ARS Question 1: Among men who have sex with men, what percent of gonorrhea or chlamydia infections are missed if only urine is screened?

A. 1. 0%
B. 2. 10%
C. 3. 40%
D. 4. ≥70%
High Proportion of Extragenital CT/GC associated with negative urine test, STD Surveillance Network (n=21994)

Between 70-90% of infections would be missed by only screening with urine

2015 CDC STD Screening Recommendations for MSM with HIV

- Gonorrhea, chlamydia, syphilis
  - During first HIV evaluation
  - At least annually and every 3-6 months if at increased risk
- Gonorrhea and chlamydia at sites of contact regardless of condom use
  - Gonorrhea: urethra, rectum, and pharynx
  - Chlamydia: urethra, rectum
- Hepatitis C
  - During first HIV evaluation
  - Annually

Targeted Prevention: Requires Asking!
Self-collected rectal/pharyngeal STI testing

- Highly acceptable, similar performance compared to clinician-collected specimens
- Self-collection can be performed at laboratory along with blood draw/urine collection or in the exam room before/after the provider visit
- May save patient an office visit
- May save the provider time
20 yo man referred by a partner "who had syphilis"

- Considers himself healthy, no symptoms
- Two episodes of rectal gonorrhea last year
- Sometimes uses meth on weekends
- 6 partners in last 3 months; receptive/insertive anal & oral sex. Last unprotected sex 12 h ago.
- No information on recent partners’ health
- Otherwise healthy, taking no medications
- Rapid HIV Ab test negative today

His physical examination is normal.

You order syphilis serology (EIA with reflexive quantitative RPR if positive) and screen for gonorrhea in pharynx, urine and rectum; chlamydia in urine and rectum.

Which of the following do you do now?

ARS Question 2: Which of the following do you do?

A. Base future treatment on results of screening tests
B. Treat him now with a single injection of BZN PCN 2.4 x 10-6 mu IM
C. Treat him now with the first of three weekly injections of BZN PCN 2.4 x 10-6 mu IM
D. Give him doxycycline to give to his most recent sex partner
Syphilis Treatment
Primary, Secondary, Early Latent

- Penicillin treatment of choice
  - Benzathine penicillin 2.4 mu IM x 1

- No benefit of additional therapy
  - Enhanced (IM + oral)
  - Single vs. 3 weekly injections under study (NCT03637660)

- Penicillin alternatives
  - Doxycycline (100 mg BID x 14 days), ceftriaxone (1-2 g daily x 10-14 days)
  - Azithromycin 2 gm (A2058G mutation/treatment failure)
    - Most common in MSM
    - Not recommended

Partner Management in Syphilis

- Sex partners of a person with primary, secondary, or early latent syphilis
  - Within 90 days before the diagnosis: treat presumptively for early syphilis, even if serologic test results are negative.
  - >90 days before the diagnosis: treat presumptively for early syphilis if serologic test results are not immediately available and opportunity for follow-up uncertain. If serology is negative, no treatment is needed. If serology is positive, base treatment on clinical and serologic evaluation and stage of syphilis.

- Sexual transmission likely occurs only when mucocutaneous syphilitic lesions are present (uncommon after first year of infection).

- Long-term sex partners of persons who have late latent syphilis: evaluate clinically and serologically and treat on basis of findings

Expedited Partner Management?

- Expedited partner management is an option for chlamydia & gonorrhea, but not for syphilis
  - Safe and effective at reducing reinfection for GC
  - Dual therapy (cefixime 400 mg + azithromycin 1 g)
  - Consider for trichomonas
  - Review laws in your state: www.cdc.gov/std/eppt

Some do not NOT recommend for MSM
>5% of MSM with bacterial STI will be diagnosed with HIV
ARS Question 3: Would you offer him doxycycline post-exposure prophylaxis for STI?

A. Yes
B. No
C. I have no idea, that sounds crazy for more reasons than I have time to discuss

Doxy-PreP/PEP for Syphilis & Chlamydia?

**Pros**
- Effective in early work
- Relatively safe drug
  - Chronic use in acne vulgaris
- Easy to administer
- Few other options for prevention
- Considerable interest among some MSM surveyed, with use already reported (Spinelli 2018)

**Cons**
- Limited data; duration?
- Costs
- Side effects of doxycycline
  - Esophagitis/ulceration
  - Photosensitivity
- Risk compensation?
- Reproductive concerns (women)?
- Antibiotic resistance*
- Microbiome effects*
FC

- 34 yo gay man
- HIV-negative
- 10-year partner is HIV+ on ART with VL <20 consistently
- Requests HIV PrEP
- Physical examination: normal
- Baseline creatinine 0.8, urinalysis negative

ARS Question 4:

What do you recommend?

