Clinical Pearls: How to Treat Commonly Seen Infections (and When Not to Treat)

John Koeppe, MD
February, 2017
Outline and Objectives

• Recurrent UTIs in Elderly Women
  – Non-antibiotic options for prevention

• Screening and treatment of latent TB
  – Populations at risk, screening tests and treatment

• Screening and treatment of syphilis
  – Populations at risk, screening tests and treatment

• PrEP
  – Populations at risk, testing and management
Disclosures

• No financial disclosures.
• Exactly who we’re supposed to be screening for Latent TB and Syphilis will remain somewhat ambiguous at the end of today’s talk.
Recurrent Urinary Tract Infection in Elderly Women
Case Presentation

- 80 y/o female with her fifth UTI in the last year.
- Urine has repeatedly grown E coli with varying sensitivities.
- UA shows large leuk esterase and treatment is initiated (eventually grows E coli).
Recurrent UTIs in Elderly Women

The best option to prevent recurrent UTIs would be:

a. Vaginal estrogen
b. Cranberry juice or capsules
c. Vaginal probiotics
d. Methenamine
e. Daily antibiotics to prevent infection
f. Symptomatic therapy when infections occur
Vaginal Estrogen

- Estrogen lowers vaginal pH
- Promotes colonization with lactobacilli
- Lactobacilli produce $\text{H}_2\text{O}_2$
- This decreases colonization with E coli and coliforms.

<table>
<thead>
<tr>
<th>Study</th>
<th>Estrogen</th>
<th>Control</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>0.5 events / year (N = 50)</td>
<td>5.9 episodes / years (N = 43)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2003</td>
<td>51 % UTI / 9 month (N = 53)</td>
<td>80 % UTI / 9 month (N = 55)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Cranberries / Cranberry products

- Anthrocyanidins are thought to inhibit binding of P-fibrinated E coli to urethral epithelium.

<table>
<thead>
<tr>
<th>Study</th>
<th>Cranberry</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>0.45 UTI / year (N = 50)</td>
<td>0.81 UTI / year (N = 50)</td>
<td>0.03</td>
</tr>
<tr>
<td>2002</td>
<td>18–20% ≥ 1 UTI / year (N = 100)</td>
<td>32% ≥ 1 UTI / year (N = 50)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>2011</td>
<td>16.9% UTI / 6 months (N = 155)</td>
<td>14.6% UTI / 6 months (N = 164)</td>
<td>0.21</td>
</tr>
<tr>
<td>2012</td>
<td>27.5% UTI / 6 months (N = 120)</td>
<td>30.4% UTI / 6 months (N = 56)</td>
<td>0.70</td>
</tr>
<tr>
<td>2013</td>
<td>29.1% UTI / 6 months (N = 55)</td>
<td>49.2% UTI / 6 months (N = 63)</td>
<td>0.043*</td>
</tr>
<tr>
<td>2016</td>
<td>8.3% UTI / 1 year (N = 92)</td>
<td>10.8% UTI / 1 years (N = 93)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Probiotics

• Lactobacilli colonization of the vagina is thought to be protective against UTIs.

<table>
<thead>
<tr>
<th>Study</th>
<th>Probiotic Vaginal Suppository</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>1.3 UTI / Year (N = 9)</td>
<td>5.0 UTI / Year (N = 9)</td>
<td>0.0007</td>
</tr>
<tr>
<td>2011</td>
<td>15% UTI / 10 weeks (N = 48)</td>
<td>27% UTI / 10 weeks (N = 48)</td>
<td>NS</td>
</tr>
</tbody>
</table>


• Lactobacilli given oral resulted in detectable vaginal colonization in 4/46 (9.5%) of post-menopausal women.

