

## HIV MANAGEMENT AND TREATMENT ISSUES DURING PREGNANCY

Billy R. Brown, PharmD\*

ABSTRACT

Most children with HIV/AIDS acquire the virus from their mothers. The United States Preventive Services Task Force recommends that clinicians screen all pregnant women for HIV. Mother-to-child transmission (MTCT) of the virus can occur during pregnancy (antepartum), during labor and delivery (intrapartum), or after delivery (postnatal). Postnatally, virtually all cases of MTCT are through breast-feeding. The rates of transmission are affected by several factors, including the mother's viral load and which type of delivery she uses. It is now established that use of highly active antiretroviral therapy (HAART) before delivery decreases the rate of MTCT with no evidence of fetal harm (with the exception of efavirenz). HAART is now recommended in HIV-infected pregnant women. Breast-feeding is recognized worldwide as offering several benefits to mother and baby. These benefits include improved nutritional, immunological, developmental, psychological, social, economical, and environmental outcomes. However, breast-feeding by an HIV-infected mother increases the risk of MTCT, and the risk is cumulative—the longer the child is breastfed, the greater the risk of being infected. Paradoxically, the risk is decreased if the mother breast-feeds exclusively and the risk is highest if the mother complements breast-feeding with other sources of nutrition. Many of the factors associated with transmission risk via breast

milk are the same as for other HIV-infected adults (ie, viral load and CD4<sup>+</sup> cell count). In infants, mucosal membrane integrity affects transmission risk, as does the infant's gender. Secondary preventive measures of MTCT include use of formula feeding, wet nursing by an HIV-negative woman, heat treatment of breast milk, or use of breast milk banks. Although the rate of MTCT is declining in the United States, each case of pediatric HIV/AIDS is potentially preventable and depends on appropriate education of the mother and her choices regarding testing, treatment, delivery, and breast-feeding.

(*Adv Stud Pharm.* 2006;3(2):78-85)

According to the Centers for Disease Control and Prevention (CDC), approximately 27% of the US cases of AIDS are in women.<sup>1</sup> Most American women with AIDS are African Americans (56.4 per 100 000), followed by Hispanics (18.6 per 100 000).<sup>1,2</sup> Therefore, it is not surprising that HIV disproportionately affects minority children, with 59% of cases (reported to the CDC from the beginning of the AIDS epidemic until 2002) in black/non-Hispanic children, 23% in Hispanic children, 17% in white/non-Hispanic children, and less than 1% in other minority groups.<sup>3</sup> The good news is that rates of infection in women are declining. From 2001 through 2004, the estimated number of HIV/AIDS cases decreased approximately 2% among males and 15% among females.<sup>1</sup>

From the beginning of the AIDS epidemic until 2002, the CDC reports that 9300 American children (ie, <13 years) were living with HIV/AIDS. Only 174 cases of pediatric HIV/AIDS were reported in 2004.<sup>1</sup> From 2000 through 2004, the estimated number of AIDS cases decreased 61% among

\*Clinical Assistant Professor, University of Mississippi School of Pharmacy, Jackson, Mississippi.

Address correspondence to: Billy R. Brown, PharmD, Clinical Assistant Professor, University of Mississippi School of Pharmacy, 350 West Woodrow Wilson Boulevard, Jackson, MS 39213. E-mail: brbrown@pharmacy.umsmed.edu.

children younger than 13 years of age.<sup>1</sup> Although pediatric AIDS is a healthcare crisis in developing nations, such as in Africa, the United States has the smallest percentage of children living with HIV/AIDS in the world.<sup>3</sup> Most of these children acquire the virus from their mothers.

The rapid decline in children becoming infected is due to several factors. These include our better understanding of how the virus is transmitted from mother to child, better screening methods and protocols, improvements in HIV treatment for the mother, and greater knowledge of the safety and efficacy of antiretroviral drugs administered during pregnancy, delivery, and postpartum.

