Initial Postnatal Management of the Neonate Exposed to HIV

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Panel's Recommendations
• All newborns perinatally exposed to HIV should receive appropriate antiretroviral (ARV) drugs as soon as possible, preferably within 6 hours, after delivery (see Antiretroviral Management of Infants with Perinatal HIV Exposure or HIV Infection) (AI). • For infants in whom presumptive HIV therapy is initiated, hemoglobin and neutrophil counts should be obtained at baseline. If combination ARV drugs are continued through 4 weeks, hemoglobin and neutrophil counts should be remeasured at that time (AI). • With subsequent monitoring of hematologic parameters in infants, clinicians need to consider the infant's baseline hematologic values, gestational age at birth, and clinical condition; whether the infant is receiving zidovudine, other ARV drugs, or certain concomitant medications; and the specific ARV drugs used in the birthing parent's antepartum drug regimen. Infants who are found to have hematologic abnormalities may need to discontinue or switch ARV drugs, and consultation with an expert in pediatric HIV infection is advised (CIII). • Nucleic acid tests (e.g., DNA and RNA polymerase chain reaction [PCR] assays) are required to diagnose HIV infection in infants aged <18 months (see Diagnosis of HIV Infection in Infants and Children) (AII). • To prevent *Pneumocystis jirovecii* pneumonia (PJP), all infants born to persons with HIV should begin PJP prophylaxis at age 4 to 6 weeks, unless adequate test information is available to presumptively exclude HIV infection (see *Pneumocystis jirovecii* Pneumonia in the Pediatric Opportunistic Infections Guidelines) (AII). • Health care providers should inquire routinely about infant feeding plans and/or breastfeeding desires, as well as the use of pre-masticated (pre-chewed or pre-warmed) food. Counseling against pre-mastication and discussion of safe infant feeding options should be provided (see Infant Feeding for Individuals with HIV in the United States) (AIII).
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

Postnatal Management of the Neonate Exposed to HIV

Following birth, infants exposed to HIV should have a detailed physical examination, and a thorough birthing parent health history should be obtained. Pregnant people with HIV may have coinfections with other pathogens that can be transmitted during pregnancy and the birthing process, such as cytomegalovirus (CMV), Zika virus, herpes simplex virus, hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis, toxoplasmosis, or tuberculosis. Infants born to a birthing parent with such coinfections should undergo appropriate evaluation to exclude the possibility of transmission of additional infectious agents. The routine primary immunization schedule for children should be followed for infants born to persons with HIV. One study examining humoral response to routine vaccination in infants who were exposed to HIV but uninfected (HEU) demonstrated robust antibody responses to vaccine antigens to support this recommendation.[1] However, the immunization schedule may need to be modified for infants with confirmed HIV infection (see the Pediatric Opportunistic Infections Guidelines for more information).

Infants should be monitored for toxicities associated with antiretroviral (ARV) drugs to which they were exposed *in utero* or the ARV drugs that they are receiving for the prevention of perinatal HIV transmission (see Antiretroviral Management of Infants with Perinatal HIV Exposure or HIV Infection). No evidence is available to enable the Panel on Treatment of HIV During Pregnancy 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

Older studies have shown that anemia is the primary hematologic complication in neonates who received a 6-week postnatal prophylaxis regimen with zidovudine (ZDV).[2] Some experts remeasure hemoglobin and neutrophil counts routinely after ZDV prophylaxis and/or when the results of diagnostic HIV nucleic acid test (NAT) assays 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.[3-7] Although a 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 with low-risk infants who received ZDV alone, these differences did not persist past 2 months of age.[6] In addition, a recent study from the European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC) evaluated 1,836 infants who were HEU 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, $P = 0.277$).[8] 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, $P = 0.113$).[9] Hemoglobin level and neutrophil count testing should be repeated following the initiation of ARV drugs and/or at the time that a diagnostic HIV NAT is performed in infants who receive regimens that contain ZDV and 3TC.[3,6]

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 birthing parent's history of ARV drugs and viral load near delivery, and mode of delivery). A 4-week ZDV regimen, compared with the 6-week ZDV regimen, has been reported to result in earlier recovery from anemia in infants who are HIV-exposed but otherwise healthy.[10] A 2-week (instead of a 4- or 6-week) ZDV neonatal regimen **is recommended** in situations where there is a low risk of perinatal HIV transmission (see specific criteria in Table 10. Neonatal Antiretroviral Management According to Risk of HIV Infection in the Infant in Antiretroviral Management of Infants with Perinatal HIV Exposure or HIV Infection).[11] The shorter ZDV regimen may mitigate the risk of anemia in infants who are HEU.

