

HIV Supporting Information

When viral loads in the mother are undetectable (i.e. < 200-500 copies/ml):

Should anti-retroviral therapy be given to the infant?

A nested case-control study in 105 women (Thea, 1997) found that those with an undetectable viral load were 6 times less likely to transmit the infection than were those with a measurable load (AOR 5.8; 95% CI 2.2-15.5).

In a nonrandomised prospective cohort study of 92 HIV-1-seropositive mothers (Dickover, 1996), none of the 63 women with viral loads of <20,000 copies/ml transmitted the infection to their infants.

A larger study in 480 zidovudine-treated women (Mofenson, 1999) found that “there was no perinatal transmission of HIV-1 among the 84 women who had HIV-1 levels below the limit of detection (500 copies per milliliter) at base line or the 107 women who had undetectable levels at delivery.”

In another, similar study of 42 women (Aleixo, 1997), perinatal transmission occurred in 2 ZDV-treated and 3 untreated women with viral loads < 100 copies/ml, raising the possibility that there is no absolute threshold below which transmission will not occur. Equally, there appears to be no upper threshold above which transmission will always occur (Cao, 1997). Anti-retroviral therapy (for both mothers and infants) was shown by the Aleixo study to reduce transmission by 78%, and this was similar to the reduction of 67% noted by the ACTG 076 study (Connor, 1994).

Treating the infants of mothers with a viral load of < 1000 copies may confer some benefit, but it is "not possible to discern from the available data" according to the combined results of 7 European and US prospective studies in a total of 1,202 women (Ioannidis, 2001).

Aleixo LF, Goodenow MM, Sleasman JW. Zidovudine administered to women infected with human immunodeficiency virus type 1 and to their neonates reduces pediatric infection independent of an effect on levels of maternal virus. *J Pediatr* 1997;130:906-14

Cao Y, Krogstad P, Korber BT, et al. Maternal HIV-1 viral load and vertical transmission of infection: the Ariel Project for the prevention of HIV transmission from mother to infant. *Nat Med* 1997;3:549-52

Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med* 1994;331:1173-80

Dickover RE, Garratty EM, Herman SA, et al. Identification of levels of maternal HIV-1 RNA associated with risk of perinatal transmission: effect of maternal zidovudine treatment on viral load. *JAMA* 1996;275:599-605

Ioannidis JP, Abrams EJ, Ammann A, et al. Perinatal transmission of human immunodeficiency virus type 1 by pregnant women with RNA virus loads <1000 copies/mL. *J Infect Dis* 2001;183:539-45

Mofenson LM, Lambert JS, Stiehm ER, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. *N Engl J Med* 1999;341:385-93

Thea DM, Steketee RW, Pliner V, et al. The effect of maternal viral load on the risk of perinatal transmission of HIV-1. New York City Perinatal HIV Transmission Collaborative Study Group. *AIDS* 1997;11:437-44

Evidence Level: III

Should delivery be by elective caesarean section?

A recent review (Mitchla, 2000) states that “There is still no information as to whether (caesarean section) provides any added benefit for women on highly active antiviral therapy with an undetectable HIV viral load”.

The American College of Obstetricians and Gynecologists originally recommended, in 1999, that caesarean section should be offered to all HIV-seropositive pregnant women. A survey of 2,000 randomly-selected obstetricians and gynaecologists in the U.S. (Rowland, 2001) found, however, that 47% of respondents disagreed with this recommendation, and 72% did not advise caesarean delivery in women with undetectable viral loads.

Current recommendations (Anon, 2001) are that there is no evidence of benefit in women with viral loads < 1000 copies/ml, but that the individual’s wishes regarding mode of delivery should be respected.

Anon. Scheduled cesarean delivery and the prevention of vertical transmission of HIV infection. ACOG committee opinion Number 234, May 2000 (Replaces Number 219, August 1999). Committee on Obstetric Practice. *Int J Gynecol Obstet* 2001;73:279-81

Mitchla Z, Sharland M. Current treatment options to prevent perinatal transmission of HIV. *Expert Opin Pharmacother* 2000;1:239-48

Rowland BL, Vermillion ST, Soper DE. Scheduled cesarean delivery and the prevention of human immunodeficiency virus transmission: a survey of practicing obstetricians. *Am J Obstet Gynecol* 2001;185:327-31

Evidence Level: V

Should breast-feeding be avoided?

In a small study involving 17 samples of breast milk from 4 HIV-positive mothers (Chantry, 2000) 15 (88%) showed measurable HIV-1 proviral DNA, despite all mothers having had low or undetectable viral loads.

Advice from the U.S. Public Health Service Task Force (Anon, 2005) is that all HIV-seropositive mothers should avoid breast-feeding.

Anon. Recommendations for 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. Public Health Service Task Force, 2005

http://aidsinfo.nih.gov/guidelines/perinatal/PER_022405.pdf

Chantry CJ, Morrison P, Panchula J, et al. Effects of lipolysis or heat treatment on HIV-1 provirus in breast milk. *J Acquir Immune Defic Syndr* 2000;24:325-9

Should the infant be tested with pro-viral DNA/RNA PCR?

A prospective study compared DNA-PCR and viral RNA amplification and detection in 44 HIV-infected infants and 9 uninfected infants (Brown, 1996). Specimens were tested at 3 stages between birth and around 35 days of age, and in each case, viral

RNA was found to be more sensitive than DNA-PCR. After the first month of life, the sensitivity of the DNA-PCR increases from 50% to 96% (Cervia, 2003).

As viral RNA levels increase rapidly from birth and reach a peak at 1-2 months of age (Shearer, 1997), testing during this period should be conclusive on the question of whether or not transmission has occurred. The available evidence, however, is at present inconclusive as to the value of testing or treating infants of mothers with undetectable viral load (see 1st question).

Brown TM, Steketee RW, Abrams EJ, et al. Early diagnosis of perinatal HIV infection comparing DNA-polymerase chain reaction and plasma viral RNA amplification. Int Conf AIDS 1996 Jul 7-12 (abstract no. Tu.B.2374)

Cervia J, Kaplan B, Schuval S, et al. Virologic testing in the management of perinatal HIV exposure. AIDS Read 2003;13:39-46

Shearer WT, Quinn TC, LaRussa P. Viral load and disease progression in infants infected with human immunodeficiency virus type 1. N Engl J Med 1997;336:1337-42

Evidence Level: V

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