#### REVISED RECOMMENDATIONS FOR HIV SCREENING FOR PREGNANT WOMEN

The US Preventive Services Task Force (USPSTF) published recommendations for screening for HIV.<sup>4</sup> The USPSTF recommends that clinicians screen all pregnant women for HIV, noting evidence that supports several important benefits. First, prenatal counseling and voluntary testing increase the proportion of HIV-infected women who receive a diagnosis and are treated before delivery. Also, the treatment regimens for HIV infection significantly reduce rates of mother-to-child transmission (MTCT) of the virus, and there is no current evidence of fetal anomalies or other fetal harm associated with current antiretroviral regimens, with the exception of those that include efavirenz.<sup>4</sup>

The benefits of screening for HIV outweigh the risks in pregnant women. The benefits include the opportunity to provide drug treatment, to counsel the mother against breast-feeding, and to avoid obstetric practices that may increase the risk for transmission, such as vaginal delivery in certain circumstances.<sup>4</sup> The disadvantages of screening result from the very small number of false-positive or false-negative cases, which can lead to antiretroviral prophylaxis before negative confirmatory results, elective pregnancy termination based on incorrect test results, anxiety, discrimination, continued risky behaviors, social stigmatization, or altered partner relationships.<sup>5</sup> The risk of suicide with prenatal diagnosis of HIV is currently unknown.<sup>6</sup>

Screening is most effective when an “opt-out” strategy is used, as opposed to an “opt-in” strategy. With the opt-out strategy, pregnant women are

informed that an HIV test will be conducted as a standard part of prenatal care unless they decline to be tested. With the opt-in policy, women are required to specifically consent to an HIV test.<sup>5</sup> The USPSTF noted that mandatory testing of pregnant women could result in avoidance of prenatal care, thus testing should be voluntary and obtained with informed consent.<sup>5,7</sup> Importantly, states vary with regard to their regulations on testing babies for HIV. Some states require that babies are tested for HIV if the status of the mother is unknown, some states require that babies are tested unless the mother refuses, and some states only require HIV testing be offered to pregnant women with the right for the mother to refuse.<sup>8</sup>

#### PREGNANCY AND VERTICAL HIV TRANSMISSION

Mother-to-child transmission can occur during pregnancy (antepartum), during labor and delivery (intrapartum), or after delivery (postnatal).<sup>5</sup> If the mother does not breast-feed, antepartum transmission is thought to account for 25% to 40% of MTCT; the remaining occur during delivery.<sup>5,9</sup> Postnatally, virtually all cases of MTCT are through breast-feeding.<sup>5</sup> A small number of children are infected through physical or sexual abuse.<sup>3</sup>

The rates of transmission are affected by several factors, including the mother’s viral load and which type of delivery she uses. Caesarean delivery (C-section) is recommended for an HIV-infected mother when: her viral load is unknown or is greater than 1000 copies/mL at 36 weeks of pregnancy; she has not taken any antiretroviral agents or has only taken zidovudine during her pregnancy; or she has not received prenatal care until 36 weeks or later into her pregnancy. A C-section should be performed at 38 weeks and before the membranes have ruptured to be most effective. If vaginal delivery is considered, it should be performed when the HIV-infected mother has been receiving prenatal care throughout her pregnancy, has a viral load less than 1000 copies/mL at 36 weeks, and she is taking zidovudine with or without other antiretroviral drugs. The Public Health Service Task Force (PHSTF) guidelines provide recommendations regarding mode of delivery to reduce MTCT based on the mother’s profile (ie, extent of prenatal care, use of antiretroviral therapy, viral load, and CD<sup>+</sup> cell count).<sup>10</sup>

It is now established that the use of highly active antiretroviral therapy (HAART) before delivery decreases the rate of MTCT. Without the use of antiretroviral prophylaxis, the risk for MTCT is 14% to 25% in developed countries.<sup>11</sup> When antiretroviral prophylaxis is used to prevent MTCT, zidovudine should always be considered as part of the regimen when feasible.<sup>12,13</sup>

