Preventing Perinatal HIV Transmission

This is a PDF version of the following document:
Section 5: Prevention of HIV
Topic 1: Preventing Perinatal HIV Transmission

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Overview

Risk of Perinatal HIV Transmission

The World Health Organization estimates that nearly 10 million cases of perinatal HIV transmission have occurred globally since the beginning of the HIV epidemic, with most of these in resource-poor settings.[1] In the United States, the annual number of infants perinatally infected with HIV peaked at 1650 cases in 1991;[2] since 2010, the number of annual perinatal HIV cases in the United States has consistently been less than 200 cases per year (Figure 1).[4] For pregnant women infected with HIV, the estimated rate of perinatal transmission of HIV in the absence of intervention is approximately 25%; among children who are infected perinatally, about 20% of the transmission events occur before 36 weeks’ gestation, 50% between 36 weeks and delivery, and 30% during active labor and delivery.[5,6] With the use of suppressive combination antiretroviral therapy during pregnancy, followed by postnatal infant antiretroviral prophylaxis (and with the judicious use of elective cesarean section and the avoidance of breastfeeding), the current rate of perinatal HIV transmission rate in the United States is less than 1%. [7,8,9]

Impact of Antiretroviral Therapy on Perinatal HIV Transmission

In 1994, the landmark Pediatric AIDS Clinical Trials Group (PACTG) 076 trial established that a three-part zidovudine regimen reduced mother-to-child HIV transmission by 67.5% when compared with placebo (Figure 2).[5] In this trial, the three-part regimen consisted of (1) oral zidovudine initiated for the mother with HIV infection at 14 to 34 weeks’ gestation and continued throughout pregnancy, (2) intravenous zidovudine given during labor and delivery, and (3) oral zidovudine given to the newborn for 6 weeks. The HIV transmission rate (determined at 18 months after birth) was 8.3% in the three-part zidovudine group (compared to 25.5% in the placebo group).[5] Later that year, the U.S. Public Health Service (USPHS) issued guidelines recommending the use of zidovudine to reduce perinatal HIV transmission. The PACTG study and the subsequent USPHS recommendations spurred a dramatic decline in the number of perinatal AIDS cases in the United States from 1994 onward (Figure 3).[10] Clinical trials and observational studies in the United States, as well as clinical trials of shorter course regimens in low-resource settings, have demonstrated that a variety of antiretroviral regimens markedly reduce the risk of perinatal HIV transmission, with the greatest risk reductions seen with longer duration of antiretroviral therapy during pregnancy (Figure 4) and with use of combination antiretroviral therapy (Figure 5).[1,10,11,12,13]

Consultation Resources

This topic review will highlight key points from the Perinatal Guidelines; the full text of the guidelines should be consulted for all management decisions and for further reading. In addition, expert consultation can be obtained by calling the National Clinician Consultation Center’s Perinatal HIV/AIDS Line (888)-448-8765) that provides information and clinical consultation to medical
providers caring for pregnant women with HIV infection and their infants. The Perinatal HIV/AIDS phone consultation service is available 24 hours a day, 7 days a week.
Screening for HIV Infection During Pregnancy

Multiple organizations strongly recommend screening all pregnant women for HIV infection.[14, 15, 16] This recommendation is grounded in data that knowledge of HIV status during pregnancy provides an opportunity to administer antiretroviral therapy to the mother during pregnancy, optimize strategies during delivery to minimize transmission risk, give post-delivery antiretroviral therapy to the newborn, and counsel women to avoid breastfeeding—all of which markedly reduce the risk of perinatal HIV transmission. The recommendation to test women for HIV infection applies to women presenting at any stage of pregnancy, including during labor. It is also important to remember that women who are at high risk for HIV acquisition and who test negative for HIV in the first trimester should undergo repeat HIV testing in the third trimester.[14] Any pregnant or breastfeeding woman who presents with symptoms suggestive of acute HIV infection should have prompt diagnostic evaluation for acute HIV infection.[17]
Antepartum Management

Indications for Antiretroviral Therapy in Pregnancy

The United States Health and Human Services document Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States, which is commonly referred to as the “Perinatal Guidelines”, recommends using combination antiretroviral therapy for all pregnant women with HIV infection, regardless of CD4 count or HIV RNA level, to decrease the risk of perinatal HIV transmission and is beneficial to the mother's health.[18] The risk of perinatal HIV transmission increases with higher maternal HIV RNA levels, but transmission can occur at low HIV RNA levels. Studies have shown that zidovudine decreases transmission risk at any HIV RNA level, including in women with an HIV RNA level less than 1000 copies/mL near the time of delivery.[19] Therefore, even pregnant women with a low HIV RNA level should receive antiretroviral therapy during pregnancy.

