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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Infant Antiretroviral Prophylaxis (Last updated January 29, 2013; last reviewed July 31, 2012)

Panel's Recommendations
• The 6-week neonatal component of the zidovudine chemoprophylaxis regimen is recommended for all HIV-exposed neonates to reduce perinatal transmission of HIV **(AI)**.
• Zidovudine, at gestational age-appropriate doses, should be initiated as close to the time of birth as possible, preferably within 6 to 12 hours of delivery **(AII)**.
• Infants born to HIV-infected women who have not received antepartum antiretroviral (ARV) drugs should receive prophylaxis with zidovudine given for 6 weeks combined with three doses of nevirapine in the first week of life (at birth, 48 hours later, and 96 hours after the second dose), begun as soon after birth as possible **(AI)**.
• In other scenarios, the decision to combine other drugs with the 6-week zidovudine regimen should be made in consultation with a pediatric HIV specialist, preferably before delivery, and should be accompanied by counseling of the mother on the potential risks and benefits of this approach **(BIII)**.
• In the United States, the use of ARV drugs other than zidovudine and nevirapine cannot be recommended in premature infants because of lack of dosing and safety data **(BIII)**.
• The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on all aspects of perinatal HIV, including infant care.
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*

General Considerations for Choice of Infant Prophylaxis

All HIV-exposed infants should receive postpartum antiretroviral (ARV) drugs to reduce perinatal transmission of HIV. The 6-week neonatal zidovudine chemoprophylaxis regimen is recommended for all HIV-exposed infants.[1, 2] Table 9 shows recommended zidovudine dosing based on the status of maternal antepartum ARV regimens. Infants born to mothers who have received standard antepartum and intrapartum ARV prophylaxis and have undetectable viral loads are at very low risk of HIV transmission and should receive the 6-week zidovudine regimen alone.

The risk of transmission is increased when maternal viral load at delivery is high or maternal antepartum and/or intrapartum prophylaxis was not received. Most experts feel that the potential benefit of combining zidovudine infant prophylaxis with additional ARV drugs may exceed the risk of multiple drug exposure to infants born to:

a. mothers who received antepartum and intrapartum ARV drugs but who had suboptimal viral suppression at delivery, particularly if delivery was vaginal;
b. mothers who received only intrapartum ARV drugs;
c. mothers who received neither antepartum nor intrapartum ARV drugs; and
d. mothers with known ARV drug-resistant virus.

In each of these situations, there is a spectrum of transmission risk that depends on a number of maternal and infant factors, including maternal viral load, mode of delivery, and gestational age at delivery. The risks and benefits of infant exposure to ARV drugs in addition to zidovudine will differ depending on where the

mother/child falls in the risk spectrum. For example, an infant delivered vaginally to a mother with an HIV RNA level ≥100,000 copies/mL at delivery has a higher risk of acquiring HIV infection than an infant born by cesarean delivery to a mother with an HIV RNA level of approximately 10,000 copies/mL at delivery. Thus, a generic recommendation cannot be made regarding use of combination drug regimens for infant prophylaxis. Each situation needs to be considered individually, balancing potential benefits (in terms of preventing perinatal transmission of HIV) with risks (in terms of toxicity to the infant). In addition, appropriate drug formulations and dosing regimens for neonates are incompletely defined and data are minimal on the safety of combination drugs in the neonate (see Short-Term Antiretroviral Drug Safety and Choice for Neonatal Prophylaxis and the *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*).

Recent data from the NICHD-HPTN 040/PACTG 1043 study have provided guidance for management of infants born to women who received no ARV prophylaxis during pregnancy. In this study, 1,746 infants born to HIV-infected women who did not receive any ARV drugs during pregnancy were randomized to 3 infant prophylaxis regimens: the standard 6-week zidovudine regimen; 6 weeks of zidovudine plus 3 doses of nevirapine given during the first week of life (first dose at birth–48 hours, second dose 48 hours after first dose, and third dose 96 hours after second dose); and 6 weeks of zidovudine plus 2 weeks of lamivudine/nelfinavir. The risk of intrapartum transmission was significantly lower compared with 6 weeks of zidovudine alone in the 2- and 3-drug arms (2.2% and 2.5%, respectively, vs. 4.9% for zidovudine alone; $P = .046$ for each experimental arm vs. zidovudine alone).[3] Although transmission rates with the 2 combination regimens were similar, neutropenia was significantly more common with the 3-drug regimen than with the 2-drug or zidovudine-alone regimen (27.5% vs. 15%, $P < .0001$). In other studies, significantly higher rates of neutropenia and anemia have been reported with coadministration of zidovudine and lamivudine to infants.[4] Thus, based on comparable efficacy and reduced toxicity, the Panel recommends 6 weeks of zidovudine plus 3 doses of nevirapine for infants whose mothers have not received antepartum ARVs (Table 9).

