What do I need to know about HIV treatment and prevention: an update

Dima Dandachi, MD, MPH

Assistant Professor of Medicine, Department of Medicine, Division of Infectious Diseases, University of Missouri – Columbia

Medical Director of the HIV/AIDS program at the University of Missouri – Columbia
Disclosures

• I have received grants funding from the National Institute of Health (NIH), National Science Foundation (NSF), Patient-Centered Outcomes Research Institute (PCORI)

• I have received research support funding from ContraFect Corporation for Staph aureus research

• Invited speaker at the Gilead Virtual Training Institute discussing: The Potential of Telehealth in Helping to Address Barriers to HIV Care.
Around the world 1.7 million new infections/year

In the US 38,000 new infections/year

A need for additional methods of HIV prevention to further reduce new HIV infections

Especially (but not exclusively) among

<table>
<thead>
<tr>
<th>Young adult</th>
<th>MSM</th>
<th>People of color</th>
</tr>
</thead>
</table>
We HAVE the means to end the HIV epidemic.
GOAL:

75% reduction in new HIV infections in 5 years and at least 90% reduction in 10 years.

Plan for America

Ending the HIV Epidemic: A Plan for America

Diagnose: all people with HIV as early as possible after infection.

Treat: the infection rapidly and effectively to achieve sustained viral suppression.

Protect: people at risk for HIV using potent and proven prevention interventions, including PrEP, a medication that can prevent HIV infections.

Respond: rapidly to detect and respond to growing HIV clusters and prevent new HIV infections.

HIV HealthForce: will establish local teams committed to the success of the Initiative in each jurisdiction.
Diagnose
What is the percentage of people with HIV who were unaware of their infection?

- Overall, all? **15%**

- Young people aged 13 – 24 years? **55%**

- Nationwide, 46% of all sexually active high school students did not use a condom the last time they had sex
Screen everyone for HIV once in their lifetime

- More frequent testing for patients with high-risk sexual behavior
- Inpatient or outpatient
- Opt-out strategy
- No need for written consent
Many People at Risk for HIV Not Tested

7 in 10 people at high risk who weren’t tested for HIV in the past year saw a healthcare provider during that time. More than 75% of them weren’t offered a test.
Case

- 55-year old female has history of DM, HTN, HLD, CAD, presented to MU on 07/2021 for worsening dysphagia, poor PO intake, abdominal pain and weight loss and found to have a mediastinal mass with esophageal involvement and a large retroperitoneal soft tissue mass.

- Patient had EBUS with biopsy and PEG tube placement. Hospital course complicated by bilateral pleural effusions s/p chest tube placement as well as Streptococcus viridans bacteremia for which patient was placed on Vancomycin, Meropenem.

- Biopsy came back as Burkitt lymphoma

- HIV test was done, was positive, ID consulted
Case

• Sexual history Has at least about 10 partners throughout her life. Did not use condom consistently. Her husband cheated on her, so she cheated on him

• CD4 7

• She then developed ileus and neutropenic enterocolitis, got also diagnosed with pulmonary mucormycosis

• The patient continued to decondition rapidly with worsening respiratory distress and mentation

• The palliative care team was consulted. After extensive conversation with family the decision to transition to comfort care was made

• The patient passed on 08/05/2021
HIV screening

Let us not be the ones who forgot or did not offer the HIV screening test
# HIV Assay Diagnostic Testing Evolution

