



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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Management of Antiretroviral Drug Resistance during Pregnancy (Updated September 14, 2011)

Panel's Recommendations

- Women who have documented zidovudine resistance and are on regimens that do not include zidovudine for their own health should still receive intravenous zidovudine during labor whenever possible, along with their established antiretroviral (ARV) regimens **(AII)**.
- In women who are receiving a stavudine-containing regimen, the drug should be discontinued during labor while intravenous zidovudine is being administered (see [Intrapartum Care](#)) **(AII)**.
- The optimal prophylactic regimen for newborns of women with ARV resistance is unknown (see [Infant Antiretroviral Prophylaxis](#)). Therefore, ARV prophylaxis for an infant born to a woman with known or suspected drug resistance should be determined in consultation with a pediatric HIV specialist, preferably before delivery **(AIII)**.

Ideally, ARV regimens used during pregnancy for treatment or prophylaxis should be chosen based upon the results of ARV resistance testing. Although most transmission occurs intrapartum, 30%–35% of transmission may occur *in utero*¹⁻³. The majority of the latter infections are believed to occur later in pregnancy¹ and they may be more likely in women with advanced HIV disease and/or high viral load²⁻³. Therefore, a delay in initiation of an ARV drug regimen to await results of resistance testing could result in *in utero* infection of the infant, particularly in women at high risk of transmission or who are late in pregnancy at the time the drugs are initiated. In such circumstances, as noted earlier, empiric initiation of the ARV drug regimen may be warranted, with modification of the regimen once resistance testing results become available.

For women who have documented zidovudine resistance and whose antepartum regimen does not include zidovudine, the drug still should be given intravenously during labor whenever possible (see [Intrapartum Care](#)). Because stavudine may be antagonistic to zidovudine, it should be stopped during the intrapartum period and restarted after delivery (see [Intrapartum Care](#)). Other ARVs should be continued orally during labor to the extent possible. The optimal prophylactic regimen for newborns of women with ARV drug-resistant virus is unknown. Therefore, ARV prophylaxis for infants born to women with known or suspected drug-resistant virus should be determined with a pediatric HIV specialist, preferably before delivery (see [Infant Antiretroviral Prophylaxis](#)).

The rationale for including zidovudine intrapartum when a woman is known to harbor virus with zidovudine resistance is based on several factors. Data thus far have suggested that only wild-type virus appears to be transmitted to infants by mothers who have mixed populations of wild-type virus and virus with low-level zidovudine resistance⁴. Other studies have suggested that drug-resistance mutations may diminish viral fitness and possibly decrease transmissibility⁵. The efficacy of the zidovudine prophylaxis appears to be based not only on a reduction in maternal HIV viral load but also on pre- and post-exposure prophylaxis in the infant⁶⁻⁸. Zidovudine crosses the placenta readily and has one of the highest maternal-to-cord blood ratios among the nucleoside analogue agents. In addition, zidovudine is metabolized to the active triphosphate within the placenta⁹⁻¹⁰, which may provide additional protection against transmission. Metabolism to the active triphosphate, which is required for activity of all nucleoside analogue agents, has not been observed within the placenta with other nucleoside analogues that have been evaluated (didanosine and zalcitabine). Zidovudine penetrates the central nervous system (CNS) better than do other nucleoside analogues except stavudine, which has similar CNS penetration; this may help to

eliminate a potential reservoir for transmitted HIV in the infant¹¹⁻¹². Thus, intrapartum intravenous administration of zidovudine currently is recommended even in the presence of known resistance because of the unique characteristics of the drug and its proven record in reducing perinatal transmission.

References

1. Rouzioux C, Costagliola D, Burgard M, et al. Estimated timing of mother-to-child human immunodeficiency virus type 1 (HIV-1) transmission by use of a Markov model. The HIV Infection in Newborns French Collaborative Study Group. *Am J Epidemiol*. Dec 15 1995;142(12):1330-1337.
2. Kuhn L, Steketee RW, Weedon J, et al. Distinct risk factors for intrauterine and intrapartum human immunodeficiency virus transmission and consequences for disease progression in infected children. Perinatal AIDS Collaborative Transmission Study. *J Infect Dis*. Jan 1999;179(1):52-58.
3. Magder LS, Mofenson L, Paul ME, et al. Risk factors for *in utero* and intrapartum transmission of HIV. *J Acquir Immune Defic Syndr*. Jan 1 2005;38(1):87-95.
4. Colgrove RC, Pitt J, Chung PH, Welles SL, Japour AJ. Selective vertical transmission of HIV-1 antiretroviral resistance mutations. *AIDS*. Dec 3 1998;12(17):2281-2288.
5. Nijhuis M, Deeks S, Boucher C. Implications of antiretroviral resistance on viral fitness. *Curr Opin Infect Dis*. Feb 2001;14(1):23-28.
6. Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med*. Nov 28 1996;335(22):1621-1629.
7. Wade NA, Birkhead GS, Warren BL, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med*. Nov 12 1998;339(20):1409-1414.
8. Melvin AJ, Burchett SK, Watts DH, et al. Effect of pregnancy and zidovudine therapy on viral load in HIV-1-infected women. *J Acquir Immune Defic Syndr Hum Retrovirol*. Mar 1 1997;14(3):232-236.
9. Qian M, Bui T, Ho RJY, Unadkat JD. Metabolism of 3'-azido-3'-deoxythymidine (AZT) in human placental trophoblasts and Hofbauer cells. *Biochem Pharmacol*. 1994;48(2):383-389.
10. Sandberg JA, Binienda Z, Lipe G, et al. Placental transfer and fetal disposition of 2',3'-dideoxycytidine and 2',3'-dideoxyinosine in the rhesus monkey. *Drug Metab Dispos*. 1995;23(8):881-884.
11. Strazielle N, Belin MF, Ghersi-Egea JF. Choroid plexus controls brain availability of anti-HIV nucleoside analogs via pharmacologically inhibitable organic anion transporters. *AIDS*. Jul 4 2003;17(10):1473-1485.
12. Thomas SA. Anti-HIV drug distribution to the central nervous system. *Curr Pharm Des*. 2004;10(12):1313-1324.