Sexually Transmitted Infections in Adolescents & Pre-Exposure Prophylaxis (PrEP)

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Division of General Pediatrics & Adolescent
Adolescent HIV Prevention ECHO Forum
Objectives

- Review the Centers for Disease and Control and Prevention recommendations for screening, prevention and treatment of sexually transmitted infections (STIs) in adolescents
- Identify adolescent populations at risk for HIV and the recommendations around pre-exposure prophylaxis (PrEP)
- Discuss barriers needed to address youth seeking PrEP in school based health settings
The STATE of STDs in the United States

1.7 million CASES OF CHLAMYDIA
22% increase since 2013

555,608 CASES OF GONORRHEA
67% increase since 2013

30,644 CASES OF SYPHILIS
76% increase since 2013

Anyone who has sex is at risk, but some groups are more affected

CDC

- YOUNG PEOPLE AGED 15-24
- GAY & BISEXUAL MEN
- PREGNANT WOMEN
SEXUALLY TRANSMITTED INFECTIONS AMONG YOUNG AMERICANS

Youth bear disproportionate share of STIs

- Americans ages 15-24 make up just 27% of the sexually active population
- But account for 50% of the 20M new STIs in the U.S. each year

Consequences are particularly severe for young women

- Undiagnosed STIs cause 24,000 women to become infertile each year

Young people account for a substantial proportion of new STIs

- 70% Gonorrhea (820,000)
- 63% Chlamydia (2.9 million)
- 49% HPV (14.1 million)
- 45% Genital Herpes (776,000)
- 26% HIV (47,500 *Ages 13-24)
- 20% Syphilis (55,400)

Many do not know they’re infected because STIs often have no symptoms

- Gonorrhea: 200,000 Diagnosed & reported, 570,000 Estimated total new infections
- Chlamydia: 1 million Diagnosed & reported, 1.8 million Estimated total new infections

Unique factors place youth at risk

- Insufficient Screening
  - Many young women don’t receive the chlamydia screening CDC recommends
- Confidentiality Concerns
  - Many are reluctant to disclose risk behaviors to doctors
- Biology
  - Young women’s bodies are biologically more susceptible to STIs
- Lack of Access to Healthcare
  - Youth often lack insurance or transportation needed to access prevention services
- Multiple Sex Partners
  - Many young people have multiple partners, which increases STI risk
Case: Erica

• Erica is a 16-year-old sexually active female who presents with vaginal discharge.

• How do you approach Erica?
Case: Erica

- Do you need to perform a pelvic exam?
  - Erica is symptomatic and sexually active.
  - A pelvic exam in this case is a diagnostic exam not an asymptomatic screening.
  - If Erica had been asymptomatic, would you perform a speculum exam?
**Trichomonas vaginalis** and Other Vaginal Infections Among Females — Initial Visits to Physicians’ Offices, United States, 1966–2016

*NOTE:* The relative standard errors for *Trichomonas vaginalis* infection estimates range from 23% to 17% and for other vaginal infection estimates range from 13% to 8%. See Section A2.5 in the Appendix and Table 44.

**SOURCE:** National Disease and Therapeutic Index, IMS Health, Integrated Promotional Services™, IMS Health Report, 1966–2016. The 2017 data were not obtained in time to include them in this report.
# Vaginitis Differential Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bacterial Vaginosis (Gardnerella vaginalis)</th>
<th>Trichomoniasis (Trichomonas vaginalis)</th>
<th>Candida vaginitis (Candida albicans)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Examination</strong></td>
<td>- Thin, off-white discharge with fishy odor - No vaginal inflammation</td>
<td>- Thin, yellow-green, malodorous, frothy discharge - Vaginal inflammation</td>
<td>- Thick, “cottage cheese” discharge - Vaginal inflammation</td>
</tr>
<tr>
<td><strong>Microbiology</strong></td>
<td>Overgrowth of bacteria species normally present in vagina with anaerobic bacteria</td>
<td><em>T vaginalis</em> is single-celled, flagellated, anaerobic protozoan parasite. Only protozoan that infects genital tract.</td>
<td>Candida species are normal flora of the skin and vagina. VVC is caused by overgrowth of <em>C. albicans</em> and other non-albicans species.</td>
</tr>
<tr>
<td><strong>Sequelae</strong></td>
<td>- Pregnancy complications; Pelvic Inflammatory Disease (PID) - Susceptibility to other STDs (HIV, HSV, CT/GC)</td>
<td>-Pregnancy Complications (pre-term delivery, low birth weight) -Increased HIV risk *Women: Vaginitis *Men: Urethritis</td>
<td>-Pregnancy Complications (pre-term delivery, low birth weight) -Increased HIV risk</td>
</tr>
</tbody>
</table>
## Vaginitis Treatment