Methenamine

• Pre and Post Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Pre-methenamine</th>
<th>Post-methenamine</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1978 (N = 20)</td>
<td>3.1 UTIs / year</td>
<td>0.7 UTIs / year</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>1981 (N = 43)</td>
<td>3.9 UTIs / year</td>
<td>2.3 UTIs / year</td>
<td>NG</td>
</tr>
</tbody>
</table>


• Control / Placebo Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Placebo / No drug</th>
<th>Methenamine</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974</td>
<td>3.6 UTIs / year (N = 40)</td>
<td>1.6 UTIs / year (N = 40)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>1982</td>
<td>63.2% recurrence (N = 68)</td>
<td>34.2% recurrence (N = 73)</td>
<td>NG</td>
</tr>
</tbody>
</table>

## Suppressive Antibiotics

<table>
<thead>
<tr>
<th>Study</th>
<th>Antibiotic (UTI/year)</th>
<th>Control (UTI/year)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974</td>
<td>Nitrofurantoin (N=61) 0.45</td>
<td>Methenamine (N=58) 0.56</td>
<td>NG</td>
</tr>
<tr>
<td></td>
<td>Trimethoprim (N=58) 0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TMP/SMX (N=62) 0.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1974</td>
<td>SMX (N=40) 2.5</td>
<td>No drug (N=40) 3.4 UTI/yr</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>TMP/SMX (N=40) 0.1</td>
<td>Methenamine (N=40) 1.6 UTI/yr</td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>Nitrofurantoin (N=56) 1.0</td>
<td>Methenamine (N=43) 2.3 UTI/yr</td>
<td>NG</td>
</tr>
<tr>
<td>1982</td>
<td>Nitrofurantoin (N=72) 25.0% recurred</td>
<td>Placebo (N=68) 63.2% recurrence</td>
<td>NG</td>
</tr>
<tr>
<td></td>
<td>Trimethoprim (N=77) 10.4% recurred</td>
<td>Methenamine (N=73) 34.2% recurrence</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>Nitrofurantoin (N=79) 0.8</td>
<td>Vaginal Estrogen (N=71) 2.0 UTI/yr</td>
<td>0.004</td>
</tr>
<tr>
<td>2009</td>
<td>Trimethoprim (N=68) 41.2%</td>
<td>Cranberry extract (N=69) 72.4% UTI/yr</td>
<td>NS</td>
</tr>
<tr>
<td>2011</td>
<td>TMP/SMX (N = 95) 1.8 % UTI / 1 year</td>
<td>Cranberry extract (N = 111) 4.0 % UTI / 1 year</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Just treat UTI symptoms?**

- Healthy women age 18 – 65...

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ibuprofen (N = 241)</th>
<th>Fosfomycin (N = 243)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics Rx’s</td>
<td>85 patients/94 scripts</td>
<td>243 patients/283 scripts</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mean symptom duration</td>
<td>5.6 days</td>
<td>4.6 days</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>5 (2%)</td>
<td>1 (0.4%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Recurrent UTI (Day 0 – 28)</td>
<td>27 (11%)</td>
<td>34 (14%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Recurrent UTI (Day 28 – 180)</td>
<td>34/189 (18.0%)</td>
<td>46/197 (23.4%)</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Recurrent UTIs in Elderly Women

• Non-antibiotic therapies for preventing UTIs;
  – Methenamine > Vaginal estrogen > Vaginal probiotics > Cranberry products.
• If using antibiotic suppression, nitrofurantoin would be my preferred choice.
• Symptomatic management of UTIs is not standard of care; but something to watch for with future research.
Screening and treatment for Latent TB
Routine Screening? For who?

- The USPSTF recommends screening for latent TB infection (LTBI) in populations at increased risk (B recommendation).

  USPSTF. Screening for Latent Tuberculosis Infection in Adults. JAMA 2016;316(9):962-969

- No studies evaluated the benefits and harms of screening versus no screening.

