STI Update Including PrEP

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Objectives

1. Updates in STI treatment

1. Identify the indications for prescribing PrEP and the barriers for patients and physicians

1. Increase awareness of PrEP in primary care providers
Syphilis

*Treponema pallidum*

- Spirochete
- Causes a diverse spectrum of disease
- Darkfield microscopy – gold standard
- Cannot be cultured
Sexually transmitted infection pyramid rates per year in USA

- **Hep B**: 19,000
- **HIV**: 41,400
- **Syphilis**: 55,400
- **Herpes Simplex Virus (Type 2)**: 776,000
- **Gonorrhea**: 820,000
- **Trichomoniasis**: 1,090,000
- **Chlamydia**: 2,860,000
- **Human Papilloma Virus**: 14,100,000

*Satterwhite et al. Sex Transm Dis 2013;40:187-93*  
[www.ashasexualhealth.org](http://www.ashasexualhealth.org)
Important Issues in STIs

1. Rates of syphilis, chlamydia, gonorrhea have increased as per the latest CDC reports
2. Increasing rates of antimicrobial resistance in Neisseria gonorrhea
3. Sexual Transmission of Hepatitis C in MSM increasingly recognized
4. Increase risk of HIV transmission in the presence of other STI’s
5. Mycoplasma genitalium (emerging concern)
The Big Three
Primary and Secondary Syphilis – Reported Cases by Sex and Sexual Behavior, 33 Areas* 2007-2013

*32 states and Washington, DC reported sex of partner data for ≥70% of cases of P&S syphilis for each year during 2007-2013.

†MSM=men who have sex with men; MSW=men who have sex with women only.
Syphilis - Natural History

- **Sexual Contact**
  - **Primary Syphilis**
  - Chancre
    - Infectious
  - 6 - 8 weeks
  - **Secondary Syphilis**
    - Latent
      - Early - < 1 year
      - Late - > 1 year
    - Rash
      - LAD
    - Clearance of infection
      - Persistent Seropositive state
      - Neurosyphilis
      - Tertiary syphilis
    - Latent
      - Early - < 1 year
      - Late - > 1 year

- **Syphilis**
  - Natural History
  - Infectious
  - Chancre
  - Rash
  - Persistent Seropositive state
  - Clearance of infection
  - Neurosyphilis
  - Tertiary syphilis
Early Syphilis (< 1 year) primary stage-localized

Infection occurs in 30-50% of exposed through:

– Genital sex, oral sex
– Kissing, touching (intimate contact)
– In utero transmission

– Firm, painless ulcer (chancre) in 2-4 weeks
– Occurs at site of inoculation (may miss it)
– Heals spontaneously in 3-8 weeks
Primary syphilis: chancre
Primary syphilis: chancres
Primary Syphilitic Chancre
Early syphilis (<1 year) - secondary stage disseminated

Occurs in fraction of untreated patients
- Systemic spread- spirochetemia (including CSF)
- Skin/mucosal involvement 90%
  - Rash (usually symmetric, maculo-papular)
  - Condylomata lata
    - wart-like lesions in warm moist areas
    - silvery gray mucous patches (oral)
  - Alopecia
- Constitutional symptoms 70%
  - Fever, HA, myalgias, weight loss, lymphadenopathy
  - Deafness, uveitis

- All symptoms disappear spontaneously!
Secondary syphilis: rash
Secondary syphilis: condyloma lata
Secondary syphilis: alopecia
Syphilis Screening Test

- Treponemal test (Elisa)
- Detects IgM and IgG against *T. pallidum*
  - Uses recombinant antigen (TpN17)
- A negative test essentially rules out recent or remote infection
- A positive test does NOT distinguish between recent and remote infection
### CDC recommendations for treatment for syphilis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Recommended</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary, Secondary, Early Latent (&lt; 1 year)</td>
<td>Benzathine PCN 2.4 MU once IM</td>
<td>Doxy 100mg PO BID for 14 days</td>
</tr>
<tr>
<td>Late latent (&gt; 1 year) Unknown duration, Tertiary</td>
<td>Benzathine PCN 2.4 MU once a week IM for 3 weeks</td>
<td>Doxy 100mg PO BID for 28 days</td>
</tr>
<tr>
<td>Neurosyphilis Ocular Disease</td>
<td>IV PCN 18-24 MU/day IV for 10-14 days</td>
<td>Desensitize for PCN</td>
</tr>
</tbody>
</table>
Jarisch-Herxheimer Reaction