A. Take more history
B. No PrEP
C. Daily TDF/FTC
D. On-demand TDF/FTC
E. Daily TAF/FTC
F. On-demand TAF/FTC

FC

- Further history reveals that the couple is monogamous and have not used condoms “in years”.
ARS Question 5:
Now, 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

PARTNER Study: Prospective Cohort Study
• 1166 serodifferent couples from 14 European countries
  • 62% heterosexual, 38% homosexual
  • Median f/u 1.3 years
  • ~58,000 condomless sex acts
  • No PrEP or PEP use in HIV- partners
  • Result: NO linked infections

Opposites Attract Study: Observational Cohort
• 343 serodiscordant MSM couples in Australia, Brazil, Thailand
  • No exclusion for ART use, VL <200, or PrEP use
  • Median f/u 1.7 years
  • ~16,800 condomless sex acts
  • Result: NO new linked infections
So, does U=U?

People who take ART daily as prescribed and achieve and maintain an undetectable viral load have effectively no risk of sexually transmitting the virus to an HIV-negative partner.

September, 2017

Science Validates Undetectable = Untransmittable HIV Prevention Message

NIAID Now | July 22, 2018

People living with HIV whose virus is completely, durably suppressed by treatment will not sexually transmit the virus to an HIV-negative partner, according to NIAID Director Anthony S. Fauci, M.D.

ARS Question 6:

Routine rectal Chlamydia NAT test+

Besides STD treatment with ceftriaxone and azithro, what do you recommend?

A. Start PrEP – he’s having unsafe sex
B. Start PrEP – his partner is having unsafe sex
C. Start PrEP and consider couples counseling
D. No PrEP
A Vexing Problem

- 33 yo man with well-controlled HIV diagnosed with rash of secondary syphilis, confirmed by serology; no indication for LP
- Treated with appropriate BZN PCN therapy
- Serum RPR 1:1024 (day of treatment)
- Two recent sex partners; both treated in same clinic

A Vexing Problem

- Returned in 3 months
- Serum RPR 1:512

A Vexing Problem

- Returned in 6 months
- Serum RPR 1:64
A Vexing Problem

- Returned in 9 months
- Serum RPR 1:32

A Vexing Problem

- Returned in 1 year
- Serum RPR 1:8
- No new partners or known exposures to syphilis
- No intercurrent STD
- What now?
• Identified 1689 reports in the literature, reviewed 20 studies that met selection criteria.

• Median proportion of patients with serological non-response was 12.1% overall (interquartile range, 4.9–25.6)

• Serofast proportion estimated from 2 studies, which ranged from 35.2–44.4 %. Serological cure was primarily associated with younger age, higher baseline nontreponemal titers, and earlier syphilis stage.

• Relationship between serological cure and HIV status inconsistent; among HIV-infected patients, CD4 count and HIV viral load was not associated with serological cure

HPI

• 26 year old female presents to your clinic to establish care.

• She asks about HIV pre-exposure prophylaxis (PREP) based on a commercial she saw on TV.

• She is in good health with no known medical problems.

• One of her male sex partners is HIV-positive. She has seen him take ART but she does not know his viral load.

Labs

• HIV 4th generation Ag/Ab test non-reactive

• CBC/BMP/LFTS normal

• Hepatitis B surface antigen positive (HbsAg+).

• Hepatitis B surface antibody negative (HbsAb-).

• HCV Antibody negative (HCV Ab-)

• STI screen negative (urine chlamydia/gonorrhea NAAT, serum RPR)

• Urine HCG test positive
Management

• Does she need PREP?

• If yes, would you prescribe tdf/ftc today?

• What additional information will help you make a decision?

Timeline

• TDF/FTC HIV PREP was approved by FDA in 2012
• USPSTF PREP Guidelines 2019
• Grade A Recommendation:
  • Pregnancy

34 y.o. HIV+ (CD4 200) man w/ rectal discharge, bleeding, pain that first occurred 2 mos prior, off ART
• Given routine GC, chlamydia, & syphilla treatment
• Symptoms recur with severe pelvic, pain radiating to back
• Monogamous with male partner; family history of Crohn’s disease and colon cancer

Colonoscopy: rectal ulcers with inflammation, friable mucosa; no abscess

Courtesy of Catherine McLean, CDC
CT scan: Perirectal wall thickening and surrounding inflammatory changes.
Limited local lymphadenopathy

ARS Question 7: What Would You Do Now?

