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Committee on Gynecologic Practice

This Committee Opinion was developed with the assistance of the HIV Expert Work Group. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. This information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Preexposure Prophylaxis for the Prevention of Human Immunodeficiency Virus

ABSTRACT: *Preexposure prophylaxis* is defined as the administration of antiretroviral medications to individuals who are not infected with human immunodeficiency virus (HIV) and are at the highest risk of acquiring HIV infection. In combination with other proven HIV-prevention methods, preexposure prophylaxis may be a useful tool for women at the highest risk of HIV acquisition. Obstetrician–gynecologists involved in the care of women using preexposure prophylaxis must reinforce adherence to daily medication. The Centers for Disease Control and Prevention's guidance for preexposure prophylaxis is likely to evolve in the coming years, and obstetrician–gynecologists should remain aware of new developments in this area. Risk reduction for all women at risk of HIV infection should include counseling about testing, safe-sex practices (including condom use), and other behavioral interventions.

Preexposure prophylaxis is defined as the administration of antiretroviral medications to individuals who are not infected with human immunodeficiency virus (HIV) and are at the highest risk of acquiring HIV infection. In 2010 and 2011, HIV infection was newly diagnosed in approximately 10,000 women in the United States with a majority (84%) infected by heterosexual contact (1). Most of these new cases of HIV occurred in women of color (1). The American College of Obstetricians and Gynecologists recommends that all women aged 13–64 years be tested for HIV at least once in their lifetime and annually thereafter based on factors related to risk (2). Obstetrician–gynecologists should be aware of and comply with legal requirements regarding HIV testing in their jurisdictions and institutions. In 2012, preexposure prophylaxis was recommended by the Centers for Disease Control and Prevention (CDC) for individuals at high risk of HIV infection as part of a comprehensive HIV-prevention strategy (3). The single pill, fixed dose of tenofovir and emtricitabine has been approved by the U.S. Food and Drug Administration (FDA) for this indication. Both drugs in this combination are HIV reverse transcriptase inhibitors. This combination of medications was originally approved in 2004 by the FDA for treatment of HIV infection. Advantages of using tenofovir

and emtricitabine for preexposure prophylaxis include once daily oral dosage, known safety and tolerability of the drug, and potent antiretroviral activity (4, 5). The purpose of this Committee Opinion is to inform obstetrician–gynecologists of this potential intervention to decrease the rate of HIV infection in women.

Data From Clinical Trials

The use of daily tenofovir and emtricitabine was shown to be effective in decreasing HIV transmission in two prospective randomized trials of heterosexual men and women (4, 6); one trial found no effect (7) (see [Table 1](#)). Daily use of tenofovir and emtricitabine reduced the rate of new HIV infection by 62% in the trial of uninfected heterosexual men and women in Botswana (6). The second trial studied heterosexual discordant couples in Uganda and Kenya; in approximately one third of the study couples, the seronegative partner was female (4). Daily use of tenofovir and emtricitabine was 75% effective in decreasing transmission in this trial. Adherence to study medication, assessed with serum drug levels, pill counts, or self-reports, was high for both of these trials.

The third trial of tenofovir and emtricitabine studied heterosexual women in a variety of settings in Africa. In this trial, daily use of tenofovir and emtricitabine showed

Table 1. Clinical Trials of Preexposure Prophylaxis to Prevent Human Immunodeficiency Virus Transmission ←

Setting	Male (n)	Female (n)	Incidence rate of HIV infection per 100 person-years	Adherence
Botswana*	54.3% (662), 100% HIV-seronegative	45.7% (557), 100% HIV-seronegative	1.2 TDF-FTC versus 3.1 placebo	84.1% TDF-FTC versus 83.7% placebo [†]
Kenya and Uganda ^{‡§}	50% (4,747), 62% HIV-seronegative	50% (4,747), 38% HIV-seronegative	0.65 TDF versus 0.50 TDF-FTC versus 1.99 placebo	84% TDF versus 84% TDF-FTC versus 85% placebo
Kenya, South Africa, and Tanzania [¶]	NA	100% (2,120), 100% HIV-negative	4.7 TDF-FTC versus 5.0 placebo	88% for both TDF-FTC and placebo [#]

Abbreviations: HIV, human immunodeficiency virus; NA, not applicable; TDF, tenofovir disoproxil fumarate; TDF-FTC, tenofovir disoproxil fumarate and emtricitabine.

*Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. TDF2 Study Group. *N Engl J Med* 2012;367:423–34.

[†]Adherence was calculated using pill count.

[‡]Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. Partners PrEP Study Team. *N Engl J Med* 2012;367:399–410.

[§]This trial included an arm of daily tenofovir, which also was effective as preexposure prophylaxis. However, tenofovir as a single agent is not currently approved by the U.S. Food and Drug Administration for preexposure prophylaxis.

^{||}Adherence was calculated using pill count, specifically bottles with 95% or more of doses taken.

[¶]Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. FEM-PrEP Study Group. *N Engl J Med* 2012;367:411–22.