The landmark Pediatric AIDS Clinical Trials Group protocol 076 was the first study to show the benefits of antiretroviral therapy in preventing MTCT. Using a 3-phase treatment with zidovudine, the risk of transmission decreased 66% overall, from 22.6% to 7.6% compared to placebo. The 3-phase regimen included starting oral zidovudine at 14 to 34 weeks' gestation and continued throughout pregnancy, intravenous zidovudine during labor and delivery, and oral zidovudine to the newborn during the first 6 weeks of life, beginning at 8 to 12 hours after birth.<sup>14,15</sup> Since this study more than a decade ago, epidemiologic data have confirmed the efficacy of zidovudine in reducing MTCT in children of women with advanced disease, low CD4<sup>+</sup> cell counts, and prior zidovudine therapy.

Pregnancy is no longer considered a reason to defer standard therapy for women who are HIV infected and become pregnant. The PHSTF currently recommends more aggressive drug regimens to maximally suppress viral replication, reduce the risk of prenatal transmission, and minimize the risk of development of resistant virus. In fact, HAART is currently recognized as standard of care in HIV-infected pregnant women.<sup>10</sup> The choice and timing of therapy may be altered, based on the woman's individual profile. Providers must consider factors, such as dose adjustments for physiologic changes with pregnancy (Table 1), potential for short- and long-term adverse events on the fetus and newborn (including potential for teratogenicity, mutagenicity, or carcinogenicity), and the effectiveness of drugs in reducing risk of perinatal transmission. Because data to evaluate these factors are limited, a detailed discussion with the pregnant woman about the known and unknown benefits and risks should accompany any treatment decision.<sup>10</sup> Of special note, these recommendations were developed for use in the United States. In other countries, particularly developing countries, the factors that affect MTCT vary widely, including the role of breast-

feeding, access to HAART and prenatal care, and options for delivery.<sup>10</sup>

The PHSTF recommendations review the clinical and preclinical data for antiretroviral drugs with regard to placental passage, long-term animal carcinogenicity studies, and animal teratogen studies. A list of antiretroviral drugs and their US Food and Drug Administration pregnancy category is provided in Table 2.<sup>10</sup> The Department of Health and Human Services has also published a supplement to their guidelines that is a review of the safety and toxicity of individual antiretroviral agents in pregnancy.<sup>16</sup>

The PHSTF recommendations use clinical scenarios to discuss their recommendations on the use of antiretroviral drugs in pregnant women (Table 3).<sup>10</sup> Because the use of zidovudine is also effective in women with advanced disease, low CD4<sup>+</sup> count, and prior zidovudine therapy, clinical situations based on CD4<sup>+</sup> count and prior zidovudine use are not presented. Weeks of gestation are also not considered in the recommendations of zidovudine because data indicate that most transmission occurs near the time of or during delivery.<sup>10</sup>

**Table 1. Physiologic Changes During Pregnancy that May Affect Antiretroviral Therapy**

- Prolonged gastrointestinal transit time
- Increase in body water and fat
- Increases in cardiac output, ventilation, and liver and renal blood flow
- Decreased plasma protein concentrations
- Increased renal sodium reabsorption
- Changes in hepatic metabolic enzyme pathways

Physiologic changes that occur during pregnancy may affect the kinetics of drug absorption, distribution, biotransformation, and elimination, thereby also affecting requirements for drug dosing and potentially altering the susceptibility of the pregnant woman to drug toxicity. Also, placental transport of drugs, compartmentalization of drugs in the embryo/fetus and placenta, biotransformation of drugs by the fetus and placenta, and elimination of drugs by the fetus, in addition to the pharmacokinetics and toxicity of transplacentally transferred drugs, need to be taken into consideration. Public Health Task Force. Recommendations for the use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. February 24, 2005. Available at: <http://www.AIDSinfo.nih.gov>. Accessed January 15, 2006.<sup>10</sup>