A. Start immunomodulatory therapy to treat for inflammatory bowel disease
B. Retreat for gonorrhea assuming infection with fluoroquinolone-resistant strain
C. Obtain diagnostic tests for Chlamydia trachomatis from rectal mucosa and start doxycycline therapy
D. Treat empirically for genital herpes and do nothing else

Results

- Colon Bx: fibropurulent debris, granulation tissue; special stains- AFB, PAS, Steiner negative
- Rectal swab of ulcer: Chlamydia trachomatis (NAAT); negative for HSV, GC, chancroid, enteric pathogens
- Urine negative for C. trachomatis, GC
- Sent for genotyping to CDC
Lymphogranuloma venereum

- Caused by L1-L3 serovars of *C. trachomatis*
- MSM presenting with proctitis should be tested with rectal NAATs (chlamydia)
  - Additional molecular testing (PCR based genotyping) can be used to differentiate LGV vs. non-LGV strains
- LGV proctitis can resemble *C. difficile*, and be mistaken for inflammatory bowel disease
- Clinical syndrome of severe proctitis should receive presumptive treatment (doxy 100 mg bid x 21 d)
  - In addition if painful perianal ulcers or mucosal ulcers (anoscopy) presumptive therapy for herpes
- CROI 2019: azithromycin 1 g orally weekly x 3 weeks was effective (Blanco no. 1011)

RP

- 47 yo woman
- HIV-negative
- No prior history of kidney disease
- HIV+ male partner, not on ART
- Requests HIV PrEP
- Physical examination: normal
- Baseline creatinine 1.0, urinalysis negative

ARS Question 8: What do you recommend?

A. Daily TDF/FTC
B. On-demand TDF/FTC
C. Daily TAF/FTC
D. On-demand TAF/FTC
E. Continue condoms -- no PrEP
RP

- Prescribed TDF/FTC daily
- Routine follow-up at 3 months
  - HIV Ag/Ab (4th generation) negative
  - Creatinine 1.2 mg/dl
  - Calculated creatinine clearance 56 cc/min
  - Urinalysis negative
  - Urine culture negative

ARS Question 9:

What do you recommend?

A. Continue daily TDF/FTC
B. Change TDF/FTC to every other day
C. Change TDF/FTC to “on-demand” dosing
D. Change to daily TAF/FTC
E. Discontinue PrEP

RP

One month later...
- Feels “dehydrated”
- Taking NSAIDs for knee pain
- Creatinine ↑ 1.4
- Calculated creatinine clearance ↓ 45 cc/min
- BP normal
- Urinalysis negative
- Renal USG negative
ARS Question 10:

In addition to encouraging hydration and holding NSAIDs, what do you recommend?

A. Continue daily TDF/FTC
B. Change TDF/FTC to every other day
C. Change TDF/FTC to “on-demand” dosing
D. Change to daily TAF/FTC
E. Discontinue PrEP

Rates of Detectable TFV/TFV-metabolite detection in Female Mucosal Tissues – Single Dose Study

- TAF 25mg
- TDF 300mg

100% 100% 100% 37%

Rectal Tissue

RP

- Changed to every other day TDF/FTC
- Repeat labs
  - Creatinine 1.03 mg/dl
  - Calculated creatinine clearance >60 cc/min
  - Serum phosphate normal
  - Urinalysis negative
- Changed back to daily TDF/FTC
4 months later…

- HIV Ag/Ab (4th generation) negative
- Creatinine 1.08 mg/dl
- Calculated creatinine clearance >60 cc/min
- Urinalysis negative

38 yo man with blurry vision

- Well-controlled HIV, CD4 488 (22%)
- Has had a week or so of increasingly blurry vision in R eye
- No other complaints
- 1 primary male partner, also HIV+, no condoms; occasional outside male partners
- Prior h/o of rectal GC; syphilis EIA negative 6 mo ago
- Normal neuro exam; ophthalmologic exam unrevealing (undilated pupils)
- You are concerned about ocular syphilis, so you initiate presumptive treatment for neurosyphilis with IV Penicillin (PCN G) and refer him immediately for ophthalmology evaluation

ARS Question 11: Assuming it is feasible, would you perform a lumbar puncture?

