

# HATiP

HIV & AIDS Treatment in Practice

Issue 11 | 07 August 2003



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# Preventing mother-to-child transmission of HIV

## Summary and key messages

Article by Julian Meldrum

Transmission of HIV from mothers to babies is almost entirely preventable but continues on a large scale, especially in Africa. It directly undermines the health of children and the wellbeing of their families and places serious burdens on healthcare systems. This article outlines some of the ways in which this transmission can be stopped, at different stages before, during and after pregnancy. ARV drugs are an important tool, but to make them work effectively means much more than supplying pills and syrup.

Key messages:

- Thinking about what is best to do has changed and will change again. Health care workers therefore need to know the principles behind the advice and treatment, as well as current guidelines and protocols.
- VCT including male partners is better than testing women alone and leads to better outcomes for babies. Ideally, this should be before women become pregnant.
- Detailed preparation for what will happen when women give birth can help their baby to receive best treatment.
- Two-dose nevirapine is an essential step for many countries towards eliminating paediatric AIDS, but is only a first step. Better regimens exist and will need further development. For women who need ARV treatment for themselves and can be provided with it, that is likely to be the best option.
- It may be hard to balance the need for babies to receive breast milk with the need to avoid breast milk transmission of HIV. Advice may need to change as new information and options become available. The starting point remains that breast milk will always be the best, the cheapest and the only food and drink needed by most young babies.
- Early diagnosis of positive infants - preferably, by 6 weeks after they are born and 4 weeks after any breast feeding ends, is important for the families and so that clinical resources can be used where they are most needed.

## When exposure happens

In principle, babies can be exposed to HIV while growing in the womb, or during childbirth, or subsequently, through breast feeding.

Babies born with high viral loads and some evidence of immune deficiency fall into the first group.

The success of interventions such as short-course antiviral treatment, given around the time of birth, points to the importance of exposure during childbirth.

The effect of elective caesarian birth in reducing HIV transmission also highlights the importance of transmission during childbirth - although in most countries, and for most women with HIV, this is neither an affordable nor a safe option for mother or child.

The first clear evidence that babies could be infected with HIV through breastfeeding came from cases where women who acquired HIV through blood transfusions after their baby was born passed the virus on to their breastfed babies. This is a good

reminder that all prevention efforts for mother to child transmission should begin with efforts to protect the mother.

## Protecting HIV negative parents

The inclusion of male partners in antenatal voluntary counselling and testing programmes is an opportunity to identify serodiscordant couples and offer them help to maximise the chances of having a healthy child and avoid HIV transmission in either direction between the parents. It is also a vital opportunity to win the support of a woman's husband or partner for whatever options are available to them both, to protect their unborn child.

There is strong evidence that when a woman's partner has been tested for HIV OR is aware of her status, she is much more likely to make use of interventions such as nevirapine to prevent HIV transmission to her baby.

A programme of research in Zambia and Rwanda, reported in several presentations at the IAS meeting in Paris, has sought to enrol serodiscordant couples in a study and to follow them over a prolonged period, to evaluate risk factors for HIV transmission. Such studies are difficult - especially when both parents need to attend a clinic together, which may mean making difficult child care and work arrangements. Retention rates in studies of HIV prevention methods may therefore be particularly low. Nonetheless, it is argued that as much as 60% of HIV transmission in Africa - and the figure may even be higher in other regions - occurs within co-habiting couples.

The role of sexually transmitted infections is likely to be different within a couple, to its role in promoting HIV transmission among single people or outside a relationship.

## Treatment for genital herpes?

Recurrent genital herpes is likely to be more important in promoting HIV transmission within cohabiting couples, as opposed to newly acquired infections. The Rwanda-Zambia group have found some evidence to support this. The next stage of research in this area will be a clinical trial, funded by the Bill and Melinda Gates Foundation, to find out whether maintenance treatment with aciclovir to prevent recurrent herpes can reduce the rate of HIV transmission within relationships.

## Assistance with safer reproduction?

The Rwanda-Zambia group found that with active support, the HIV transmission rate among the HIV negative partners in the couples they recruited could be brought down from an annual rate of around 20% to less than 10%, but this remains shockingly high.

One obvious reason why the rate is high is that these are couples who for the most part wish to have children. One question this raises, is whether they could be given more help in identifying ways to achieve this without taking the risks they have clearly been taking.

