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AND NOW: *PRE*-EXPOSURE PROPHYLAXIS FOR HIV

This week, amidst happy news about the likely cure of a perinatally infected infant*, we bring you an update on the recent Food and Drug Administration (FDA) approval of a medication for pre-exposure prophylaxis against HIV or "PrEP." PrEP has been practiced quietly for a few years by people with access to antiretroviral drugs on the assumption (hope?) that it would be effective. The FDA approval signals that sufficient evidence now supports the official labeling of the combination of tenofovir (TDF) and emtricitabine (FTC), also known as Truvada®, for PrEP in people at high risk for HIV infection.

PrEP's cousin, post-exposure prophylaxis after non-occupational high-risk needle or sexual exposures (nPEP), has already been around for several years, but you'll get a bonus update on nPEP herein.

WHY PrEP?

Effective antiretroviral treatment (ART) and condom use reduce the risk of HIV transmission. However, some people with HIV may not be aware of their infection, may not disclose their status, or may have high viral loads despite ART. Also, not everyone uses condoms consistently or effectively (e.g., decreased sensation, diminished sense of intimacy, substance use). In July 2012, the U.S. FDA approved Truvada® (TDF/FTC) for PrEP among adult men who have sex with men (MSM), and heterosexual males and females at high risk of acquiring HIV infection.

THE EVIDENCE FOR PrEP

In 3 of 4 trials among MSM, heterosexually active women and men, and HIV-discordant couples,† PrEP reduced new HIV infections by 44% to 75%. Relative reductions in new infections were greatest among participants with measurable TDF/FTC in their blood, suggesting that prevention failures were largely a consequence of missed PrEP doses. For example, in the Pre-exposure Prophylaxis Trial (iPrEx), new infections were 44% lower in the treatment group overall, but 92% lower among treatment group participants with detectable drug levels. The fourth trial, among African women, demonstrated no reduction in new infections, but overall adherence was low.[1]

PrEP with TDF/FTC appears to be well-tolerated. The most frequent side effect is nausea; the most significant is mild elevations in creatinine.[2] Development of drug resistance was uncommon in trials. Although no adverse effects have been found among infants exposed to TDF/FTC during pregnancy and breastfeeding, data are limited and TDF/FTC should be used advisedly during pregnancy or breastfeeding.

Interestingly, although a person might feel bulletproof while taking PrEP, in fact, iPrEx participants increased condom use and had fewer sex partners. Still, view this pleasant surprise with some circumspection: all participants were encouraged to employ standard risk reduction strategies and both the placebo *and* the active drug group reduced sexual risk taking. When people "know" they are taking an effective preventive therapy, they might not be so cautious.

CONSIDERING PrEP?

Before initiating PrEP

- Assess likelihood of recurring high risk behavior (Tables 1 and 2, *verso*). Typically, this is someone with an HIV-infected sex or drug partner, women or men who change partners frequently, and men who have sex with men.
- Get an HIV antibody test. Test for acute HIV infection if patient has consistent symptoms. Don't give PrEP to someone who is known to be HIV-infected.
- Assess ability of the patient to take medication daily. Success of PrEP is closely linked to adherence.
- Get a pregnancy test in reproductive-aged women. If pregnant, discuss potential risks and benefits of PrEP.

Beginning PrEP

- Prescribe Truvada® (tenofovir disoproxil fumarate [300 mg] and emtricitabine, [200 mg]), 1 tablet daily, renewable every 90 days only after repeat HIV testing.
- Deliver or refer patient to additional prevention services, such as condoms and risk-reduction counseling.
- Emphasize the importance of adherence for efficacy. Refer to adherence counseling if needed.

Follow-up

Conduct follow-up visits every 2–3 months to repeat HIV testing, review side effects, adherence, risk behaviors and pregnancy status if female.

BRIEF nPEP OVERVIEW

The risk of HIV infection after any single exposure is low (< 1%) (Table 1). Nevertheless, timely use of nPEP reduces risk of infection after a high-risk expo-

Table 1. Estimated HIV transmission risk to uninfected person from infected source by exposure type.

