Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Initial Postnatal Management of the Neonate Exposed to HIV  

Postnatal Management of the Neonate Exposed to HIV

Following birth, infants who were exposed to HIV should have a detailed physical examination, and a thorough maternal history should be obtained. Women with HIV may have coinfections with other pathogens that can be transmitted from mother to child, such as cytomegalovirus, Zika virus, herpes simplex virus, hepatitis B, hepatitis C, syphilis, toxoplasmosis, or tuberculosis. Infants born to mothers with such coinfections should undergo the appropriate evaluations to exclude the possibility of transmission of additional infectious agents. The routine primary immunization schedule for children should be followed for infants born to women with HIV. The schedule may need to be modified for infants with known HIV infection (see the Pediatric Opportunistic Infection Guidelines for more information).

Infants should be monitored for the toxicities that are associated with the antiretroviral (ARV) drugs they were exposed to in utero or the ARV drugs that they are receiving for the prevention of perinatal HIV transmission (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection).

Comprehensive care also includes appropriate HIV diagnostic testing and infant feeding support to assist mothers in abstaining from breastfeeding. No evidence is available to enable the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission to assess whether any changes in routine bathing practices, or timing of circumcision, are indicated for newborns with perinatal HIV exposure.

Hematologic Toxicity

A complete blood count and differential should be performed before initiating ARV drugs in newborns who were exposed to HIV (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection).

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
Infection). Decisions about the timing of hematologic monitoring after birth depend on several factors, including the infant’s baseline hematologic values, gestational age at birth, and clinical condition; the infant’s ARV drugs and concomitant medications; and the maternal antepartum ARV drug regimen.

Older studies have shown that anemia is the primary complication seen in neonates who received a 6-week postnatal prophylaxis regimen with zidovudine (ZDV). Some experts remeasure hemoglobin and neutrophil counts routinely after 4 weeks of ZDV prophylaxis and/or when the results of diagnostic HIV polymerase chain reaction (PCR) tests are obtained. Data are limited and somewhat mixed on infants who received ZDV in combination with other ARV drugs. Higher rates of hematologic toxicity have been observed in infants who received ZDV plus lamivudine (3TC) and other combination infant ARV regimens, such as ZDV plus 3TC plus nevirapine (NVP), than in those who received ZDV alone. Although a recent study from Thailand observed significantly higher Grade 2 anemia at age 1 month in high-risk infants who received ZDV plus 3TC plus NVP compared to low-risk infants who received ZDV alone, these differences did not persist past 2 months of age. In addition, a recent study from the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) evaluated 1,836 infants who were exposed to HIV but who did not contract HIV and who were receiving ARV drugs. The presence of Grade 3 or 4 anemia in the first 6 months of life was not associated with the infants’ ARV regimens (adjusted odds ratio [aOR] 1.04 for one-drug regimens, \( P = 0.879 \); aOR 1.60 for three-drug vs. two-drug regimens, \( P = 0.277 \)). Likewise, the presence of Grade 3 or 4 neutropenia in the first 6 months of life was not associated with the infants’ ARV regimens (aOR 1.33 for one-drug regimens, \( P = 0.330 \); aOR 1.98 for three-drug vs. two-drug regimens, \( P = 0.113 \)).

Hemoglobin level and neutrophil count testing should be repeated 4 weeks after initiating ARV drugs and/or at the time that diagnostic HIV PCR testing is done in infants who receive regimens that contain ZDV and 3TC. Older studies have previously shown that the association between in utero exposure to maternal ARV drugs and anemia and/or neutropenia in infants was greater in infants with in utero exposure to combination ARV drug regimens than in infants with exposure to ZDV alone. In PACTG 316, where 77% of mothers received antenatal combination therapy, significant Grade 3 or higher anemia was noted in 13% of infants and significant Grade 3 or higher neutropenia was noted in 12% of infants. Some experts recommend more intensive hematologic monitoring in infants who were exposed to combination ARV drug regimens in utero or during the neonatal period. These tests should be performed at birth and when diagnostic HIV PCR tests are also obtained.

Infants who are found to have hematologic abnormalities may need to discontinue ARV drugs. Clinicians should base the decision to discontinue ARV drugs on the individual needs of the patient. Considerations include the extent of the abnormality, whether related symptoms are present, the duration of ARV drugs received by the infant, and the risk of HIV infection (as assessed by maternal history of ARV drugs, maternal viral load near delivery, and mode of delivery). A 4-week ZDV regimen has been reported to result in earlier recovery from anemia in HIV-exposed but otherwise healthy infants than the 6-week ZDV regimen. A 4-week (instead of a 6-week) ZDV neonatal regimen is recommended when the mother has received standard antiretroviral therapy (ART) during pregnancy and has had consistent viral suppression and appropriate adherence; the shorter regimen may mitigate the risk of anemia in infants who have been exposed to HIV but who have not contracted HIV (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection).

**Hyperlactatemia**

Hyperlactatemia has been reported in infants with in utero exposure to ARV drugs, but it appears to be transient and, in most cases, asymptomatic. Routine measurement of serum lactate to assess for potential mitochondrial toxicity is not recommended in asymptomatic neonates because the clinical relevance of hyperlactatemia is unknown and the value of lactate levels as a predictive measure of toxicity appears to be poor. However, serum lactate measurement should be considered for infants who develop severe clinical symptoms of unknown etiology, particularly neurologic symptoms. ARV drugs should be discontinued in cases where infants develop symptoms or when serum lactate levels are significantly abnormal (i.e., levels >5
mmol/L). An expert in pediatric HIV infection should be consulted about initiating alternative ARV regimens or the discontinuation of ARV drugs.

**Prophylaxis Against Pneumocystis jirovecii Pneumonia**

To prevent *Pneumocystis jirovecii* pneumonia, all infants born to women with HIV should begin trimethoprim-sulfamethoxazole prophylaxis at age 4 to 6 weeks, after completing the infant ARV regimen, unless there is adequate virologic test information to presumptively exclude HIV infection (see the Pediatric Opportunistic Infection Guidelines).  

**HIV Testing of the Infant**

All infants who were perinatally exposed to HIV require virologic HIV testing (i.e., HIV RNA and HIV DNA nucleic acid tests) to diagnose or exclude HIV infection. For a detailed discussion of HIV testing, including types of tests and the recommended HIV testing schedule, see Diagnosis of HIV Infection in Infants and Children.

**Infant Feeding Practices and Risk of HIV Transmission**

In the United States, it is recommended that women with HIV refrain from breastfeeding their infants as safe infant feeding alternatives are available. Maternal ART is likely to reduce free virus in breast milk, but cell-associated virus (intracellular HIV DNA) remains unaffected and may continue to pose a transmission risk. However, clinicians should be aware that some women may face considerable social, familial, and personal pressures to breastfeed despite this recommendation (see Counseling and Managing Women Living with HIV in the United States Who Desire to Breastfeed). It is important to address a woman’s desire to breastfeed and potential barriers to formula feeding as early as possible in the antenatal period.

Some HIV transmission events that occurred in later infancy are thought to have resulted from infants being fed solid food that had been premasticated (prechewed or prewarmed) by caregivers with HIV. Phylogenetic comparisons of virus from cases and suspected sources as well as supporting clinical history identified the practice of feeding premasticated foods to infants as a potential risk factor for HIV transmission. Health care providers should routinely inquire about premastication, instruct caregivers with HIV not to perform this feeding practice, and advise on safer feeding options.

**References**


