CDC, 2018
How is 2-1-1 done?

**Example 1:** One sex episode.
2 PrEP tablets 2-24 hours before sex; 1 PrEP tablet 24 hours after and another 48 hours after the double dose.
How is 2-1-1 done?

Example 2: Multiple sex episodes.
Continue 1 PrEP tablet every 24 hours until 2 days after last “sex day.”

Saberi P. and Scott HM. J Gen Intern Med. 2019
Example 3: Multiple sex episodes in one week.
If there are <7 days between end of one on-demand dosing period and beginning of another, take one single PrEP tablet to restart.
If there are ≥7 since last PrEP dose, start again with 2 PrEP tablets.

Saberi P. and Scott HM. J Gen Intern Med. 2019
IPERGAY Findings

- RCT in France and Canada of MSM and TGW randomized to on-demand PrEP vs. Placebo
- Median # of pills per month: 15
- 16 new HIV infections
  - TDF-FTC: 2 (0.91/100 PY)
  - Placebo: 14 (6.60/100 PY)
- Relative risk reduction of 86% (95% CI, 40-98; P=0.002)
- NNT 17

Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study

Jean-Michel Molina, Isabelle Charreau, Bruno Spire, Laurent Cotte, Julie Chas, Catherine Capitant, Cecile Tremblay, Daniela Rojas-Castro, Eric Cua, Armelle Pasquet, Camille Bernaud, Claire Pintado, Constance Delaugerre, Luis Sagaon-Teyssier, Soizic Le Mestre, Christian Chidiac, Gilles Pialoux, Diane Ponscarrne, Julien Fonsart, David Thompson, Mark A Wainberg†, Veronique Doré, Laurence Meyer, for the ANRS IPERGAY Study Group*

- Open-label extension of the IPERGAY trial
- All participants were offered on-demand PrEP (n=361)
- Median duration of follow-up: 18.4 months
- Only 2 transgender women (2/361); all other participants were cis men

Findings

- Low incidence of HIV infections
  - On-demand: 0.19/100 PY
  - Placebo: 6.6/100 PY
  - RRR: 97% (CI, 81-100)
- Similar safety data as randomized trial
TDF/FTC PrEP efficacy and Adherence (iPrEx)

Grant RM et al. Lancet Inf. Disease. 2014

\[
\begin{align*}
\text{HIV incidence (infections per 100 person-years)} & \quad \text{Tenofovir diphosphate concentration (fmol per punch)} \\
<2 \text{ tablets per week} & \quad 0 - 350 \\
2-3 \text{ tablets per week} & \quad 350 - 700 \\
4-6 \text{ tablets per week} & \quad 700 - 1250 \\
7 \text{ tablets per week} & \quad 1250 - 1500 \\
\end{align*}
\]

\{ 2-3 doses \text{ wk} \} \quad \{ 4 \text{ doses and more/week} \}
What about less frequent sex?

- Post-hoc analyses of 270 participants (134 person-years) who had periods of less frequent sex (15 pills or fewer per month) and high PrEP adherence

<table>
<thead>
<tr>
<th></th>
<th>IPERGAY RCT</th>
<th>2017 Sub-Analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median # of sex acts/month</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Median # of pills taken/month</td>
<td>15</td>
<td>9.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Person-years</th>
<th># HIV infections</th>
<th>HIV incidence rate/100 py (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>64.8</td>
<td>6</td>
<td>9.3 (3.4-20.1)</td>
<td></td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>68.9</td>
<td>0</td>
<td>0.0 (0.0-5.4)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Antoni et al. Lancet HIV. 2020
Who can be offered on-demand PrEP?

<table>
<thead>
<tr>
<th></th>
<th>2-1-1 PrEP</th>
<th>Daily PrEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who can use it?</td>
<td>Only studied in MSM, Small numbers of TGW who have sex with men (no frontal sex)</td>
<td>Anyone</td>
</tr>
<tr>
<td>Chronic HBV</td>
<td>Can trigger a flare</td>
<td>Can be used safely</td>
</tr>
<tr>
<td>Planning</td>
<td>Need to plan sex at least 2 hours in advance</td>
<td>No planning needed</td>
</tr>
<tr>
<td>“Forgiveness”</td>
<td>Not forgiving of missed doses</td>
<td>Forgiving of missed doses during the week</td>
</tr>
</tbody>
</table>

What do you recommend?