• Self-limited reaction to anti-treponemal therapy
  — Fever, malaise, nausea/vomiting; may be associated with chills and exacerbation of secondary rash

• Occurs within 24 hours after therapy

• NOT an allergic reaction to penicillin

• More frequent after treatment with penicillin and treatment of early syphilis
Additional considerations

• All patients with syphilis should be tested for HIV and other STI’s (and vice versa)

• Reportable disease (local health dept)

• Treat partners presumptively if seen within 90 days of early syphilis contact with benzathine PCN 2.4 MU IM once

• Follow-up with RPR; syph screen remains (+)
*Neisseria gonorrhea* spectrum of disease

### ASYMPTOMATIC
- Urethra
- Endocervix
- Rectum
- Pharynx

### SYMPTOMATIC
- Urethritis, Cervicitis
- Pharyngitis, Proctitis
- Conjunctivitis

### COMPLICATIONS
- Salpingitis, Infertility
- PID, Perihepatitis,
- Epididymitis, Prostatitis
- Reiter’s
Clinical syndrome, point-of-care testing, screening

- Mucopurulent urethral and/or cervical discharge

- Gram stain: ≥2 WBC’s per oil immersion field and intracellular Gram-negative diplococci is diagnostic
  - Specificity >99% and sensitivity >95%

- Nucleic acid amplification tests (NAAT)

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>urethral/urine</td>
<td>98%</td>
<td>96%</td>
</tr>
<tr>
<td>oropharynx</td>
<td>66-95%</td>
<td>100%</td>
</tr>
<tr>
<td>rectal (MSM)</td>
<td>54-100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

APTIMA Combo 2: sensitivity 96-100%, specificity 99-100%
Gonorrhea
*Neisseria gonorrhoeae*

- Gram negative intracellular diplococci
Gonorrhea — Rates of Reported Cases by Age and Sex, United States, 2013

Men

Rate (per 100,000 population)

<table>
<thead>
<tr>
<th>Age</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>4.8</td>
</tr>
<tr>
<td>15-19</td>
<td>220.9</td>
</tr>
<tr>
<td>20-24</td>
<td>320.1</td>
</tr>
<tr>
<td>25-29</td>
<td>198.7</td>
</tr>
<tr>
<td>30-34</td>
<td>122.0</td>
</tr>
<tr>
<td>35-39</td>
<td>82.1</td>
</tr>
<tr>
<td>40-44</td>
<td>50.8</td>
</tr>
<tr>
<td>45-54</td>
<td>17.1</td>
</tr>
<tr>
<td>55-64</td>
<td>3.7</td>
</tr>
<tr>
<td>65+</td>
<td>109.5</td>
</tr>
<tr>
<td>Total</td>
<td>102.4</td>
</tr>
</tbody>
</table>

Women

<table>
<thead>
<tr>
<th>Age</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>21.0</td>
</tr>
<tr>
<td>15-19</td>
<td>459.2</td>
</tr>
<tr>
<td>20-24</td>
<td>541.6</td>
</tr>
<tr>
<td>25-29</td>
<td>258.4</td>
</tr>
<tr>
<td>30-34</td>
<td>126.6</td>
</tr>
<tr>
<td>35-39</td>
<td>62.9</td>
</tr>
<tr>
<td>40-44</td>
<td>30.2</td>
</tr>
<tr>
<td>45-54</td>
<td>12.1</td>
</tr>
<tr>
<td>55-64</td>
<td>3.1</td>
</tr>
<tr>
<td>65+</td>
<td>0.5</td>
</tr>
<tr>
<td>Total</td>
<td>102.4</td>
</tr>
</tbody>
</table>
Neisseria gonorrhoeae — Percentage of Isolates, with Penicillin, Tetracycline, and/or Ciprofloxacin Resistance, Gonococcal Isolate Surveillance Project (GISP), 2013

PenR = penicillin-resistant
TetR = tetracycline-resistant
QRNG = quinolone-resistant
MDR
## Treatment for Gonorrhea