In Europe, a number of centres have tried and are now offering a range of services to serodiscordant heterosexual couples who wish to have children. These include sperm washing and, more recently, in-vitro fertilisation of the woman's egg with her partner's sperm. However, such techniques are likely to remain unaffordable in most countries.

A strategy that has been used in the past in some western countries has been to apply the rhythm method, training women to find out when they are most fertile and restrict unprotected sex to a limited period each month. However, there have been no recent reports on this approach.

## Using ARVs to reduce transmission risk

In theory, the use of antiretrovirals might also reduce transmission risk.

Combination therapy that reduces the level of HIV in a man's semen should reduce the risk of HIV transmission to a woman. However, it cannot be assumed that suppressing the virus in the blood will suppress it in the semen too, or from the nucleus of cells in the semen. It is likely to depend on the particular ARV drugs used. Practical, let alone affordable, tests to confirm that the virus is suppressed remain to be developed, tested or adopted by communities.

Alternatively, ARV treatment for an HIV negative woman might be protective, but the risk of exposing an early foetus to potent drugs will always raise major concerns. A crucial method of collecting information on ARV safety for mothers and babies, would be the establishment of a register of children born to women on ARV treatment, as advocated by HATIP advisory panel member Dr Henry Barigye of Mulago in Uganda. If this includes information on women who actually conceived while undergoing treatment, including the precise regimen they were taking at the time as well as later in their pregnancy, this could help build up confidence to the point where the same drugs could be offered to HIV negative women.

## When a woman is HIV positive and pregnant

One of the clearest factors determining the risk of HIV being transmitted to a baby is the health - and particularly the CD4 count and viral load - of the mother. In this case, a CD4 count of around 350 is considered by the Ghent Group (see Sources and Further Information, below) to mark the divide between women who are more or less likely to transmit the virus to their babies.

An obvious implication is that if possible, women with a CD4 count of 350 or below should be treated with an effective ARV regimen of three or more drugs, even if the standard threshold for treatment in the community is 200 or below.

The practicality of doing this is being explored by a number of projects within the scheme known as MTCT Plus, on which HATIP will be reporting again, later this year. It is also discussed below, in relation to breastfeeding.

Transmission can happen before birth, during birth, or after birth, and different interventions are possible at each stage.

## HIV transmission across the placenta

While the baby is growing in the womb, HIV transmission is preventable by treating a woman during her pregnancy with a combination of ARVs that suppress her own viral load. It may also help to treat with one or more drugs that can cross the placenta and achieve levels in the foetus which should be high enough to prevent infection. This is a reason why the combination of nevirapine, AZT and 3TC is widely recommended for treatment during pregnancy, when a mother needs ARV treatment for her own health. However, there may be increased risks from nevirapine, in particular, when it is given as treatment to women with higher CD4 counts - in the form of relatively rare but very serious liver damage associated with an immune reaction.

Another potential prevention measure relates to malaria. A poster presentation at the recent Paris conference, from Cameroon, showed elegantly that the rate of mother-to-child transmission in a patient population given nevirapine at the time of birth, but heavily

exposed to malaria, rises and falls with the level of rainfall three months before the child's birth. The effect is highly significant and substantial - a fourfold increase in risk, comparing the wettest and driest months. Even before this study, however, placental malaria (normally seen only in first pregnancies, though this risk may extend to later pregnancies in HIV positive women) had been linked to increased HIV transmission risk. If antimalarial drug treatment during the pregnancy would be considered worthwhile anyway, then it may be doubly worthwhile for women who are HIV positive.

[Reference: Ayouba A et al. Mother-to-child transmission of HIV-1 in relation to season in Yaoundé, Cameroon. *Antiviral Therapy* 8 (Suppl. 1): abstract 1023. 2003.]

## Use of ARVs around the time of birth

The first study to show that any ARV could reduce mother to child transmission gave AZT monotherapy to mothers from an early stage during pregnancy and by injection during childbirth, followed by a course to the baby after the birth. This NIH/ANRS study, however, was immediately seen as difficult or impossible to apply in low-resource settings where women are commonly seen for antenatal care only very late in pregnancy. The regimen was therefore adapted into what is commonly known as the Thai short course AZT regimen where the woman starts treatment at week 36 in the pregnancy and the child is also treated briefly.