Timing of Initiating Antiretroviral Therapy in Pregnancy

Due to the overwhelming benefits of antiretroviral therapy in preventing perinatal HIV transmission, the Perinatal Guidelines recommend all women with HIV infection who become pregnant and are not receiving antiretroviral therapy should start antiretroviral therapy without delay.[20] A French prospective cohort study reported that perinatal transmission was inversely related to duration of antenatal antiretroviral therapy, with higher rates of transmissions occurring in patients with a short duration of antenatal antiretroviral therapy, as well as in those with preterm delivery at less than 33 weeks.[9] A subsequent nested case control study of the initial French cohort showed that high HIV RNA levels in the early part of pregnancy were responsible for cases of HIV transmission from women who received antiretroviral therapy and had low or undetectable HIV RNA levels near delivery.[21] Given that approximately 80% of perinatal transmissions occur between 36 weeks and the time of birth, intense efforts are warranted to lower HIV RNA levels as much as possible prior to the delivery, even in women who are diagnosed with HIV late in pregnancy.[1,6]

Women Already on Antiretroviral Therapy who Become Pregnant

In general, a woman who is already taking fully suppressive combination antiretroviral therapy and becomes pregnant should continue her current antiretroviral regimen; discontinuing therapy could cause a viral rebound that could increase the risk of HIV transmission to the fetus.[22] The Perinatal Guidelines now recommend that women taking an efavirenz-based regimen who present for care during pregnancy, including during the first trimester, can continue to take efavirenz, if the regimen is adequately suppressing HIV RNA levels.[22] The rationale for the recommendation to not restrict efavirenz use in the first trimester is twofold: (1) the risk of neural tube defects is limited to the first 5 to 6 weeks of pregnancy and confirmation of pregnancy typically occurs after week 6, and (2) unnecessary changes in antiretroviral therapy could lead to loss of suppression of HIV RNA levels. In recent years, the issue of efavirenz use in pregnancy has become less important since efavirenz is no longer included as a preferred antiretroviral regimen for adults. Women taking a regimen that contains didanosine, stavudine, or full-dose ritonavir should not continue on any of these medications during pregnancy.[22]

Women with Prior Antiretroviral Treatment But Currently NOT on Therapy

Some women with HIV who become pregnant may have previously received antiretroviral therapy, but are not currently taking any antiretroviral medications at the time when they are first evaluated during their pregnancy. In this situation, it is very important to review the history and medical records to obtain detailed information regarding past regimens, tolerance of prior medications, adherence with past regimens, evidence of prior virologic failure, and resistance testing data, if available.[23] If the woman's current HIV RNA level is above the threshold for resistance testing
(e.g. greater than 500-1,000 copies/mL depending on the laboratory performing the testing), then resistance testing should ideally be performed prior to starting the antiretroviral regimen during pregnancy. After the drug resistance test has been ordered, antiretroviral therapy should be restarted, with modification of the regimen as needed when results from the drug resistance test become available.[23] For women who previously took antiretroviral therapy and have no history of virologic failure or HIV drug resistance, then reinitiating antiretroviral therapy is relatively straightforward. For those women with prior virologic failure and HIV drug resistance, choosing an antiretroviral regimen is more complicated and should ideally be done in conjunction with an HIV treatment specialist.[23]

Recommended Antiretroviral Regimens in Treatment-Naïve Pregnant Women

The Perinatal Guidelines provide recommendations for initial combination regimens for antiretroviral-naïve pregnant women that include four categories: (1) preferred initial regimens in pregnancy (Table 1), (2) alternative initial regimens in pregnancy (Table 2), (3) insufficient data in pregnancy to recommend routine use in initial regimen (Table 3), and (4) not recommended for initial antiretroviral therapy in pregnancy (Table 4).[24] The preferred antiretroviral regimens for use in pregnancy consist of a dual nucleoside reverse transcriptase inhibitor (NRTI) backbone combined with either a protease inhibitor (PI) boosted with low-dose ritonavir or an integrase strand transfer inhibitor (INSTI).[24] Some experts recommend utilizing raltegravir in women who start antiretroviral therapy late in pregnancy and in women taking antiretroviral therapy who have failed virologic suppression late in pregnancy, since integrase inhibitors, including raltegravir, generate a very rapid decline in HIV RNA levels (estimated 2 log decline in 2 weeks).[25,26] Nevertheless, the benefit of this approach remains unproven and it is not endorsed in the Perinatal Guidelines.[27]
Intrapartum Management

In Labor without Antepartum Antiretroviral Therapy

For women who present in labor and have unknown HIV antibody status, expedited fourth-generation HIV antigen/antibody testing is recommended followed by an HIV-1/HIV-2 differentiation assay. Women who have a reactive test (preliminary positive) should be assumed to have HIV infection and all available prevention measures (for the mother and the infant) should be initiated to reduce the risk of perinatal transmission. Continuation of antiretroviral therapy for the mother and infant will depend on subsequent HIV confirmatory tests. Since most perinatal transmission of HIV occurs at or near the time of delivery, intrapartum antiretroviral therapy should be provided to all women with HIV infection who are newly diagnosed at the time of labor and to women with known HIV infection who are not taking antiretroviral therapy late in their pregnancy. Intravenous zidovudine, when given early in labor, rapidly crosses the placenta and thus can efficiently provide high systemic levels of zidovudine for the infant. For pregnant women with HIV infection who are not on antiretroviral therapy late in their pregnancy, the use of intrapartum and postpartum zidovudine reduces the risk of perinatal transmission from 27% to 10%. Most experts recommend cesarean delivery section for women newly diagnosed with HIV at the time of labor and for those with known HIV who are not on antiretroviral therapy, since these women are likely to have an HIV RNA level above 1000 copies/mL—the threshold for elective cesarean section. The benefit of cesarean section after rupture of membranes or onset of labor is unknown.