**Table 2. Antiretroviral Drugs and US FDA Pregnancy Category**

<i>Nucleoside and Nucleotide Analogue Reverse Transcriptase Inhibitors</i>	
Abacavir	C
Didanosine	B
Emtricitabine	B
Lamivudine	C
Stavudine	C
Tenofovir DF	B
Zalcitabine	C
Zidovudine	C
<i>Non-nucleoside Analogue Reverse Transcriptase Inhibitors</i>	
Delavirdine	C
Efavirenz	D
Nevirapine	C
<i>Protease Inhibitors</i>	
Amprenavir	C
Atazanavir	B
Fosamprenavir	C
Indinavir	C
Lopinavir/ritonavir	C
Nelfinavir	B
Ritonavir	B
Saquinavir	B
<i>Fusion Inhibitors</i>	
Enfuvirtide	B

## US FDA Pregnancy Categories:

- A. Adequate and well-controlled studies in pregnant women fail to demonstrate a risk to the fetus during the first trimester of pregnancy (and no evidence exists of risk during later trimesters).
- B. Animal reproduction studies fail to demonstrate a risk to the fetus, and adequate but well-controlled studies of pregnant women have not been conducted.
- C. Safety in human pregnancy has not been determined; animal studies are positive for fetal risk or have not been conducted, and the drug should not be used unless the potential benefit outweighs the potential risk to the fetus.
- D. Positive evidence of human fetal risk that is based on adverse reaction data from investigational or marketing experiences, but the potential benefits from the use of the drug among pregnant women may be acceptable despite its potential risks.
- X. Studies among animals or reports of adverse reactions have indicated that the risk associated with the use of the drug for pregnant women clearly outweighs any possible benefit.

US FDA = US Food and Drug Administration.

Public Health Task Force. Recommendations for the use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. February 24, 2005. Available at: <http://www.AIDSinfo.nih.gov>. Accessed January 15, 2006.<sup>10</sup>

Development of resistant HIV strains is as much of a concern in pregnant women as it is with other adults and adolescents. The PHSTF offers recommendations to reduce the risk of developing drug-resistant strains and guidelines for resistance testing in HIV-infected pregnant women. These recommendations are summarized in Table 4.<sup>10</sup> Optimal adherence is a key part of the strategy to reduce development of resistance.

**TRANSMISSION THROUGH BREAST-FEEDING**

Breast-feeding by HIV-negative women is recognized worldwide as offering several benefits to mother and baby. These benefits provide positive nutritional, immunological, developmental, psychological, social, economical, and environmental outcomes. The policy statement on breast-feeding published by the American Academy of Pediatrics (AAP) states that “breast-feeding ensures the best possible health as well as the best developmental and psychosocial outcomes for the infant.”<sup>17</sup> The World Health Assembly, along with UNICEF (United Nations Children’s Fund) and the World Health Organization, state that infants should be breast-fed exclusively for the first 6 months of life to achieve optimal growth, development, and health. After 6 months, they should receive nutritionally adequate and safe complementary foods while breast-feeding continues up to 24 months or beyond.<sup>18</sup>

As reviewed by the AAP, the immunologic benefits of breast-feeding include decreased rates of a wide range of infectious diseases, including bacterial meningitis, bacteremia, diarrhea, respiratory tract infection, necrotizing enterocolitis, otitis media, urinary tract infection, and late-onset sepsis in preterm infants. Health outcomes include decreased mortality rates and decreased rates of sudden infant death syndrome, with some studies suggesting decreased incidence of type 1 and type 2 diabetes, lymphoma, leukemia, Hodgkin’s disease, overweight and obesity, hypercholesterolemia, and asthma. Breast-feeding may also enhance cognitive development and provide a source of analgesia, but more research in these areas is needed. For the mother, breastfeeding decreases postpartum bleeding and contributes to a more rapid return to prepregnancy weight. Breast-feeding also decreases the risk of ovarian and breast cancer, in addition to potentially decreasing the risk of hip fracture and postmenopausal osteoporosis.