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bacterial Vaginosis (Gardnerella vaginalis)</th>
<th>Trichomoniasis (Trichomonas vaginalis)</th>
<th>Candida vaginitis (Candida albicans)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td>- Amsel’s criteria:</td>
<td></td>
<td>- Clinically by the presence of external dysuria and vulvar pruritus, pain, swelling, and redness.</td>
</tr>
<tr>
<td></td>
<td>- Positive Whiff</td>
<td></td>
<td>- Wet Prep (10% KOH)</td>
</tr>
<tr>
<td></td>
<td>- pH&gt;4.5</td>
<td></td>
<td>- Culture</td>
</tr>
<tr>
<td></td>
<td>- Thin, white discharge</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Clue cells (&gt;20% of the cells)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>- Metronidazole 500 mg PO BID x 7 days</td>
<td>- 2 grams Metronidazole</td>
<td>- Diflucan 150 mg PO X 1</td>
</tr>
<tr>
<td></td>
<td>- Metronidazole gel 0.75% OD x 5</td>
<td>- 2 grams Tinidazole</td>
<td>- Topically applied azole drugs are more effective than nystatin.</td>
</tr>
<tr>
<td></td>
<td>- Clindamycin cream or 7 days</td>
<td>- Alternative: Metronidazole</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>500 mg PO BID x 7 days</td>
<td></td>
</tr>
<tr>
<td><strong>Treatment Failure/Alternative</strong></td>
<td>- Tinidazole 2 gm PO X 2 days</td>
<td>- Re-treat with metronidazole 500 mg PO BID x 7 days</td>
<td>- Culture*</td>
</tr>
<tr>
<td></td>
<td>- Tinidazole 1 gm PO X 5 days</td>
<td>- If repeat failure, treat w/ tinidazole or metronidazole 2 gm PO X 5 days</td>
<td>- 7–14 days of topical therapy or a 100-mg, 150-mg, or 200-mg oral dose of fluconazole every third day for a total of 3 doses [day 1, 4, and 7]</td>
</tr>
<tr>
<td></td>
<td>- Clindamycin 300 mg PO BID X 7 days</td>
<td></td>
<td>- Weekly for 6 months</td>
</tr>
<tr>
<td></td>
<td>- Clindamycin ovules 100 mg OD, QHS X 3 days</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Newer Trichomonas Diagnostics

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Turnaround Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSOM</td>
<td>&gt;83%</td>
<td>&gt;97%</td>
<td>10 min POC</td>
</tr>
<tr>
<td>Affirm VPii</td>
<td>&gt;83%</td>
<td>&gt;97%</td>
<td>45 min POC</td>
</tr>
<tr>
<td>Aptima* (NAAT)</td>
<td>74-98%</td>
<td>87-98%</td>
<td>FDA approved April 2011 (women)</td>
</tr>
</tbody>
</table>

*APTIMA Trichomonas vaginalis Assay (point of care trading). CDC 2010 STD Treatment Guideline.

*Diflucon 150 mg PO X 1

*Culture*
## Screening Recommendations

<table>
<thead>
<tr>
<th></th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAP</td>
<td>NOT routinely recommended for asymptomatic. Consider screening ♀ if individual or population-based risk factors</td>
</tr>
<tr>
<td>ACOG</td>
<td>NOT routinely recommended. Consider screening ♀ based on local prevalence</td>
</tr>
<tr>
<td>CDC*</td>
<td>NOT routinely recommended: HIV+ ♀. Consider Trichomonas screening persons receiving care in high-prevalence settings, i.e., STD clinics, correctional facilities or if high risk (e.g., multiple sex partners, or h/o STD)</td>
</tr>
</tbody>
</table>
Management of Sex Partners

- Treatment of partners with BV is not routinely recommended
  - Female’s response to therapy and likelihood of relapse or recurrence are not affected by treatment of her sex partner(s)

- Sex partners of patients with *T. vaginalis* should be treated

- Treatment of sex partners who have Candida is not recommended (unless recurrent or symptomatic)
Additional Concerns

- Because she is a sexually active 16-year-old, she is also at risk for cervicitis.