Indication for Intravenous Zidovudine During Labor

The Perinatal Guidelines recommend the use of intravenous zidovudine during delivery for women if, near the time of delivery, the HIV RNA level is either unknown or greater than 1000 copies/mL. Although use of intrapartum zidovudine is not required in women who have an HIV RNA level equal to or less than 1000 copies/mL near the time of delivery (and who are reliably taking combination antiretroviral therapy), some experts recommend using intravenous zidovudine if there is any level of detectable viremia near delivery. Data from several recent studies support the new recommendation to use 1000 copies/mL as the cutoff for administering intravenous zidovudine.

Dosing of Zidovudine in Labor

The recommended intravenous dose of zidovudine during labor is 2 mg/kg over the first hour, followed by a continuous infusion of 1 mg/kg/hour until delivery. For women scheduled to have a cesarean delivery, the intravenous infusion should be started 3 hours prior to the scheduled delivery.

Single-dose Nevirapine in Labor

In the United States, single-dose nevirapine is not recommended for any women with HIV infection during labor, regardless of whether they have received antepartum combination antiretroviral prophylaxis. A single dose of nevirapine had previously been given during labor to women who did not receive combination antiretroviral therapy during pregnancy, but the PACTG 316 trial found that nevirapine provided no additional benefit to standard antiretroviral therapy (as determined and prescribed by the woman's health care clinician) in reducing perinatal transmission, and it was associated with increased rates of antiretroviral resistance in the mother and in the infants who became infected with HIV. A subsequent clinical trial in Botswana also found no benefit of maternal single-dose nevirapine at the time of delivery in the setting of maternal zidovudine and infant zidovudine prophylaxis.

Indications for Cesarean Section Delivery
In the years before combination antiretroviral therapy was recommended for all pregnant women with HIV infection, cesarean section markedly reduced the risk of perinatal HIV transmission.[34] Current Perinatal Guidelines recommend performing a cesarean section at 38 weeks for all women with HIV infection who have an HIV RNA level greater than 1000 copies/mL (near the time of delivery), regardless of whether they are receiving antiretroviral therapy.[29] In addition, scheduled cesarean section at 38 weeks is also recommended for women with unknown HIV RNA near the time of delivery. The woman’s CD4 cell count has no bearing on recommendations regarding cesarean delivery. Insufficient data exist as to whether cesarean section would further reduce the risk of HIV transmission for women receiving antiretroviral therapy who have detectable low-level viremia (less than 1000 copies/mL) near the time of delivery. For women who have a detectable HIV RNA level above 1000 copies/mL, but who present with rupture of membranes (or present after the onset of labor), the benefit of cesarean is unknown; a meta-analysis has found that the risk of HIV transmission increases by 2% every hour following rupture of membranes.[29] These complex cases should be managed in consultation with an HIV expert.

**Timing for Cesarean Section Delivery**

Despite the potential risk of iatrogenic prematurity, the American Congress of Obstetricians and Gynecologists (ACOG) and the Perinatal Guidelines recommend performing the elective cesarean for women with HIV RNA levels greater than 1000 copies/mL (or unknown HIV RNA levels) at 38 weeks to avoid onset of labor before the scheduled cesarean section.[29] If the patient has an HIV RNA level less than 1000 copies/mL and the decision is made to perform a cesarean section, the elective cesarean should be performed at 39 weeks’ gestation.

**Obstetric Procedures and Risk of HIV Transmission**

Although limited data exist regarding the impact of obstetrical procedures on HIV transmission risk, the Perinatal Guidelines recommend against the routine use of any of the following procedures: artificial rupture of membranes, invasive fetal scalp monitoring with scalp electrodes, operative delivery with forceps or vacuum extractor, and episiotomy.[12,35] If, however, any of these procedures are deemed to have a clear obstetrical indication, they should be performed. The possible risk of HIV transmission from these procedures is likely lower in women who have an undetectable HIV RNA level at the time of delivery. Epidural anesthesia is considered safe for women with HIV infection in labor, regardless of the antiretroviral regimen the woman is receiving.

