### Intrapartum Care  (Last updated December 7, 2018; last reviewed December 7, 2018)

#### Intrapartum Antiretroviral Therapy/Prophylaxis

<table>
<thead>
<tr>
<th>Panel’s Recommendations</th>
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<tbody>
<tr>
<td>• Women should continue taking their antepartum combination antiretroviral therapy (ART) on schedule as much as possible during labor and before scheduled cesarean delivery (AIII).</td>
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<td>• Intravenous (IV) zidovudine:</td>
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<tr>
<td>• Should be administered to women living with HIV if HIV RNA is known or suspected to be &gt;1,000 copies/mL (or if HIV RNA is unknown) near delivery (AI).</td>
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<tr>
<td>• Is not required for women who are receiving ART regimens and who have HIV RNA ≤50 copies/mL during late pregnancy and near delivery and no concerns regarding adherence to the ART regimen (BII).</td>
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<tr>
<td>• May be considered for women with HIV RNA between 50 and 999 copies/mL. There are inadequate data to determine whether administration of IV zidovudine to women with HIV RNA levels between 50 and 999 copies/mL provides any additional protection against perinatal transmission. <strong>This decision can be made on a case by case basis, taking into consideration the woman’s recent ART adherence, her preferences, and involving expert consultation if needed (CII).</strong></td>
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<tr>
<td>• Scheduled cesarean delivery at 38 weeks’ gestation (compared to 39 weeks for most indications) is recommended for women who have HIV RNA &gt;1,000 copies/mL near delivery (see Transmission and Mode of Delivery) (AI).</td>
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<td>• Women who present in labor with unknown HIV status should undergo expedited antigen/antibody HIV testing (AII).</td>
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<td>• If the results are positive, an HIV-1/HIV-2 antibody differentiation test and an HIV-1 RNA assay should be done as soon as possible and maternal (IV zidovudine)/infant (combination antiretroviral [ARV] prophylaxis) ARV drugs should be initiated pending results of the differentiation test (AII).</td>
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<tr>
<td>• If the maternal HIV differentiation test is positive or if acute infection is suspected because the HIV RNA test is positive but the differentiation test is negative infant ARV drugs should be managed as discussed in Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV (AI). Women with positive expedited testing should not initiate breastfeeding until HIV infection is definitively ruled out (see Postpartum Follow-Up of Women Living with HIV Infection) (AII).</td>
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<tr>
<td>• If the maternal HIV differentiation test is negative and acute HIV infection has been reasonably excluded with a negative HIV RNA test, the maternal and infant ARV drugs should be stopped (AIII).</td>
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</table>

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

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### Women Who Have Received Antepartum Antiretroviral Drugs

#### Use of Intravenous Zidovudine During Labor

The PACTG 076 zidovudine regimen included a continuous intravenous (IV) infusion of zidovudine during labor for all women. Antiretroviral therapy (ART) regimens are now recommended for treatment of HIV and prevention of perinatal transmission of HIV in all pregnant women, regardless of CD4 T lymphocyte (CD4) cell count and HIV viral load; the additional benefit of IV zidovudine in women receiving combination regimens has not been evaluated in randomized clinical trials.

The French Perinatal Cohort evaluated transmission in >11,000 pregnant women with HIV who were receiving antiretroviral (ARV) drugs (10% of women were receiving zidovudine alone, 18% were receiving dual-ARV regimens, and 72% were receiving triple-ARV regimens) and who delivered between 1997 and 2010, stratified by viral load at delivery; 95% of these women received IV intrapartum zidovudine. The overall rate of perinatal transmission was 0.9% (95/10,239 infants) with IV zidovudine and 1.8% (9/514 infants, *P* = 0.06) without IV zidovudine. Among women with HIV RNA <1,000 copies/mL at delivery, no transmission occurred among 369 women who did not receive IV zidovudine compared to a transmission rate of 0.6% (47/8,132, *P* > 0.20) among those who received IV zidovudine. Among women with HIV RNA >1,000 copies/mL whose infants received only zidovudine for prophylaxis, the risk of transmission...
was 10.2% without maternal IV zidovudine and 2.5% with maternal IV zidovudine ($P < 0.01$) The risk of transmission was no different (4.8% vs. 4.1%, $P = 0.83$) if the neonate received intensified prophylaxis with two or more ARV drugs. In a cohort of 717 women who delivered between 1996 and 2008 in Miami, the majority of whom were receiving an ART regimen and had HIV RNA <1,000 copies/mL at delivery, lack of receipt of IV zidovudine during labor was not associated with an increased risk of transmission. Among a European cohort of infants considered at high risk of transmission, lack of IV zidovudine during labor was associated with transmission on univariate analysis but was not significantly associated with transmission once the results were adjusted for maternal HIV RNA and other factors (adjusted odds ratio with IV zidovudine = 0.79; 95% CI, 0.55–1.15; $P = 0.23$). In a cohort of Irish women with HIV RNA <1,000 copies/mL who received ART for at least 4 weeks before delivery, no transmission occurred among 61 women who received either no zidovudine during labor or <4 hours of IV zidovudine.