The HIVNET 012 regimen consists of one dose of nevirapine for the mother at the time of onset of labour, followed by one dose to the baby after the baby's birth. The trial, much discussed recently (see links to news reports in the second section of this newsletter, [here](#)) showed unexpected superiority for nevirapine over short-course AZT, sustained for two years in babies born to mothers who breast-fed them. It is unknown, since the trial was not placebo-controlled, whether the short-course AZT had any effect, and it does seem that adherence to the AZT course was less good than to the NVP.

If the mother's dose is taken at least one hour before the baby was born, then the baby's dose should be deferred for 72 hours to maximise the period of protection from the drug. If the drug was only taken in the final hour of labour, then the baby is treated immediately after birth.

Involving the woman's male partner, if possible, in the process has been shown to increase substantially the chance that she will remember to take the first dose. Familiarising the woman with the staff and setting where it is intended that she will give birth, so she does not have to disclose her HIV status to strangers at the time of birth, can greatly increase the chance that her baby will also receive the treatment intended.

More recent studies - in Africa and in Thailand - use the HIVNET 012 regimen in addition to short-course AZT or AZT/3TC. These have already shown extra benefit, compared to using either regimen on its own. The only question now being asked by the Thai study (which will be completed later in 2003) is whether the NVP given to the baby is of specific benefit.

## Mode of delivery

While elective caesarian section is not considered practical or safe for use in settings with limited resources, HIV has led to reviews of other obstetric practices.

In particular, early rupture of membranes has been linked to an increased risk of HIV transmission, so this practice is best avoided.

Similarly, there is advice against using instruments to assist delivery if at all possible, and to avoid the use of scalp electrodes.

### Infant feeding - breast or formula?

In settings where infant mortality is high and related to unsafe water supplies, many services continue to promote breast feeding for the babies of HIV positive women, with an emphasis on exclusive breast feeding where only breast milk and, where needed, medical treatments are given to the baby. In many other settings, the woman is encouraged and supported to choose for herself between exclusive breast feeding and exclusive formula feeding. In industrialised countries where formula feeding can be safely provided, its use is strongly advised and supported.

The best reason for breast feeding is because it is the natural and the best option for a healthy mother and baby. Other reasons for breastfeeding are likely to include economic necessity and general social pressure, which may be felt as severe stigma by women who choose not to breast feed.

Reasons for using formula are likely to include firstly, a determination not to transmit the virus to the baby and secondly, in some cases, not feeling well enough to breast feed or being unable to do so. Another reason can be for convenience, to allow shared child care and in some societies because breast feeding is stigmatised among some people.

As discussed in a recent aidsmap news story, from the Paris IAS conference (see reference at the end of this article), there is a growing body of evidence on the safety of formula feed - when carefully supported and monitored by well-trained healthcare staff - in urban settings with access to clean water supplies. However, advocates for breast feeding counter that the numbers in these studies are too small and follow-up not detailed or long enough to make a proper judgement of the risks of formula feed.

In Khayelitsha, Cape Town, South Africa, where women with HIV are provided with free formula for 9 months and the overwhelming majority have used it in preference to breast feeding, it is clear that mutual support among women attending the clinic is critical for their ability to make use of the formula. Some of the ways that women found to answer questions about why they were not breast feeding included, "having tuberculosis", "chronic diseases, such as hypertension", "bad milk", "having had a bad experience with a previous child", and "having had a caesarian section".

On the other hand, there is also a strong body of evidence that exclusive breast feeding is the best way of feeding babies, especially those born with HIV. This may be one of several strong reasons for seeking access to early diagnosis - preferably using a nucleic acid based test on dried blood spots, first taken shortly after a baby is born.

For mothers who may be HIV negative, there is no question that breast feeding is better than using formula. It is a major concern that in communities heavily affected by HIV, the culture of breast feeding among women may be lost and be very hard to recover. Mathematical modeling shows that if a mother's HIV status is unknown, then it is always better to breast feed than to give formula, yet mothers who are scared to find out their own status may be tempted to give formula to be on the safe side with counter-productive and possibly tragic results.

Another concern is that even when formula feed is provided free, it may not be made up correctly at full strength and with clean water; that it may also be shared between mothers or given to siblings so that the baby for whom it is intended is under-nourished.

There are also very serious problems for health care staff and for relationships between women and health services, when complex and changing advice is given by experts. In any event, women's decisions on breast feeding are often strongly influenced by female relatives. Reconciling the possible need for community-wide education about infant feeding options with preserving the confidentiality of women who are taking up those options will remain a challenge for as long as HIV status is stigmatised in any community.