Case Presentations

- 30 y/o male from Mexico. Came to U.S. at age 25.
- 36 y/o female refugee from Somalia. Came to the U.S. at 23.
- 28 y/o female with Crohn’s disease who is planning to start Humira.
- 22 y/o pre-med student who has lived in Colorado his whole life. QuantiFERON requested prior to volunteering at hospital is positive.
Increased risk of TB exposure

- Two thirds of new infections are among foreign born.
  - Africa, Asia, Eastern Europe, Latin America, Middle East
- Close contact with persons who have TB.
- Work or residence in:
  - Homeless shelters, Correctional facilities, Nursing homes or Homes for persons with HIV

[https://www.cdc.gov/tb/publications/ltbi/targetedtesting.htm#identifyingTBDisease](https://www.cdc.gov/tb/publications/ltbi/targetedtesting.htm#identifyingTBDisease)
Increased risk of TB progression

- HIV Infection
- IVDA
- Radiographic evidence of prior healed TB
- Other medical conditions
  - Silicosis
  - Diabetes mellitus
  - CRI or HD
  - Gastrectomy or jejunoileal bypass
  - Solid organ transplant
  - Head and neck cancer
  - Other immunocompromising conditions including use of TNF-α antagonists
- Persons with a recent conversion or 10 mm or more increase in size of TST
- Infants under the age of five

https://www.cdc.gov/tb/publications/ltbi/targetedtesting.htm#identifyingTBDisease
Isn’t screening done at the time of immigration???

For applicants 2–14 years of age:
- Medical history
- Physical examination
- Tuberculin skin test or IGRA
- TST ≥10 mm or IGRA-positive

For applicants ≥15 years of age:
- Medical history
- Physical examination
- Chest radiograph
- Medical history, examination, or chest radiograph suggestive of tuberculosis or HIV infection
- Three sputum smears and cultures for *Mycobacterium tuberculosis*
- Drug susceptibility testing of positive cultures

- Screening only for individuals seeking permanent residency.
- Screening is often an out of pocket expense.

Michelle Haas, M.D.

TB Immunology and Testing

B. PRIMARY PULMONARY TUBERCULOSIS (>3 weeks)

- Alveolar macrophage
- IL-12
- Class II MHC
- T-cell receptor
- MTB antigen
- T-cell
- \( T_{H1} \)
- IFN-\( \gamma \)
- "Activated" macrophage
- iNOS
- Nitric oxide and free radicals
- Tuberculin positivity ("hypersensitivity")
- Bactericidal activity ("immunity")
# Tuberculin Skin Test (TST) Screening

<table>
<thead>
<tr>
<th>&gt; 5 mm Induration</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Infection</td>
</tr>
<tr>
<td>Recent contact with a person who has active tuberculosis</td>
</tr>
<tr>
<td>Fibrotic changes on CXR consistent with prior TB</td>
</tr>
<tr>
<td>Organ transplant patients, persons on ≥ 15 mg a day prednisone or use of TNF-α antagonists or other immunosuppressive agents</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>&gt; 10 mm Induration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons from areas prevalence areas who arrived in the last 5 years</td>
</tr>
<tr>
<td>IVDA</td>
</tr>
<tr>
<td>Persons living or working in high risk areas (i.e. Homeless shelter)</td>
</tr>
<tr>
<td>Laboratory workers who work with TB</td>
</tr>
<tr>
<td>Persons with increased risk of progression to TB (other than listed above, i.e. DM)</td>
</tr>
<tr>
<td>Children less than 4</td>
</tr>
<tr>
<td>Children and adolescents exposed to high risk groups</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>&gt; 15 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons with no known risks</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/tb/publications/ltbi/targetedtesting.htm#identifyingTBdisease
Interferon Gamma Release Assay Screening (IGRA)

QuantiFERON-TB Gold—ELISA

T-Spot TB Test—ELISPOT

## Sensitivity and Specificity of LTBI Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PPD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 mm</td>
<td>0.79</td>
<td>0.30 – 0.97</td>
</tr>
<tr>
<td>10 mm</td>
<td>0.79</td>
<td>0.97</td>
</tr>
<tr>
<td>15 mm</td>
<td>0.52</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>T-Spot</strong></td>
<td>0.90</td>
<td>0.95</td>
</tr>
<tr>
<td><strong>QuantiFERON</strong></td>
<td>0.80</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Note: There is no gold standard test for diagnosing LTBI.

