Women with HIV  (Last updated October 25, 2018; last reviewed October 25, 2018)

This section focuses on some unique clinical and therapeutic issues to consider and basic principles to follow when caring for cisgender women living with HIV. Cisgender women are defined as women who were assigned female at birth and who identify themselves as women. Some topics discussed in this section, such as contraception, drug-drug interactions between antiretroviral (ARV) drugs and hormonal therapy, and pregnancy, also apply to transgender men (men assigned female at birth), and individuals assigned female at birth who identify as nonbinary (gender identities that are not exclusively feminine or masculine) or gender fluid (gender identity is not fixed). A new section focused on transgender health and HIV is currently in development and will be added to the Special Patient Population section soon. Clinicians who care for pregnant patients should consult the current Perinatal Guidelines for a more in-depth discussion and guidance on managing these patients.

Sex Difference Considerations in Antiretroviral Therapy

In general, studies to date have not shown sex differences in virologic responses to antiretroviral therapy (ART). However, there are limited data showing that pharmacokinetics (PKs) for some ARV drugs may differ between men and women, possibly because of variations in factors such as body weight, plasma
volume, gastric emptying time, plasma protein levels, cytochrome P (CYP) 450 activity, drug transporter function, and excretion activity.5-7

**Adverse Effects**

Several studies with older ARV drugs have suggested that sex may influence the frequency, presentation, and severity of some ARV-related adverse events. Most notably, women are more likely to develop severe symptomatic hepatotoxicity with nevirapine (NVP) use8,9 and are more likely to develop symptomatic lactic acidosis with prolonged use of older nucleoside reverse transcriptase inhibitors (NRTIs) such as zidovudine (ZDV), stavudine, and didanosine.10 These agents are no longer recommended for use in people with HIV in the United States; although ZDV is still administered intravenously (IV) to some patients during delivery, it is not generally recommended for long-term use.

Some studies have investigated how metabolic complications associated with ARV use differ between women and men. Over 96 weeks following initiation of ART, women with HIV are less likely to have decreases in limb fat but more likely to have decreases in bone mineral density (BMD) than men with HIV.11,12 Women have an increased risk of osteopenia, osteoporosis, and fractures, particularly after menopause, and this risk is exacerbated by HIV and ART.13-16 ART regimens that contain tenofovir disoproxil fumarate (TDF), ritonavir-boosted protease inhibitors (PI/r), or both are associated with a significantly greater loss of BMD than regimens containing other NRTIs and raltegravir.17-20 Abacavir, NRTI-sparing regimens, and tenofovir alafenamide (a new oral tenofovir prodrug that induces less bone loss than TDF) may be considered as alternatives to the use of TDF in patients who are at risk of osteopenia or osteoporosis. Recommendations for management of bone disease in people with HIV have been published.21

**Adults and Adolescents with HIV Who Are of Childbearing Potential**

All adults and adolescents with HIV who are of childbearing potential should be offered comprehensive reproductive and sexual health counseling and care as part of routine primary medical care. Topics for discussion should include safe sex practices, reproductive desires and options for conception, the HIV status of sex partner(s), and use of effective contraception to prevent unplanned pregnancy. Counseling should also include discussion of special considerations pertaining to ARV use when using hormonal contraceptives, when trying to conceive, and during pregnancy (see the Perinatal Guidelines).

**Antiretroviral Regimen Considerations When Trying to Conceive or For Individuals Who Cannot Use Effective Contraception**

Efavirenz (EFV) is teratogenic in nonhuman primates. However, a meta-analysis that included data from 23 studies found no evidence for an increased risk of birth defects in infants born to women on EFV during the first trimester compared with infants born to women on other ARV drugs during the first trimester.22 EFV can be used in individuals of childbearing potential who are not using effective contraception or who are contemplating pregnancy. Individuals who become pregnant on EFV-containing regimens should continue their current regimens.

A preliminary report from an observational surveillance study of birth outcomes among pregnant women on ART in Botswana found an increase in the risk of in neural tube defects (NTDs) in infants born to women who received dolutegravir (DTG) prior to conception. In this report, four infants born to 596 women (0.67%) who initiated a DTG-based regimen prior to pregnancy and who were still receiving that regimen at the time of conception were affected compared to 0.1% of infants born to women who received other ARV drugs.23,24 This study is ongoing. By contrast, the same study identified no NTDs in the infants born to 116 women who initiated DTG-based regimens during the first trimester or the infants born to 396 women who initiated EFV-based regimens.25

DTG is not recommended for individuals who are pregnant and within 12 weeks post-conception. It is also not recommended if an individual of childbearing potential is sexually active and cannot use effective
contraception or is contemplating pregnancy, unless there is no alternative option (AII). For those not known to be pregnant, a negative pregnancy test result should be documented prior to the initiation of DTG (AIII). Women who are currently receiving DTG or who wish to start DTG should be counseled about the potential risk of NTDs when DTG is taken near the time of conception. In a patient with multidrug-resistant HIV who has no alternatives to DTG, the decision of whether to use DTG should be made after careful consideration of the risk of NTDs in the infant if pregnancy occurs while a patient is taking DTG, and the risks of persistent viremia in the patient and potential HIV transmission to the fetus if pregnancy occurs while the patient is not on effective ART.