**Methylergonovine for Postpartum Hemorrhage**

Methylergonovine and other ergot alkaloids, which are generally the first-line treatment for postpartum hemorrhage due to uterine atony, are metabolized primarily by the P450 CYP3A4 enzyme system. Potent CYP3A4 inhibitors, such as ritonavir or cobicistat, significantly increase systemic levels of methylergonovine whereas CYP34A inducers, such as efavirenz or nevirapine, lower systemic levels of methylergonovine. Co-administering methylergonovine with medications that may cause a drug interaction can lead to overtreatment (with resulting excessive vasoconstriction) or undertreatment of uterine atony, respectively. Accordingly, other treatment options for uterine atony and bleeding should be considered. [35]
Management of the Infant Exposed to HIV

Approach to Postpartum Prevention of Perinatal Transmission

Appropriate management of an infant (following birth from a mother with HIV infection) plays a significant role in preventing perinatal HIV transmission. The major prevention measure include administering postpartum antiretroviral therapy to all infants in this setting and avoiding breastfeeding.

Antiretroviral Prophylaxis for the Infant

All infants born to a mother with HIV infection should have antiretroviral prophylaxis initiated as soon as possible after birth, ideally within 6 to 12 hours following delivery. The choice of infant antiretroviral prophylaxis regimen depends on the mother’s antiretroviral history and HIV RNA levels near delivery, as outlined below. Zidovudine is a component of all postpartum infant HIV prophylaxis regimens; the zidovudine dosing is weight-based and depends on gestational age.

Mother Took Antepartum Antiretroviral Drugs with Effective Viral Suppression

For women with suppressed HIV RNA levels near delivery, zidovudine monotherapy is recommended for the infant. The standard duration for infant zidovudine prophylaxis is 6 weeks; this may be shortened to a 4-week course if the mother received suppressive combination antiretroviral therapy throughout the pregnancy, there was sustained viral suppression during the pregnancy, and there are no concerns related to maternal adherence during pregnancy.

Mother Took Antepartum Antiretroviral Drugs with Suboptimal Viral Suppression Near Delivery

Infants born to mothers who received antiretroviral therapy but had HIV RNA levels greater than 1000 copies/mL near delivery, should receive combination antiretroviral therapy consisting of a 6-week regimen of zidovudine plus 3 doses of nevirapine (given at birth, 48 hours later, and 96 hours after the second dose). The first doses of zidovudine and nevirapine should be given to the infant as soon as possible after birth. This recommendation to use combination therapy is based on findings from a large international trial (HPTN 040/PACTG 1043) that enrolled women with HIV infection who did not receive antiretroviral therapy during pregnancy and demonstrated a significantly lower risk of acquiring HIV among infants who received combination antiretroviral therapy (with a two- or three-drug regimen) than infants who received zidovudine only.

Many of the panel members on the perinatal guideline committee have recommended administering a 2 to 6 weeks of triple antiretroviral therapy with zidovudine, lamivudine, and nevirapine for infants at high risk of HIV acquisition, such as those born to mothers with high HIV RNA levels at the time of delivery, but safety and efficacy data with this approach are limited, especially in premature and low-birth weight babies. With this approach, nevirapine is given at a dose of 6 mg/kg twice daily. A decision to administer triple antiretroviral therapy to a neonate should include consultation with a pediatric HIV specialist, ideally beginning prior to delivery. Several studies are ongoing investigating the safety and efficacy of triple treatment.

Mother Received Only Intrapartum Antiretroviral Drugs, or no Intrapartum or Antepartum Antiretroviral Drugs

Infants born to mothers who received antiretroviral therapy only at delivery, or who did not receive combined antiretroviral therapy during pregnancy or delivery, should receive the same combination antiretroviral therapy regimen as infants born to mothers with suboptimal HIV RNA suppression: a 6-week regimen of zidovudine plus 3 doses of nevirapine (given at birth, 48 hours later, and 96 hours after the second dose). As noted above, those infants considered high-risk for HIV acquisition should also be considered for triple antiretroviral therapy (zidovudine plus lamivudine plus...
Pneumocystis Pneumonia Prophylaxis for the Infant

After completing 4 to 6 weeks of zidovudine prophylaxis, all infants born to women with HIV infection should begin prophylaxis for *Pneumocystis* pneumonia with trimethoprim-sulfamethoxazole, unless HIV infection can be presumptively excluded with virologic testing.[38]

Initial Care of the Neonate Exposed to HIV Infection

Following delivery, infants born to mothers with HIV infection require hematological monitoring in addition to routine infant care; there is no evidence that changes in routine bathing practices or timing of circumcision are required.[38] A complete blood count (CBC) and differential should be performed at birth prior to the initiation of infant antiretroviral drug prophylaxis and again at 4 weeks of age since anemia is the primary complication of zidovudine prophylaxis.[38] In addition, some experts advise checking serum chemistry and liver function tests depending on which antiretroviral therapies the infant was exposed to in utero.