- Yes
- No
In Favor
- CNS involvement in early syphilis is common (40%) & predicted clinical neurosyphilis in the pre-antibiotic era
- BZN PCN does not penetrate CNS
- Syphilis contained by cell-mediated immunity, and may be more severe in HIV

Against
- Frequency of serious neurosyphilis low in both untreated syphilis & early syphilis treated with BZN PCN
- PCN in CNS may not be needed to suppress early CNS invasion
- Cost & inconvenience of LP

Recommendation: careful evaluation for signs & symptoms, treatment failure

Evaluation of CNS Involvement
- Clinical signs (neurologic, ocular, auditory, meningitis, stroke) warrant investigation
- CNS invasion in early syphilis is common
- CSF abnormalities
  - Unknown clinical significance in absence of signs or symptoms
- Neurosyphilis: CSF tests + reactive RPR + signs/sx
- Lumbar puncture (LP): neuro/ocular symptoms, serologic treatment failure, tertiary
  - Some studies in HIV+ showed association with CSF abnormalities*
  - RPR ≥ 1:32 and/or CSF OD4 ≥ 0.8
- Unless neurologic signs/symptoms, value of LP unknown

* Marra 2004; Libois A, STD 2007; Ghanem CID; Marra CID 2008

LP in Syphilis / HIV

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Recommendation: careful evaluation for signs & symptoms, treatment failure
AC

• 27 yo gay man
• Baseline HIV Ag/Ab test negative
• Starts PrEP with daily TDF/FTC
• Reports excellent adherence
• Intermittently uses condoms
• Week 4: HIV Ag/Ab test negative
• Week 12: HIV Ag/Ab test negative
• Week 24: HIV Ag/Ab test positive, Immunoblot for HIV-1 and HIV-2 negative, HIV RNA <20 copies/ml

ARS Question 12:
What is your interpretation?
A. He’s not infected -- this is a false positive Ag/Ab test.
B. He is infected -- this is a false negative Immunoblot test.
C. He is infected -- PrEP has decreased the HIV RNA level.
D. I need more information.
Timeline Following HIV Infection

AC
Repeat testing 1 week later shows:
- HIV Ag/Ab test positive
- Immunoblot for HIV-1 and HIV-2 negative
- HIV RNA <20 copies/ml

ARS Question 13:
Now what?
A. Continue PrEP and retest
B. Add a PI to his PrEP and retest
C. Add an II to his PrEP and retest
D. Stop PrEP and retest
Managing Ambiguous HIV Tests in PrEP

<table>
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<tr>
<th>Possible Strategy</th>
<th>Pros</th>
<th>Cons</th>
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<td>Continue PrEP</td>
<td>If adherent, low pre-test probability of HIV; ↓ risk of HIV infection</td>
<td>If infected, may select drug mutations</td>
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<tr>
<td>Start ART (PrEP + PI or II)</td>
<td>If infected, prevent drug resistance and ↓ seeding of reservoirs</td>
<td>If uninfected, unnecessary ART exposure; diagnosis and insurance issues</td>
</tr>
<tr>
<td>Discontinue PrEP</td>
<td>May facilitate diagnosis quickly by allowing HIV replication</td>
<td>If uninfected, ↑ risk of HIV infection</td>
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Follow-up

- Off PrEP, repeat testing shows:
  - HIV Ag/Ab test negative
  - HIV Ag/Ab DIFFERENT test negative
  - Immunoblot for HIV-1 and HIV-2 negative
  - HIV RNA <20 copies/ml
  - HIV DNA negative

Bonus Cases
- 16 yr old previously healthy female presented to the dermatologist with facial rash for past 2 months, which started on her arm and spread to her axilla, chest and face
- Pt was seen by primary care provider for this rash about a month ago, prescribed topical steroids with no improvement
- Rash was not itchy, no redness, no pain
- Denied fever, URI, headache, malaise, anorexia, sore throat, myalgias, weight loss and lymphadenopathy
- Social history: recently at summer camp, denied being sexually active (ever)

Exam: 1 cm hypopigmented macules with central sparing, on face, extending to trunk, few spots scattered on arms, no palm/sole involvement
Q14: What is the rash from?
A. Pityriasis rosea  
B. Treponema pallidum  
C. Tinea corporis  
D. Discoid lupus  
E. Eczema

