Intrapartum Care  (Last updated December 24, 2019; last reviewed December 24, 2019)

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 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 (ZDV):</td>
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<td>• Should be administered to women with HIV if HIV RNA is known or suspected to be &gt;1,000 copies/mL (or if HIV RNA is unknown) near delivery (AII).</td>
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<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) (AII).</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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<td>• May be considered for women with HIV RNA between 50 copies/mL and 999 copies/mL. There are inadequate data to determine whether administration of IV ZDV to women with HIV RNA levels between 50 copies/mL and 999 copies/mL provides any additional protection against perinatal HIV transmission. This decision can be made on a case-by-case basis, taking into consideration the woman’s recent ART adherence and her preferences and involving expert consultation if needed (CII).</td>
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<td>• Women who present in labor with unknown HIV status should undergo expedited antigen/antibody HIV testing (AII). See Maternal HIV Testing and Identification of Perinatal HIV Exposure for more information.</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 ZDV and infant combination antiretroviral (ARV) prophylaxis should be initiated pending results of the differentiation test (AII).</td>
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<td>• If the maternal HIV differentiation test is positive or if acute infection is suspected because the differentiation test is negative but the HIV RNA test is positive, infant ARV drugs should be managed as discussed in Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection (AI). Women with positive expedited test results should not initiate breastfeeding until HIV infection is definitively ruled out (see Postpartum Follow-Up of Women Living with HIV Infection) (AI).</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 result, the maternal and infant ARV drugs should be stopped (AIII).</td>
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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

Women Who Have Received Antepartum Antiretroviral Drugs

Use of Intravenous Zidovudine During Labor

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

The French Perinatal Cohort evaluated HIV transmission in >11,000 pregnant women with HIV who were receiving antiretroviral (ARV) drugs (10% of women were receiving ZDV 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 ZDV. The overall rate of perinatal HIV transmission was 0.9% (95 of 10,239 infants) with maternal IV ZDV and 1.8% (9 of 514 infants, \( P = 0.06 \)) without maternal IV ZDV. Among women with HIV RNA <1,000 copies/mL at delivery, no transmission occurred among 369 women who did not receive IV ZDV; the transmission rate was 0.6% (47 of 8,132 infants, \( P > 0.20 \)) among those who received IV ZDV. Among women with HIV RNA >1,000 copies/mL...
whose infants received only ZDV for prophylaxis, the risk of transmission was 10.2% without maternal IV ZDV and 2.5% with maternal IV ZDV ($P < 0.01$). If a neonate received combination prophylaxis with two or more ARV drugs, there was no difference in the risk of transmission between women who received IV ZDV and those who did not (4.8% vs. 4.1%, $P = 0.83$).

In a cohort of 717 women who delivered between 1996 and 2008 in Miami, the majority of whom were receiving ART and had HIV RNA <1,000 copies/mL at delivery, not receiving IV ZDV during labor was not associated with an increased risk of perinatal HIV transmission. Among a European cohort of infants who were considered to be at high risk of transmission, lack of IV ZDV during labor was associated with transmission on univariate analysis; however, lack of IV ZDV was not significantly associated with transmission once the results were adjusted for maternal HIV RNA and other factors (adjusted odds ratio with IV ZDV was 0.79; 95% confidence interval, 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 ZDV during labor or <4 hours of IV ZDV.

The results of these studies indicate that IV ZDV should continue to be administered to women with HIV RNA >1,000 copies/mL near delivery (or to women with HIV who have unknown HIV RNA levels), regardless of a woman’s antepartum regimen. IV ZDV is not required for women who are receiving ART and who have HIV RNA ≤1,000 copies/mL in late pregnancy and/or near delivery and for whom there are 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 ZDV to women with HIV RNA between 50 copies/mL and 999 copies/mL provides any additional protection against perinatal transmission. They recommend administering intrapartum IV ZDV 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 copies/mL to 999 copies/mL than when it is <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. The clinician should use clinical judgement when making the decision to use intrapartum IV ZDV, regardless of the patient’s viral load.

In women with HIV RNA >1,000 copies/mL who are undergoing a scheduled cesarean delivery for prevention of transmission, IV ZDV administration should begin 3 hours before the scheduled operative delivery. This recommendation is based on a pharmacokinetic (PK) study in which ZDV was administered orally during pregnancy and as a continuous infusion during labor. Maternal ZDV levels were measured at baseline, after the initial IV loading dose, and then every 3 to 4 hours until delivery. ZDV levels were also measured in cord blood. Systemic and intracellular ZDV levels increased from baseline but appeared to stabilize after 3 hours of infusion; cord blood ZDV 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, administering IV ZDV is not required.

