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

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Intrapartum Care

Intrapartum Antiretroviral Therapy/Prophylaxis (Last updated July 31, 2012; last reviewed July 31, 2012

Panel's Recommendations
• Women who are receiving an antepartum combination antiretroviral (ARV) drug regimen should continue this regimen on schedule as much as possible during labor and before scheduled cesarean delivery **(AIII)**.
• Intravenous (IV) zidovudine should be administered to HIV-infected women with HIV RNA ≥400 copies/mL (or unknown HIV RNA) near delivery, regardless of antepartum regimen or mode of delivery **(AI)**.
• IV zidovudine is not required for HIV-infected women receiving combination ARV regimens who have HIV RNA <400 copies/mL near delivery **(BII)**.
• For women who have received antepartum ARV drugs but have suboptimal viral suppression near delivery (that is, HIV RNA >1,000 copies/mL), scheduled cesarean delivery is recommended (see Mode of Delivery) **(AI)**.
• Women whose HIV status is unknown who present in labor should undergo rapid HIV antibody testing **(AII)**. If the results are positive, a confirmatory HIV test should be done as soon as possible and maternal (IV zidovudine)/infant (combination ARV prophylaxis) ARV drugs should be initiated pending results of the confirmatory test **(AII)**. If the confirmatory HIV test is positive, infant ARV drugs should be continued for 6 weeks (see Infant Antiretroviral Prophylaxis) **(AI)**; if the test is negative, the infant ARV drugs should be stopped.
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 regimen included a continuous intravenous (IV) infusion of zidovudine during labor (initial loading dose of 2 mg/kg IV over 1 hour, followed by continuous infusion of 1 mg/kg/hour until delivery) for all women. This regimen along with maternal antepartum and infant zidovudine reduced perinatal transmission by 66% overall. Combination antiretroviral (ARV) regimens are now recommended for treatment and prevention of perinatal transmission of HIV; 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 >5,000 HIV-infected pregnant women receiving ARV (19% zidovudine alone, 33% dual ARV, and 48% triple ARV) who delivered between 1997 and 2004, stratified by viral load at delivery; 96% received IV intrapartum zidovudine.[1] Overall, intrapartum IV zidovudine prophylaxis was associated with lower risk of transmission (1.2% [59/5,006] transmission with intrapartum prophylaxis vs. 3.1% [7/230] without intrapartum prophylaxis, P =.025) but this association was related to HIV RNA level at delivery. In 364 women who had HIV RNA >10,000 copies/mL at delivery, intrapartum prophylaxis was strongly associated with a lower risk of transmission: 5.3% (18/339) with intrapartum prophylaxis versus 22.7% (5/22) without intrapartum prophylaxis (P =.009). However, intrapartum prophylaxis was not associated with transmission in 2,845 women with HIV RNA <400 copies/mL at delivery: 0.6% (17/2,750) with intrapartum prophylaxis versus 0% (0/95) without intrapartum prophylaxis. Data were not provided for women with viral load 400 to 9,999 copies/mL. Based on this study, IV

zidovudine is not required for HIV-infected women receiving combination ARV regimens with HIV RNA <400 copies/mL near delivery but should continue to be administered to HIV-infected women with HIV RNA ≥400 copies/mL near delivery (or unknown HIV RNA levels), regardless of antepartum regimen.

In women with HIV RNA >400 copies/mL receiving 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, and in cord blood.[2] Systemic and intracellular zidovudine levels increased from baseline but appeared to stabilize after 3 hours of infusion; cord blood zidovudine levels were assocated with maternal levels and maternal infusion duration. If cesarean section is being performed for other indications and maternal viral load is <400 copies/mL near the time of delivery, administration of IV zidovudine is not required.

If antenatal use of zidovudine was precluded by known or suspected zidovudine resistance, intrapartum use of the drug still should be recommended in women with HIV RNA >400 copies/mL near delivery, except in women with documented histories 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 Management of Antiretroviral Drug Resistance during Pregnancy).