In all other scenarios, decisions about use of combination ARV prophylaxis in infants should be made in consultation with a pediatric HIV specialist before delivery, if possible, and should be accompanied by a discussion with the mothers about potential risks and benefits of this approach.

Despite the paucity of available data, the use of combination ARV prophylaxis for infants in high-risk situations is increasing. Surveillance of obstetric and pediatric HIV infection in the United Kingdom and Ireland through the National Study of HIV in Pregnancy and Childhood noted that between 2001 and 2004, 9% of HIV-exposed infants received triple-drug prophylaxis compared with 13% between 2005 and 2008.[5] Similarly, in a web-based poll of 134 U.S.-based perinatal HIV service providers, 62% reported using combination postnatal prophylaxis in high-risk situations in the past year. Zidovudine, lamivudine, and nevirapine was the combination regimen used most often.[6]

The National Perinatal HIV Hotline (1-888-448-8765)

The *National Perinatal HIV Hotline* is a federally funded service providing free clinical consultation to providers caring for HIV-infected pregnant women and their infants.

Recommendations for Infant Antiretroviral Prophylaxis in Specific Clinical Situations

Infants Born to Mothers Who Received Antepartum/Intrapartum Antiretroviral Drugs with Effective Viral Suppression

The risk of HIV acquisition is small in infants born to women who received standard ARV prophylaxis regimens during pregnancy and labor and had undetectable viral loads at delivery or born by scheduled cesarean section to mothers with low viral loads at delivery. Such infants should receive the 6-week

zidovudine infant prophylaxis regimen. In that situation, combining zidovudine with additional ARV drugs to reduce transmission risk is not recommended because the benefit would be very limited.

Infants Born to Mothers Who Have Received Antepartum/Intrapartum Antiretroviral Drugs But Have Suboptimal Viral Suppression Near Delivery

The risk of perinatal transmission is related to maternal antepartum viral load in women on no ARV drugs as well as women receiving ARVs.[7-9] Scheduled cesarean delivery is recommended for prevention of perinatal transmission in women who have received antepartum ARV drugs but have detectable viremia (HIV RNA >1,000 copies/mL) near the time of delivery (see Intrapartum Care and Transmission and Mode of Delivery). In PACTG 316, transmission occurred in 0% of 17 infants when maternal HIV RNA levels at delivery were >10,000 copies/mL and delivery was by scheduled cesarean delivery.[2] However, not all women with detectable viremia near delivery will undergo cesarean delivery. The risk of acquisition of HIV will be higher in infants born to mothers with higher viral loads near delivery, particularly if delivery is vaginal. The gradient of transmission risk is based on HIV RNA levels. In the Women and Infants Transmission Study (WITS), the risk of transmission of HIV was ≤1.8% in women who received triple-combination ARV prophylaxis and had HIV RNA levels <30,000 copies/mL at delivery; it increased to 4.8% in women with HIV RNA levels ≥30,000 copies/mL.[9]

All infants should receive zidovudine for 6 weeks. No specific data address whether a more intensive combination infant prophylaxis regimen (2 or 3 drugs) provides additional protection against transmission when maternal antepartum/intrapartum prophylaxis is received but viral replication near delivery is significant. Elective cesarean section is recommended for pregnant women with HIV RNA levels >1,000 copies/mL near delivery. Extrapolation of findings from the previously discussed NICHD-HPTN 040/PACTG 1043 study[3] suggests that combination infant prophylaxis should be considered, depending on assessment of risk based on maternal viral load and mode of delivery. That decision should be made in consultation with a pediatric HIV specialist before delivery and accompanied by maternal counseling on the potential risks and benefits of this approach.