**Table 3. Clinical Scenarios and Recommendations for the Use of Antiretroviral Drugs to Reduce Perinatal HIV-1 Transmission**
**SCENARIO #1**
**HIV-1–infected pregnant women who have not received prior ART**

- Pregnant women with HIV-1 infection must receive standard clinical, immunologic, and virologic evaluation. Recommendations for initiation and choice of ART should be based on the same parameters used for persons who are not pregnant, although the known and unknown risks and benefits of such therapy during pregnancy must be considered and discussed.
- The 3-part ZDV chemoprophylaxis regimen, initiated after the first trimester, is recommended for all pregnant women with HIV-1 infection, regardless of antenatal HIV-RNA copy number, to reduce the risk for perinatal transmission.
- The combination of ZDV chemoprophylaxis with additional antiretroviral drugs for treatment of HIV-1 infection is recommended for infected women whose clinical, immunologic, or virologic status requires treatment or who have HIV-1 RNA over 1000 copies/mL regardless of clinical or immunologic status, and can be considered for women with HIV-1 RNA <1000 copies/mL.
- Women who are in the first trimester of pregnancy may consider delaying initiation of therapy until after 10–12 weeks' gestation.

**SCENARIO #2**
**HIV-1–infected women receiving ART during the current pregnancy**

- HIV-1–infected women receiving ART in whom pregnancy is identified after the first trimester should continue therapy. ZDV should be a component of the antenatal ART regimen after the first trimester whenever possible, although this may not always be feasible.
- For women receiving ART in whom pregnancy is recognized during the first trimester, the woman should be counseled regarding the benefits and potential risks of antiretroviral administration during this period, and continuation of therapy should be considered. If therapy is discontinued during the first trimester, all drugs should be stopped and reintroduced simultaneously to avoid the development of drug resistance.
- Regardless of the antepartum antiretroviral regimen, ZDV administration is recommended during the intrapartum period and for the newborn.

**SCENARIO #3**
**HIV-1–infected women in labor who have had no prior therapy**

- Several effective regimens are available. These include:
  - Intrapartum intravenous ZDV followed by 6 weeks of ZDV for the newborn;
  - Oral ZDV and lamivudine during labor, followed by 1 week of oral ZDV and lamivudine for the newborn;
  - A single dose of nevirapine at the onset of labor followed by a single dose of nevirapine for the newborn aged 48 hours; and
  - The single-dose maternal/infant nevirapine regimen combined with intrapartum intravenous ZDV and 6-week ZDV for the newborn.
- If single-dose nevirapine is given to the mother, alone or in combination with ZDV, consideration should be given to adding maternal ZDV and lamivudine starting as soon as possible (intrapartum or immediately postpartum) and continuing for 3–7 days, which may reduce development of nevirapine resistance.
- In the immediate postpartum period, the woman should have appropriate assessments (eg, CD4<sup>+</sup> count and HIV-1–RNA copy number) to determine whether ART is recommended for her own health.

**SCENARIO #4**
**Infants born to mothers who have received no ART during pregnancy or intrapartum**

- The 6-week neonatal ZDV component of the ZDV chemoprophylactic regimen should be discussed with the mother and offered for the newborn.
- ZDV should be initiated as soon as possible after delivery, preferably within 6–12 hours of birth.
- Some clinicians may choose to use ZDV in combination with other antiretroviral drugs, particularly if the mother is known or suspected to have ZDV-resistant virus. However, the efficacy of this approach for prevention of transmission has not been proven in clinical trials, and appropriate dosing regimens for neonates are incompletely defined for many drugs.
- In the immediate postpartum period, the woman should undergo appropriate assessments (eg, CD4<sup>+</sup> count and HIV-1–RNA copy number) to determine if ART is required for her own health. The infant should undergo early diagnostic testing so that if HIV infected, treatment can be initiated as soon as possible.

Discussion of treatment options and recommendations should be noncoercive, and the final decision regarding the use of antiretroviral drugs is the responsibility of the woman. A decision to not accept treatment with ZDV or other drugs should not result in punitive action or denial of care. Use of ZDV should not be denied to a woman who wishes to minimize exposure of the fetus to other antiretroviral drugs and who therefore chooses to receive only ZDV during pregnancy to reduce the risk for perinatal transmission.

ART = antiretroviral therapy; HIV-1 = human immunodeficiency virus type 1; ZDV = zidovudine.