- What are the most common identifiable causes of cervicitis?
  - Chlamydia
  - Gonorrhea
Chlamydia — Rates of Reported Cases by Age Group and Sex, U.S., 2017

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Men Rate (per 100,000 population)</th>
<th>Women Rate (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>11.9</td>
<td>93.6</td>
</tr>
<tr>
<td>15-19</td>
<td>924.5</td>
<td>3265.7</td>
</tr>
<tr>
<td>20-24</td>
<td>1705.4</td>
<td>3985.8</td>
</tr>
<tr>
<td>25-29</td>
<td>1091.9</td>
<td>1725.4</td>
</tr>
<tr>
<td>30-34</td>
<td>598.9</td>
<td>725.7</td>
</tr>
<tr>
<td>35-39</td>
<td>351.1</td>
<td>361.8</td>
</tr>
<tr>
<td>40-44</td>
<td>197.5</td>
<td>170.8</td>
</tr>
<tr>
<td>45-54</td>
<td>106.3</td>
<td>63.3</td>
</tr>
<tr>
<td>55-64</td>
<td>37.5</td>
<td>17.9</td>
</tr>
<tr>
<td>65+</td>
<td>6.7</td>
<td>2.5</td>
</tr>
<tr>
<td>Total</td>
<td>363.1</td>
<td>687.4</td>
</tr>
</tbody>
</table>

Source: https://www.cdc.gov/std/stats17/adolescents.htm
Gonorrhea — Rates of Reported Cases by Age Group and Sex, U.S., 2017

Source: https://www.cdc.gov/std/stats17/adolescents.htm
Chlamydia & Gonorrhea — Rates by Race and Hispanic Ethnicity, United States, 2013–2017

Chlamydia rates by race/ethnicity

Gonorrhea rates by race/ethnicity
Southern States with the highest rates in 2017

Chlamydia Rates

Gonorrhea Rates
# Chlamydia and Gonorrhea Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chlamydia</th>
<th>Gonorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Examination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>Heavy or prolonged menses, spotting, dysmenorrhea, discharge, dyspareunia</td>
<td>Yellow or bloody vaginal discharge, burning/painful urination, bleeding with vaginal Intercourse</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>Penile discharge, dysuria</td>
<td>White, yellow/green pus from the penis with pain, burning during urination, swollen/painful testicles</td>
</tr>
<tr>
<td><strong>Preferred diagnostic test:</strong></td>
<td>Nucleic Acid Amplified Tests (NAAT)</td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>vaginal swab preferred</td>
<td></td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>urine acceptable</td>
<td></td>
</tr>
<tr>
<td><strong>Sequelae</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>- Symptomatic PID occurs in 10-15% of women with untreated Chlamydia</td>
<td>- Cramps and pain, vomiting, fever → PID, infertility, Ectopic pregnancy , HIV</td>
</tr>
<tr>
<td></td>
<td>- Increased risk of HIV transmission</td>
<td></td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>Epididymitis, reactive arthritis, HIV transmission, proctitis</td>
<td>- Rare  →  Prostate complications, epididymis, HIV</td>
</tr>
</tbody>
</table>
Chlamydia Treatment

- Rx not changed
- Effectiveness: azithromycin < doxycycline
  - Data from meta-analysis of 12 randomized clinical trial
    - Urogenital chlamydial infection demonstrated that the treatments were equally efficacious, with microbial cure rates of 97% and 98%, respectively
    - Conclusion: doxy marginally superior to azithro
- Doxycycline delayed release 200 mg tabs (Doryx)
  - ↓ GI upset
  - Qday x 7 days
  - ↑$
Gonorrhea Dual Therapy: Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose

PLUS

Azithromycin 1 g orally

• Doxy no longer recommended as 2nd antimicrobial for GC Rx
  o Substantially ↑↑ prevalence of GC resistance to tetracycline vs azithromycin

www.cdc.gov/std/tg2015/gonorrhea.htm
What Does Dual Therapy Mean?

• Ceftriaxone and azithromycin administered on same day
  – Preferably simultaneously and under direct observation
  – Challenge if ceftriaxone IM in office and Rx for azithromycin to fill in pharmacy
    • Must be given within 24 hr time period for adequate treatment
Gonorrhea Treatment Alternatives 2015: Anogenital Infections

**ALTERNATIVE CEPHALOSPORINS:**
- Cefixime 400 mg orally once
  - **PLUS**
- Dual treatment with azithromycin 1 g OR
- doxycycline 100 mg BID x 7 days

> Doxy only allowed for allergy

www.cdc.gov/std/tg2015/gonorrhea.htm
**Gonorrhea Treatment Alternatives**

**Anogenital Infections**

*IN CASE OF SEVERE ALLERGY:*

- Azithromycin 2 g orally once
  
  *(Caution: GI intolerance, emerging resistance)*

- Gentamicin 240 mg IM + azithromycin 2 g PO
- Gemifloxacin 320 mg orally + azithromycin 2 g PO