Based on the results of these studies, IV zidovudine should continue to be administered to women with HIV RNA >1,000 copies/mL near delivery (or to women living with HIV who have unknown HIV RNA levels), regardless of antepartum regimen. IV zidovudine is not required for women receiving ART and have HIV RNA ≤1,000 copies/mL in late pregnancy and/or near delivery and have no concerns about adherence to or tolerance of their ART regimens. However, many experts feel that there are inadequate data to determine whether administration of intrapartum IV zidovudine to women with HIV RNA between 50 and 999 copies/mL provides any additional protection against perinatal transmission. They recommend intrapartum IV zidovudine administration to women with HIV RNA levels in this range, as the transmission risk is slightly higher (approximately 1% to 2%) when HIV RNA is in the range of 50 to 999 copies/mL compared to <50 copies/mL (transmission risk is ≤1%). In addition, a recent study noted that 6% of women with suppressed HIV RNA levels during pregnancy had viral load rebound near delivery. Regardless of viral load, the clinician may elect to use or not use intrapartum IV zidovudine based on clinical judgment.

In women with HIV RNA >1,000 copies/mL who are undergoing a scheduled cesarean delivery for prevention of transmission, IV zidovudine administration should begin 3 hours before the scheduled operative delivery. This recommendation is based on a pharmacokinetic (PK) study of zidovudine given orally during pregnancy and as a continuous infusion during labor. Maternal zidovudine levels were measured at baseline, after the initial IV loading dose, and then every 3 to 4 hours until delivery. Zidovudine levels were also measured in cord blood. Systemic and intracellular zidovudine levels increased from baseline but appeared to stabilize after 3 hours of infusion; cord blood zidovudine levels were associated with maternal levels and maternal infusion duration. If cesarean delivery is being performed for other indications and maternal viral load is ≤1,000 copies/mL near the time of delivery, administration of IV zidovudine is not required.

If zidovudine was not used in the antenatal ART regimen because of known or suspected zidovudine resistance, intrapartum use of the drug is still recommended in women with HIV RNA >1,000 copies/mL near delivery unless a woman has a documented history of hypersensitivity. This intrapartum use of the drug is recommended because of the unique characteristics of zidovudine and its proven record in reducing perinatal transmission, even in the presence of maternal resistance to the drug (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy).

In some international studies, oral (rather than IV) zidovudine has been administered during labor. Data are limited on the PKs of oral versus IV zidovudine during labor. In studies of oral dosing in labor, zidovudine levels were lower than with IV dosing, and PK parameters suggested erratic absorption during labor. Therefore, in women with HIV RNA >1,000 copies/mL near delivery for whom zidovudine is recommended, IV would be preferred to oral administration in the United States; in situations where IV administration is not possible, oral administration of zidovudine using a 600-mg loading dose and 400 mg every 3 hours can be considered.

### Continuation of Antenatal Antiretroviral Drugs during Labor

Women who are receiving an antepartum ART regimen should continue that regimen on schedule as much as possible during the intrapartum period to provide maximal virologic suppression and to minimize the
chance of developing drug resistance. If the woman is to receive IV zidovudine and oral zidovudine as part of the antepartum regimen, the oral zidovudine component of the regimen can be held while she receives IV zidovudine. When cesarean delivery is planned, oral medications can be administered preoperatively with sips of water. Medications requiring food ingestion for absorption can be taken with liquid dietary supplements, contingent on consultation with the attending anesthesiologist during the preoperative period. If the maternal ARV drug regimen must be interrupted temporarily (meaning for <24 hours) during the peripartum period, all drugs should be stopped and reinstituted simultaneously to minimize the chance that resistance will develop.

**Women Who Have Received Antepartum Antiretroviral Drugs but Have Suboptimal Viral Suppression Near Delivery**

Women who have received ART regimens may not achieve complete viral suppression by the time of delivery because of factors such as difficulty with adherence, viral resistance, or late entry into care. Regardless of the reason, all women who have HIV RNA levels >1,000 copies/mL or presumed >1,000 copies/mL near the time of delivery should be offered a scheduled cesarean delivery at 38 weeks, which may significantly reduce the risk of transmission (see Transmission and Mode of Delivery).

Women with HIV RNA levels above 1,000 copies/mL at the time of delivery should receive IV zidovudine along with oral administration of their other ARVs, as described above. While additional maternal ART, such as single-dose nevirapine, is not recommended, in certain high-risk situations, additional medications for prophylaxis in infants may be warranted. These situations include cases where maternal HIV RNA levels are high at or near the time of delivery, especially if delivery is not a scheduled cesarean delivery (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV and Table 9).