Public Health Task Force. Recommendations for the use of antiretroviral drugs in pregnant HIV-1–infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. February 24, 2005. Available at: <http://www.AIDSinfo.nih.gov>. Accessed January 15, 2006.<sup>10</sup>

**Table 4. Recommendations Related to Antiretroviral Drug Resistance and Drug Resistance Testing for HIV-1–Infected Pregnant Women**

- Monotherapy with zidovudine can be considered for women in whom combination antiretroviral therapy would be considered optional (HIV-1 RNA <1000 copies/mL) and who wish to restrict their exposure to antiretroviral drugs during pregnancy. The regimen should follow the 3-phase plan used in the PACTG 076 study.
  - Development of resistance should be minimized by limited viral replication (assuming HIV-1–RNA levels remain low) and time-limited exposure to zidovudine.
  - Monotherapy with zidovudine does not suppress HIV-1 replication to undetectable levels in most cases. Theoretically, such therapy may select for zidovudine-resistant viral variants, potentially limiting future treatment options. These considerations should be discussed with the pregnant woman.
- Recommendations for resistance testing for HIV-1–infected pregnant women are the same as for nonpregnant patients: acute HIV-1 infection, virologic failure, suboptimal viral suppression after initiation of antiretroviral therapy, or high likelihood of exposure to resistant virus based on community prevalence or source characteristics.
- Women who have a history of presumed or documented zidovudine resistance and are on antiretroviral regimens that do not include zidovudine for their own health should still receive intravenous zidovudine intrapartum and oral zidovudine for their infants according to the PACTG 076 protocol whenever possible.
  - A key mechanism by which zidovudine reduces perinatal transmission is likely through pre- and postexposure prophylaxis of the infant, which may be less dependent on drug sensitivity than is reduction of viral replication. However, these women are not good candidates for zidovudine alone.
- Optimal antiretroviral prophylaxis of the infant born to a woman with HIV-1 known to be resistant to zidovudine or other agents should be determined in consultation with pediatric infectious disease specialists, taking into account resistance patterns, available drug formulations, and infant pharmacokinetic data, when available.
- If women receiving combination therapy require temporary discontinuation for any reason during pregnancy, all drugs should be stopped and reintroduced simultaneously to reduce the potential for emergence of resistance.
- Optimal adherence to antiretroviral medications is a key part of the strategy to reduce the development of resistance.
- Because the prevalence of drug-resistant virus is an evolving phenomenon, surveillance is needed to monitor the prevalence of drug-resistant virus in pregnant women over time and the risk of transmission of resistant viral strains.

HIV-1 = human immunodeficiency virus type 1; PACTG 076 = Pediatric AIDS Clinical Trials Group protocol 076.

Public Health Task Force. Recommendations for the use of antiretroviral drugs in pregnant HIV-1–infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. February 24, 2005. Available at: <http://www.AIDSinfo.nih.gov>. Accessed January 15, 2006.<sup>10</sup>

Importantly, breast-feeding also acts as a very effective method of birth control in the postpartum period, especially if the mother is breast-feeding exclusively. Finally, economical benefits include decreased annual healthcare costs, decreased costs for public health programs (eg, the Supplemental Nutrition Program for Women, Infants, and Children), decreased environmental burden for disposal of formula cans and bottles, and decreased energy demands for production and transport of artificial feeding products. However, the AAP notes that some of the cost savings would be offset by increased costs for physician visits, lactation specialist consultations, and breast pumps.<sup>17</sup>

Breast-feeding by an HIV-infected mother increases the risk of MTCT (beyond that incurred during pregnancy or delivery) by an additional 15%, when breastfeeding continues for 2 or more years.<sup>18,19</sup> Studies have shown that the risk is cumulative—the longer the child is breast-fed, the greater the risk of being infected with HIV from the mother.<sup>18,20–24</sup> Paradoxically, the risk is decreased if the mother breast-feeds exclusively, and risk is highest if the mother complements breast-feeding with other sources of nutrition. Exclusive breast-feeding carries a significantly lower risk of HIV infection than mixed feeding (hazard ratio 0.56, 95% confidence interval [CI] 0.32–0.98) and is similar to never breastfeeding (hazard ratio 1.19, 95% CI 0.63–2.22). The cause is unclear and may involve transfer of immunoglobulin or cellular immunity through breast milk to protect against infection or increasing susceptibility in the gut through mechanical or inflammatory mechanisms with switching milk sources.<sup>18</sup>