Alternative Urogenital GC Regimens

- Non-comparative randomized trial in adults with urethral or cervical gonorrhea
  1. Gentamicin 240 mg IM + azithromycin 2 g PO, or
  2. Gemifloxacin 320 mg PO + azithromycin 2 g PO

- Rationale for regimens
  - Additive effect between gentamicin and azithromycin (*in vitro*)
  - Gemifloxacin more active against GC with known ciprofloxacin resistance

<table>
<thead>
<tr>
<th>Location</th>
<th>Gentamicin / Azithromycin</th>
<th>Gemifloxacin / Azithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>% (L 95% CI)</td>
</tr>
<tr>
<td>Urethra/Cervix</td>
<td>202/202</td>
<td>100% (98.5%)</td>
</tr>
<tr>
<td>Pharynx</td>
<td>10/10</td>
<td>100%</td>
</tr>
<tr>
<td>Rectum</td>
<td>1/1</td>
<td>100%</td>
</tr>
</tbody>
</table>

Kirkcaldy, CID 2014
GC Test of Cure

• Patients with pharyngeal GC treated with an alternative regimen
  – Obtain test of cure 14 days after treatment, using either culture or NAAT

• Cases of suspected treatment failure
  – Culture and simultaneous NAAT
  – Call your local health department
Cephalosporin Treatment Failures

• Oral cephalosporin treatment failures reported worldwide
  – Japan, Hong Kong, England, Austria, Norway, France, South Africa, and Canada

• Ceftriaxone treatment failures in pharyngeal gonorrhea and a few isolates with high-level ceftriaxone resistance reported

Suspected GC Treatment Failure After Recommended Dual Therapy: What do I do?

REPORT: ECDOH STD program ASAP (within 24 hours)

CULTURE: if GC culture not available, call ECDOH

REPEAT TREATMENT: Gemifloxacin 320 mg + AZ 2g OR gentamicin 240 mg IM + AZ 2g

TREAT PARTNERS: Within 60 days with same regimen as patient receives

TEST OF CURE (TOC): Patient returns in 7-14 days for TOC culture and NAAT

- If reinfection suspected instead of treatment failure, repeat Tx with CTX 250mg + AZ 1g
Recommendations for Screening

• CDC, AAP, USPSTF, ACOG, AAFP recommend:
  – Annual screening for CT/NG for ♀ ages 15-24 years

CDC Recommendations for Screening and Prevention in Males

• Consider screening young men for CT in high prevalence clinical settings or in populations with high burden of infection (e.g. MSM)
• MSM should be screened at least annually for sexually active MSM at sites of contact (urethra, rectum, oral) regardless of condom use
• MSM should be screened annually for syphilis

Potential High-Prevalent Settings

- Incarcerated populations, military recruits, and patients receiving care at public STI clinics
- Communities that experience racial segregation, in adequate access, high rates within sexual networks that contributes to racial/ethnic disparities
USPSTF Risk-based Screening

- New sex partner
- >1 sex partner
- H/o or coexisting STIs or sex partner w/ STI infection
- Inconsistent condom use;
- H/o exchanging sex for money or drugs
U.S. Preventive Services Task Force: High Priority Evidence Gaps

- USPSTF 4th Annual Report identified:
  - Effectiveness of screening strategies to identify high-risk adolescents
  - Long-term harms of HIV antiretroviral therapy
  - Interventions to prevent STIs in low-risk adolescents and high-risk adolescents
Dr. Sanders Recommendations

- Base decisions about STI screening on sexual behaviors, and the anatomy/body parts used for sex as identified through the sexual history
- Base frequency on new sexual partners & history of a prior sexually transmitted infection
- Encourage barrier methods including:
  - Condoms for sex involving penetration with penis or sex toys
  - Condoms or dental dams for oral/vaginal or oral/anal contact
Case

• 18 year old male presents with non-healing ulcer & a new onset rash on trunk
Differential Diagnosis