Type of exposure**	Transmission/event
Contaminated needle or injection drug equipment with skin puncture	0.7%
Receptive anal intercourse	0.5%
Receptive penile-vaginal intercourse	0.1%
Insertive penile-vaginal intercourse	<.01%
Receptive oral intercourse	<.01%
Insertive oral intercourse	<.01%

** All estimates for sexual exposures assume a condom was not used. Other factors such as viral load of the source, trauma, genital ulcer disease or cervical ectopy can increase risk of HIV transmission

* http://www.nytimes.com/2013/03/04/health/for-first-time-baby-cured-of-hiv-doctors-say.html?pagewanted=all&_r=0

† Alas, no Oregonians.

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Table 2. Exposures that do and do not warrant consideration of HIV PrEP or nPEP.

Prep or nPEP warranted	PrEP or nPEP *NOT* warranted
Receptive or insertive anal or vaginal sex	Kissing or other mouth-to-mouth contact without mucosal damage
Mouth-to-anus contact with visible blood	Mouth-to-anus contact without visible blood exposure
Penis-to-mouth contact without condom and with ejaculation, or without ejaculation in presence of patient oral pathology	Penis-to-mouth contact with condom, or without condom and without ejaculation, unless evidence of patient oral pathology
Mouth-to-vagina contact with blood exposure	Mouth-to-vagina contact without blood exposure
Exposure of mucosal surface or non-intact skin to blood or genital secretions	Exposure of intact skin to saliva, tears, sweat, or urine
Reuse of a needle previously used by another person	Masturbation without contact between potentially infectious body fluids and non-intact skin or mucous membranes

sure and should be considered. [*N.B.* Identifying patients who have ongoing high-risk behaviors, represents a key opportunity to link them to other prevention services, such as PrEP, risk reduction counseling and screening for HIV and other STDs.]

The first nPEP dose should be given as early as possible since effectiveness decreases rapidly over time and wanes completely after ≥72 hours have elapsed since exposure.

CONSIDERING nPEP?

Before initiating nPEP

- Assess patient's possible exposure to potentially infectious fluid (Tables 1 and 2).
- If possible, assess the HIV status of the patient's partner. If the partner is HIV-positive with an accessible medication history, call the national PEPline at (888-448-4911.)
- Do an HIV test for pre-existing HIV infection. Do not delay nPEP while awaiting HIV results.

Beginning nPEP

- Prescribe 1 tablet of Truvada® (tenofovir disoproxil fumarate [300 mg] and emtricitabine, [200 mg]) daily and 4 tablets of Kaletra® (lopinavir [200 mg] and ritonavir [50 mg]) once daily. If alternative medications are being considered, call the PEPline at 888-448-4911 for assistance in choosing medications for nPEP.
- Give first dose as early as possible after the exposure. Provide nPEP "starter pack" with enough nPEP medication to complete at least four days of therapy.
- Refer patient to additional prevention services, such as condoms, risk-reduction counseling, and testing for other sexually transmitted diseases.
- Emphasize the importance of adherence for efficacy. Refer to medication adherence counseling if needed.

Follow-up

- Within 4 days, and before exhaustion of the initial supply of nPEP medications, patient must be seen by a licensed health care provider to assess need for the full 28-day course of nPEP and whether additional tests or treatment are needed.
- Test patient for HIV at six weeks, three months and six months following the exposure to determine whether HIV infection has occurred.

RESOURCES

PrEP and nPEP

- Training: The Northwest AIDS Education and Training Center (AETC). Visit http://bit.ly/VFE6mE.
- Patient Assistance Programs: The Truvada® Partnership for Prescription Assistance may be able to help eligible patients pay for medications. Visit www.pparx.org or call 1-888-477-2669.

PrEP

- Information and tools: Gilead PrEP materials for clinicians and patients are available at http://bit.ly/VA2fFP.
- Guidance: CDC interim guidance for clinicians prescribing PrEP
  - For MSM (http://1.usa.gov/11DrSwF)
  - For heterosexually active women and men (http://1.usa.gov/VA2oZZ).

nPEP

- Consultation: National Clinicians' Post-Exposure Prophylaxis Hot-line: 888-448-4911.

REFERENCES

1. Centers for Disease Control and Prevention. Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults. MMWR 2012; 61: 586–9.
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3. Smith, DK., et al., Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep 2005; 54(RR-2): 1–20.