**Sensitivity** = (Positive Test) / (Positive Tests + Negative Tests) done in persons with *active tuberculosis*.

**Specificity** = (Negative Test) / (Negative Tests + Positive Tests) done in countries with *low TB prevalence*.

USPSTF. Screening for Latent TB Infection in Adults. JAMA 2016;316(9):962-969.

Costs of LTBI Testing at UCH

- Nurse visit with ppd placement and follow-up ppd reading: $300.69.

- QuantiFERON Gold blood draw and laboratory testing: $96.53 + $492.01 = $588.54

Thanks to David Baez, Clinical Business Supervisor
30 y/o male from Mexico.

PPV of 12 mm positive ppd = 90.1% (???)

Annual risk of developing TB disease = 0.09%

Risk of developing TB disease by age 80 = 4.51%

Risk of clinically significant drug induced hepatitis = 0.3%

My Answers:

Should testing be done? Yes

Should treatment be given if testing is positive? Yes
36 y/o female from Ethiopia.

PPV positive IGRA = 98.0% (???)

Annual risk of developing TB disease = 0.1%

Risk of developing TB disease by age 80 = 4.31%

Risk of clinically significant drug induced hepatitis = 1.2%

My Answers:
Should testing be done? Yes
Should treatment be given if testing is positive? Yes
52 y/o female from Vietnam.

PPV positive IGRA = 98.0% (???)

Annual risk of developing TB disease = 0.1%

Risk of developing TB disease by age 80 = 2.74%

Risk of clinically significant drug induced hepatitis = 2.3%

My answers:
Should screening be done? No
Should treatment be given if testing is positive? Maybe
28 y/o female from Colorado about to start Humira.

PPV of positive IGRA = 98.0% (???)

Annual risk of developing TB disease = 0.52%

Risk of developing TB disease by age 80 = 27.26%

Risk of clinically significant drug induced hepatitis = 0.3%

My answers:
Should screening be done?  Yes
Should treatment be given if testing is positive?  Yes
22 y/o male from Colorado about to start volunteering at a local hospital. QuantiFERON is positive.

PPV of positive IGRA = 98.0% (???)

Is this PPV or Specificity???

If prevalence of LTBI is 1% then PPV = 37%
If prevalence of LTBI is 25% then PPV = 93%

My Answer: Repeat the test
My Calculations if Interested...

**LTBI Prevalence 1%**

<table>
<thead>
<tr>
<th></th>
<th>Disease Present</th>
<th>Disease Absent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Positive</td>
<td>(A) 800</td>
<td>(B) 1,980</td>
<td>2,780</td>
</tr>
<tr>
<td>Test Negative</td>
<td>(C) 200</td>
<td>(D) 97,020</td>
<td>97,220</td>
</tr>
<tr>
<td></td>
<td>1000</td>
<td>99,000</td>
<td>100,000</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{A}{A + C} = \frac{800}{800+200} = 0.80 \)

Specificity = \( \frac{D}{D + B} = \frac{97,020}{97,020+1,980} = 0.98 \)

**PPV** = \( \frac{A}{A + B} = \frac{800}{800+1,980} = 0.37 \)

**NPV** = \( \frac{D}{D + C} = \frac{97,020}{97,020 + 200} = 0.99 \)

**LTBI Prevalence 25%**

<table>
<thead>
<tr>
<th></th>
<th>Disease Present</th>
<th>Disease Absent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Positive</td>
<td>(A) 20,000</td>
<td>(B) 1,500</td>
<td>21,500</td>
</tr>
<tr>
<td>Test Negative</td>
<td>(C) 5,000</td>
<td>(D) 73,500</td>
<td>78,500</td>
</tr>
<tr>
<td></td>
<td>25,000</td>
<td>75,000</td>
<td>100,000</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{A}{A + C} = \frac{20,000}{20,000+5,000} = 0.80 \)

Specificity = \( \frac{D}{D + B} = \frac{73,500}{73,500+1,500} = 0.98 \)

**PPV** = \( \frac{A}{A + B} = \frac{20,000}{20,000+1,500} = 0.93 \)

**NPV** = \( \frac{D}{D + C} = \frac{73,500}{73,500 + 5,000} = 0.93 \)
False positive IGRA testing

• Low LTBI risk with a positive baseline IGRA test:
  – 67/118 (56.8%) QuantiFERON Gold were negative when repeated.
  – 92/144 (63.9%) T-Spot were negative when repeated.

• Converted their IGRA test during the study:
  – 81/106 (76.4%) QuantiFERON Gold were negative when repeated.
  – 91/118 (77.1%) T-Spot were negative when repeated.

• Two sets of tubes were drawn on the same day:
  – 10/172 (5.8%) QuantiFERON Gold were discordant
  – 10/153 (6.5%) T-Spot were discordant

Treatment of LTBI

• INH (5 mg/kg; max 300 mg) daily for 6 – 9 months.
• Rifampin 10 mg/kg; max 600 mg) daily for 4 months.

• LFTs at baseline if: Age > 35, h/o liver dz, regular EtOH use, HIV, pregnancy or immediately post-partum.
• Pyridoxine (B6) 25 – 50 mg/day if any risk factors for neurologic disease (i.e. older adults, DM...)
Important Resources

• Michelle Haas, M.D.  
  [Michelle.Haas@dhha.org](mailto:Michelle.Haas@dhha.org); Office: 303-602-5052.

• Robert Belknap, M.D., director;  
  [Robert.Belknap@dhha.org](mailto:Robert.Belknap@dhha.org); Office 303-602-7244.

• Ann Scarpita, TB Nurse; CDPHE; Office 303-692-2656.

• ID Group Practice. 720-848-0191.
Screening and treatment of LTBI

• Screening may be reasonable in recent immigrants from high prevalence areas; especially those who are under 50.
• INH x 9 months or Rifampin x 4 months are both reasonable options.
Screening and treatment for Syphilis
Case Presentation

• 34 y/o male on presents for initial visit
• Reports some right sided arm and leg pain and subjective weakness.
• Meds: None.
• Social: MSM, occasional marijuana.
• Exam: Unremarkable.
• Syphilis ordered due to neurologic symptoms and risks factors. TPPA positive with an RPR titer of 1:16.
Who to screen / test for Syphilis

• Screening HIV-positive or MSM for syphilis every 3 months is associated with improved syphilis detection.
  – 61% of primary and secondary syphilis among MSM in 2014 (MSM make up 2% of US pop.).
  – USPSTF. JAMA 2016;315(2):2328-2337
  – http://www.cdc.gov/hiv/group/msm/

• Anyone requesting other STD testing
• Anyone with signs or symptoms concerning for syphilis.
# Serologic testing for Syphilis

<table>
<thead>
<tr>
<th></th>
<th>Treponemal</th>
<th>Non-Treponemal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test names</strong></td>
<td>TPPA, FTA-AB</td>
<td>RPR, VDRL</td>
</tr>
<tr>
<td><strong>Antigen(s) targeted</strong></td>
<td><em>T. pallidum Ag</em></td>
<td><em>Cardiolipin</em></td>
</tr>
<tr>
<td><strong>Positive after treatment</strong></td>
<td>Yes</td>
<td>No (Hopefully)</td>
</tr>
<tr>
<td><strong>Measure of disease activity</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>86%</td>
<td>70%</td>
</tr>
<tr>
<td>Secondary</td>
<td>&gt; 95%</td>
<td>&gt; 95%</td>
</tr>
<tr>
<td>Tertiary</td>
<td>&gt; 95%</td>
<td>70%</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>High</td>
<td>Poor (SLE, other rheumatic dz, HIV, Hep C)</td>
</tr>
</tbody>
</table>
Serologic testing for Syphilis