Genital Sores

Chancroid

Trauma

LGV

Syphilis

Herpes

SOLITARY PAINLESS ULCER WITH INDURATED BORDER

PAINLESS PAPULE, SHALLOW EROSION OR ULCER

PAINFUL ULCER WITH SHARP BORDERS

CLUSTER OF PAINFUL (SOMETIMES) SORES

PAINFUL ULCER WITH SHARP BORDERS
# Herpes and Syphilis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Herpes Simplex Virus (HSV)</th>
<th>Syphilis</th>
</tr>
</thead>
</table>
| **Examination** | **Types:** First clinical episode (primary/non-primary), recurrent symptomatic infection, asymptomatic infection  
- Mostly asymptomatic (90%)  
- Painful blisters/open sores (can be preceded by tingling/burning)  
- Sores typically disappear in 2-3 weeks (virus lies latent leading to future outbreaks) | **3 Stages:**  
- Primary (9-90days): One or more skin lesions called chancre  
- Secondary (6weeks-6months): Skin rash and mucous membrane lesions, flu-like symptoms  
- Late/latent: symptoms disappear, internal damage ensues |
| **Laboratory findings** | Tzanck smear: multinucleated giant cells (insensitive) | Large numbers of organisms present in exudates of lesion and in lymph nodes and |
| | | Highly infectious; diagnosis by dark field microscopy |
| **Sequelae** | - Aseptic meningitis  
More common in primary infection  
Generally no neurological sequelae  
- Rare complications include:  
Stomatitis and pharyngitis  
Radicular pain, sacral paresthesias  
Transverse myelitis  
Autonomic dysfunction  
- Psychological distress | two- to five-fold increased risk of acquiring HIV infection when syphilis is present |
## Herpes and Syphilis

<table>
<thead>
<tr>
<th>Screening</th>
<th><strong>Herpes Simplex Virus (HSV)</strong></th>
<th><strong>Syphilis</strong></th>
</tr>
</thead>
</table>
| Current CDC guidelines do not recommend universal screening with serology. | Consider testing if:  
- Past inconclusive work up for genital lesions—negative herpes culture or NAAT  
- Have a partner with genital HSV  
- MSM  
- Are HIV infected | NOT recommended  
Screening in correctional facilities based on local and institutional prevalence; MSM. Screen Q3-6 mo if hi risk w/ multiple partners or HIV+ |

### Diagnosis

| **Culture:** Specificity > sensitivity  
- requires a new lesion and high viral load | **Classically:**  
1.) Non-treponemal (RPR/VDRL)  
THEN  
2.) Treponemal (TPPA/FTA)  
**New:**  
1.) Treponemal (TPPA,FTA, EIA)  
THEN  
2.) Non-treponemal (RPR/VDRL) |

| **Type-specific serology:** Most HSV-1 is not sexually transmitted | **PCR:** Sensitivity decreases as lesion heals |

*NOTES:*
# Herpes and Syphilis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Herpes Simplex Virus (HSV)</th>
<th>Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td><strong>Acute therapy:</strong>&lt;br&gt;- Acyclovir 400 mg PO TID x 7-10 days&lt;br&gt;- Acyclovir 200 mg PO 5x/day x7-10 days&lt;br&gt;- Famciclovir 250 mg PO TID 7-10 days&lt;br&gt;- Valacyclovir 1 g PO BID x 7-10 days</td>
<td><strong>Primary, Secondary, and Early Latent:</strong>&lt;br&gt;Benzathine Penicillin G—2.4 million units IM x 1 dose</td>
</tr>
<tr>
<td></td>
<td><strong>Suppressive Therapy:</strong>&lt;br&gt;- Acyclovir 400 mg PO BID&lt;br&gt;- Famciclovir 250 mg PO BID&lt;br&gt;- Valacyclovir 500 mg PO daily&lt;br&gt;- Valacyclovir 1.0 g PO daily</td>
<td><strong>Late Latent:</strong>&lt;br&gt;Benzathine Penicillin G—2.4 million units IM x 3 doses</td>
</tr>
<tr>
<td></td>
<td>****Treatment can be extended if healing is incomplete after 10 days of therapy.</td>
<td><strong>Alternative treatment:</strong>&lt;br&gt;Doxycycline 100 mg PO BID x 14 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>OR</strong>&lt;br&gt;Tetracycline 500 mg PO QID x 14 days</td>
</tr>
</tbody>
</table>
Case

- 18 year old male reports anal sex without a condom occurred 14 days ago
- Last HIV test (oral rapid test) was 8 weeks ago.
Which test do you order?