### Safer breast milk

A low-tech approach to protecting infants is wet nursing - where one woman breast-feeds another's baby. Apart from the social challenge of recruiting women able and willing to do this, there is also an ethical challenge, that if the baby is HIV positive then the wet nurse herself may be at risk of HIV. Cases were reported from Ukraine, some years ago, where mothers did become HIV positive from their babies who had been infected through medical procedures. Plainly, this risk could be overcome if the breast milk was expressed first and fed to the baby from a clean cup. Questions of practicality, if this is to be applied for more than a very short period in a hospital setting, remain to be answered.

One approach that has been evaluated biologically in South Africa, but also remains to be translated into large-scale programmes, is the use of expressed breast milk, pasteurised to inactivate HIV using cheap and readily available equipment. An even simpler possibility is to store expressed breast milk for some hours in a covered container before feeding it to the baby. A related approach, which is also under discussion but remains to be proven safe, is the use of a chemical disinfectant to inactivate HIV in breastmilk. [A candidate substance was discussed in a Paris presentation.]

The challenge of all of these approaches is that they require a certain level of openness and acceptance of HIV status, at the very least within a household. The big advantage is that they might match the protection level of formula feed at a small fraction of the cost.

### Improved breast care

The health of the mother's breast - and especially the presence of mastitis or any kind of sore or ulcer - has a major impact on the risk of HIV transmission. Therefore, raising the level of health care to deal with these problems and advising mothers to avoid feeding the baby from a less healthy breast may be an effective way to reduce HIV transmission risks.

### Avoiding mixed feeding

There is evidence, though it is only from observational studies (rather than a randomised trial) that exclusive breast feeding - where the only food or drink that a baby receives comes from the mother's breast - is much less likely to transmit HIV than when any kind of mixed feeding is given.

Other evidence, going back well before HIV and AIDS were known about, shows that exclusive breast feeding is strongly protective against infant diarrhoea and pneumonia, which are two of the leading causes of death [for babies] in many countries.

Reasons given for mixed feeding have been given as conflicting advice from health care workers and also pressure from female relatives. Myths - for example, that babies need food or drink in addition to milk from an early age, or that a woman cannot produce enough milk to feed twins - must be countered.

## Protection while breastfeeding

The SIMBA study, reported on *aidsmap* (see Sources and Further Information, below) is best regarded as preliminary evidence for the efficacy of ARVs to prevent HIV transmission through breast milk, by giving ARVs to HIV negative babies. Among other things, this would clearly require the use of early nucleic-acid-based tests to make sure that monotherapy is not given to positive babies. It may also be desirable to target such treatment on babies born to the mothers who are most likely to transmit, which means mothers with low CD4 counts (which depends, of course, on having tests available).

An alternative strategy would be to treat the mother with ARVs to control the viral load in her milk as well as in her blood. The limitation of this approach, at present, is that too many mothers are only testing HIV positive relatively late in their pregnancy. This gives no time to go through the preparation that is needed for successful initiation of ARV treatment. Having to cope with initial side effects of treatment while pregnant is also an unattractive prospect. In addition, with most ARV regimens, 'nullundetectable' viral load often takes 8 weeks or more to achieve.

It has been estimated in South Africa that only around 20 to 25% of HIV positive pregnant women have a sufficiently low CD4 count (under 200) to qualify for immediate ARV treatment. There are proposals in some countries that for pregnant women the relevant threshold might be set higher, up to 350. These are the women most likely to transmit the virus through breast feeding and for whom the benefits of treatment, if it could be provided early enough, could be most effective. Unfortunately, a proportion might still be too unwell to breast feed in any case. Clearly, further research is needed.

Further research that is being done, and will be reported over the next year or two, is still exploring the use of micronutrients given to pregnant and breast feeding women and to their babies to improve their general health and resistance to disease. The possibility of iron and vitamin deficiencies does need to be taken seriously.

## Weaning

Where breast feeding is practiced, there is still some discussion about how long it should continue, to maximise any health benefit that can be gained for the baby and to avoid engorgement and related health problems for the mother. However, the general advice is not to continue breast feeding after six months. Using expressed breast milk, fed in a cup, can help to accustom a baby to the end of breast feeding. Contraception may also need to be discussed, to try and ensure that births are spaced as they would have been with more extended breast feeding, with benefits for the health of mother and child.

## Diagnosing HIV infection in babies

Identifying HIV negative babies - those who do not have HIV - is important because it can lift a great emotional and psychological burden from their parents or other carers. The earlier this happens, the better.

Identifying HIV positive babies may be of immediate benefit, if it happens early enough to allow a mother to be advised to breast feed her baby, since there is strong evidence that HIV positive babies are at greatly increased risk of diarrhoeal diseases and pneumonia when formula-fed in settings where this may be a problem.

Early diagnosis becomes even more important, when any service moves towards providing effective treatment options. These may include extended prophylaxis with co-trimoxazole (normally, from 6 weeks of age) as well as ARV therapy to keep babies out of hospital. As Dr Fareed Abdullah, who heads the HIV/AIDS programme of the Western Cape Province in South Africa explains, sick babies generate even more pressure than adults on health care services. Furthermore, in South Africa and possibly in other countries, providing such treatment free of charge is an effective anti-poverty measure, as many poor families will otherwise spend more than they can afford on treatment for a sick baby.

Unfortunately, the tests needed to prove a baby's HIV status by the age of 6 weeks are more expensive than those which can be used later, when the mother's antibodies have been lost by the child. However, there are very strong economic as well as humanitarian reasons for such tests to be used.

The most practical way of testing in most settings will be through using a PCR or viral load test on blood spot samples, collected from the baby onto paper, dried and then sent by mail or courier to a central laboratory. The cost can be brought down below US \$10 per test through methods that the South African National Health Laboratory Service, among others, are currently developing. There appears to be no significant loss of accuracy with dried blood samples compared to using fresh blood, so available alternatives such as heat-dissociated p24 antigen tests are probably not worth pursuing.

Antibody tests (either ELISA or Rapid Tests) cannot give accurate results for a baby until after the mother's antibodies have been lost, normally by 18 months. It might be possible to bring this date forwards by using oral fluid collection systems, although these may not be approved for paediatric use. A preliminary South African study lends some support to this idea, although negative results may still be down to the inadequacy of samples rather than the true absence of antibodies.

In many settings diagnosis for babies without signs of illness now depends on antibody tests. Even if other tests are used, this is likely to remain worthwhile as a final screening test, though for reasons already stated it is less than ideal for this to be the only test used.

## Sources and further information

In December 2002, the International AIDS Society sponsored an expert meeting in Ghent, Belgium, to review mother to child transmission. Presentations made at that meeting are available through a dedicated website, [www.ghentgroup.org](http://www.ghentgroup.org). This article is also based on information presented at the recent IAS Conference on HIV Pathogenesis and Treatment in Paris, France, and at the first national South African Conference on AIDS recently held in Durban (see news links, earlier in this report, for discussion of nevirapine for PMTCT).

Other recent related *aidsmap* coverage includes:  
Formula feed is 'medicine to prevent HIV'

<http://www.aidsmap.com/news/newsdisplay2.asp?newsId=2186>

With growing evidence that formula feed can be provided safely to babies born to HIV positive women in many African settings, health researchers are calling for formula feed to be provided free of charge to HIV positive women who need it, can use it safely, and currently do not have the resources to access it.

Treatment for babies can block HIV breast milk transmission

<http://www.aidsmap.com/news/newsdisplay2.asp?newsId=2187>

The preliminary results of the SIMBA study, reported as a late breaker at the 2nd IAS Conference on HIV Pathogenesis and Treatment in Paris, are that treating breast-fed babies with either nevirapine (NVP) or lamivudine (3TC) can greatly reduce, though not eliminate, breast milk transmission of HIV.

HAART effective at preventing illness and death in babies

<http://www.aidsmap.com/news/newsdisplay2.asp?newsId=2169>

The provision of HAART to HIV-positive babies in the first six months of life effectively prevents the early onset of HIV disease, according to French data presented to the Second International AIDS Society Conference on HIV Pathogenesis and Treatment in Paris on July 14th.

## about HATiP

A regular electronic newsletter for health care workers and community-based organisations on HIV treatment in resource-limited settings.

The newsletter is edited by Theo Smart (Cape Town) and Keith Alcorn, NAM's Senior Editor (London).

For further information please visit the HATIP section of [aidsmap.com](http://aidsmap.com)