Reproductive Options for Serodiscordant Couples

An individual who wishes to conceive with a serodiscordant partner should be informed of options to prevent sexual transmission of HIV while attempting conception. Interventions include screening and treating both partners for sexually transmitted infections (STIs), use of ART to maximally suppress and maintain the viral load of the partner with HIV, use of pre-exposure prophylaxis by the partner without HIV, male circumcision, and/or self-insemination with the sperm of the partner without HIV during the periovulatory period of the individual with HIV.

Hormonal Contraception

Safe and effective reproductive health and family planning services to prevent unplanned pregnancies and perinatal transmission of HIV are an essential component of care for individuals with HIV of childbearing age. These individuals should receive ongoing counseling on reproductive issues. Regardless of hormonal contraceptive use, individuals with HIV should be advised to consistently use condoms (male or female) during sex and adhere to an HIV regimen that effectively maintains viral suppression. Both strategies are crucial to prevent transmission of HIV to partners without HIV and to protect against infection with other STIs. The following sections describe some factors to consider when hormonal contraceptives are used.

Drug-Drug Interactions

PK interactions between ARV drugs and hormonal contraceptives may reduce contraceptive efficacy. However, there are limited clinical data regarding drug interactions between ARVs and hormonal contraceptives, and the clinical implications of these interactions are unclear. The magnitudes of changes in drug concentrations that may reduce contraceptive efficacy or increase the risk of adverse effects are not known for all forms of contraceptives.

- **Combined Oral Contraceptives (COCs):** Several PIs, EFV, and elvitegravir/cobicistat (EVG/c)-based regimens have drug interactions with COCs. Interactions include either a decrease or an increase in blood levels of ethinyl estradiol, norethindrone, or norgestimate (see Tables 21a, 21b, and 21d), which potentially decreases contraceptive efficacy or increases the risk of estrogen- or progestin-related adverse effects (e.g., thromboembolism). EFV can decrease etonogestrel bioavailability and plasma progestin concentrations of COCs containing ethinyl estradiol and norgestimate. Several regimens that include a cobicistat-boosted PI, PI/r, and EVG/c decrease oral contraceptive estradiol levels. One PK study showed that DTG did not affect ethinyl estradiol or norgestimate levels. Several studies have shown that use of etravirine, rilpivirine, and NVP did not significantly affect estradiol or progestin levels in individuals with HIV using COCs.

- **Injectable Contraceptives:** Small studies of women with HIV who were receiving injectable depot-medroxyprogesterone acetate (DMPA) while on ART showed no significant interactions between DMPA and EFV, lopinavir/ritonavir (LPV/r), NVP, nelfinavir (NFV), or NRTI drugs.

- **Contraceptive Implants:** Contraceptive failure of the etonogestrel implant in women on EFV-based therapy has been reported. Studies of women with levonorgestrel- and etonogestrel-releasing implants reported that participants receiving EFV-based ART had decreased bioavailability of levonorgestrel and
etontogestrel.\textsuperscript{45-47} These studies did not identify any change in hormone concentrations when the implants were used in those taking NVP\textsuperscript{45,47} or LPV/r.\textsuperscript{46} Similarly, two retrospective cohort evaluations conducted in Swaziland and Kenya showed an increased risk of contraceptive failure in women using contraceptive implants and receiving EFV.\textsuperscript{48,49}

Concerns about PK interactions between oral or implantable hormonal contraceptives and ARV drugs should not prevent clinicians from prescribing hormonal contraceptives for individuals on ART who prefer this contraceptive method. However, an alternative or additional effective contraceptive method is recommended when there are significant drug interactions between hormonal contraceptives and ARV drugs (see drug interaction Tables 21a, 21b, and 21d and the Perinatal Guidelines).

Risk of HIV Acquisition and Transmission

Studies have produced conflicting data on the association between hormonal contraception and the risk of acquisition of HIV.\textsuperscript{50} Most of the retrospective studies were done in the setting where the partners with HIV were not taking ART. A retrospective secondary analysis of two studies of serodiscordant couples in Africa in which the partner with HIV was not receiving ART found that, compared to women who did not use hormonal contraception, those using hormonal contraception (with the majority of study participants using injectable DMPA) had a two-fold increased risk of acquiring or transmitting HIV. Higher genital HIV RNA concentrations have been found in women with HIV using hormonal contraception than in those not using hormonal contraceptives.\textsuperscript{51}

Oral contraceptive use was not significantly associated with transmission of HIV; however, the number of women using oral contraceptives in this study was insufficient to adequately assess risk. A World Health Organization expert group reviewed all available evidence regarding hormonal contraception use and HIV transmission to a partner without HIV and recommended that individuals living with HIV can continue to use all existing hormonal contraceptive methods without restriction.\textsuperscript{52} Further research is needed to definitively determine whether hormonal contraceptive use is an independent risk factor for acquisition and transmission of HIV, particularly in the setting of ART. Regardless, the potential association of hormonal contraceptive use and HIV transmission in the absence of ART underscores the importance of ART-induced viral suppression to reduce transmission risk.