1. Determine HIV-1/2 Ag/Ab Combo
2. INSTI HIV-1/HIV-2 Antibody Test
3. HIV-1 RNA Qualitative Assay
# HIV test technologies

<table>
<thead>
<tr>
<th>HIV test</th>
<th>Method</th>
<th>Window</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; gen EIA (Ab)</td>
<td>viral lysate</td>
<td>~ 4-6 wks</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; gen EIA (Ab)</td>
<td>purified HIV-1/2 Ag or recombinant</td>
<td>~ 3-4 wks</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; gen EIA (Ab)</td>
<td>synthetic peptide, “antigen sandwich”</td>
<td>~ 2-3 wks</td>
</tr>
<tr>
<td></td>
<td>detects IgM</td>
<td></td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt; gen assay</td>
<td>detects either antibody or p24 Ag</td>
<td>~ 2 wks</td>
</tr>
<tr>
<td>(Ab plus p24 Ag)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled HIV RNA (HIV NAAT)</td>
<td></td>
<td>&lt;1-2 wks</td>
</tr>
</tbody>
</table>

Adapted from Stekler CID 2007
HIV Testing Diagnostic Algorithm

**Figure 1: HIV Laboratory Diagnostic Testing Algorithm (adapted from CDC and APHL-Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. 2014)**

- **Step 1**: HIV-1/2 Antigen/Antibody Combination Immunoassay
  - (+): HIV-1/2 antibody differentiation immunoassay
  - (-): Negative for HIV-1 and HIV-2 antibodies and p24 Ag

- **Step 2**: HIV-1/HIV-2 antibody differentiation immunoassay
  - HIV-1 (+), HIV-2 (-): HIV-1 antibodies detected
  - HIV-1 (-), HIV-2 (+): HIV-2 antibodies detected
  - HIV-1 (+), HIV-2 (+): HIV antibodies detected*
  - HIV-1 (-) or indeterminate: HIV-2 (-)
    - NAT
      - NAT (+): Acute HIV-1 infection
      - NAT (-): Negative for HIV

---

*Additional testing required to rule out dual infection with HIV-1 and HIV-2

(+): Indicates reactive test result
(-): Indicates non-reactive test result
NAT: Nucleic acid test
Timing of Positivity for HIV tests

- **HIV RNA**
- **4th Generation Antigen-Antibody**
  - Lab
  - POC
- **3rd Generation Antibody**
  - Lab
  - POC
- **Western blot**

Days following HIV Acquisition

Source: University of Washington, National HIV Curriculum
CDC HIV Testing Recommendations: Revised 2006

- Screening performed routinely for all patients aged 13-64 years using an “OPT OUT” strategy
  - Based on state HIV testing laws
- Pre-/post test counseling not required
- All patients seeking treatment for STI
- Repeat screening at least yearly for those at high risk
- Repeat testing when initiating a new sexual relationship
- Consider the benefits of offering more frequent screening (e.g., once every 3 or 6 months) to youth at increased risk for acquiring HIV infection (e.g., young MSM)

Source: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm
https://www.cdc.gov/mmwr/volumes/66/wr/mm6631a3.htm
Pre-exposure Prophylaxis

- PrEP is a prevention method for adolescents and adults who are HIV negative and at-risk for HIV to reduce their risk of becoming infected with HIV.

- Co-formulated tablet with Emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)
PrEP Recommendations & approvals

2012

FDA & EC approved in persons ≥ 35 kg in 2018

2015

World Health Organization

2012

U.S. FOOD & DRUG ADMINISTRATION

2015

2016
Who should take PrEP?
<table>
<thead>
<tr>
<th>HIV Positive Partner</th>
<th>No Condom Use</th>
<th>Multiple Sex Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td><img src="no_condom.png" alt="No Condom" /></td>
<td><img src="multiple_partners.png" alt="Multiple Sex Partners" /></td>
</tr>
<tr>
<td>HIV-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Engage in Sex Work</th>
<th>Bacterial STIs</th>
<th>Injection Drug Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="sex.png" alt="Sex Work" /></td>
<td><img src="bacterial_stis.png" alt="Bacterial STIs" /></td>
<td><img src="injection.png" alt="Injection" /></td>
</tr>
</tbody>
</table>
What is the evidence behind PrEP?

- Risk for HIV is reduced by up to 97% when PrEP is taken regularly
- Well tolerated with few side effects

https://www.hhs.gov/blog/2019/02/05/ending-the-hiv-epidemic-a-plan-for-america.html
### PrEP Randomized Control Trials among Adults

