HUMAN IMMUNODEFICIENCY VIRUS (HIV)
Supporting Information

This guideline and has been prepared with reference to the following:

BHIVA. British HIV Association guidelines for the management of HIV in pregnancy and postpartum 2018 (2019 interim update). 2019. BHIVA

https://www.bhiva.org/pregnancy-guidelines

Children's HIV Association of UK and Ireland (CHIVA). The Child with HIV and acute illness. 2016. CHIVA

https://www.chiva.org.uk/files/3314/9493/5383/HIV-and-acute-illness_2016.pdf

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).

A Cochrane Review of 25 trials with a total of 18,901 participants (Siegfried, 2011) concluded that: “A regimen combining triple antiretrovirals is most effective for preventing transmission of HIV from mothers to babies. The risk of adverse events to both mother and baby appears low in the short-term but the optimal antiretroviral combination and the optimal time to initiate this to maximise prevention efficacy without compromising the health of either mother or baby remains unclear. Short courses of antiretroviral drugs are also effective for reducing mother-to-child transmission of HIV and are not associated with any safety concerns in the short-term. ZDV given to mothers during the antenatal period, followed by ZDV+3TC intrapartum and postpartum for one week, and sd-NVP given to infants within 72 hours of delivery and ZDV for one week, may be most effective when considering short antiretroviral courses. Where HIV-infected women present late for delivery, post-exposure prophylaxis with a single dose of NVP immediately after birth plus ZDV for the first 6 weeks after birth is beneficial. The long term implications of the emergence of resistant mutations following the use of these regimens, especially those containing Nevirapine, require further study.”

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
http://www.nejm.org/doi/full/10.1056/NEJM199908053410601#t=articleTop

Siegfried N, van der Merwe L, Brocklehurst P, et al. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD003510
http://onlinelibrary.wiley.com/enhanced/doi/10.1002/14651858.CD003510.pub3

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: I

Should delivery be by elective caesarean section?

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.

The European Collaborative Study (Boer, 2010), a cohort study on 5238 mother-child pairs (MCPs), found that, amongst MCPs with maternal HIV RNA<400 HIV-1 RNA copies/mL (n=960), elective caesarean section (CS) was associated with 80% decreased transfer risk (AOR 0.20; 95% CI 0.05-0.65). Two infants born to 559 women with viral loads <50 copies/mL were infected, one of whom was delivered by elective CS (transmission rate 0.4%; 95% CI 0.04-1.29).

Boer K, England K, Godfried MH, et al. Mode of delivery in HIV-infected pregnant women and prevention of mother-to-child transmission: changing practices in Western Europe. HIV Medicine 2010;11:368-78
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3428890/

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 BHIVA (2012) and the U.S. Public Health Service Task Force (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2015) is that all HIV-seropositive mothers should avoid breast-feeding. “To prevent the transmission of HIV infection during the postpartum period, the British HIV Association and Children's HIV Association (BHIVA/CHIVA) continue to recommend the complete avoidance of breast feeding for infants born to HIV-infected mothers, regardless of maternal disease status, viral load or treatment.” (see top of page)

Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. 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. Public Health Service Task Force, 2015
https://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf

British HIV Association (BHIVA). Guidelines for the management of HIV infection in pregnant women 2012
http://www.bhiva.org/PregnantWomen2012.aspx

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

Evidence Level: IV

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

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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
http://www.nejm.org/doi/full/10.1056/NEJM199705083361901#t=articleTop

Evidence Level: V

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