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<td>Specificity</td>
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<td>Poor (SLE, other rheumatic dz, HIV, Hep C)</td>
</tr>
</tbody>
</table>
25 y/o male with a positive TPPA and negative RPR. This could be consistent with?

a. Previously treated syphilis
b. Primary syphilis
c. Secondary syphilis
d. Tertiary syphilis
e. a, b and d
Serologic testing for Syphilis

25 y/o male with a positive TPPA and negative RPR. *Prior records show a RPR titer of 1:32 two years ago and treatment with benzathine PCN.* This is most consistent with?

a. Previously treated syphilis
b. Primary syphilis
c. Secondary syphilis
d. Tertiary syphilis
e. a, b and d
What are the signs and symptoms of syphilis???
Primary Syphilis (Verse 1)
There was a man from Back Bay
Who thought Syphilis just went away
He believed that a chancre
Was only a canker
That healed in a week and day.
Signs and Symptoms of Syphilis

**Secondary Syphilis (Verse 2)**

But now he has “acne vulgaris”—
(Or whatever they call it in Paris);
On his skin it has spread
From his feet to his head,
And his friends want to know where his hair is.
Signs and Symptoms of Syphilis

Tertiary syphilis (Verse 3)
There’s more to this terrible plight:
His pupils won’t close in the light
His heart is cavorting,
His wife is aborting,
And he squints through his gunbarrel sight.
Signs and Symptoms of Syphilis

Tertiary syphilis and beyond (Verse 4)
Arthralgia cuts into his slumber,
His aorta is in need of a plumber,
But now he has tabes,
And sabershinned babies,
While gummas he has quite a number.
Signs and Symptoms of Syphilis

Tertiary syphilis and beyond (Verse 5)
He’s been treated in every known way,
But his spirochetes grow day by day;
He’s developed paresis,
Has long talks with Jesus,
And thinks he’s the queen of May.


Syphilis treatment

Primary and latent syphilis up to one year:
- Benzathine Penicillin 2.4 MU IM x 1
  - Alternatives
    - Doxycycline 100 mg bid x 14 days
    - Ceftriaxone 1 gram IV or IM x 10 – 14 days

All other syphilis excluding neurosyphilis
- Benzathine Penicillin 2.4 MU IM x 3
  - Alternatives
    - Doxycycline 100 mg bid x 28 days
    - Ceftriaxone 1 gram IV or IM x ?? Days

Neurosyphilis
- Penicillin G IV 18 – 24 MU / day x 10 – 14 days
Syphilis treatment response

- 4 fold drop in the RPR by one year; or the RPR becomes undetectable.
- “Serofast state” is when RPR doesn’t drop despite appropriate treatment. Doesn’t mean failure.
- TPPA will remain positive.
Syphilis screening and treatment

• Screening is recommended for high risk populations, including gay men not in committed relationships or persons seeking STD testing.
• Screening is done using serologic tests
  – TPPA: Treponemal, sensitive and specific.
  – RPR: Non-treponemal, measures disease activity.
• Treatment is with IM Penicillin in non-allergic individuals.
  – Less than one year: IM injection x 1
  – Neurosyphilis: IV Penicillin starting in the hospital
  – Everything else: IM injection x 3
Case Presentation

• 34 y/o gay male. Recently diagnosed with and treated for syphilis.
PrEP Basics

• **Pre-Exposure Prophylaxis** for HIV.
• Truvada (Tenofovir/Emtricitabine), 1 tab daily for the prevention of HIV.
• Truvada is the backbone of most HIV regimens today.
• Risks are *kidney injury* (generally seen as a slow rise in the creatinine rather than sudden renal toxicity) and some uncertain degree *bone density loss.*
PrEP Questions

- What are the absolute benefits of PrEP in different populations?