Infants Born to Mothers Who Received Only Intrapartum Antiretroviral Drugs

All infants whose mothers have received only intrapartum ARV drugs should be given zidovudine for 6 weeks. This infant prophylaxis regimen is a critical component of prevention when no maternal antepartum ARV drugs have been received. The PETRA study demonstrated that intrapartum prophylaxis alone, without infant prophylaxis, is ineffective in reducing perinatal transmission.[10] A study in Thailand indicated that longer infant prophylaxis with zidovudine (6 weeks vs. 3 days) is required for optimal efficacy when maternal antenatal exposure to zidovudine is <4 weeks.[11] Infant prophylaxis with zidovudine should be initiated as soon after delivery as possible. In addition to zidovudine, three doses of nevirapine should be administered in the first week of life (first dose at birth–48 hours, second dose 48 hours after first dose, and third dose 96 hours after second dose). In the NICHD-HPTN 040/PACTG 043 trial previously discussed, 41% of women received zidovudine during labor. Administration of intrapartum zidovudine did not affect transmission rates.[3]

Infants Born to Mothers Who Did Not Receive Antepartum or Intrapartum Antiretroviral Drugs

The two-drug regimen of 6 weeks of zidovudine plus three doses of nevirapine in the first week of life (first dose at birth–48 hours, second dose 48 hours after first dose, and third dose 96 hours after second dose) is recommended based on the results of the NICHD-HPTN 040/PACTG 1043 study, which demonstrated increased efficacy of combination regimens in reducing intrapartum transmission compared with use of zidovudine alone in infants.[3] Prophylaxis should be initiated as soon after delivery as possible.

The interval during which infant prophylaxis can be initiated and still be of benefit is undefined. In the New York State study, when prophylaxis was delayed beyond 48 hours after birth, no efficacy could be demonstrated. Data from animal studies indicate that the longer the delay in institution of prophylaxis, the less likely that infection will be prevented. In most studies of animals, ARV prophylaxis initiated 24 to 36 hours after exposure usually has been ineffective in preventing infection, although a delay in administration has been associated with decreased viremia.[12-14] In the NICHD-HPTN 040/PACTG 1043 study, infant regimens were initiated within 48 hours of life and usually within 12 hours of life.[3] Initiation of infant prophylaxis after age 2 days is not likely to be efficacious in preventing transmission and, by age 14 days, infection already would be established in most infants.[15] Initiating prophylaxis as soon after delivery as possible increases its potential efficacy and minimizes potential harm, such as development of resistant virus, if infection has occurred.

Infants Born to Mothers with Antiretroviral Drug-Resistant Virus

The optimal prophylactic regimen for newborns delivered by women with ARV drug-resistant virus is unknown. ARV prophylaxis for infants born to mothers with known or suspected drug resistance should be determined in consultation with a pediatric HIV specialist before delivery.

Data from the WITS suggest that in women who have mixed zidovudine-resistant and -sensitive viral populations, the zidovudine-sensitive rather than -resistant virus may be preferentially transmitted.[16, 17] Thus, the 6-week infant zidovudine prophylaxis (along with maternal intravenous intrapartum zidovudine prophylaxis) continues to be recommended, even when maternal zidovudine-resistant virus with thymidine-associated mutations is identified.

Some studies have suggested that ARV drug-resistant virus may have decreased replicative capacity (reduced viral fitness) and transmissibility.[17] However, transmission from mother to child of multidrug-resistant virus has been reported.[18-20]

For these newborns, use of zidovudine in combination with other ARV drugs, selected on the basis of maternal virus resistance testing, should be considered. The efficacy of this approach for prevention of transmission, however, has not been proven in clinical trials, and for many drugs, appropriate dosing regimens for neonates have not been established. Decisions regarding use of additional drugs should be made in consultation with a pediatric HIV specialist and will depend on maternal history of past and current ARV drug exposure, HIV RNA levels at or near delivery, current and previous maternal resistance testing, and availability of drug formulation and dosing information in the infant.

Short-Term Antiretroviral Drug Safety and Choice for Neonatal Prophylaxis

Infant prophylaxis with zidovudine has been associated with only minimal toxicity, consisting primarily of transient hematologic toxicity (mainly anemia), which generally resolves by age 12 weeks (see Initial Postnatal Management). Data are limited on the toxicity to infants of exposure to multiple ARV drugs.

The latest information on neonatal dosing for ARV drugs can be found in the *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*. Other than zidovudine, lamivudine is the nucleoside reverse transcriptase inhibitor (NRTI) with the most experience in use for neonatal prophylaxis. In early studies, neonatal exposure to combination zidovudine/lamivudine was generally limited to 1[10, 21, 22] or 2 weeks.[3] Six weeks of infant zidovudine/lamivudine exposure also has been reported; these studies suggest that hematologic toxicity may be increased over that seen with zidovudine alone, although the infants also had *in utero* exposure to maternal combination therapy.