Discharge/Follow-up
- Dermatology: Biopsy of the axillary lesion performed  
- Patient was sent home with diagnosis of possible discoid lupus  
- A week later, path results prompted patient to be recalled to care

Labs
- Biopsy revealed *Treponema pallidum* on Warthin Starry silver stain  
- RPR 1:64, TPPA positive  
- HIV Ag-Ab test positive
A 45 year old woman is diagnosed with HIV (CD4 = 26, VL = 265,000). She is started on dolutegravir & TAF/FTC. She returns 4 weeks after initiating ART with painful genital lesions, myalgias and fevers. She has never had these symptoms before and denies a history of genital herpes. She has one long-term sexual partner. Last sex was 2 months ago. Her examination shows:

Exam

Q 15: Which of the following is the most likely cause of her symptoms?
A. Primary HSV-2
B. Fixed drug eruption
C. HSV-2 IRIS
D. Erosive lichen planus
E. Secondary syphilis
Key Points: HSV-2 & IRIS
- Can occur in 6 months after ART initiation
- More severe than recurrences with local and systemic symptoms
- Most people with HSV-2 are not aware of their infection (like this patient); consider HSV-2 serologic screening in HIV care
- For patients with known HSV-2 and low CD4 counts initiating ART, consider suppressive therapy.

Accurate HSV Serology: Type Specific
- Glycoprotein gG tests
  - Western blot
  - gG ELISA
  - gG membrane tests
  - gG immunoblot

Genital Herpes: HIV OI Guidelines Preventing Recurrence
- Suppressive therapy for HSV may be continued indefinitely, without regard for improved CD4 cell count, although need for continuation should be addressed on an annual basis, particularly if immune reconstitution has occurred (BIII).
- In persons starting ART with CD4 cell counts <250 cells/mm³, there is an increased risk of HSV-2 shedding and genital ulcer disease in the first 6 months; suppressive ACV decreases the risk of GUD nearly 60% compared to placebo, and may be recommended for persons with CD4 cell counts <250 cells/mm³ starting ART (Bii).
- The use of daily suppressive therapy (when compared to episodic therapy) has been associated with a lower risk of development of acyclovir-resistant HSV in hematopoietic stem cell recipients; there are no specific data for persons with HIV infection.

U.S. O.I. Guidelines, September 2015 (no revisions on this in recent updates)
47-y.o. man complaining of painful lesion penis for 2 weeks

Sexual history: 1 male partner in past 3 months; oral sex (both insertive and receptive) and insertive anal sex only

No history of STIs

No history of (injection) drug use

Last HIV test >2 years ago (negative)

2.5 cm round, superficial ulceration on shaft

No lymphadenopathy

HIV (rapid test): reactive

24 y.o. male complaining of initially non-painful penile lesions for 1 month; they have gradually become more uncomfortable

Pt denies new female partners, sex with men, or injection drug use

No history of STI

Last HIV test: 4 months ago – negative by self-report
Large, partly confluent, superficial erosions inside foreskin, corona and extending onto glans penis, painful to the touch
Tender, bilateral inguinal lymphadenopathy

Q16: What do you do now?

A. Treat for primary syphilis
B. Treat for genital herpes
C. Treat for syphilis and herpes
D. Provide NSAIDs and await test results (syphilis serology; HSV2 PCR)
Both Cases

- Initially treated for syphilis and herpes
- Herpes cultures positive for HSV-2
- CD4 counts 23 and 12, respectively
- Syphilis serologies negative

---

Healthy HIV+ 40 y.o. man sexually active with men, receptive/insertive anal/oral sex "usually" with condoms if receptive anal only
- Screening last week at all sites revealed +NAAT for *N. gonorrhoeae* at the pharynx.
- He reports hives on receipt of penicillin as a child, and has not received penicillin since.

---

Q17: What do you do?

A. Treat with IM ceftriaxone, 250 mg, now
B. Document negative skin testing for PCN allergy prior to treatment with ceftriaxone
C. Treat with oral azithromycin, 2 gram, now
D. Treat with IM gentamicin (240 mg) and oral azithromycin (2 gram) now
2015 CDC Gonorrhea Treatment Guidelines

PENICILLIN ALLERGY
RECOMMENDED THERAPY

- Gentamicin
  240 mg IM x 1
- Azithromycin
  2 g PO x 1
- Gemifloxacin
  320 mg PO x 1

NOTES:
- Urogenital infections only
- Nausea is a common side effect of these regimens

Source: CDC and Prevention. MMWR. 2015.64(3)