Evaluating the Infant for HIV Infection

Initial HIV testing in infants should be performed using an HIV nucleic acid amplification test (NAAT), either an HIV DNA or an HIV RNA assay. Routine HIV antibody testing should not be used in newborns since maternal HIV antibody crosses the placenta and can persist through 18 months of age in infants exposed to HIV.[38] Virologic testing with either an HIV DNA or HIV RNA test should be performed at 14 to 21 days of life, 1 to 2 months of age, and 4 to 6 months of age. For higher risk situations, such as when the mother does not have virologic suppression near the time of delivery, some experts recommend obtaining an HIV NAAT on the infant at birth.[38] The Perinatal Guidelines make a distinction between presumptive and definitive exclusion of HIV in infants born to mothers with HIV infection. According to these guidelines, HIV can be presumptively excluded with two or more negative HIV NAATs: one at age 14 days or older and the other at age 1 month or older. Definitive exclusion of HIV in non-breastfed infants can be based on two negative HIV NAATs, with one test performed at age 1 month or older and the other test at age 4 months or older. Negative HIV antibody testing at age 12 to 18 months provides further confirmation of the child’s HIV negative status.[38]

Breastfeeding Recommendations

In the United States, where replacement feeding with infant formula is generally affordable, readily available, and safe, clear recommendations exist that mothers with HIV infection should not breastfeed, due to a 1 to 5% risk of transmitting HIV to their newborn, even with antiretroviral prophylaxis administered to either the infant or the mother.[38,39] Colostrum and breastmilk can efficiently transmit HIV from mother to infant, with especially high transmission risk (25 to 30%) occurring if the mother is infected with HIV during the postpartum period while breastfeeding.[40] Studies have shown that infants who become infected with HIV through breastfeeding when the mother is taking antiretroviral therapy have an increased risk of acquiring drug-resistant HIV.[39,41]

Postpartum Antiretroviral Therapy for the Mother

Pregnant women with HIV infection who receive antiretroviral therapy during pregnancy should continue to receive antiretroviral therapy after delivery, both for their own health and to prevent forward sexual transmission of HIV.[42] The HPTN 052 study, among others, has shown that antiretroviral therapy markedly reduces the risk of sexual HIV transmission to uninfected partners in HIV-serodiscordant couples.[43] Taking antiretroviral therapy in the postpartum period may be very challenging due to the mother’s fatigue, psychosocial stress, and demands and responsibilities of
taking care of a newborn. The Perinatal Guidelines emphasize the importance of coordinating maternal services with the woman’s HIV medical provider, with decisions about antiretroviral therapy ideally made prior to delivery.

**Long-term Follow-up of Infants Born to Mothers with HIV Infection**

The long-term effects of *in utero* exposure to antiretroviral therapy and to HIV itself (even if the infant was not infected) are not fully known. Nevertheless, based on available data that have shown rates of birth defects for infant antiretroviral exposure during the first trimester does not differ from exposure later in pregnancy,[44,45,46] the Perinatal Guidelines now recommend that women can be counseled that, in general, taking antiretroviral therapy during pregnancy does not increase the risk of birth defects.[47] Data on neurodevelopmental outcomes of HIV-exposed infants are limited, and confounding factors (maternal substance abuse, poverty, prematurity due to antiretroviral therapy, or other obstetrical causes) make it difficult to assess the possible effects of HIV and of antiretroviral therapy.[48] A recent review found that infants who acquired HIV during fetal and early life display lower developmental scores than children not exposed to HIV, though early initiation of combination antiretroviral therapy seems to confer benefits in those children who acquired HIV as infants.[48] Multiple studies and surveillance projects, at both the state and national levels, are ongoing. The Perinatal Guidelines recommend that any children with *in utero/perinatal* exposure to antiretroviral therapy who develop organ system abnormalities, particularly neurological or cardiac, should be evaluated for mitochondrial dysfunction, and follow-up of children exposed to antiretroviral medications should continue lifelong due to potential carcinogenicity of nucleoside reverse transcriptase inhibitor drugs.[49]
Acute HIV in Pregnancy

Diagnosis of Acute HIV in Pregnancy or in Breastfeeding Mothers

Acute HIV infection of a woman during pregnancy or while breastfeeding confers a very high risk of HIV transmission to the child because of high HIV RNA levels in the mother’s plasma, genital tract, and breastmilk that occur with acute infection. In one cohort study in New York state, investigators reported the rate of perinatal transmission was 22% among neonates born to mothers who acquired HIV during pregnancy compared to 1.8% of newborns whose mothers did not acquire HIV during pregnancy.[50] Therefore, pregnant or breastfeeding women with symptoms of acute retroviral syndrome should undergo prompt evaluation for acute HIV infection.[17] When acute HIV is suspected during pregnancy or while breastfeeding, the evaluation should include an HIV RNA assay in combination with antibody testing (preferably a fourth-generation antigen-antibody test).[17]

