Optimizing STD Management for Patients Living with HIV

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The views expressed herein do not necessarily reflect the official policies of the City and County of San Francisco; nor does mention of the San Francisco Department of Public Health imply its endorsement.

I will be discussing off-label use of Gonorrhea, Chlamydia and Trichomonas NAATs with local laboratory validation procedures

Overview

• Lots of STDs in patients at risk for HIV or living with HIV
• Case based review of key clinical management issues

http://www.cdc.gov/std/tg2015/CDC Treatment Guidelines App for iOS and Android Available now, FREE! (accept no competitors)

In New York City, Prior STD places men at risk for HIV

As PrEP Expands, STD screening is important

Expert STD clinical services are a Key Factor in Reducing HIV in the United States

Volk et al. CID 2015; slide courtesy Dr. Volk
High Prevalence of STDs in people living with HIV/AIDS

Kalichman S C et al. Sex Transm Infect 2011;87:183-190

Median point prevalence 12%

Multiple, Continued Recommendations to Screen for STDs in HIV-infected Patients

Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America

All patients

Recommended annual gonorrhea and chlamydia screening lags behind lipid screening in seven HIV-care clinics

In your practice, what is the single biggest barrier to routine STD screening?

1. Want to do it, not enough time
2. STD screening not a priority
3. STD lab tests not readily available
4. Challenges incorporating screening into visit
5. Patients decline screening
6. Other barrier (not listed here)
7. No barrier - I routinely screen
Practical Provider Tools for Sexual History

Case 1

David is a 28 year old HIV positive man, new to your practice. His CD4 is 989 and VL undetectable on ABC/3TC/DTG. He feels fine and is here to establish primary care. His partners are all men. During the visit, he says that while he has not had any symptoms or been notified of any exposure, but would like an STD check – whatever you recommend.

What would you recommend?

1. Urine for Gonorrhea and Chlamydia
2. Syphilis serology
3. Rectal Gonorrhea and Chlamydia swab
4. Pharyngeal Gonorrhea and Chlamydia swab
5. All of the above
6. No screening indicated – he is asymptomatic
7. I would like more info before deciding

Screening: Which STDs and How Often?

For any HIV-infected patient, on entry and then at least annually - as often as every 3-6 months for those at higher risk:

- Gonorrhea
- Chlamydia
- Syphilis
- Hepatitis C serology ('at least yearly')
- Hepatitis A and B serology on entry (if negative, vaccinate)
- Trichomonas (women)
- HPV (anal cancer): Annual digital rectal exam may be useful, some centers perform anal Pap and HRA for ASC-US or worse.

CDC 2015 STD Treatment Guidelines
Unlike Urethral Infections, most Rectal Gonorrhea and Chlamydia infections in MSM are Asymptomatic.

Can we screen a single anatomic site (i.e. urine) and assume concordance at the pharynx and rectum?

No, will miss majority of cases.

Case 1, continued

Patient’s results: rectal GC NAAT+, all else neg. You call to give him the results and to arrange treatment.

To make life more interesting - he is traveling out of state and just before he hangs up says that he once had a severe reaction to cephalosporins that landed him in the hospital.
Which of these is now the best option for treating GC in this patient?

1. Cefixime 400mg PO x 1 AND azithromycin 1g PO x 1
2. Azithromycin 2g PO x 1
3. Gemifloxacin 320 mg PO x 1 and Azithromycin 2g PO x 1
4. Gentamicin 240mg IM x 1 and Azithromycin 2g PO x 1

Gonorrhea Treatment is one of CDC's key strategies to reducing risk of resistant Neisseria gonorrhoeae

Gonorrhea changes: 2015 Treatment Guidelines

- Doxycycline no longer recommended (leave only Ceftriaxone + Azithromycin as recommended tx)
- Limit Test of cure only to pharyngeal GC treated with alternative regimen, may extend interval to 14 days
- For cephalosporin allergic, add 2 regimens
  - Gentamicin 240 mg IM (or 5mg/kg IM) with azithromycin 2g orally
  - Gemifloxacin 320 mg orally with azithromycin 2g orally
The Efficacy and Safety of Gentamicin Plus Azithromycin and Gemifloxacin Plus Azithromycin as Treatment of Uncomplicated Gonorrhea

Kirkcaldy CID 2014

Primary Outcome

<table>
<thead>
<tr>
<th></th>
<th>Gentamicin/Azithro</th>
<th>Gemifloxacin/Azithro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethral/cervical</td>
<td>(n/N=202/202)</td>
<td>(n/N=198/199)</td>
</tr>
<tr>
<td></td>
<td>100% (95%CI 98.5% – 100%)</td>
<td>99.5% (95% CI 97.6% - 100%)</td>
</tr>
</tbody>
</table>

Secondary Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Gentamicin/Azithro</th>
<th>Gemifloxacin/Azithro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngeal</td>
<td>n/N= 10/10 (100%)</td>
<td>n/N=15/15 (100%)</td>
</tr>
<tr>
<td>Rectal</td>
<td>N=1/1 (100%)</td>
<td>N=5/5 (100%)</td>
</tr>
</tbody>
</table>

Mild-mod GI side effects were common in both arms (47-55%)

Resistant Gonorrhea: More to Come?

- Routine gonorrhea surveillance: Seven isolates from Honolulu with high level Azithromycin resistance
- Very Concerning: Five of seven also with reduced susceptibility to ceftriaxone (first cases documented in US)
- No treatment failures with CDC recommended dual treatment

Case 2

28 year old woman, Suzette, is new to your practice. She previously injected drugs but not in the past 10 years. HCV screen negative and she is asymptomatic. Stable on ARVs with undetectable VL and high CD4.

The lab calls to tell you that the patient’s syphilis results are:

EIA+, RPR nonreactive

Best next step?

1. Treat with benzathine PCN 2.4 mu IM x 1
2. Treat with benzathine PCN 2.4 mu IM x 3
3. Need more information before proceeding
4. Do nothing as this is unlikely to be syphilis
5. Perform an LP to rule out neurosyphilis

Syphilis Screening Paradigm

TRADITIONAL

Non-treponemal tests (e.g., RPR, VDRL)
- NON-SPECIFIC ANTIBODY TO LIPOIDAL ANTIGENS
- QUANTITATIVE
- REACTIVITY DECLINES WITH TIME

Treponemal tests (e.g., TPPA, FTA-Abs)
- SPECIFIC TO TP
- QUALITATIVE
- REACTIVITY PERSISTS OVER LIFETIME
Syphilis Screening Paradigm

Reverse Algorithm

Treponemal tests (e.g., EIA, CIA, MBA)
- SPECIFIC TO TP
- QUALITATIVE
- REACTIVITY PERSISTS OVER LIFETIME

Non-treponemal tests (e.g., RPR, VDRL)
- NON-SPECIFIC ANTIBODY TO LIPOIDAL ANTIGENS
- QUANTITATIVE
- REACTIVITY DECLINES WITH TIME

Second treponemal test (TPPA) is 'tie-breaker'

EIA+ RPR- TPPA + cannot distinguish old vs. new infection so must review diagnosis and treatment history! Call public health!

Syphilis Natural History

Primary: painless chancre, lymphadenopathy
Secondary: systemic symptoms, cutaneous rash, mucus patches, condylomata lata, alopecia, hepatitis, glomerulonephritis, CNS involvement including eye and ear sx and signs
Latent (Early & Late, Unknown duration): no symptoms, relapse into secondary possible in early latent
Tertiary: late complications (skin, heart, brain)

Neurosyphilis can occur at any stage!!

Primary Syphilis

Early
- < 1 yr
- public health priority: more infectious
- Shorter treatment

Late
- >1 yr
- Lower public health risk
- Longer treatment

Primary Syphilis
Chancres may be multiple, cannot easily distinguish from herpes

Chancres may be perirectal, not noticed by patient

Chancres may be vaginal or cervical, not noticed by patient

Chancres may be oral or on lip
Secondary syphilis

Secondary rash may mimic drug rash or other derm conditions

Secondary rash – scrotum

Secondary rash – soles of feet
Condylomata lata

Mucous patch

Same patient, 1 week after treatment with benzathine penicillin

Syphilis Treatment — no change in 2015 Guidelines

Primary, Secondary & Early Latent:
- Benzathine penicillin G 2.4 million units IM in a single dose

Late Latent and Unknown Duration:
- Benzathine Penicillin G 7.2 million units total, given as 3 doses of 2.4 million units each at 1 week intervals

Neurosyphilis:
- Aqueous Crystalline Penicillin G 18-24 million units IV daily administered as 3-4 million IV q 4 hr for 10-14 d

No enhanced efficacy of additional doses of penicillin, amoxicillin or other antibiotics even if HIV infected!

CDC 2015 STD Tx Guidelines www.cdc.gov/std/treatment
Primary, Secondary & Early Latent:

Alternatives (non-pregnant penicillin-allergic adults):
- Doxycycline 100 mg po bid x 2 weeks
- Tetracycline 500 mg po qid x 2 weeks
- Ceftriaxone 1 g IV (or IM) qd x 10-14 d
- Azithromycin 2 g po in a single dose*

* Should be used with caution and not in MSM or pregnant women

In pregnancy, benzathine penicillin is the only recommended therapy. No alternatives

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

Syphilis – When to LP?

- Clinical signs of neurosyphilis
  - Cranial nerve dysfunction, meningitis, stroke, acute or chronic altered mental status, auditory or ophthalmic abnormalities
- Serologic treatment failure
- Evidence of active tertiary syphilis (e.g. aortitis, gumma)
- HIV positive and late latent syphilis or syphilis of unknown duration

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

Syphilis Stage Determines Treatment

If you cannot ascertain that infection has happened in < 1 year, then must treat for late disease

What can help pinpoint timing of infection?

- Signs or symptoms of primary or secondary
- Can recall those symptoms in past year
- Contact to a known case in past year
- Negative non-treponemal serology (RPR or VDRL) in the past year
  - In HIV-infected patients at higher risk for syphilis, consider getting RPR with every CD4 or VL

Syphilis Management Pearls

- Public Health will interview P&S patients in order to prevent primary syphilis in exposed partners – please prepare patients!
- Public health may be able to help track down prior syphilis labs or treatment
- If classic signs of secondary but negative RPR, consider prozone phenomenon (false neg RPR in setting of extremely high titer) and ask lab to dilute specimen and retest
- If delay between lab draw with positive RPR and treatment, re-draw day of treatment titer
**In Late Latent Syphilis, What is the Maximum Time Allowed Between Benzathine PCN Doses?**

- Clinical experience suggests 10-14 days ok for non-pregnant adults
- <9 days is best based on limited pharmacologic data
- In pregnancy, must adhere to strict 7 days between doses
  - 40% of pregnant women are below treponemical levels after 9 days
  - If a dose is missed, the entire series must be restarted

Collart 1980, Fretz 1984, Hagrup 1986

**Case 2, continued**

Your patient Suzette has completed a full course of treatment. Assuming she continues to have no symptoms, when (if at all) would she need follow up testing?

1. Test of cure at 3 weeks
2. Rescreen at 3 months
3. Resume annual screen
4. As needed per her request

**Additional Screening after an STD infection**

- Women with CT, GC or trich should be rescreened for all at 3 months after treatment.
- Men with CT or GC should be rescreened at 3 months after treatment.
- Patients diagnosed with syphilis should undergo follow up serologic testing every 3-6 months.
- HIV testing should also be considered in all HIV-uninfected patients with a prior STD history.

Should also perform pregnancy testing in women diagnosed with an STD

**Congenital Syphilis increased 38% in the US between 2012-14**

Screen all pregnant women at start of prenatal care, and if high risk at start of 3rd trimester and again at delivery (3 total screens)

CDC 2015 STD Treatment Guidelines
**Additional Points on Preventing Congenital Syphilis**

- Congenital cases are sentinel events for clinical delivery systems AND public health
- Public health prioritizes female partners of male syphilis cases – please prepare patients and encourage them to work with us to ensure partners are treated
- Remember that penicillin is the only acceptable treatment for pregnant women with syphilis – must desensitize if serious true allergy
- Must adhere to strict 7-day interval for weekly benzathine penicillin in pregnant patients with late latent syphilis. If longer, must restart series. Reinforces importance of annual (at least) screening which narrows infection window and allows us to stage as early syphilis and rx with benzathine PCN 2.4mu IM x 1

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**One last, Important Syphilis Item: Clusters of Ocular Syphilis in Western States**

Cluster of four cases Washington State Dec 2014 – Jan 2015
- All MSM, 75% HIV-infected
- Two patients with permanent visual loss

Subsequently eight cases identified in San Francisco Dec 2014-March 2015
- (75% MSM, 88% HIV-infected)

Providers should have a high suspicion for syphilis in patients with visual complaints, especially HIV-infected MSM

Treatment for ocular syphilis is IV PCN as for neurosyphilis even if the CSF lab tests are negative

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**Thank You!**

2015 CDC STD Treatment Guidelines:
http://www.cdc.gov/std/tg2015/

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