[#]Adherence was calculated using pill count. However, approximately 20–26% of women with HIV seroconversion had subtherapeutic drug levels in serum samples.

no reduction in new HIV infections when compared with placebo; the authors hypothesized this was due to poor adherence to the study drug because only 15–25% of those who seroconverted had therapeutic serum levels of tenofovir (7, 8). No unusual adverse effects or safety concerns were noted among HIV-negative participants taking daily tenofovir and emtricitabine. The most common adverse effects included nausea and diarrhea, and these problems were frequently mild and resolved without treatment.

Candidates for Preexposure Prophylaxis

Women at the highest risk of acquiring HIV infection (eg, a woman not infected with HIV with a male sexual partner who is known to be infected with HIV) should be considered candidates for preexposure prophylaxis. Other potential candidates may include women who engage in sexual activity within a high HIV-prevalence area or social network and one or more of the following: inconsistent or no condom use; diagnosis of sexually transmitted infections; exchange of sex for commodities (such as money, shelter, food, or drugs); use of intravenous drugs or alcohol dependence or both; incarceration; or partner(s) of unknown HIV status with any of the factors previously listed (9). An abbreviated version of the interim CDC guidelines appears in **Box 1**. Risk reduction for all women at risk of HIV infection should include

counseling about testing, safe-sex practices (including condom use), and other behavioral interventions.

The use of daily oral preexposure prophylaxis during pregnancy and lactation for women without HIV with HIV-infected partners has had limited study, and specifically was not addressed in the studies previously cited. The drug combination of tenofovir and emtricitabine is commonly used during pregnancy and has a reassuring safety profile. Human immunodeficiency virus infection is one of the few contraindications to breastfeeding (10), and clinicians should be vigilant for new HIV seroconversion in lactating women at risk of new HIV infection.

Adherence Counseling and Other Interventions

In the previously discussed preexposure prophylaxis clinical trials, adherence to study medication was the most important factor in reducing risk of HIV infection. Obstetrician–gynecologists involved in the care of women using preexposure prophylaxis must reinforce adherence to daily medication. In addition, safe-sex practices, especially consistent condom use, must be emphasized to maximize HIV prevention and prevent transmission of other sexually transmitted infections, and patients should be asked the reason they are not using condoms in order to assess whether the patient feels safe negotiating condom use. A combination of testing, education, and brief

Box 1. Adapted Centers for Disease Control and Prevention's Interim Guidance on Human Immunodeficiency Virus Preexposure Prophylaxis ↵

Before providing preexposure prophylaxis

- Document negative human immunodeficiency virus (HIV)-antibody status immediately prior to starting preexposure prophylaxis medication
- Confirm that patient currently is at very high risk of acquiring HIV infection
- Document the pregnancy intention of the patient
- Determine method of contraception
- Prescribe no more than a 90-day supply of medication (preexposure prophylaxis medication, not contraception)
- Screen for hepatitis B infection, and vaccinate if susceptible
- Screen and treat for sexually transmitted infections

Follow-up during preexposure prophylaxis

- Perform an HIV-antibody test every 2–3 months
- Evaluate medication adherence at each follow-up visit
- Assess risk behaviors and provide risk-reduction counseling and condoms every 2–3 months
- Test for bacterial sexually transmitted infections and treat as indicated

Discontinuing preexposure prophylaxis

- Discontinue preexposure prophylaxis at patient request, for safety concerns, or if HIV infection is acquired
- Test for antiretroviral resistance and refer for HIV care, if HIV positive
- Continue risk-reduction counseling, if HIV negative

Data from Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep* 2012;61:586–9.

behavioral interventions can help reduce the rate of HIV infection and its complications.

Cost and Access

The success of preexposure prophylaxis for preventing HIV infection in U.S. women is tied to issues of cost and access. The average wholesale price for a standard dose of preexposure prophylaxis (300-mg of tenofovir and 200-mg of emtricitabine; one tablet daily) is estimated at \$1,425 per month (11). Currently, no generic versions are available. Furthermore, the cost for the individual patient includes laboratory services and other professional fees (eg, follow-up visits and counseling for adherence and risk reduction), in addition to daily medication (11). To date, no private plan has publicly released its

preexposure prophylaxis coverage policy and it is not covered by Medicaid or Medicare (11). A list of pharmaceutical company patient assistance programs and copayment assistance programs is available through the National Alliance of State and Territorial AIDS Directors (<http://www.nastad.org/docs/PrEP%20and%20PEP%20PAP%20fact%20sheet.pdf>).

Conclusion

In combination with other proven HIV-prevention methods, preexposure prophylaxis may be a useful tool for women at the highest risk of HIV acquisition. Adherence to prescribed prophylaxis may be the most critical variable in preventing HIV infection with preexposure prophylaxis. The CDC's guidance for preexposure prophylaxis is likely to evolve in the coming years, and obstetrician–gynecologists should remain aware of new developments in this area. Any infection prevention strategy should include ongoing emphasis on safe-sex practices and risk reduction interventions.

Resources

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