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Recommended regimen</th>
<th>Alternative regimen</th>
<th>Follow-up testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated infections of the cervix, urethra and rectum</td>
<td>Ceftriaxone 250 mg IM x 1 dose + azithromycin 1 g PO x 1 dose</td>
<td>Gemifloxacin PO x 1 dose + azithromycin 2g PO x 1 dose</td>
<td>Repeat NAAT in 3 months</td>
</tr>
<tr>
<td>Uncomplicated gonococcal infection of the pharynx</td>
<td>Ceftriaxone 250 mg IM x 1 dose + azithromycin 1 g PO x 1 dose</td>
<td></td>
<td>Repeat NAAT in 14 days after treatment</td>
</tr>
</tbody>
</table>

**Chlamydia classification**

<table>
<thead>
<tr>
<th>Serovars</th>
<th>Human disease</th>
<th>Method of spread</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>A, B, Ba and C</td>
<td>Ocular trachoma</td>
<td>Hand to eye, fomites and eye-seeking flies</td>
<td>Conjunctivitis, and conjunctival and corneal scarring</td>
</tr>
<tr>
<td>D, Da and E, F, G, H, I, J, Jb, Jc and K</td>
<td>Oculogenital disease</td>
<td>Sexual and perinatal</td>
<td>Cervicitis, urethritis, endometritis, pelvic inflammatory disease, tubal infertility, ectopic pregnancy, neonatal conjunctivitis and infant pneumonia</td>
</tr>
<tr>
<td>L1, L2 and L3</td>
<td>Lymphogranuloma venereum</td>
<td>Sexual</td>
<td>Submucosa and lymph-node invasion, with necrotizing granulomas and fibrosis</td>
</tr>
</tbody>
</table>

*Chlamydia pneumoniae* and *psittaci* belong to the same family as *Chlamydia trachomatis* and can cause respiratory tract infections.
## Chlamydia — Rates of Reported Cases by Age and Sex, United States, 2013

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>Rate (per 100,000 population)</th>
<th>Women</th>
<th>Rate (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>14.7</td>
<td>108.9</td>
<td>3043.3</td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td>715.2</td>
<td>15-19</td>
<td>3621.1</td>
<td></td>
</tr>
<tr>
<td>20-24</td>
<td>1325.6</td>
<td>20-24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-29</td>
<td>757.9</td>
<td>25-29</td>
<td>1428.3</td>
<td></td>
</tr>
<tr>
<td>30-34</td>
<td>390.9</td>
<td>30-34</td>
<td>599.2</td>
<td></td>
</tr>
<tr>
<td>35-39</td>
<td>207.5</td>
<td>35-39</td>
<td>273.4</td>
<td></td>
</tr>
<tr>
<td>40-44</td>
<td>116.6</td>
<td>40-44</td>
<td>118.3</td>
<td></td>
</tr>
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<td>45-54</td>
<td>55.9</td>
<td>45-54</td>
<td>41.4</td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td>17.0</td>
<td>55-64</td>
<td>11.3</td>
<td></td>
</tr>
<tr>
<td>65+</td>
<td>4.0</td>
<td>65+</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>262.6</td>
<td>Total</td>
<td>623.1</td>
<td></td>
</tr>
</tbody>
</table>
Infection in Men

Urethritis
- >50% are asymptomatic
- Dysuria and mild-to-moderate whitish or clear discharge
- Complications
  - Epididymitis: typically with unilateral scrotal pain and swelling
  - Reiter’s syndrome (urethritis, conjunctivitis, arthritis)

Pharyngeal/Rectal Infection
- Mostly asymptomatic
Infection in Women

Pelvic Inflammatory Disease

- Ascending infection involving uterus, Fallopian tubes, ovaries, and peritoneal tissues
- Lower abdominal pain is cardinal presenting symptom; usually bilateral
- May be associated with vaginal discharge, uterine bleeding, fever, chills, dyspareunia
- Fitz-Hugh-Curtis syndrome (perihepatitis): acute onset severe R upper quadrant pain

Urethritis/Cervicitis

- Majority asymptomatic
- Dysuria, frequency, pyuria
- Mucopurulent endocervical discharge
- Ascending infection resulting in endometritis and salpingitis