In some international studies, oral, rather than IV zidovudine has been administered during labor (see Lessons from Clinical Trials of Antiretroviral Interventions to Reduce Perinatal Transmission of HIV). Data are limited on the PKs of oral compared with IV zidovudine during labor. Additionally, the drug levels needed for prophylaxis are unknown, although extrapolations have been made using therapeutic drug level targets. In a study of oral intrapartum zidovudine 300 mg every 3 hours in Thailand, most cord blood zidovudine levels were at therapeutic levels but were lower than those reported after continuous IV administration; 17% of infants had subtherapeutic levels at birth.[3] In another study, the PKs of two dosing regimens of oral zidovudine during labor were evaluated in 10 HIV-infected pregnant women.[4] The oral regimen was well tolerated; plasma zidovudine concentrations were substantially lower with 300 mg every 3 hours given orally during labor than previously reported with continuous IV therapy. A revised regimen with a 600-mg oral loading dose, followed by 400 mg every 3 hours, resulted in increased zidovudine concentrations but inter-patient variance was significant. In both cohorts, PK parameters suggested erratic absorption during labor. Therefore, in women with HIV RNA >400 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 can be considered.

Continuation of Antenatal Antiretroviral Drugs during Labor

Women who are receiving an antepartum combination ARV drug regimen should continue that regimen on schedule as much as possible during the intrapartum period to provide maximal virologic effect and to minimize the chance of development of drug resistance. If oral zidovudine is part of the antepartum regimen and a woman's HIV-1 RNA viral load is >400 copies/mL, the oral zidovudine component of her regimen should be stopped while she receives IV zidovudine. When cesarean delivery is planned, oral medications can be continued 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 in the preoperative period. If the maternal ARV regimen must be interrupted temporarily (meaning for less than 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 combination ARV drug regimens may not achieve complete viral suppression by the time of delivery because of factors such as poor adherence, viral resistance, or late entry into care. Regardless of the reason, all women who have HIV RNA levels >1,000 copies/mL near the time of delivery should be offered a scheduled cesarean delivery at 38 weeks, which may significantly reduce risk of transmission (see Transmission and Mode of Delivery).

Women with incomplete viral suppression at the time of delivery should receive IV zidovudine along with their other ARVs orally, as described above. In certain high-risk situations, additional medications for prophylaxis in infants may be warranted, such as in 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 Infant Antiretroviral Prophylaxis 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 with rapid HIV testing unless they decline (opt-out screening). Rapid HIV testing is also recommended for women presenting in labor who tested negative for HIV in early pregnancy but are at increased risk of HIV infection and were not retested in the third trimester.[5] Factors that may increase risk of infection include diagnosis of a sexually transmitted disease, illicit drug use or exchange of sex for money or drugs, multiple sexual partners during pregnancy, a sexual partner at risk of HIV infection, signs/symptoms of acute HIV infection, or living in a region with an elevated incidence of HIV in women of childbearing age and not undergoing repeat HIV testing in the third trimester.[5]

Rapid HIV antibody 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 rapid testing vary from state to state; see http://www.nccc.ucsf.edu/consultation_library/state_hiv_testing_laws for a review of state HIV testing laws. Current information on rapid testing also should be available at all facilities with a maternity service and/or neonatal intensive care unit.

Women with positive rapid HIV antibody tests should be presumed to be infected until standard HIV antibody confirmatory testing clarifies their infection status. IV zidovudine should be started immediately in all women with positive rapid HIV tests in labor to prevent perinatal transmission of HIV, as discussed below.

In the postpartum period, along with confirmatory HIV antibody testing, these women should receive appropriate assessments as soon as possible to determine their health status, including CD4 T-lymphocyte count and HIV-1 RNA viral load. Arrangements also should be made for establishing HIV care and providing ongoing psychosocial support after discharge.

Choice of Intrapartum/Postpartum Antiretroviral Regimen for Women without Antepartum Antiretroviral Therapy

All HIV-infected women who have not received antepartum ARV drugs should have IV zidovudine started 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 inhibitor drugs and non-nucleoside reverse transcriptase inhibitor drugs cross the placenta well, whereas

protease inhibitors do not (see Table 5).

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 mother-to-child transmission of HIV for mothers who have received no antepartum ARV drugs (see Infant Antiretroviral Prophylaxis). In this study, women who had not received antepartum ARV drugs received IV zidovudine if they were identified in labor or no zidovudine when diagnosed immediately postpartum, and 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 compared with zidovudine alone. Therefore, no additional intrapartum drugs, including intrapartum maternal single-dose nevirapine, are indicated for a woman in this situation.[6]

References:

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