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generation</strong></td>
<td>1st</td>
<td>2nd</td>
<td>3rd</td>
<td>4th</td>
<td>5th</td>
</tr>
<tr>
<td><strong>Antigen (Ag) Source</strong></td>
<td>Virus Infected Cell Lysate</td>
<td>Lysate &amp; Recombinant</td>
<td>Recombinant &amp; Synthetic peptides</td>
<td>Recombinant &amp; Synthetic peptides</td>
<td>Recombinant &amp; Synthetic peptides</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>95-98%</td>
<td>&gt;99%</td>
<td>&gt;99.5%</td>
<td>99.5%</td>
<td>99.5%</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>99%</td>
<td>&gt;99.5%</td>
<td>&gt;99.5%</td>
<td>&gt;99.8%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Negative Window</strong></td>
<td>8-10 weeks</td>
<td>4-6 weeks</td>
<td>2-3 weeks</td>
<td>2 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td><strong>Detects Antibody (Ab) and Ag</strong></td>
<td>IgG Anti HIV-1</td>
<td>IgG anti HIV-1 and IgG anti HIV-2</td>
<td>IgG and IgM anti HIV-1, HIV-2 and Group O</td>
<td>IgG and IgM anti HIV-1, HIV-2 and Group O</td>
<td>IgG and IgM anti HIV-1, HIV-2 and Group O</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>Single result</td>
<td>Single result</td>
<td>Single result</td>
<td>Single result; does not differentiate Ab from Ag positivity</td>
<td>Separate HIV-1 and HIV 2 Ab and Ag results</td>
</tr>
<tr>
<td><strong>Confirming Tests</strong></td>
<td>HIV-1 western blot (WB) or immunofluorescence (IFA)</td>
<td>HIV-1 WB or IFA, HIV-2 ELISA and WB if HIV-1 confirm is negative</td>
<td>HIV-1 WB or IFA, HIV-2 ELISA and WB if HIV-1 confirm is negative</td>
<td>HIV-1.2 differentiation Assay followed by qualitative HIV-1 RNA PCR if differentiation assay is negative</td>
<td>Not determined at the time of this writing</td>
</tr>
</tbody>
</table>
Preliminary positive result from the HIV-1/2 Antigen/Antibody Immunoassay leads to a Confirmation test. The HIV-1/HIV-2 Antibody Differentiation Immunoassay further differentiates between HIV-1 and HIV-2 antibodies. A negative result for HIV-1 and HIV-2 antibodies and p24 Ag indicates a negative test.

- **HIV-1 (+)** and **HIV-2 (-)**: HIV-1 antibodies detected.
- **HIV-1 (-)** and **HIV-2 (+)**: HIV-2 antibodies detected.
- **HIV-1 (+)** and **HIV-2 (+)**: HIV antibodies detected.
- **HIV-1 (-)** or Indeterminate: Requires further testing.
- **HIV-1 NAT (+)**: Acute HIV-1 infection.
- **HIV-1 NAT (-)**: Negative for HIV-1.
Treat
A 33-year-old heterosexual man with HIV is taking a 3-drug ART regimen and has maintained HIV VL as UD for longer than 1 year. He has sex only with women and has a new female partner who very recently tested negative for HIV.

Assuming he continues to consistently maintain undetectable HIV VL, what is the likelihood that he will transmit HIV to his female partner if they regularly have condomless vaginal sex?

- <0.1%
- 15%
- 5%
- 10%
A 33-year-old heterosexual man with HIV is taking a 3-drug ART regimen and has maintained HIV VL as UD for longer than 1 year. He has sex only with women and has a new female partner who very recently tested negative for HIV.

Assuming he continues to consistently maintain undetectable HIV VL, what is the likelihood that he will transmit HIV to his female partner if they regularly have condomless vaginal sex?

- <0.1%
- 15%
- 5%
- 10%
When to start?

In 2012, the CDC recommended ART initiation to all patients regardless of CD4 count (Universal).

Same day ART rapid start
Potential benefits for rapid ART initiation

- Increased engagement in care and the proportion of individuals who achieve viral suppression

- 2 Major studies START and TEMPRANO that showed clinical benefits, better outcomes when ART started early for patients with CD4 >500

- Increased evidence of Direct HIV effects on various end organs and indirect effect through HIV-associated inflammation

- Earlier ART might prevent end-organ damage: CVD, HIV associated nephropathy, neurocognitive decline, malignancies, liver disease progression with Hep B and/or Hep C

- **Blunted immunological response, Poor CD4 Cell Recovery** 15% to 20% of individuals who initiate ART at very low CD4 counts may plateau at abnormally low CD4 cell counts

TasP Treatment as prevention

- Supported by multiple studies, all of which show HIV VL **consistently undetectable** result in NO sexual transmission of HIV

- Prevention is one of the main reasons to recommend ART for all persons with HIV

- Do not address transmission among people who inject drugs (PWID)
Test-and-Treat Strategy Suppresses Viral Load Quickly and is Highly Acceptable

Same-day treatment suppressed almost two and half times as fast as conventional...

RAPID pilot (2013-5) - 56 days to Undetectable Viral Load (UVL)

Universal Era (2010-3) - 132 days to UVL

Graph shows the percentage of patients on ART over days after ART offer, comparing RAPID and Universal strategies.
U.S. Prevalence-based HIV Care Continuum, 2016

- Diagnosed: 86%
- Receipt of Care: 64%
- Retained in Care: 49%
- Viral Suppression: 53%

Linked to Care: 78% of persons with diagnosed HIV infection were linked to care within 1 month of diagnosis.
In what occasions it is important to delay ART treatment?