Antiretroviral Therapy for Acute HIV in Pregnancy

Given the high risk of HIV transmission to the fetus in the setting of acute maternal HIV infection, a pregnant woman with acute HIV infection should immediately begin triple antiretroviral therapy while a genotype is pending, preferable with a regimen that includes a protease inhibitor-based regimen.[17] The use of dolutegravir plus tenofovir DF-emtricitabine is also considered a reasonable option in this situation; a raltegravir-based regimen is not recommended if the HIV RNA level is high, since raltegravir does not have a high genetic barrier to resistance.[17] If needed, adjustments to the regimen can be made once the genotype results are known.[17] If acute HIV infection is diagnosed late in pregnancy, cesarean section will likely be necessary since there may not be adequate time to reduce maternal HIV RNA levels below the threshold of 1000 copies/mL (the threshold above which cesarean section is recommended).[17]

Acute HIV in the Postpartum Period

If acute HIV infection is suspected in the postpartum period, the newly diagnosed mother should be counseled to stop breastfeeding until acute HIV infection is ruled out (if HIV infection is confirmed, breastfeeding should be permanently discontinued).[17] In this situation, expert consultation should be obtained regarding the evaluation and management of the breastfeeding infant who may have been exposed to HIV.
Summary Points

- All pregnant women should undergo screening for HIV infection, including women who present in labor without prior testing during the pregnancy.
- For pregnant women with HIV infection, perinatal HIV transmission rates less than 1% can be achieved with a comprehensive, multipronged approach that includes suppressive combination antiretroviral therapy during pregnancy, use of elective cesarean section (when indicated), intravenous zidovudine during labor (when indicated), postnatal infant antiretroviral prophylaxis, and avoidance of breastfeeding.
- All women diagnosed with HIV infection during pregnancy should start combination antiretroviral therapy and continue it throughout the pregnancy.
- Women with known HIV infection who become pregnant and are not receiving antiretroviral therapy should start antiretroviral therapy and continue therapy throughout the pregnancy.
- Women with established HIV infection who become pregnant and are already taking fully suppressive antiretroviral therapy should continue the same regimen.
- The risk of perinatal HIV transmission correlates with maternal HIV RNA levels, but there is no HIV RNA level cutoff at which transmission cannot occur.
- Due to concerns about teratogenicity, efavirenz should be avoided in the first trimester, if possible, but women who are already taking efavirenz when they become pregnant can continue it.
- The dosage of lopinavir-ritonavir and atazanavir (with or without ritonavir), two protease inhibitors that are approved for use in pregnancy, may need to be increased in the third trimester to maintain adequate plasma levels.
- Laboratory monitoring of HIV RNA levels should occur every 3 months during pregnancy to evaluate for viral suppression; obtaining an HIV RNA level at 34 to 36 weeks is important in making decisions about delivery and newborn management.
- Approximately 80% of perinatal transmission takes place between gestation week 36 and birth, so women who present late to prenatal care should start on antiretroviral therapy immediately, and additional interventions, including intravenous zidovudine and elective cesarean section may be recommended to help decrease the risk of perinatal transmission.
- For pregnant women with HIV infection, cesarean section and intravenous zidovudine during labor are indicated if the HIV RNA level is greater than 1000 copies/mL near the time of delivery (or if they have an unknown HIV RNA level near the time of delivery).
- The evaluation for HIV infection of infants born to mothers with HIV infection requires use of HIV nucleic acid amplification tests; HIV antibody testing is not reliable since maternal HIV antibody crosses the placenta and persists in the infant for months.
- Infants born to mothers with HIV infection should receive antiretroviral prophylaxis with zidovudine for 4 to 6 weeks; if the mother with HIV infection was not treated with antiretroviral therapy during pregnancy or has a high HIV RNA at the time of delivery, combination antiretroviral therapy is recommended for the infant (though the ideal number of antiretroviral drugs and duration of therapy remains contested).
- Women with HIV infection in the United States are advised to avoid breastfeeding due to the possibility of transmitting HIV through colostrum and breastmilk and the availability of affordable, safe, and acceptable feeding alternatives.
Citations


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30. European Mode of Delivery Collaboration.. Elective caesarean-section versus vaginal delivery


References


Figures

Figure 1 Perinatal HIV Infections in the United States, 2010-2015

In the Pediatric AIDS Clinical Trials Group (PACTG) Protocol 076, pregnant women with HIV infection were randomized to receive either zidovudine or placebo. The zidovudine regimen consisted of antepartum oral zidovudine, intravenous zidovudine during labor and delivery, and postpartum oral zidovudine for the infant. The proportion of babies who were determined to have HIV infection at 18 months postpartum was 67.5% lower in the zidovudine arm.

Figure 3 Perinatal HIV Transmission Rates in United States, 1990-1999

This graphic shows trends in maternal-to-infant HIV transmission rates during the years 1990-1999. A major decline occurred in 1994 concurrent with clinician implementation of findings from PATG 076 and then again in 1996 with the more widespread use of antenatal combination antiretroviral therapy.

