



**COMMENT AND CONTROVERSY**  
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## Human immunodeficiency virus infection and pregnancy

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**Abstract** Human immunodeficiency virus infection profoundly affects the medical community and is spreading rapidly in women of childbearing age worldwide. Transmission of HIV from mother to child can occur in utero, during labor, or after delivery through breast-feeding. Most of the infants are infected during delivery.

We focus on the factors affecting the transmission of HIV, diagnostic and resistance tests, strategies to prevent mother-to-child transmission with special reference to mode of delivery, infant feeding, and use of antiretroviral therapy. The risk of infection for the infant can be decreased by reducing maternal viral load, by elective cesarean delivery, and by avoidance of breast-feeding. The efficacy of antiretroviral treatment should be balanced against the possibility of embryonic or fetal toxicity. The choice of therapy should be based on the woman's treatment history, the clinical status, and the available prognostic markers, which are related to the progression of disease in the mother and the risk of mother-to-child transmission HIV transmission.

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### Introduction

During 2003, HIV infection killed more than 3 million people, and almost half of the 42 million people living with the virus around the world are women in their reproductive years who became infected mainly as a result of heterosexual transmission.<sup>1</sup> More than 2 million HIV-infected women across the world become pregnant each year, especially in developing countries, and close to 600,000 of HIV-infected

women die each year because of complications of pregnancy and childbirth.<sup>2</sup>

Human immunodeficiency virus infection rates in pregnant women range from below 1% to more than 40% in different countries. The highest rates are mainly in Africa, the Caribbean, and South and Southeast Asia. Similarly, an estimated 3.2 million children and adolescents younger than 15 years are infected with HIV, most of whom live in sub-Saharan Africa and have acquired HIV through perinatal transmission.<sup>3</sup> In the United States, the prevalence of HIV/AIDS among women varies dramatically by geographic region, with the largest share of AIDS cases in the northeast and southeast regions of the country. One third of new HIV-positive patients in 2000 were women,<sup>3</sup> and the nationwide seroprevalence of HIV during pregnancy has been reported to be 1.7 per 1000 pregnancies.<sup>4</sup> The vertical

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transmission of the virus from mother to child occurred during pregnancy in 4.4% of cases, during delivery in 60%, and during breast-feeding in 35.6%.<sup>5</sup>

## Mother-to-child HIV transmission and risk factors

Mother-to-child transmission (MTCT), also known as vertical transmission, may occur in utero, intrapartum, or postpartum through breast-feeding, with most cases occurring around the time of delivery.<sup>6,7</sup> The risk of MTCT is associated with maternal HIV disease status, fetal exposure to infected maternal body fluids, and breast-feeding, but the exact mechanism of viral transmission is not understood. There are numerous risk factors that increase the chance of MTCT of HIV infection, including maternal, obstetrical, and neonatal factors.

### Maternal factors

In most recent studies, maternal HIV-1 RNA level at delivery remains the most consistent predictor of MTCT.<sup>8,9</sup> Increasing geometric mean level of plasma HIV-1 RNA is generally associated with increasing rates of perinatal transmission. The highest rate of transmission was found among women whose HIV plasma level is more than 100 000 copies/mm. Conversely, transmission is a rare event when viral loads are undetectable.

The more effective a drug regimen is at reducing viral load, the greater the likelihood that it will succeed in preventing neonatal infection. Even when analysis, however, is limited to women with viral loads less than 1000 copies/mL, those on antiretroviral therapy (ARVT) still have lower rates of transmission.<sup>10</sup> Low maternal CD4+ cell count is associated with higher transmission of HIV.<sup>11,12</sup> Maternal viral properties, such as viral homogeneity and rapid replication kinetics, have also been linked to an increased risk of HIV transmission.<sup>13</sup> There is limited and conflicting evidence that viral resistance may increase the likelihood of MTCT.<sup>14</sup>

Other factors such as the use of tobacco and illicit drugs, especially cocaine, should be discouraged for reasons of general health. Furthermore, unprotected sex with HIV-infected men or those at risk of acquiring infection should be avoided because it has been suggested that this may increase the risk of vertical transmission.

### Obstetrical factors

Prolonged rupture of membranes has been shown to be a risk factor for HIV transmission among women treated and untreated with ARVT during pregnancy.<sup>15,16</sup> The risk of infection is related to the duration of membrane rupture and is particularly increased when this duration is more than 4 hours.<sup>17</sup> Prolonged rupture of membrane appears to be a particular risk among women with low CD4+ cell

counts<sup>18,19</sup> and women at preterm gestation.<sup>20</sup> Preterm delivery is an additional risk factor for intrapartum HIV transmission.<sup>21</sup> Chorioamnionitis, an infection of the chorion-amnion space, increases the risk of MTCT.<sup>22,23</sup> Some studies that do not adjust for plasma HIV-1 RNA level have demonstrated increased transmission with intrapartum maternal hemorrhage,<sup>20</sup> maternal sexually transmitted infections,<sup>20</sup> and amniocentesis.<sup>20,24</sup>

Delivery by cesarean birth decreases the risk of transmission by about 25%.<sup>17</sup> In twins, the firstborn has a higher likelihood of being infected than the second, presumably because of more prolonged neonatal exposure to maternal mucocutaneous vaginal secretions.<sup>25</sup>

### Neonatal factors

Neonatal variables such as premature birth at less than 35 weeks' gestation<sup>26</sup> and birth weight less than 2500 g<sup>15,17</sup> are associated with neonatal HIV acquisition.

Nutritional factors may affect viral transmission. In 1 study,<sup>27</sup> maternal vitamin A deficiency promoted disease transmission, increased infant mortality, and impaired infant growth in height and weight during the first year of life. Another study reported that vitamin A levels in the third trimester did not affect the risk of vertical transmission, although no cases of maternal vitamin A deficiency occurred in the study.<sup>28</sup> Maternal vitamin A deficiency was strongly associated with the presence of retroviral DNA in breast milk.<sup>29</sup> The effect of vitamin A deficiency on disease transmission is uncertain, and vitamin A deficiency could be a surrogate marker for another nutritional deficiency.

## Diagnosis of HIV in pregnancy

Given the many successful interventions now available to prolong AIDS-free survival and to reduce MTCT, attention has focused in ensuring universal HIV testing among pregnant women. Furthermore, a test should also be offered to their sexual partners. Test results should always be given in person and in private. Immediately after a positive test result, a woman requires detailed and specific counseling and support. Subsequent decisions about personal treatment, the continuation of pregnancy, and the use of interventions to reduce the risk of vertical transmission must be taken after a thorough discussion about the risks and benefits of the various options.

For woman with negative test results, it is important to assess the presence of behavioral risk factors for HIV infection or infection by other sexually transmitted agents. For women who have an initial negative test result and are known to be at high risk of HIV infection, repeat testing during pregnancy and postnatal is recommended, taking into consideration maternal infection close to delivery or transmission through breast-feeding.

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