**Women Who Have Not Received Antepartum Antiretroviral Drugs**

**Women Who Present in Labor without Documentation of HIV Status**

All women without documentation of HIV status at the time of labor should be screened for HIV with expedited testing unless they decline (i.e., “opt-out” screening). Expedited repeat HIV testing is also recommended for women presenting in labor who tested negative for HIV in early pregnancy, but who are at increased risk of HIV infection and were not retested in the third trimester. Factors that may increase the risk of infection include diagnosis of a sexually transmitted disease, illicit drug use, exchange of sex for money or drugs, multiple sexual partners during pregnancy, a sexual partner at risk of or with known HIV infection, signs/symptoms of acute HIV infection, or living in a region with an elevated incidence of HIV in women of childbearing age.

Initial testing for HIV should be done with a Food and Drug Administration (FDA)-approved antigen/antibody combination immunoassay that detects HIV-1 and HIV-2 antibodies, and an HIV RNA assay to screen for both acute and established HIV-1 infection. No further testing is required for specimens that are nonreactive on the initial immunoassay. Women with a positive initial antigen/antibody combination immunoassay result should be tested with an FDA-approved antibody immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies. Reactive results on the initial antigen/antibody combination immunoassay and the HIV-1/HIV-2 antibody differentiation immunoassay should be interpreted as positive for HIV-1 antibodies; HIV-2 antibodies; or HIV antibodies, undifferentiated (see Revised Recommendations for HIV Testing in Adults, Adolescents, and Pregnant Women in Health-Care Settings and the resource page for laboratory testing for HIV). Those with high HIV-1 RNA and a negative confirmatory HIV assay most likely have acute HIV infection.

Expedited HIV testing should be available on a 24-hour basis at all facilities with a maternity service and/or neonatal intensive care unit. Statutes and regulations regarding expedited testing vary from state to state (see State HIV Testing Laws from the Clinician Consultation Center for a review of these laws). Current information about testing also should be available at all facilities with a maternity service and/or neonatal intensive care unit.
Women who test positive on the initial test should be presumed to have HIV until follow-up testing clarifies their infection status. IV zidovudine should be started immediately in all women with positive initial HIV tests in labor to prevent perinatal transmission of HIV, as discussed below. Women with positive initial testing should not initiate breastfeeding until HIV infection is definitively ruled out.

During the postpartum period, clinicians should follow up with these women on the results of confirmatory HIV-1/HIV-2 antibody differentiation immunoassay and HIV-1 RNA testing and provide appropriate assessments of their health status as soon as possible, including CD4 cell count and HIV genotype for resistance. Arrangements also should be made for establishing HIV care and providing ongoing psychosocial support after discharge. The infant should receive combination ARV prophylaxis as outlined in the section on Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV. If the follow-up antibody testing is negative, results of the HIV RNA test should be reviewed to rule out acute infection as a cause of the initial positive test before ART is stopped (see Acute HIV Infection).

Choice of Intrapartum/Postpartum Antiretroviral Regimen for Women who Have Not Received Antepartum Antiretroviral Therapy

All women with HIV who have not received antepartum ARV drugs should start IV zidovudine immediately to prevent perinatal transmission of HIV. Although intrapartum/neonatal ARV medications will not prevent perinatal transmission that occurs before labor, most transmission occurs near to or during labor and delivery. Pre-exposure prophylaxis for the fetus can be provided by giving mothers a drug that rapidly crosses the placenta, producing fetal systemic ARV drug levels during intensive exposure to HIV in maternal genital secretions and in blood during birth. In general, zidovudine and other nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and the integrase inhibitor raltegravir cross the placenta well, whereas protease inhibitors do not (see Table 10). A small PK study and placental perfusion data suggest moderate-to-high placental transfer of elvitegravir. For dolutegravir, a PK study found the median cord blood/maternal plasma concentration ratio was 1.25 in 18 infants, corroborating data from case reports and placental perfusion models showing moderate-to-high placental transfer of dolutegravir.

Considerations for postpartum regimen choice are similar to those for women who have never received ART (see Pregnant Women Living with HIV Who Have Never Received Antiretroviral Drugs).

A large international trial (NICHD-HPTN 040/PACTG 1043) demonstrated that adding ARV agents to the neonatal portion of the intrapartum/neonatal zidovudine regimen can further reduce perinatal transmission of HIV for mothers who have received no antepartum ARV drugs (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). In this study, women who had not received antepartum ARV drugs received IV zidovudine if HIV infection was diagnosed during labor or no zidovudine if HIV was diagnosed immediately postpartum; their infants received either 6 weeks of zidovudine alone or zidovudine in combination with other agents. The combination infant regimens resulted in a 50% reduction in transmission when compared with zidovudine alone. Adding maternal single-dose nevirapine to a regimen of maternal short-course zidovudine and infant single-dose nevirapine did not reduce the risk of perinatal transmission in the Mashi trial conducted by Shapiro et al. in Botswana. Therefore, intrapartum maternal single-dose nevirapine is not recommended for a woman who has received no antepartum ARV drugs. The efficacy of newer drugs, such as integrase inhibitors, in this situation has not been evaluated. In the United States, where replacement feeding is affordable, feasible, acceptable, sustainable, and safe, women diagnosed with HIV infection during labor or the early postpartum period should be counseled against breastfeeding.

References