Intrauterine devices (IUDs) appear to be a safe and effective contraceptive option for individuals with HIV.\textsuperscript{53-55} Although studies have focused primarily on IUDs that do not contain hormones (e.g., copper IUD), several small studies have found that levonorgestrel-releasing IUDs are also safe and not associated with increased genital tract shedding of HIV.\textsuperscript{56-58}

Pregnancy

Clinicians caring for pregnant adults and adolescents with HIV should review the Perinatal Guidelines. The use of combination ARV regimens is recommended for all pregnant persons with HIV, regardless of virologic, immunologic, or clinical parameters, for their own health and to prevent transmission of HIV to the fetus (AI). Pregnant individuals with HIV should be counseled regarding the known benefits and risks of ARV use during pregnancy to the woman, fetus, and newborn. They should be counseled and strongly encouraged to receive ART for their own health and that of their infants. Open, nonjudgmental, and supportive discussion should be used to encourage them to adhere to care.

Prevention of Perinatal Transmission of HIV

The use of ART and the resultant reduction of HIV RNA levels decrease the risk of perinatal transmission of HIV.\textsuperscript{59-61} The goal of ART is to achieve maximal and sustained viral suppression throughout pregnancy. Long-term follow-up is recommended for all infants who were exposed to ART \textit{in utero}, regardless of the infant’s HIV status (see the Perinatal Guidelines).
Antiretroviral Regimen Considerations

Pregnancy should not preclude the use of optimal ARV regimens. As in nonpregnant individuals, genotypic resistance testing is recommended for all pregnant persons before ARV initiation (AIII) and for those with detectable HIV RNA while on ART (AI). However, ART initiation should not be delayed pending genotypic resistance test results. The ARV regimen can be modified, if necessary, once the resistance test results are available (BIII). Unique considerations that influence recommendations on the ARVs to use during pregnancy include the following:

- Physiologic changes associated with pregnancy that potentially change the PKs of ARV drugs, which may affect ARV dosing at different stages of pregnancy;
- Potential ARV-associated adverse effects in pregnancy;
- Potential for nonadherence to a particular regimen during pregnancy; and
- Potential short-term and long-term effects of an ARV drug on the fetus and newborn, which are unknown for many drugs.

ART is considered the standard of care for pregnant individuals with HIV, both to treat HIV infection and prevent perinatal transmission of HIV. Clinicians should review the Perinatal Guidelines for ARV recommendations for individuals who have recently received an HIV diagnosis or those who become pregnant while on ART.

Based on preliminary data from Botswana that reported neural tube defects in infants born to women who were taking a DTG-based regimen at the time of conception, DTG is currently not recommended for use in those who are pregnant and within 12 weeks post-conception (AII). Those who are pregnant and at 12 weeks post-conception or later may initiate or continue DTG-based regimens (CIII). Discontinuing DTG is unlikely to confer any benefit after the neural tube has formed, and medication changes during pregnancy could increase the risk of viremia and perinatal transmission.

If maternal HIV RNA is ≥1,000 copies/mL (or unknown) near delivery, IV infusion of ZDV during labor is recommended regardless of the mother’s antepartum regimen and resistance profile and the mode of infant delivery (AI). Administration of combination ART should continue during labor and before a cesarean delivery (oral medications can be administered with sips of water during this time).

Clinicians who are treating pregnant individuals with HIV are strongly encouraged to report cases of prenatal exposure to ARV drugs (either administered alone or in combinations) to the Antiretroviral Pregnancy Registry. The registry collects observational data regarding exposure to Food and Drug Administration-approved ARV drugs during pregnancy to assess potential teratogenicity.

Postpartum Management

Following delivery, clinical, immunologic, and virologic follow-up should continue as recommended for nonpregnant adults and adolescents. Because maternal ART reduces but does not eliminate the risk of transmission of HIV in breast milk and postnatal transmission can occur despite maternal ART, individuals should be counseled to avoid breastfeeding. Persons with HIV should not premasticate food and feed it to their infants because the practice has been associated with mother-to-child transmission of HIV. ART is currently recommended for all individuals with HIV (AI); therefore, maternal ART should be continued after delivery. For more information regarding postpartum management, refer to the Perinatal Guidelines.

Several studies have demonstrated that adherence to ART may decline in the postpartum period. Clinicians should address ART adherence at each clinic visit postpartum, including an evaluation of specific facilitators of and barriers to adherence. Clinicians may recommend an intervention to improve adherence (see Adherence to the Continuum of Care).
References