In a French study, more severe anemia and neutropenia were observed in infants exposed to 6 weeks of zidovudine/lamivudine for prophylaxis plus maternal antepartum zidovudine/lamivudine than in a historical

cohort exposed only to maternal and infant zidovudine. Anemia was reported in 15% and neutropenia in 18% of infants exposed to zidovudine/lamivudine, with 2% of infants requiring blood transfusion and 4% requiring treatment discontinuation for toxicity.[4] Similarly, in a Brazilian study of maternal antepartum and 6-week infant zidovudine/lamivudine prophylaxis, neonatal hematologic toxicity was common, with anemia seen in 69% and neutropenia in 13% of infants.[23]

Experience with other NRTI drugs for neonatal prophylaxis is more limited.[24, 25] Hematologic and mitochondrial toxicity may be more common with exposure to multiple versus single NRTI drugs.[4, 26-29]

Nevirapine is the only non-nucleoside reverse transcriptase inhibitor drug with a pediatric drug formulation and neonatal dosing information (see *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*).[30] In rare cases, chronic multiple-dose nevirapine has been associated with severe and potentially life-threatening rash and hepatic toxicity. These toxicities have not been observed in infants receiving single-dose nevirapine, the two-drug zidovudine regimen plus three doses of nevirapine in the first week of life in NICHD-HPTN 040/PACTG 1043), or in breastfeeding infants receiving nevirapine prophylaxis daily for 6 weeks to 6 months to prevent transmission of HIV via breast milk.[3, 31-34] Resistance to nevirapine can occur, however, with exposure to nevirapine in infants who become infected despite prophylaxis.[35, 36] ARV drug-resistance testing is recommended for all HIV-infected infants before initiation of antiretroviral therapy (see *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*).

Of the protease inhibitors (PIs), although nelfinavir, lopinavir/ritonavir, ritonavir, tipranavir, and fosamprenavir have pediatric drug formulations, their use in neonates is not recommended. Pharmacokinetic (PK) studies of nelfinavir in newborn infants show highly variable plasma concentrations and no single dose that results in safe but adequate nelfinavir concentrations in all infants has been defined.[25, 37, 38] In addition, nelfinavir powder is no longer commercially available in the United States. No PK data are available for the other PIs in infants in the first 2 weeks of life. PK data are available for treatment of HIV-infected infants 2 to 6 weeks of age with lopinavir/ritonavir. Although the lopinavir area under the curve (AUC) was significantly lower with dosing 300 mg lopinavir/75 mg ritonavir/m^2 body surface area twice daily than observed for infants >6 weeks of age, treatment was well tolerated and 80% of 10 infants had viral control at 6 months.[39] Studies are ongoing but data are not yet available for infants <2 weeks of age. However, in 4 premature infants (2 sets of twins) started on lopinavir/ritonavir from birth, heart block developed that resolved after drug discontinuation.[40, 41] In studies of adults, both ritonavir and lopinavir/ritonavir cause dose-dependent prolongation of the PR interval, and cases of significant heart block, including complete heart block, have been reported. Elevation of 17-hydroxyprogesterone and dehydroepiandrosterone-sulfate has also been associated with administration of lopinavir/ritonavir compared with zidovudine in the neonatal period. Levels of 17-hydroxyprogesterone were greater in infants who were also exposed to lopinavir/ritonavir *in utero* compared with those exposed only in the neonatal period. Term infants were asymptomatic but 3 premature newborns experienced life-threatening symptoms compatible with adrenal insufficiency, including hyponatremia and hyperkalemia with, in 1 case, cardiogenic shock.[42] Based on these and other post-marketing reports of cardiac toxicity (including complete atrioventricular block, bradycardia, and cardiomyopathy), lactic acidosis, acute renal failure, adrenal dysfunction, central nervous system depression, respiratory complications leading to death, and metabolic toxicity,[43] predominantly in preterm neonates, the Food and Drug Administration now recommends that lopinavir/ritonavir NOT be administered to neonates before a postmenstrual age (first day of the mother's last menstrual period to birth plus the time elapsed after birth) of 42 weeks and a postnatal age of at least 14 days.