Bartholinitis

- Exudative infection of Bartholin’s ducts
### Treatment of *Chlamydia*

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Recommended regimen</th>
<th>Alternative regimen</th>
<th>Follow-up testing</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C. trachomatis</em> urethritis/cervicitis</td>
<td>Azithromycin 1 g PO x 1 dose; Or Doxycycline 100 mg PO BID x 7d</td>
<td>Levofloxacin 500 mg PO Qdaily x 7 days; Ofloxacin 300 mg PO BID x 7 days</td>
<td>Repeat NAAT in 3-4 weeks after treatment completion</td>
</tr>
</tbody>
</table>
STI Conclusions

• **Syphilis**
  • < 1 year: benz PCN x 1
  • Unknown or > 1 year: benz PCN x 3
  • Follow up with RPR titers in 3 months

• **Chlamydia**
  • Azithromycin 1g once
  • Follow up NAAT in 1-3 months

• **GC**
  • Ceftriaxone 250mg IM with azithromycin 1g once
  • Males/Females 15-30, MSM any age
  • Follow-up NAAT in 1-3 months
How many in the audience have heard of or prescribed PREP?
HIV in US - 2015

1.2 million people living with HIV

39,513 individuals newly diagnosed with HIV

New diagnoses has fallen 19% since 2005

https://www.cdc.gov/hiv/statistics/overview/ataglance.html
Engagement in HIV care and Treatment

HIV Care Continuum Shows Where Improvements are Needed

In the US, 1.2 million people are living with HIV. Of those:

- **Diagnosed**: 86%
- **Engaged in Care**: 40%
- **Prescribed ART**: 37%
- **Virally Suppressed**: 30%

Sources: CDC National HIV Surveillance System and Medical Monitoring Project, 2011.

*Antiretroviral therapy

https://www.aids.gov/federal-resources/policies/care-continuum
CDC recommends daily HIV prevention pill for those at substantial risk (May 14, 2014)

FDA approved the combination of tenofovir + emtricitabine (Truvada) for use of PrEP in MSM, heterosexuals, and people who inject drugs aged 18 and over (2012)

# Indications for PrEP

## Summary of Guidance for PrEP Use

<table>
<thead>
<tr>
<th>Detecting substantial risk of acquiring HIV infection:</th>
<th>Men Who Have Sex With Men</th>
<th>Heterosexual Women and Men</th>
<th>Injection Drug Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sexual partner with HIV</td>
<td></td>
<td>• Sexual partner with HIV</td>
<td>• HIV-positive injecting partner</td>
</tr>
<tr>
<td>• Recent bacterial STD</td>
<td></td>
<td>• Recent bacterial STD</td>
<td>• Sharing injection equipment</td>
</tr>
<tr>
<td>• High number of sex partners</td>
<td></td>
<td>• High number of sex partners</td>
<td>• Recent drug treatment (but currently injecting)</td>
</tr>
<tr>
<td>• History of inconsistent or no condom use</td>
<td></td>
<td>• History of inconsistent or no condom use</td>
<td></td>
</tr>
<tr>
<td>• Commercial sex work</td>
<td></td>
<td>• Commercial sex work</td>
<td></td>
</tr>
<tr>
<td>• Lives in high-prevalence area or network</td>
<td></td>
<td>• Lives in high-prevalence area or network</td>
<td></td>
</tr>
</tbody>
</table>

| Clinically eligible:                                    |                           |                           |                       |
| • Documented negative HIV test before prescribing PrEP |                           | • No signs/symptoms of acute HIV infection |                       |
| • No signs/symptoms of acute HIV infection             |                           | • Normal renal function, no contraindicated medications |                       |
| • Normal renal function, no contraindicated medications|                           | • Documented hepatitis B virus infection and vaccination status |                       |

Key points of the CDC guidance:

- PrEP is not a stand-alone solution for HIV Prevention
- Individuals prescribed PrEP must be confirmed as HIV-negative prior to use
- Should be delivered as part of a comprehensive package of prevention services:
  - counseling to reduce risk behavior
  - counseling for adherence to the qd pill regimen
  - management of STIs (hopefully few)
  - access to condoms
Potential Components of a Combination Prevention Strategy for HIV Infection

1. Screening the blood supply
2. Education and Behavior Modification
3. HIV testing and counseling
4. ARV treatment for HIV-infected persons
5. Condom use
6. Treatment/prevention of drug and alcohol abuse
7. Providing clean syringes – pharmacy or needle exchange
8. ARVs to prevent mother to child HIV transmission
9. Post-exposure prophylaxis by using ART
What medication to use?