Many of the factors associated with risk of transmission via breast milk are the same as for those with other adults, such as RNA viral load in plasma and breast milk and HIV-related immune status (ie, CD4+ cell count). Importantly, RNA viral load in blood appears to correlate only partly with that in breast milk, and differences between breasts and over time can be highly variable.<sup>18</sup> Clinical or subclinical mastitis (inflammation of the breast) can also be associated with transmission risk, as can suboptimal maternal nutritional status.<sup>18,25,26</sup>

In the infant, mucosal membrane integrity affects transmission risk. Conditions that damage the mucous membranes, such as oral thrush

(*Candida* infection), may increase risk. As noted earlier in this article, infants who receive only breast milk have a healthier gut lining, which may be less permeable to viral infection.<sup>18</sup> Interestingly, female infants appear to be much less likely to become infected than male infants with regard to late post-natal transmission (ie, after 4 weeks of age). The risk is highest for males breast-fed by mothers with low CD4<sup>+</sup> cell counts (<200 cells/mm<sup>3</sup>), followed by males breast-fed by mothers with CD4<sup>+</sup> counts 200 to 499 cells/mm<sup>3</sup>, then females breast-fed by mothers with counts lower than 200 cells/mm<sup>3</sup>. The cause is unclear and may be due to male infants being more likely to receive mixed feeding at an earlier age than female infants.<sup>18,23</sup>

Beyond primary prevention (ie, avoiding HIV infection in the mother), secondary preventive measures of MTCT include use of formula feeding, wet nursing by an HIV-negative woman, heat treatment of breast milk, or use of breast milk banks (which are currently available in California, Colorado, Delaware, Iowa, North Carolina, and Texas).<sup>18</sup> In general, HIV-infected women need to consider the risk of transmission of the virus with the benefits of breast-feeding. HIV-infected women should be counseled regarding all of their options.

## CONCLUSIONS

Although the rate of MTCT is declining in the United States, each case of pediatric HIV/AIDS is potentially preventable and depends on appropriate education of the mother and her choices regarding testing, treatment, delivery, and breast-feeding. After more than 20 years into the HIV epidemic, we now possess the educational resources, in addition to the antiretroviral arsenal, needed to help a pregnant, HIV-infected woman reduce the risk of MTCT during pregnancy, delivery, or through breast-feeding. We also have broad evidence and guidelines to support the use of HAART in pregnant women.