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk</th>
<th>Incidence / 100 pt year</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td>PrEP</td>
</tr>
<tr>
<td>1</td>
<td>MSM; 16 partners / 12 weeks</td>
<td>4.38</td>
<td>2.32</td>
</tr>
<tr>
<td>2</td>
<td>Serodiscordant heterosexual couples</td>
<td>2.80</td>
<td>0.67</td>
</tr>
<tr>
<td>3</td>
<td>MSM; 8 partners / 2 months</td>
<td>6.60</td>
<td>0.91</td>
</tr>
<tr>
<td>4</td>
<td>MSM; 63 – 65% STD / 12 months</td>
<td>9.0</td>
<td>1.2</td>
</tr>
<tr>
<td>5</td>
<td>Heterosexual men &amp; women; 1 partner / month</td>
<td>3.1</td>
<td>1.2</td>
</tr>
<tr>
<td>6</td>
<td>IDU; Most &lt; 1 / week; 1 partner / 12 weeks</td>
<td>0.68</td>
<td>0.35</td>
</tr>
<tr>
<td>7</td>
<td>African women; &gt; 98% reported a primary partner; &gt; 12% sex for money / 12 weeks</td>
<td>5.0</td>
<td>4.7</td>
</tr>
<tr>
<td>8</td>
<td>African women; 20 – 24% with 2 or more partners in last 3 months; 15 – 18% with GC, Chlamydia or Syphilis at baseline</td>
<td>5.41</td>
<td>5.88</td>
</tr>
</tbody>
</table>
PrEP Questions

• What labs should I be checking?
  – Baseline:
    • HIV Ab/Ag test
    • Syphilis, GC/Chlamydia screen
    • HBsAb, HBsAg
    • BMP
  – Every 3 – 6 months:
    • HIV Ab/Ag test
    • BMP
    • GC/Chlamydia screen, syphilis screening per your judgement (Err on the side of testing).
PrEP Questions

• Who should I prescribe PrEP to?
  – PrEP is indicated for sexually active gay men; as well as heterosexuals who may have sex with a HIV+ individual and persons with IDVA.
  – The CDC estimates 1.2 million Americans many qualify for PrEP.
## PrEP Questions

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Ardent PrEP Advocate</th>
<th>John Koepppe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gay male with 30 different sexual partners in the last 6 months. Condoms “Most of the time.”</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Gay male with 4 lifetime sexual partners. Monogamous when in a relationship. Uses condoms until sure of the relationship and partners status.</td>
<td>Yes</td>
<td>Maybe…</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of Truvada toxicity although low may be as great as the risk of HIV.</td>
</tr>
</tbody>
</table>
## PrEP Questions

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Ardent PrEP Advocate</th>
<th>John Koepple</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gay male in a monogamous relationship with a HIV positive partner. Partner is intermittently adherent with his HAART.</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Gay male in a monogamous relationship with a HIV positive partner. Partner is adherent with his HAART.</td>
<td>Yes</td>
<td>Maybe... Probably not...</td>
</tr>
</tbody>
</table>
PrEP Uncertainties

- Will PrEP lead to decreased condom use?

PrEP Uncertainties

• Will PrEP promote HIV resistance?
  – 10/9237 (0.1%) drug resistance mutations so far in RCTs.
  – Half patients who had resistance mutations, had acute HIV at the time of initiation of PrEP.
  – All were M184V.

PrEP Uncertainties

• What does PrEP cost?
  – 30 days Truvada = $1,500
  – Annual cost = $18,250
  – Annual medication costs for 1.2 million people = $22 Billion
  – Cost analyses:
    • $ 160,000 / QALY.
    • Cost savings.

http://www.goodrx.com/truvada
PrEP Uncertainties

• 22 Billion dollars in context...
  – U.S. Population = 322,000,000
  – $ 68 dollars to each persons health care.

• What else could we do with that money?
  – Four years at CU Boulder ~ $100,000
  – Pay for 200,000 to 220,000 4 year college degrees.
PrEP

• In high risk individuals PrEP (daily Truvada) has been shown to reduce the risk of HIV transmission.

• From a complexity of care standpoint, PrEP is less complicated than many things PCPs already do on a daily basis.

• Many uncertainties remain about how PrEP may effect condom use and what the ultimate cost of PrEP will be.
Questions...