Neonatal Antiretroviral Drug Dosing

Table 9. Recommended Neonatal Dosing for Prevention of Mother-to-Child Transmission of HIV

All HIV-Exposed Infants (initiated as soon after delivery as possible)		
Zidovudine (ZDV)	**Dosing**	**Duration**
ZDV	**≥35 weeks' gestation at birth:** 4 mg/kg/dose PO twice daily, started as soon after birth as possible and preferably within 6–12 hours of delivery (or, if unable to tolerate oral agents, 3 mg/kg/dose IV, beginning within 6–12 hours of delivery, then every 12 hours)	Birth through 6 weeks
ZDV	**≥30 to <35 weeks' gestation at birth:** 2 mg/kg/dose PO (or 1.5 mg/kg/dose IV), started as soon after birth as possible, preferably within 6–12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours at age 15 days	Birth through 6 weeks
ZDV	**<30 weeks' gestation at birth:** 2 mg/kg body weight/dose PO (or 1.5 mg/kg/dose IV) started as soon after birth as possible, preferably within 6–12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours after age 4 weeks	Birth through 6 weeks
Additional Antiretroviral Prophylaxis Agents for HIV-Exposed Infants of Women who Received No Antepartum Antiretroviral Prophylaxis (initiated as soon after delivery as possible)		
In addition to ZDV as shown above, administer **Nevirapine (NVP)**	**Weight Band Dosing** **Birth weight 1.5-2 kg: 8 mg TOTAL for each dose** **Birth weight >2 kg: 12 mg TOTAL for each dose**	3 doses in the first week of life • 1st dose within 48 hours of birth (birth–48 hours) • 2nd dose 48 hours after 1st • 3rd dose 96 hours after 2nd

Key to Abbreviations: IV = intravenously; NVP = nevirapine; PO = orally; ZDV = zidovudine

The recommended dose of zidovudine for post-exposure prophylaxis in full-term neonates is 4 mg/kg body weight orally (PO) twice daily for the first 6 weeks of life, beginning as soon after birth as possible and preferably within 6 to 12 hours of delivery.[10, 31, 44-51] (Table 9) If the infant is unable to tolerate oral medications, the 6-week zidovudine prophylaxis regimen can be administered intravenously (IV). The zidovudine dosing requirements differ for premature infants and term infants (see Antiretroviral Drug Dosing for Premature Infants).

In the United Kingdom and many other European countries, a 4-week neonatal chemoprophylaxis regimen is recommended for infants born to mothers who have received antenatal combination ARV drug regimens.[52, 53] This approach also can be considered in cases where adherence to or toxicity from the 6-week zidovudine prophylaxis regimen is a concern. In an Irish observational study, a transmission rate of 1.1% was observed in 916 infants who received 4 weeks of zidovudine infant prophylaxis following antenatal maternal combination ARV prophylaxis. That is the standard regimen in Ireland and the transmission rate was similar to that observed in the United States, where 6 weeks of infant zidovudine prophylaxis is standard.[53] A prospective, observational study reported that the 4-week zidovudine regimen allowed earlier recovery from anemia in otherwise healthy infants compared with the 6-week zidovudine regimen.[54] The optimal duration

of neonatal zidovudine chemoprophylaxis, however, has not been established in clinical trials, and in the United States, the standard 6-week infant zidovudine regimen is recommended unless there are concerns about adherence or toxicity. Consultation with an expert in pediatric HIV infection is advised if early discontinuation of prophylaxis is considered.

PKs and safety of the single-dose nevirapine regimen to mother and infant[55] and chronic nevirapine administration to infants to prevent HIV transmission during breastfeeding have been studied.[56] The 3-dose extended nevirapine regimen that was used in NICHD-HPTN 040/PACTG 1043 and is recommended for HIV-exposed infants whose mothers did not receive ARV during the antepartum period has also been studied.[30] In the NICHD-HPTN 040/PACTG 1043 study, nevirapine concentrations were measured in 14 newborns participating in a PK substudy during the second week of life and in single samples from 30 more newborns on Days 10 to 14. The median nevirapine elimination half-life was 30.2 hours (range: 17.8–50.3 hours) and the concentration remained greater than the target of 100 ng/mL in all infants through Day 10 of life.[30]

Antiretroviral Drug Dosing for Premature Infants

Dosing recommendations for premature infants is available for only zidovudine and nevirapine (see Table 9). Zidovudine is primarily cleared through hepatic glucuronidation to an inactive metabolite; this metabolic pathway is immature in neonates, leading to prolonged zidovudine half-life and clearance compared with older infants. Clearance is further prolonged in premature infants because their hepatic metabolic function is even less mature than in term infants.[57, 58] The recommended zidovudine dosage for infants less than 35 weeks' gestation at birth is 2 mg/kg body weight per dose PO every 12 hours (or 1.5 mg/kg/dose IV every 12 hours), increasing to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours at age 15 days. For infants born at less than 30 weeks' gestation, 2 mg/kg/dose PO (or 1.5 mg/kg/dose IV) started as soon after birth as possible, preferably within 6 to 12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours after age 4 weeks is recommended.