Truvada
(Emricitabine and Tenofovir)

2 NRTIs - commonly used in HIV treatment

One pill once a day
## Side Effects

<table>
<thead>
<tr>
<th>Short Term</th>
<th>Long Term (Rare)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI Upset, Nausea</td>
<td>Kidney Injury/Fanconi Syndrome</td>
</tr>
<tr>
<td>Headache</td>
<td>Decrease BMD/Osteopenia/Osteoporosis</td>
</tr>
</tbody>
</table>
# Labs

<table>
<thead>
<tr>
<th>Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV antibody</td>
</tr>
<tr>
<td>BMP, UA</td>
</tr>
<tr>
<td>Hepatitis B Surface Ag, Surface Ab, Core Ab</td>
</tr>
<tr>
<td>Hepatitis C antibody</td>
</tr>
<tr>
<td>STI Screening – GC/CT/RPR*</td>
</tr>
<tr>
<td>Pregnancy Test*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV antibody</td>
<td>HIV antibody</td>
</tr>
<tr>
<td>STI Screening – GC/CT/RPR*</td>
<td>Screening – GC/CT/RPR*</td>
</tr>
<tr>
<td>BMP, UA</td>
<td>BMP, UA</td>
</tr>
</tbody>
</table>

* indicates optional tests.
Cost of PrEP

- What is the monthly out of pocket cost of Truvada (Emtricitabine/Tenofovir)?
  - $1300 – 1600 a month, $12,000 - $15,000 a year¹
- Will insurance cover Truvada (Emtricitabine/Tenofovir)?
  - Most insurances do cover Truvada – need correct diagnosis code
- If my insurance does cover Truvada, what are the monthly copays?
  - Upper tier copay
  - (e.g. UPMC Commercial Insurance - $90)

Cost of PrEP

- Are there any financial assistance programs for Truvada? YES!!!
  - Gilead Advancing Access Program
    - Help lower co-pay or find other co-pay support
    - Help with financial support if you have government insurance
    - Help with financial support if you are uninsured
  - Patient access network foundation
  - Clinical Trials – (e.g. TDF vs TAF Phase III Clinical Trial)
  - Drug assistance programs will soon cover PrEP
  - *** PrEP is available to patients without insurance ***

Barriers to PrEP

Adherence is Key!

Barriers to PrEP

Adherence – Follow up
- Follow up appointments
- Lab Work

Access
- Cost of PrEP and Insurance issues
- Rural settings (lack of PrEP-competent physicians and clinics)
- Language Barriers (lower PrEP access to Latinos)

Barriers to PrEP

PrEP Education
- CDC reports that 1/3 of primary care providers have never heard of PrEP\(^1\)
- Physician knowledge and comfort level in prescribing PrEP
- Public awareness of PrEP
- Does PrEP cause an increase in sexual behavior?

Stigma
- Both patient and physician

Side Effects
- GI Upset, nausea
- Renal Toxicity
- Decrease in bone mineral density
Future of PrEP
IPERGAY Study – “On demand” PrEP

- French study - MSM
- 2 tablets of Truvada 2 to 24 hours before having intercourse
- Then 1 tablet 24 and 48 hours after having intercourse
- **Average 4 doses a week**
- Study showed reduced risk of contracting HIV by 86 percent
- Two individuals in the on demand PrEP group acquired HIV compared to 16 people in the placebo
- Those who contracted the virus were not taking PrEP at the time (by checking drug levels)

IPERGAY Study – “On demand” PrEP

- Benefits
  - Improve adherence
  - Safety
  - Cost-effectiveness

- Concerns:
  - Study reproducible?
  - Resistance?
  - Self reported adherence vs. drug levels
  - Not FDA approved

TAF in PREP

- Emtricitabine/Tenofovir Alafenamide (Descovy)
- Approved for treatment of HIV
- Less renal and bone toxicity
- Smaller pill then Truvada
- Study of Descovy on Macaques show protection from rectal HIV
- Not approved in humans for HIV prevention
- Low penetration of the drug into rectal and vaginal tissues and genital fluids
- Phase III clinical trial TAF vs TDF

Thank you