Hyperbilirubinemia

Hyperbilirubinemia has been observed in HIV-exposed infants receiving raltegravir (RAL) through 6 weeks of life. The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network P1110 study reported Grade 3 to Grade 4 levels of increased bilirubin in 3 of 52 infants. However, no bilirubin levels exceeded 16 mg/dL, and no infants required phototherapy or other

clinical treatment for hyperbilirubinemia.[12] RAL at extremely high levels may displace unconjugated bilirubin from albumin, increasing the potential risk of bilirubin-induced neurologic dysfunction.[13] Because of the possible risk of hyperbilirubinemia, serum total and direct bilirubin measurement may be considered in infants receiving RAL.

Prophylaxis Against *Pneumocystis jirovecii* Pneumonia

To prevent *Pneumocystis jirovecii* pneumonia, all high-risk infants born to people with HIV should begin trimethoprim-sulfamethoxazole prophylaxis at age 4 to 6 weeks, unless adequate virologic test information exists to presumptively exclude HIV infection (see the *Pneumocystis jirovecii* Pneumonia section of the Pediatric Opportunistic Infections Guidelines).[14] With appropriate follow-up to support the recommended diagnostic testing schedule, most infants with perinatal HIV exposure do not require trimethoprim-sulfamethoxazole prophylaxis because HIV can be presumptively excluded by the time their postnatal ARV regimen is completed (see Diagnosis of HIV Infection in Infants and Children).

Testing for Viral Coinfections in the Infant

The prevalence of congenital CMV (cCMV) is higher in infants with perinatal exposure to HIV than in the general population. Screening for cCMV is recommended in the first 21 days of life. Early diagnosis allows appropriate monitoring and antiviral intervention with (val)ganciclovir, which improves clinical outcomes for associated comorbidities, including sensorineural hearing loss. The Pediatric Opportunistic Infection Guidelines recommend testing for cCMV in urine and/or saliva using a polymerase chain reaction (PCR) assay, and a routine newborn audiologic evaluation. For infants diagnosed with cCMV, longitudinal audiologic follow-up and neurodevelopmental assessments are recommended (see Cytomegalovirus).[15] In certain states, universal newborn screening for cCMV is recommended using dried blood spots. This test currently serves as an adjunct to urinary and salivary testing for CMV pending further validation.

HCV screening with an anti-HCV antibody test is recommended for all pregnant people during each pregnancy.[16,17] The Centers for Disease Control and Prevention (CDC) recommends HCV testing for all infants and children born to pregnant people with current or probable HCV infection. Infants with perinatal exposure to HCV should receive a NAT for HCV RNA at age 2 to 6 months to identify children in whom chronic HCV infection might develop. Parents or caregivers should receive counseling about the need for testing and follow-up (see Hepatitis C Virus/HIV Coinfection). Infants with detectable HCV RNA should be managed in consultation with a health care provider who has expertise in pediatric HCV management. Infants with an undetectable HCV RNA result do not require further follow-up unless clinically warranted.[18]

It is recommended that HBV screening for hepatitis B surface antigen (HBsAg) for all pregnant people occur during each pregnancy, preferably in the first trimester, regardless of vaccination status or history of testing.[19] The CDC recommends that infants born to people who are HBsAg positive be tested for HBsAg and hepatitis B surface antibody seromarkers. All infants born to people with positive HBsAg screening, including those with perinatal HIV exposure, should receive hepatitis B immune globulin and the first dose of the HBV vaccine series as soon as possible, preferably within 12 hours after birth, followed by the routine HBV vaccine series. See Evaluating and Managing Infants Who Were Exposed to HIV in Hepatitis B Virus/HIV Coinfection for additional information. Infants with detectable HBV DNA should be managed in consultation with a health care provider with expertise in pediatric HBV management.

HIV Testing of the Infant

All infants who are perinatally exposed to HIV require nucleic acid testing (HIV RNA or HIV DNA assays) to diagnose or exclude HIV infection. For a detailed discussion of HIV testing, including types of tests and the recommended HIV testing schedule, see Table 13. Recommended Virologic Testing Schedules for Infants Who Were Exposed to HIV According to Risk of Perinatal HIV Acquisition at and After Birth in Diagnosis of HIV Infection in Infants and Children.

Infant Feeding Practices and Risk of HIV Transmission

People with HIV should receive evidence-based, patient-centered counseling to support shared decision-making about infant feeding prior to conception or as early as possible in pregnancy. Plans for infant feeding should be reviewed throughout pregnancy and again after delivery. At postnatal visits, it is important to discuss infant feeding to assess feeding practices, identify barriers, and provide supports for the appropriate implementation of their chosen method (see Infant Feeding for Individuals with HIV in the United States). For information on ARV prophylaxis duration and HIV screening frequency for breastfeeding infants, see Antiretroviral Management of Infants with Perinatal HIV Exposure or HIV Infection, Pregnancy and Postpartum HIV Testing and Identification of Perinatal and Postnatal HIV Exposure, and Diagnosis of HIV Infection in Infants and Children.

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