PKs in low birth weight infants receiving a single dose of nevirapine have been described. In a study of 81 infants less than 37 weeks' gestation, of which 29.6% were small for gestational age, half-lives were very long—median 59 hours in infants whose mothers received single-dose nevirapine and 69 hours in infants whose mothers did not receive single-dose nevirapine. AUC of nevirapine was higher and clearance lower ($P < .0001$) in small-for-gestational-age infants.[59]

Use of ARV drugs other than zidovudine and nevirapine cannot be recommended at this time in premature infants because data on dosing and safety are lacking. Immature renal and hepatic metabolism can increase the risk of overdosing and toxicity. However, in situations where there is a high risk of infant HIV infection, consultation with a pediatric HIV specialist is recommended to determine if the benefits of combination ARV prophylaxis other than zidovudine and nevirapine outweigh the potential risks.

Breastfeeding Infants of Mothers Diagnosed with HIV Infection Postpartum

Breastfeeding should be stopped until infection is confirmed or ruled out in women who are breastfeeding at the time of HIV diagnosis or suspected to be HIV infected. Pumping and temporarily discarding breast milk can be recommended to mothers who are suspected of being HIV infected but whose infection is not yet confirmed and who want to continue to breastfeed. If HIV infection is ruled out, breastfeeding can resume.

The risk of acquisition of HIV associated with breastfeeding depends on multiple infant and maternal factors, including maternal viral load and CD4 T-lymphocyte (CD4-cell) count.[60] Infants of women who develop acute HIV infection while breastfeeding are at greater risk of becoming infected than are those of women with chronic HIV infection[61] because acute HIV infection is accompanied by a rapid increase in viral load and a corresponding decrease in CD4-cell count.[62]

Other than discontinuing breastfeeding, optimal strategies for managing infants born to HIV-infected mothers

who breastfed their infants before HIV diagnosis have yet to be defined. Some experts would consider the use of post-exposure prophylaxis in infants for 4 to 6 weeks after cessation of breastfeeding. Post-exposure prophylaxis, however, is less likely to be effective in this circumstance compared with other nonoccupational exposures because the exposure to breast milk is likely to have occurred over a prolonged period rather than in a single exposure.[63]

Several studies of infants breastfed by women with chronic HIV infection have shown that daily infant nevirapine or nevirapine plus zidovudine can reduce the risk of postnatal infection during breastfeeding.[31-33] The NICHD-HPTN 040/PACTG 043 study demonstrated that combination ARV prophylaxis was more effective than zidovudine prophylaxis alone for preventing intrapartum transmission in mothers who have not received antepartum ARV drugs.[3] However, whether the combination regimens in this trial are effective for preventing transmission after cessation of breastfeeding in mothers with acute HIV infection is unknown.

An alternative approach favored by some experts would be to offer a combination ARV regimen that would be effective for treatment of HIV should the infant become infected. If this route is chosen, current recommendations for treatment should guide selection of an appropriate combination ARV regimen (see *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*). Regardless of whether post-exposure prophylaxis or "preemptive therapy" is chosen, the optimal duration of the intervention is unknown. A 28-day course may be reasonable based on current recommendations for nonoccupational HIV exposure.[63] As in other situations, decisions regarding administration of a prophylactic or preemptive treatment regimen should be accompanied by consultation with a pediatric HIV specialist and maternal counseling on the potential risks and benefits of this approach.

Infants should be tested for HIV infection at baseline and 4 to 6 weeks, 3 months, and 6 months after recognition of maternal infection to determine HIV status. In infants younger than age 18 months, HIV DNA or RNA polymerase chain reaction (PCR) tests should be used for diagnosis. HIV DNA PCR is preferable for infants who are receiving combination ARV prophylaxis or preemptive treatment. HIV antibody assays can be used in infants older than age 18 months. Post-exposure ARV prophylaxis or preemptive treatment should be discontinued in infants who are found to be HIV infected while receiving one of these regimens. Resistance testing then should be performed and an appropriate combination therapy regimen initiated (see *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*).

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