START ART as soon as possible

Only in few exceptions short delay before initiating ART may be warranted

• Cryptococcal meningitis 2 -10 weeks
• Bartonella CNS or ophthalmic lesions 2- 4 weeks
• CMV retinitis, CMV CNS disease > 2 weeks
• TB
  • Within 2 weeks after TB treatment initiation if CD4 count <50 cells/mm³
  • within 8 weeks of starting anti-TB treatment in those with higher CD4 cell counts
Long acting ART injectables

On January 21 2021, FDA Approves First Extended-Release, Injectable Drug Regimen for PWH

Cabotegravir and rilpivirine, injectable formulation
- A complete regimen for the Rx of HIV-1
- Adults
- Those who are virologically suppressed on a stable ART
- No history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.
Long acting ART injectables

- Intramuscular (IM) gluteal injection

- Monthly injection, up to **7 days before or after the date** the patient is scheduled to receive monthly injections

- Prior to initiating treatment with LA-injectable, oral lead-in should be used for approximately 1 month (at least 28 days) to assess the tolerability of cabotegravir and rilpivirine
Protect people at risk
HIV Status-Neutral Care Continuum

- New York City has pioneered an approach that re-orient HIV-related services using an “HIV status neutral” model.

- It all starts with an HIV test

- Any result, positive or negative, kicks off further engagement with the healthcare system, leading to a common final goal, where HIV is neither acquired nor passed.
PreP (Pre-exposure HIV prophylaxis)

In 2012, Tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) formulated as a combination pill has been approved for HIV prevention.

In 2019, tenofovir alafenamide and emtricitabine (TAF/FTC) has been approved to reduce the risk of acquiring HIV from sex only among men who have sex with men (MSM).

- The efficacy of TAF-FTC for PrEP in heterosexual, women, and people who inject drugs has not yet been evaluated.

1 pill once a day
## Indications

<table>
<thead>
<tr>
<th>Preventing HIV sexual transmission</th>
<th>Preventing HIV in Persons Who Inject Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. HIV + sexual partner</td>
<td>1. HIV-positive injecting partner</td>
</tr>
<tr>
<td>2. Recent bacterial STI (past 6 months; gonorrhea, chlamydia, syphilis)</td>
<td>2. Sharing injection equipment</td>
</tr>
<tr>
<td>3. High numbers of sex partners</td>
<td></td>
</tr>
<tr>
<td>4. History of inconsistent or no condom use</td>
<td></td>
</tr>
<tr>
<td>5. Commercial sex work</td>
<td></td>
</tr>
</tbody>
</table>
PrEP efficacy

- Adherence is the most important factor, when taken consistently
  - PrEP reduces HIV from sex 99%
  - PrEP reduces HIV 74%, for people who inject drugs

- Relationship between adherence and PrEP efficacy, has been demonstrated in multiple studies and in all populations (MSM, heterosexual men and women, PWID)

- How someone is exposed to HIV affects effectiveness
  - 6 - 7 doses/week are needed to protect from HIV through vaginal sex
  - MSM, HIV-1 risk reduction of 76% for 2 doses per week
Which one of the following is considered a contraindication for initiating PrEP with tenofovir alafenamide-emtricitabine?

- Concurrent administration of a proton pump inhibitor
- Chronic hepatitis C virus infection
- An estimated creatinine clearance less than 30 mL/min
- A history of methamphetamine use in the prior 6 months
Which one of the following is considered a contraindication for initiating PrEP with tenofovir alafenamide-emtricitabine?

- Concurrent administration of a proton pump inhibitor
- Chronic hepatitis C virus infection
- An estimated creatinine clearance less than 30 mL/min
- A history of methamphetamine use in the prior 6 months
PreP side effects

• There was no significant difference between PrEP vs placebo in risk of serious adverse events or withdrawal because of adverse events

• Clinical trials have described mild gastrointestinal adverse effects (eg, nausea, vomiting) usually resolve during the first 4 weeks

• Concerns for renal and bone toxicity with long-term use
  • TDF was associated with increased risk of renal adverse events.
  • Renal abnormalities were primarily mild elevation of serum creatinine and generally resolved following PrEP cessation or with ongoing PrEP
  • TDF has been associated with reductions in bone density, ? Clinically significant, risk of fracture
The use of PrEP as an HIV prevention strategy has been modestly increasing in the US since TDF-FTC was approved for PrEP in 2012.

The CDC estimates that approximately 1.2 million people are eligible for PrEP in the U.S.

The number of individuals initiating PrEP represents a small fraction of people who have indications for PrEP only 100,000 (less than 10% of those who needed it) were using PrEP in 2017.