## REFERENCES

- Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report 2004. Atlanta, Ga: US Department of Health and Human Services, CDC. Available at: <http://www.cdc.gov/hiv/stats/2004SurveillanceReport.pdf>. Accessed January 15, 2006.
- Centers for Disease Control and Prevention Web site. Fact sheet: HIV/AIDS among women. Available at: <http://www.cdc.gov/hiv/pubs/facts/women.htm>. Accessed January 15, 2006.
- National Institutes of Allergy and Infectious Diseases Web site. HIV infection in infants and children fact sheet. Available at: [www.niaid.nih.gov/factsheets/hivchildren.htm](http://www.niaid.nih.gov/factsheets/hivchildren.htm). Accessed January 15, 2006.
- United States Preventive Services Task Force. Screening for HIV: recommendation statement. *Ann Intern Med*. 2005;143:32-37.
- Chou R, Smits AK, Huffman LH, et al. Prenatal screening for HIV: review of the evidence for the US Preventive Services Task Force. *Ann Intern Med*. 2005;143:38-54.
- Green L, Ardron C, Catalan J. HIV, childbirth and suicidal behaviour: a review. *Hosp Med*. 2000;61:311-314.
- Nakchbandi IA, Longenecker JC, Ricksecker MA, et al. A decision analysis of mandatory compared with voluntary HIV testing in pregnant women. *Ann Intern Med*. 1998;128:760-767.
- Department of Health and Human Services AIDSinfo Web site. HIV testing and pregnancy fact sheet. Available at: <http://aidsinfo.nih.gov>. Accessed January 15, 2006.
- Centers for Disease Control and Prevention. Revised recommendations for HIV screening of pregnant women. *MMWR Recomm Rep*. 2001;50:63-85.
- Public Health Task Force. Recommendations for the use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. February 24, 2005. Available at: <http://www.AIDSinfo.nih.gov>. Accessed January 15, 2006.
- Working Group on Mother-to-Child Transmission of HIV. Rates of mother-to-child transmission of HIV-1 in Africa, America, and Europe: results from 13 perinatal studies. *J Acquir Immune Defic Syndr Hum Retroviro*. 1995;8:506-510.
- Department of Health and Human Services AIDSinfo Web site. Delivery options for HIV-positive pregnant women. Available at: <http://www.aidsinfo.nih.gov>. Accessed January 15, 2006.
- Centers for Disease Control and Prevention. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Available at: <http://www.AIDSinfo.nih.gov>. Accessed January 15, 2006.
- Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med*. 1994;331:1173-1180.
- 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*. 1996;335:1621-1629.
- Department of Health and Human Services. Supplement: safety and toxicity of individual antiretroviral agents in pregnancy. Available at: [http://www.AIDSinfo.nih.gov/ContentFiles/PerinatalGLSafetyTox\\_Sup.pdf](http://www.AIDSinfo.nih.gov/ContentFiles/PerinatalGLSafetyTox_Sup.pdf). Accessed January 15, 2006.

17. American Academy of Pediatrics. Policy statement. Breastfeeding and the use of human milk. *Pediatrics*. 2005;115:496-506.
18. World Health Organization. *HIV Transmission through Breastfeeding*. Geneva, Switzerland: World Health Organization; 2004.
19. Dunn DT, Newell ML, Ades AE, Peckham CS. Risk of human immunodeficiency virus type 1 transmission through breastfeeding. *Lancet*. 1992;340:585-588.
20. Miotti PG, Taha TE, Kumwenda NI, et al. HIV transmission through breastfeeding: a study in Malawi. *JAMA*. 1999;282:744-749.
21. Leroy V, Newell ML, Dabis F, et al. International multicentre pooled analysis of late postnatal mother-to-child transmission of HIV infection. *Lancet*. 1998;352:597-600.
22. Leroy V, Karon JM, Alioum A, et al. Twenty-four months efficacy of a maternal short-course zidovudine regimen to prevent mother-to-child transmission of HIV-1 in West Africa. *AIDS*. 2002;16:631-641.
23. Read JS, et al. Late postnatal transmission of HIV in breastfed children: an individual patient data meta-analysis (The Breastfeeding and HIV International Transmission Study). Paper presented at: 10th Conference on Retroviruses and Opportunistic Infections; February 10-14, 2003; Boston, Mass.
24. The Petra Study Team. Efficacy of short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother-to-child in Tanzania, South Africa and Uganda (Petra study): a randomized double-blind, placebo-controlled trial. *Lancet*. 2002;359:1178-1186.
25. Semba RD, Kumwenda N, Hoover DR, et al. Human immunodeficiency viral load in breastmilk, mastitis and mother-to-child transmission of human immunodeficiency virus type 1. *J Infect Dis*. 1999;180:93-98.
26. John GC, Nduati RW, Mbori-Ngacha D, et al. Correlates of mother-to-child human immunodeficiency virus type 1 (HIV-1) transmission: association with maternal plasma HIV-1 RNA load, genital HIV-1 DNA shedding and breast infections. *J Infect Dis*. 2001;183:206-212.

Galen Publishing, LLC  
NO REPRODUCTION WITHOUT PERMISSION FROM THE PUBLISHER.