<table>
<thead>
<tr>
<th>Study (population)</th>
<th>Regimen</th>
<th>Relative Risk Reduction (95% CI)</th>
<th>All Subjects</th>
<th>Adherent Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners (discordant male/fem)*</td>
<td>TDF oral once a day</td>
<td>0.67 (0.44 – 0.81)</td>
<td></td>
<td>0.86 (0.57–0.95)</td>
</tr>
<tr>
<td></td>
<td>TDF/FTC oral once a day</td>
<td>0.75 (0.55 – 0.87)</td>
<td></td>
<td>0.90 (0.56–0.98)</td>
</tr>
<tr>
<td>CDC TDF2 (hetero men/women)*</td>
<td>TDF/FTC oral once a day</td>
<td>0.62 (0.22 – 0.83)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iPrEX (MSM, TGW)*</td>
<td>TDF/FTC oral once a day</td>
<td>0.44 (0.15 – 0.63)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEM-PrEP (young African women)</td>
<td>TDF/FTC oral once a day</td>
<td>0.06 (-0.41 – 0.52)</td>
<td></td>
<td>Adherence too low to assess efficacy. Trial stopped early</td>
</tr>
<tr>
<td>VOICE (women)*</td>
<td>TDF oral once a day</td>
<td>-0.49 (-1.30 – 0.04)</td>
<td>-0.04 (-0.50 – 0.30)</td>
<td>No difference</td>
</tr>
<tr>
<td>CAPRISA 004 (women)*</td>
<td>Tenofovir (TFV) gel BAT24</td>
<td>0.39 (0.04 – 0.60)</td>
<td></td>
<td>&gt;1,000 CVF increased RRR</td>
</tr>
<tr>
<td>VOICE (women)*</td>
<td>TFV gel once a day</td>
<td>0.15 (-0.20 – 0.40)</td>
<td></td>
<td>0.34 (0.13-0.87)</td>
</tr>
<tr>
<td>Bangkok (PWID)*</td>
<td>TDF once a day</td>
<td>0.49 (0.10 – 0.72)</td>
<td></td>
<td>0.70 (0.02–0.91)</td>
</tr>
</tbody>
</table>

*Adherent subjects defined by plasma/ peripheral blood mononuclear cell (PBMC)/ cervico-vaginal fluid (CVF) concentration) have greater relative risk reduction.

¥ Small numbers of transgender women (TW) were included in this study.

TDF/FTC is effective in TW who had detectable blood levels, however, questions still exist about the interaction of TDF/FTC with hormones (Deutsch MB, Lancet, 2015).
Rates of PrEP use

1 MILLION AMERICANS AT SUBSTANTIAL RISK FOR HIV

U.S. PrEP DATA BY AGE

- ≤24: 11%
- ≥25: 89%

Siegler et al. Annals of Epidemiology, 2018
HIV Rates Disproportionate Among Young Black Same Gender Loving Men

Source: CDC; HIV Surveillance Data, 2017
Number of PrEP users by sex and race/ethnicity in U.S. 2014 - 2016

Adherence by Race/Ethnicity

TFV-DP level

Overall  White  Latino  Mixed  Black/AA

4+ doses (≥700 fmol per punch)

Slide Courtesy of Sybil Hosek
Factors associated with sub-protective levels

• Black race
• Kicked out of home due to sexual orientation
• Depressive symptoms
• Low perceived risk
• Mistrust of medications
• Fear others might see medications

Arrington-Sanders JAIDS, 2019
How to start someone on PrEP

• Assess knowledge of and attitudes toward PrEP
• Discuss perception of risk (how risky do they feel that they are at risk for HIV)
• Identify behaviors that may be putting the participant at risk for HIV
• Discuss barriers around PrEP
PrEP Barriers

– Insurance
– Access (don’t know how to get a prescription)
– Mistrust
– Parental consent
– Concerns about confidentiality
PrEP is for YOUnth Program

1. More than once daily pill

2. Multidisciplinary team (Psychiatrist, SW, Navigators)
   a. Counseling about condom use
   b. Education about harm reduction
   c. Counseling to promote adherence to PrEP
   d. Assessing other needs
      a. Substance use, housing, employment and mental health

BUT...PrEP Involves More Than Just A Pill...
Approach to keep at-risk HIV negative individuals healthy
Labs

- Labs:
  - HIV test (4th generation Ab/Ag test)
  - Creatinine
  - Hepatitis A, B, C serology
  - Gonorrhea/Chlamydia (oral, rectal, urine)
  - Syphilis RPR
  - Urine HCG (for biologic females)

- Follow up:
  - 1 month and 3 months after PrEP start, then at least every 3 months
  - Only 90 day supply of medication prescribed
Follow up

• At each appointment
  • Screen for difficulties with daily adherence
  • Screen for adverse effects
  • Screen for STI symptoms
  • Discuss risk reduction and provide condoms
• **Recommended testing every 3 months**
  • HIV test and pregnancy test
• **Recommended testing every 6 months**
  • Serum creatinine and STI tests
• **Recommend annually** - Hepatitis C
• **Adolescents benefit from more frequent appointments**
Side Effects