If ZDV was not used in the antenatal ART regimen because of known or suspected ZDV 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 ZDV and its proven record in reducing the risk of perinatal HIV 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) ZDV has been administered during labor. Data are limited on the PKs of oral versus IV ZDV during labor. In studies of oral dosing in labor, ZDV levels were lower than they were with IV dosing, and PK parameters suggested erratic absorption during labor. Therefore, IV administration is recommended over oral administration in the United States for women with HIV RNA >1,000 copies/mL near delivery; in situations where IV administration is not possible, clinicians can consider administering oral ZDV using a 600-mg loading dose and then ZDV 400 mg every 3 hours.
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 maintain maximal virologic suppression and to minimize the chance of developing drug resistance. If a woman is receiving oral ZDV as part of her antepartum regimen and she requires intrapartum IV ZDV, the oral ZDV component of the regimen can be held while she receives IV ZDV. When cesarean delivery is planned, oral medications can be administered preoperatively with sips of water. Medications that must be taken with food 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 Who Have Suboptimal Viral Suppression Near Delivery

Women who are receiving ART may not achieve complete viral suppression by the time of delivery due to factors such as difficulty with adherence, viral resistance, or late entry into care. Regardless of the reason, all women who have HIV RNA >1,000 copies/mL or who are presumed to have HIV RNA >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 ZDV along with oral administration of their other ARV drugs, as described above. While additional maternal ARV drugs, such as single-dose nevirapine (NVP), is not recommended, additional medications for prophylaxis in infants may be warranted in certain high-risk situations. 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 8).

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 who present in labor and who tested negative for HIV in early pregnancy, but who are at increased risk of HIV infection and who were not retested in the third trimester. Factors that may increase the risk of infection include diagnosis of a sexually transmitted infection, illicit drug use, exchange of sex for money or drugs, multiple sexual partners during pregnancy, a sexual partner who is at risk of HIV infection or who is known to have HIV, signs or 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 of Adults, Adolescents, and Pregnant Women in Health-Care Settings and the resource page for laboratory testing for HIV from the Centers for Disease Control and Prevention). Those with high levels of HIV-1 RNA and a negative confirmatory HIV assay most likely have acute HIV infection.

Expeditied 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 HIV status. IV ZDV should be started immediately in all women in labor who have positive initial HIV test results to prevent perinatal transmission of HIV, as discussed below. Women with positive initial test results 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 the 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 performing a CD4 count and HIV genotypic resistance testing. Arrangements also should be made for establishing HIV care and providing ongoing psychosocial support after discharge. The infant should receive an appropriate ARV regimen for infants at high risk of perinatal HIV transmission (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection and Table 8). If the follow-up antibody test result is negative, results of the HIV RNA test should be reviewed to rule out acute infection as a cause of the initial positive test result 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 ZDV 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 can be provided for the fetus by giving mothers a drug that rapidly crosses the placenta. This produces systemic ARV drug levels in the fetus before the fetus experiences intensive exposure to HIV in maternal genital secretions and blood during birth. In general, ZDV and other nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and the integrase strand transfer inhibitor (INSTI) raltegravir cross the placenta well, whereas protease inhibitors do not (see Table 8). A small PK study and placental perfusion data suggest moderate-to-high placental transfer for elvitegravir.12,13 For dolutegravir (DTG), a PK study found that the median cord blood-to-maternal-plasma concentration ratio was 1.25 in 18 infants, corroborating data from case reports and placental perfusion models that showed moderate-to-high placental transfer of DTG.14-16 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 ZDV regimen can further reduce the risk of perinatal HIV transmission for mothers who have received no antepartum ARV drugs (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection). In this study, women who had not received antepartum ARV drugs received IV ZDV if HIV infection was diagnosed during labor or no ZDV if HIV was diagnosed immediately postpartum; their infants received either 6 weeks of ZDV alone or ZDV in combination with other agents. The combination infant regimens resulted in a 50% reduction in transmission risk when compared with ZDV alone.17 Adding maternal single-dose NVP to a regimen of maternal short-course ZDV and infant single-dose NVP did not reduce the risk of perinatal transmission in the Mashi trial conducted by Shapiro et al. in Botswana. Therefore, intrapartum single-dose NVP is not recommended for a woman who has received no antepartum ARV drugs.18 The efficacy of newer drugs, such as INSTIs, has not been evaluated in this situation. In the United States, where replacement feeding is affordable, feasible, acceptable, sustainable, and safe, women who receive a diagnosis of HIV infection during labor or during the early postpartum period should be counseled to avoid breastfeeding.
References