a) No PrEP (*No, the patient should be given the option for taking PrEP given that he is MSM*)

b) Daily TDF/FTC (definitely an option)

c) On-demand TDF/FTC (likely effective if able to adhere to regimen)

d) Daily TAF/FTC (*Yes, if willing to take daily, on-demand has not been studied with TAF/FTC*)

e) On-demand TAF/FTC (*No, on-demand has not been studied with TAF/FTC*)
Case 3:

• 34 yo MSM presents for routine STI screening.
• He has a remote history of chlamydia and has no other prior STI history. He is asymptomatic at present and has had 2 new partners since his last visit 1 year ago. You order labs which return as follows:
  • Syphilis EIA Negative
  • HIV Ab/AG Non-reactive
  • Urine GC PCR: Negative
  • Urine CT PCR: Negative
Case Cont'd

• He messages you 1 week later and states that his most recent partner told him he recently tested positive for chlamydia. The patient denies any sexual activity since last testing but reports that he has had both receptive anal and oral intercourse with this partner. He continues to deny any symptoms at present.

• What (if any) additional testing would you order?
Extragenital Chlamydia and Gonorrhea Among Community Venue—Attending Men Who Have Sex with Men — Five Cities, United States, 2017

**MMWR / April 12, 2019 / 68(14);321–325**

- 2371 eligible MSM screened at community sites in 5 US cities
- 34% had not been screened in prior yr; rates of STI no different

**Take home:** Sexually active MSM should be screened at least annually for chlamydia and gonorrhea at all exposed anatomic sites; higher risk, every 3-6 months
GU and Extragenital GC/CT among MSM

Figure FF. Gonorrhea and Chlamydia — Proportion* of MSM STD Clinic Patients Tested and Testing Positive† for Pharyngeal Gonorrhea and Chlamydia by Jurisdiction, STD Surveillance Network (SSuN), 2018

* Results based on data obtained from unique patients with known sex of sex partners tested for pharyngeal gonorrhea (n=23,695) and for pharyngeal chlamydia (n=21,767) ≥1 time in 2018.
† Percent positive among those tested for pharyngeal gonorrhea or chlamydia.
NOTE: See section A2.2 in the Appendix for SSuN methods.
ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men.
Association of HIV Preexposure Prophylaxis With Incidence of Sexually Transmitted Infections Among Individuals at High Risk of HIV Infection


- Overall incidence of STI 91/100 person years
- PrEP use was associated with increased STI Risk, has not been consistently shown across trials
- In this study extragenital infections made up 74% of Chlamydia and 82% Gonococcal infections
Case Cont'd

• You obtain oropharyngeal and rectal NAAT for Chlamydia and Gonorrhea. The patient is diagnosed with rectal chlamydia and prescribed 1g of azithromycin.

• Three months later, he returned to clinic. He denied having receptive anal intercourse in the interim.

• A repeat rectal swab was collected per patient request, which came back positive for rectal chlamydia.

• How would you treat him?
Case 3 of persistent rectal chlamydia

A. Retreat with 1g of azithromycin
B. Doxycycline 100 mg BID for 7 days
C. Levofloxacin 500 mg once daily for 7 days
D. Erythromycin 500 mg four times a day for 7 days
### Recommended Regimens

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>1 g orally in a single dose</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg orally twice a day for 7 days</td>
</tr>
</tbody>
</table>

### Alternative Regimens

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin base</td>
<td>500 mg orally four times a day for 7 days</td>
</tr>
<tr>
<td>Erythromycin ethylsuccinate</td>
<td>800 mg orally four times a day for 7 days</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>500 mg orally once daily for 7 days</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>300 mg orally twice a day for 7 days</td>
</tr>
</tbody>
</table>

**CDC 2015 Treatment Guidelines**
Doxycycline may be more effective at treating rectal chlamydia than azithromycin

- Meta-analysis (2014) found much higher cure rates with doxycycline than azithromycin for rectal chlamydia:
  - Doxycycline: 99.6%
  - Azithromycin: 82.9%
  - Efficacy difference: 19.9%, CI: 11.4% to 28.3%

Kong et al. BMC Infect Dis. 2014
Rectal CT are common in women

• 6% of women who attend STI clinic who were tested for rectal chlamydia tested positive

• 68% of women who tested positive for urogenital chlamydia had concurrent rectal chlamydia

• 2.2% had rectal only positivity

• Reported anal intercourse was not associated with rectal chlamydia

Chandra et al. Sex Transm Infect. 2018
- Prospective multicenter cohort study
  - Doxycycline 100 mg twice daily for 7 days for women initially positive for rectal CT
  - Azithromycin 1g single dose in vaginally positive and rectally untested or rectally negative

- Microbiological cure for rectal infections:
  - Doxycycline: 95.5%
  - Azithromycin: 78.5%

- Microbiological cure for vaginal infections:
  - Doxycycline: 95.4%
  - Azithromycin: 93.5%

Doxycycline may be more effective than azithromycin in treating rectal CT in women.
Clinical Considerations

- **Azithromycin:**
  - 1 dose only
  - Easier to do expedited partner treatment
  - May take during pregnancy
  - Effective for genital CT

- **Doxycycline:**
  - 7 day treatment, need to assess for adherence issues
  - SE: photosensitivity, GI side effects
  - Contraindicated in pregnancy
  - May be more effective at treating rectal CT
Case of persistent rectal chlamydia

A. Retreat with 1g of azithromycin
B. Doxycycline 100 mg BID for 7 days
C. Levofloxacin 500 mg once daily for 7 days
D. Erythromycin 500 mg four times a day for 7 days
Gonococcal Resistance

Figure CC. *Neisseria gonorrhoeae* — Percentage of Urethral Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin* and Ceftriaxone† by Sex and Sex of Sex Partners, Gonococcal Isolate Surveillance Project (GISP), 2009–2018

A. Azithromycin

<table>
<thead>
<tr>
<th>Year</th>
<th>MSM</th>
<th>MSW</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td></td>
<td>2%</td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td>3%</td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td>4%</td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td>4%</td>
</tr>
</tbody>
</table>

B. Ceftriaxone

<table>
<thead>
<tr>
<th>Year</th>
<th>MSM</th>
<th>MSW</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td></td>
<td>1%</td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td>2%</td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td>2%</td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td>2%</td>
</tr>
</tbody>
</table>

* Elevated Azithromycin MIC: ≥2.0 μg/mL.
† Elevated Ceftriaxone MIC: ≥3.0 μg/mL.

ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men; MSW = Men who have sex with women only.
Gonorrhea Treatment

• Uncomplicated GC infection of urethra, cervix, pharynx, rectum:
  • Preferred:
    • Ceftriaxone 250mg IM x 1
    • Azithromycin 1g PO x 1
  • Alternative: (not for pharyngeal infection)
    • Cefixime 400mg PO x 1
    • Azithromycin 1g PO x 1
  • Cephalosporin Allergy:
    • Gemifloxacin 320mg PO x 1 OR Gentamycin 240mg IM x 1 + Azithromycin 2g PO x 1

• Disseminated Infection:
  • Ceftriaxone 1g IM/IV q day, Azithromycin 1g- Treat for total of 7 days
Case 4: Non-gonococcal urethritis

• 36 yo man who has sex with women presents with a clear penile discharge and dysuria.
• Empirically treated with azithromycin 1000 mg and ceftriaxone 150 mg IM in clinic.
• Urine GC/CT NAAT collected, along with 4th generation HIV screening test and treponemal ab. All tests were negative.
• Patient returns a week later with persistent symptoms.
• How would you treat him?
How would you treat him?

A) Treat with doxycycline 100 mg BID x 7 days
B) Treat with moxifloxacin 400 mg PO daily x 7 days
C) Get more testing
D) Treat with moxifloxacin 400 mg PO daily x 7 days and metronidazole 2 g PO for one dose
Non-gonococcal urethritis is the most common sexually transmitted syndrome in men

• Major causative organisms of urethritis in men:
  • C. trachomatis (32.7%)
  • N. gonorrhoeae (24.2%)
  • M. genitalium (22.2%)
  • T. vaginalis (5.2%)
  • Co-infection with C. trachomatis and M. genitalium (5.9%)
  • Co-infection with C. trachomatis and N. gonorrhoeae (5.9%)

• Other causative organisms (rare): HSV 1/2, adenovirus, Ureaplasma urealyticum, anaerobes

Gaydos et al. Sex Transm Infect. 2009
Mycoplasma Genitalium

• One of the smallest known free-living organism; smallest genome of any species!
• Only pathogenic in the urogenital tract
• Men: discharge, dysuria, urethral stinging/itching, penile tip irritation, asymptomatic
• Women: cervicitis, pelvic inflammatory disease, infertility

Moi et al. BMC Infectious Diseases. 2015; Workowski et al. MMWR Recomm Rep. 2015
Image credit: https://images.app.goo.gl/7gkShz9d9RVVKXHD8
Diagnostic and Treatment Challenges

• Until 2019, there was no FDA-approved assay to detect M. Gent and macrolide resistance.
  • FDA approves Hologic’s Aptima M. Gent assay (Jan 2019) for vaginal, endocervical, urethral and urine
• Increasing resistance to antibiotics
  • Single dose azithromycin can induce macrolide resistance in M. Gent.
    • Widespread use of azithromycin may explain the rise in M. Gent resistance
  • Low cure rates with doxycycline (20-40%). Preferred first-line for NGU if M. gent unknown b/c:
    • 1) reduces organism load
    • 2) does not induce resistance

Chart Credit: UCSF Grand Rounds, Stephanie Cohen, 2019
NGU: A new treatment approach?