- Mild symptoms
  - GI: nausea, diarrhea, indigestion
  - Occasional Headache or dizziness
    - Symptoms resolve 1-2 months

- Renal toxicity (<4%)*
- Slight decreased bone mineral density*
  - Mild non-progressive decrease in CrCl and bone mineral density that was reversible if medication stopped
Minor Consent

- No state expressly prohibits minors’ access to PrEP or other HIV prevention methods
- When counseling around PrEP make it apart of routine HIV testing and prevention counseling
Access

HEALTH AND SCIENCE

Free daily HIV prevention pills will soon be available to private insurance holders

PUBLISHED TUE, JUN 11 2019·1:50 PM EDT | UPDATED TUE, JUN 11 2019·4:19 PM EDT

Berkeley Lovelace Jr.
@BERKELEYJR
@/IN/BERKELEYLOVELACE

KEY POINTS

• Patients with private health insurance will soon be able to get HIV prevention medication at no cost.

• The U.S. Preventive Services Task Force gave PrEP a grade A recommendation, meaning insurers will now be obligated to cover the medication at no cost to their policyholders.

• Find a PrEP provider

• https://www.truvadahcp.com/prep-locator-widget

• https://preplocator.org/
Provider Barriers

• In a study of 162 of adolescent medicine providers in SAHM

- Actual PrEP Rx in adolescents associated with:
  - nPEP use & perceived adolescent adherence
  - HIV positive patients

- Providers unaware that PrEP exists
  - 34% primary care docs and nurses haven’t heard of HIV PrEP

- Discomfort performing sexual history
- Discomfort caring for sexual and gender minority groups
- Discomfort prescribing HIV medication
- Concern that patients on PrEP may engage in riskier behaviors

Hart-Cooper, et al. JAH, 2018
Mullins, et al. AIDS Patient Care & STDs, 2017
STI rates

- Meta-analysis of PrEP on sexual risk behavior in MSM
  - Pooled OR was 1.24 (0.99-1.54), p value 0.059
  - Increased any rectal STI - 1.39 (1.03-1.87) & rectal CT 1.59 (1.19-2.13)
  - **Nonsignificant increase** in syphilis (OR, 1.12; 95% CI, .86–1.47; P = .41), CT (OR, 1.23; 95% CI, 1.00–1.51; P = .051), and GC (OR, 1.13; 95% CI, .78–1.64; P = .515) infection from any anatomical site
Those at greatest risk also have the greatest need!

Many STIs are asymptomatic. Comprehensive STI screening is recommended, including at all sites of exposure. It is estimated that 95% of gonorrhea infections among MSM would be missed by screening the urethra only. 86% of rectal chlamydia and 84% of rectal gonorrhea infections are asymptomatic.

51% of people newly diagnosed with HIV had an STI history that included chlamydia, gonorrhea, or syphilis in a real-world study (n=214).

CDC=Centers for Disease Control and Prevention.
Difficult adherence

• Pill boxes and alarms
• Mobile applications
• Other formulations
• Efficacy of PrEP improves with better adherence
  • Females – 20 days for protection
  • In males:
    • ~99% decreased risk with 7 doses/week
    • ~96% decreased risk with 4 doses/week
    • ~76% decreased risk with 2 doses/week
Post-exposure Prophylaxis

PEP 101

If you may have been exposed to HIV in the last 72 hours, talk to your health care provider, an emergency room doctor, or your local health department about PEP right away. PEP can reduce your chance of becoming HIV-positive.

• Taking medications after possible exposure to HIV
• Must be started within 72 hours of exposure
• Eligibility for PEP:
  – Sexual assault
  – Unprotected anal or vaginal sex
  – Needle sharing (drug use, hormones)
• 28-day regimens
  – **Preferred**: TDF/FTC plus raltegravir (RAL) 400 mg twice daily or dolutegravir (DTG) 50 mg daily
  – **Alternative**: TDF/FTC plus DRV + RTV
• Providers should routinely prescribe PrEP despite barriers
  • Those youth are at greatest risk have the biggest need
• Requires multi-disciplinary teams that are willing to routinely provide information about PrEP, help youth to prioritize their health and understand their risk, and address psychosocial factors that impact risk for HIV including:
  • Unemployment, inadequate housing, structural racism, and comprehensive sex education
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  - Arik V. Marcell, MD, MPH
  - Christopher Reed
  - Miles Oliva
  - James Conley
  - Noah Wheeler, MPH
• Primary Care Development Corporation (PCDC) Provides High Impact Prevention (HIP)   Email: hip@pcdc.org   Website: www.pcdc.org/hip
• https://www.truvadahcp.com