Uptake has been particularly limited in populations at greatest risk for HIV infection, AA, women.
PrEP concerns

• In meta-analysis published in JAMA: there were **no significant differences** in risk of gonorrhea, chlamydia, or syphilis

• The higher risk of STIs in a subset of PrEP users should not be a reason to withhold PrEP but rather an opportunity for counseling and more frequent screening.

• Among patients who become HIV infected while receiving PrEP, most are unlikely to develop drug-resistant virus

• Money issues
PrEP concerns

Money issues
Alternative dosing approaches, other than daily

- May be an option for certain patients who can reliably predict when they will have sex

- Intermittent dosing should **not** be used in patients with chronic HBV infection

- For patients who anticipate a discrete period of risk (eg, going on vacation):
  - 1 week prior to the period when the patient is planning to have condomless sex for males, and 3 weeks prior for women,
  - Continue daily PrEP for 1 month after
  - This approach is supported by pharmacokinetic data but has not been completely evaluated in clinical trials
Event driven “sex driven” PrEP

- Instead of daily,
- Loading dose (2 tablets of TDF-FTC) 2 - 24 hours prior to sexual activity
  → 1 tablet daily while sexually active
  → 2 more days after sexual activity has stopped

- Several studies showed that it did work in preventing HIV infection only in MSM, effectiveness as compared to daily PrEP conflicting evidence
- Not evaluated in heterosexual men or women, PWID
- Approved for use in France and is being offered in the Netherlands and other European countries
- Not approved in the US, data will be submitted to the FDA
Table 2. When ED-PrEP could be considered

<table>
<thead>
<tr>
<th>For whom is ED-PrEP appropriate?</th>
<th>For whom is ED-PrEP NOT appropriate?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• a man who has sex with another man:</td>
<td>• cisgender women or transgender women</td>
</tr>
<tr>
<td>– who would find ED-PrEP more effective and convenient</td>
<td>• transgender men having vaginal/frontal sex</td>
</tr>
<tr>
<td>– who has infrequent sex (for example, sex less than 2 times per week on average)</td>
<td>• men having vaginal or anal sex with women</td>
</tr>
<tr>
<td>– who is able to plan for sex at least 2 hours in advance, or who can delay sex for at least 2 hours</td>
<td>• people with chronic hepatitis B infection.</td>
</tr>
</tbody>
</table>
PEP

Occupational or Nonoccupational Exposure to HIV
Evaluation

1. The HIV status of the exposed person
2. The source person’s HIV status
3. Details regarding the type of exposure involved
4. Timing and frequency of the exposure(s)
5. Any available information related to ART taken by the source patient if they are known to be infected with HIV
Algorithm for antiretroviral nonoccupational postexposure prophylaxis (nPEP).
PEP

- 28-day course of a 3-drug ART

Preferred regimen
- Tenofovir with emtricitabine + dolutegravir 50 mg once daily

Alternative regimen
- Tenofovir with emtricitabine + Darunavir/ritonavir once daily
• A 19-year-old male recently presented to start pre-exposure prophylaxis (PrEP).

• The patient reported having unprotected anal sex with his HIV-positive partner for the past two months.

• His partner is on ART, with the most recent HIV VL 500 copies/mL “a few months ago.”

• Their last unprotected intercourse was the day prior to the clinic visit.

• The patient was in good health, taking no medications.

• HIV 1, 2 antigen-antibody test was done and sent to the lab during the appointment.
Is this patient a candidate for PrEP? If so, what are the considerations?

- Not at this moment, PrEP is an excellent option after further evaluation

- PrEP needs to be delayed until the patient has completed PEP because he had an unprotected sexual exposure within the 72 hours window, so he is a candidate for 28-day course of (PEP)

- After the 28-day course of PEP, the patient can be transitioned to daily PrEP if he hasn’t acquired HIV
Take home messages

✓ **Screening** everyone and linking them to care, HIV 1/2 Ag Ab → confirmation test

✓ **Treat, TasP, U = U**

✓ **Prevent**
  ✓ Prevent perinatal transmission, screen, treat mother and baby, CS, avoid breastfeeding
  ✓ Offer PrEP for at risk patients, It is very effective, has minimal side effects,
  ✓ There is no proven association/causality with increase in STI, HIV resistance, cost should not be an issue
  ✓ 2 medications are now approved for PreP TDF/FTC (all indications) and TAF/FTC (ONLY for MSM)
  ✓ Assess indications, clinical eligibility, CI (renal), willing to adhere, prescribe not more than 3 months, and FU every 3 months
  ✓ PEP 3 drug regimen, substantial risk, within 72 hours, draw baseline tests for source and person exposed
  ✓ Other measures of prevention, behavioral risk reduction, condom, ? Circumcision, syringe program
Thank you