**CDC 2015**

- **Recommended Regimens**
  - Azithromycin 1 g orally in a single dose
  - Doxycycline 100 mg orally twice a day for 7 days

- **Alternative Regimens**
  - Erythromycin base 500 mg orally four times a day for 7 days
  - Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days
  - Levofloxacin 500 mg orally once daily for 7 days
  - Ofloxacin 300 mg orally twice a day for 7 days

**SFDPH STD Clinic 2019**

- NGU/other syndromes: Doxy 100 mg BID x 7d
- NAAT for GC/CT/Mgen
- Mgen(+): Moxi 400 mg Qd x 7 days
- If moxi fails: Minocycline 100 mg BID x 14 days

**Australian Protocol**

- NGU/cervicitis/PID/proctitis/contact to MG: doxy 100 mg BID x 7 d
- NAAT for GC/CT/Mgen & macrolide resistance mutation (MSM) assay
- Mgen+/MRM+: Moxi 400 mg qd x 7 days
- Mgen+/MRM-: azithro 1g then 500 mg qd x 3d

Cure rates: Doxy/azithro: 95.4%; Doxi/Moxi: 92%

How would you treat him?

A) Treat with doxycycline 100 mg BID x 7 days
B) Treat with moxifloxacin 400 mg PO daily x 7 days
C) Get more testing, if positive for Mgen → tx with moxifloxacin
D) Treat with moxifloxacin 400 mg PO daily x 7 days and metronidazole 2 g PO for one dose
Follow-up and Management NGU:

- Treat partners
- If M. gent positive, obtain TOC >3 weeks after treatment
- If GC/CT+, screen for reinfection in 3 months
- If persistent, eval for possible reinfection, resistance or trichomonas
  - May treat pre-emptively with metronidazole 2g orally as a single dose or tinidazole 2g orally in a single dose
<table>
<thead>
<tr>
<th></th>
<th>Chlamydia</th>
<th>Gonorrhea</th>
<th>HIV</th>
<th>Syphilis</th>
<th>Trich</th>
<th>HBV</th>
<th>HCV**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cis-Women</td>
<td>&lt;25 or risk</td>
<td>&lt;25 or risk</td>
<td>13-64yo</td>
<td>*</td>
<td>Hi Prev/risk</td>
<td>Hi Risk</td>
<td>Born 1945-65, Hi risk</td>
</tr>
<tr>
<td>Pregnant</td>
<td>&lt;25 or risk</td>
<td>&lt;25 or risk</td>
<td>All</td>
<td>Yes</td>
<td></td>
<td>HBsAg</td>
<td>Born 1945-65, Hi risk</td>
</tr>
<tr>
<td>MSW</td>
<td>*Hi Prev</td>
<td>*</td>
<td>13-64</td>
<td>*</td>
<td></td>
<td>Hi Risk</td>
<td>Born 1945-65, Hi risk</td>
</tr>
<tr>
<td>MSM</td>
<td>Q3-12mo</td>
<td>Q3-12mo</td>
<td>&gt;q12mo*</td>
<td>Q3-12 mo</td>
<td>Yes</td>
<td></td>
<td>Born 1945-65, Hi risk</td>
</tr>
<tr>
<td>HIV+ M</td>
<td>Dx, q12mo</td>
<td>Dx, q12mo</td>
<td>Dx, 12 mo</td>
<td></td>
<td>HBsAg, cAb, sAb</td>
<td>Dx, q12mo MSM</td>
<td></td>
</tr>
<tr>
<td>HIV+ F</td>
<td>Dx, q12mo</td>
<td>Dx, q12mo</td>
<td>Dx, q12mo</td>
<td>Dx, q12mo</td>
<td>HBsAg, cAb, sAb</td>
<td>Dx</td>
<td></td>
</tr>
<tr>
<td>Adolescents</td>
<td>F- Yes, M-*hi Prev</td>
<td>F-Yes, M-*</td>
<td>13+</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*= consider in high prevalence settings  **= USPSTF recommends screening all adults age 18-79
Thank you! Questions?