Figure 4 Timing of Abbreviated Regimens of Zidovudine and Risk of Maternal-Child Transmission of HIV

Figure 5 Antenatal Antiretroviral Therapy and Impact on Perinatal HIV Transmission

### Table 1. Perinatal Guidelines: Recommendations for Use of Antiretroviral Drugs During Pregnancy

#### Antiretroviral-Naïve Pregnant Women: Preferred Initial Regimens in Pregnancy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comment</th>
</tr>
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<tbody>
<tr>
<td><strong>Preferred Two-NRTI Backbone</strong></td>
<td></td>
</tr>
<tr>
<td>Abacavir-lamivudine</td>
<td>Available as fixed-dose combination. Can be administered once daily. Abacavir <strong>should not be used</strong> in patients who test positive for HLA-B*5701 because of risk of hypersensitivity reaction. Abacavir-lamivudine with either ritonavir-boosted atazanavir or efavirenz is not recommended if pretreatment HIV RNA is &gt;100,000 copies/mL.</td>
</tr>
<tr>
<td>Tenofovir DF-emtricitabine or Tenofovir DF plus lamivudine</td>
<td>Tenofovir DF-emtricitabine is available as a fixed-dose combination. Either tenofovir DF-emtricitabine (coformulated) or tenofovir DF with separate lamivudine can be administered once daily. Tenofovir DF has potential renal toxicity, thus tenofovir DF-based dual NRTI combinations should be used with caution in patients with renal insufficiency.</td>
</tr>
<tr>
<td><strong>Preferred PI Regimens</strong></td>
<td></td>
</tr>
<tr>
<td>Atazanavir boosted with ritonavir plus a Preferred Two-NRTI Backbone</td>
<td>Once-daily administration. Extensive experience in pregnancy. Maternal hyperbilirubinemia; no clinically significant neonatal hyperbilirubinemia or kernicterus reported, but neonatal bilirubin monitoring recommended.</td>
</tr>
<tr>
<td>Darunavir boosted with ritonavir plus a Preferred Two-NRTI Backbone</td>
<td>Better tolerated than lopinavir-ritonavir. PK data available. Increasing experience with use in pregnancy. Must be used twice daily in pregnancy.</td>
</tr>
<tr>
<td><strong>Preferred Integrase Inhibitor Regimen</strong></td>
<td></td>
</tr>
<tr>
<td>Raltegravir plus a Preferred Two-NRTI Backbone</td>
<td>PK data available and increasing experience in pregnancy. Rapid viral load reduction (potential role for women who present for initial therapy late in pregnancy). Useful when drug interactions with PI regimens are a concern. Twice-daily dosing required. If there are concerns about adherence or medication discontinuation postpartum, a PI regimen is preferred instead of an integrase inhibitor regimen, to minimize the risk of resistance.</td>
</tr>
</tbody>
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**Abbreviations:** NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor

Table 2. Perinatal Guidelines: Recommendations for Use of Antiretroviral Drugs During Pregnancy

Antiretroviral-Naïve Pregnant Women: Alternative Initial Regimens in Pregnancy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alternative Initial Regimens in Pregnancy:</strong></td>
<td></td>
</tr>
<tr>
<td>- Regimens with clinical trial data demonstrating efficacy in adults but one or more of the following apply: experience in pregnancy is limited, data are lacking or incomplete on teratogenicity, or regimen is associated with dosing, formulation, toxicity, or interaction issues.</td>
<td></td>
</tr>
<tr>
<td><strong>Alternative Two-NRTI Backbone</strong></td>
<td></td>
</tr>
<tr>
<td>Zidovudine-lamivudine</td>
<td>Available as fixed-dose combination. NRTI combination with most experience for use in pregnancy but has disadvantages of requirement for twice-daily administration and increased potential for hematologic toxicities.</td>
</tr>
<tr>
<td><strong>PI Regimens</strong></td>
<td></td>
</tr>
<tr>
<td>Lopinavir-ritonavir plus a Preferred Two-NRTI Backbone</td>
<td>Abundant experience and established pharmacokinetics (PK) in pregnancy. More nausea than with preferred agents. Twice-daily administration. Dose increase recommended in third trimester. Once-daily lopinavir-ritonavir is not recommended for use in pregnant women</td>
</tr>
<tr>
<td><strong>NNRTI Regimen</strong></td>
<td></td>
</tr>
<tr>
<td>Efavirenz plus a Preferred Two-NRTI Backbone</td>
<td>Concern because of birth defects seen in primate study; data not borne out in human studies, but cautionary text remains in package insert. Preferred</td>
</tr>
<tr>
<td>Drug</td>
<td>Comment</td>
</tr>
<tr>
<td>----------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Ripivirine-tenofovir DF-emtrictabine or</td>
<td>Rilpivirine not recommended with pretreatment HIV RNA &gt;100,000 copies/mL or CD4 cell count &lt;200 cells/mm³. Do not use with proton pump inhibitors. PK data available in pregnancy but relatively little experience with use in pregnancy. Available in coformulated single-pill, once-daily regimen.</td>
</tr>
<tr>
<td>Rilpivirine plus a Preferred Two-NRTI Backbone</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor

**Source:**
Table 3. **Perinatal Guidelines: Recommendations for Use of Antiretroviral Drugs During Pregnancy**

**Antiretroviral-Naïve Pregnant Women: Insufficient Data in Pregnancy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insufficient Data in Pregnancy to Recommend Routine Use in Initial Regimens for Antiretroviral-Naïve Women:</strong></td>
<td></td>
</tr>
<tr>
<td>- Drugs that are approved for use in adults but lack adequate pregnancy-specific pharmacokinetic (PK) or safety data.</td>
<td></td>
</tr>
<tr>
<td>Cobicistat</td>
<td>Limited data on use of cobicistat (including coformulations with atazanavir or darunavir) in pregnancy.</td>
</tr>
<tr>
<td>Dolutegravir</td>
<td>Limited data on use of dolutegravir in pregnancy.</td>
</tr>
<tr>
<td>Elvitegravir-cobicistat-tenofovir DF-emtricitabine</td>
<td>Limited data on use of elvitegravir-cobicistat component in pregnancy.</td>
</tr>
<tr>
<td>Fosamprenavir</td>
<td>Limited data on use in pregnancy.</td>
</tr>
<tr>
<td>Maraviroc</td>
<td>Maraviroc requires tropism testing before use. Few case reports of use in pregnancy.</td>
</tr>
<tr>
<td>Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine</td>
<td>Limited data on use of elvitegravir-cobicistat in pregnancy; no data on use of tenofovir alafenamide in pregnancy.</td>
</tr>
<tr>
<td>Tenofovir alafenamide-emtricitabine</td>
<td>No data on use of tenofovir alafenamide in pregnancy.</td>
</tr>
<tr>
<td>Rilpivirine-tenofovir alafenamide-emtricitabine</td>
<td>No data on use of tenofovir alafenamide in pregnancy.</td>
</tr>
</tbody>
</table>

Source:

- Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the
### Table 4. Perinatal Guidelines: Recommendations for Use of Antiretroviral Drugs During Pregnancy

**Antiretroviral-Naïve Pregnant Women: Not Recommended for Initial ART in Pregnancy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Not Recommend for Initial Antiretroviral Therapy in Pregnancy:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drugs whose use is not recommended as part of initial regimens in pregnancy because of toxicity, lower rate of viral suppression or because not recommended in antiretroviral therapy-naïve populations.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Note:</strong> Drugs not recommended for initial use because of toxicity* (stavudine, didanosine, treatment-dose ritonavir) should also be stopped in women who present during pregnancy while taking these medications.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other medications listed below may be continued in women who present during pregnancy, as long as they are well tolerated and result in sustained virologic suppression.</td>
</tr>
<tr>
<td>Abacavir-lamivudine-zidovudine</td>
<td>Generally not recommended due to inferior virologic efficacy.</td>
</tr>
<tr>
<td>Stavudine*</td>
<td>Not recommended due to toxicity.</td>
</tr>
<tr>
<td>Didanosine*</td>
<td>Not recommended due to toxicity.</td>
</tr>
<tr>
<td>Indinavir boosted with ritonavir</td>
<td>Nephrolithiasis, maternal hyperbilirubinemia.</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Lower rate of viral suppression with NFV compared to lopinavir-ritonavir or efavirenz in adult trials.</td>
</tr>
<tr>
<td>Ritonavir*</td>
<td>Treatment-dose ritonavir as a single PI is not recommended because of inferior efficacy and increased toxicity.</td>
</tr>
<tr>
<td>Saquinavir boosted with ritonavir</td>
<td>Not recommended based on potential toxicity and dosing disadvantages. Baseline ECG is</td>
</tr>
<tr>
<td>Drug</td>
<td>Comment</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Saquinavir/r</td>
<td>recommended before initiation of saquinavir/r because of potential PR and QT prolongation; contraindicated with preexisting cardiac conduction system disease. Limited data in pregnancy. Large pill burden. Twice-daily dosing required.</td>
</tr>
<tr>
<td>Etravirine</td>
<td>Not recommended in antiretroviral-naive populations.</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Not recommended because of greater potential for adverse events, complex lead-in dosing, and low barrier to resistance. Nevirapine should be used with caution when initiating antiretroviral therapy in women with CD4 cell count &gt;250 cells/mm³. Use nevirapine and abacavir together with caution; both can cause hypersensitivity reactions within the first few weeks after initiation.</td>
</tr>
<tr>
<td>Enfuvirtide</td>
<td>Not recommended in antiretroviral-naive populations.</td>
</tr>
<tr>
<td>Tipranavir boosted with ritonavir</td>
<td>Not recommended in antiretroviral-naive populations.</td>
</tr>
</tbody>
</table>

Source:
