

PREVENTING MOTHER-TO-CHILD TRANSMISSION OF HIV-1 IN SOUTH AFRICA

Recommendations for best practice

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1. INTRODUCTION

These guidelines for best practice for the prevention of mother-to-child transmission (MTCT) of HIV-1 are intended to provide health workers with information to enable an informed decision on the most appropriate management regimen for HIV-positive pregnant women. Resources and circumstances differ across different practice settings. These guidelines recognise the need for any management strategy to be adapted to the available infrastructure and finance and to the stage of pregnancy and clinical condition of the mother. The various strategies and treatment recommendations for HIV-positive pregnant women are constantly evolving. The guidelines will be updated as and when new information becomes available.

At present MTCT of HIV remains the main source of HIV infection in children younger than 10 years of age. The United Nations agencies estimate that 1 600 infected children are born daily worldwide, the overwhelming majority in the developing world, especially in sub-Saharan Africa.^{1,2} Since 1994 prevention programmes have been developed and implemented. The more complex regimens, consisting of prolonged antenatal antiretroviral treatment, combined with scheduled caesarean section at term and treatment of the child for 6 weeks, have decreased transmission rates from an average of 25 - 30% to less than 2%. A range of antiretroviral interventions has become standard practice in developed countries, with marked declines in transmission rates,³ while in resource-limited settings both financial and political factors have hindered

implementation of scientifically sound preventive measures.

As a continuum of reproductive care, MTCT prevention encompasses three aspects:

- primary prevention of HIV infection among parents to be
- prevention of unwanted pregnancies
- prevention of viral transmission from mother to child as part of routine antenatal care.

The use of antiretroviral regimens is integrated with changes in routine obstetric practice, expanding access to care and support for HIV-positive mothers and their families, treatment of opportunistic infections and accelerating access to HIV treatment.

2. PERINATAL TRANSMISSION OF HIV IN SOUTH AFRICA

Rates of HIV infection in pregnant women in South Africa continue to rise. In the anonymous antenatal survey conducted by the Department of Health in the year 2000, 24.5% of women attending public sector antenatal clinics were HIV-positive.⁴ The rates ranged from 36.2% in KwaZulu-Natal to 8.7% in the Western Cape. In the absence of any preventive intervention, which is the current status in most public sector facilities, at least one-third of these women will transmit HIV to their child. With an estimated 1 million deliveries per year in South Africa, this translates to almost a quarter of a million HIV-positive pregnant women each year, and upwards of 80 000 infected children.

3. MECHANISM AND TIMING OF PERINATAL TRANSMISSION

HIV can be transmitted from mother to infant in three ways:

- Direct infection may occur *in utero*, via **trans-placental** passage
- HIV can be transmitted to the infant **at the time of delivery** by ascending infection, by breaks in the skin and subsequent direct exposure to infected blood or secretions, or by ingestion of maternal blood or other fluids
- HIV can be transmitted **through breast-milk**.

The relative contribution of each of these routes will depend on the presence or duration of breast-feeding. In non-breast-fed infants, around one-third of transmission occurs in the intra-uterine period, and two-thirds during or close to delivery. Where infants are breast-fed, about half of the transmission occurs around the time of delivery, around one-third through breast-feeding and a smaller proportion *in utero*.^{5,6}

4. FACTORS INFLUENCING THE RISK OF HIV TRANSMISSION

The risk of MTCT is affected by a number of factors, maternal, fetal, viral and behavioural. These are summarised in Table I.

TABLE I. RISK FACTORS ASSOCIATED WITH INCREASED OVERALL RISK OF MOTHER-TO-CHILD TRANSMISSION⁶

STRONG EVIDENCE	LIMITED EVIDENCE
Maternal High viral load Viral characteristics Advanced disease Immune deficiency HIV infection acquired during pregnancy or breast-feeding period	Vitamin A deficiency Anaemia Sexually transmitted disease Chorio-amnionitis Frequent unprotected sexual intercourse Multiple sex partners Smoking Injecting drug use
Obstetric Vaginal delivery (compared with caesarean) Prolonged rupture of membranes	Invasive procedures Episiotomy
Infant Prematurity Breast-feeding	Lesions of skin and/or mucous membranes (oral thrush)

STRONG EVIDENCE

- **Maternal viral load.** Multiple studies have confirmed the importance of maternal viral load in

predicting the risk of HIV transmission to the infant. Transmission is markedly reduced where treatment has reduced viral load to very low levels. In a recent collaborative analysis from seven US and European studies, perinatal HIV-1 transmission occurred in only 1% of treated women with RNA virus loads below 1 000 copies/ml.^{7,8}

- **Maternal CD4 count.** Clinically or immunologically advanced HIV disease has been associated with an increased risk of transmission from mother to infant. Mayaux *et al.* noted a 43% transmission rate among women whose CD4 counts were less than 200 cells/ μ l versus 15% when the CD4 count was over 600 cells/ μ l.^{9,10}
- **Mode of delivery.** The European Collaborative Study demonstrated that elective caesarean section was associated with a decreased risk of perinatal transmission (relative risk 0.56).¹¹ In a meta-analysis of over 8 500 mother-infant pairs in prospective MTCT studies, the risk of perinatal transmission was decreased by 50% in women who underwent an elective caesarean section when compared with other modes of delivery.¹² In this analysis, transmission rates in the absence of antiretroviral therapy were 10.4% in the elective caesarean section group and 19% with other modes of delivery. Where women also received antiretroviral treatment, rates were 2% and 7.3% respectively.
- **Premature rupture of membranes.** This has been associated with a higher risk of perinatal HIV transmission, probably related to increased contact of the infant to infected cervicovaginal secretions. In the Women and Infants Transmission Study (WITS), the rate of perinatal transmission was 25% when the membranes ruptured more than 4 hours before delivery as opposed to 14% when the membranes ruptured 4 hours or less before delivery.¹³ This increased risk was independent of the mode of delivery.
- **Breast-feeding.** HIV transmission from breast-feeding is well documented and contributes significantly to HIV transmission in children in developing countries. Several studies have shown that breast-feeding is independently associated with an additional transmission risk of 14 - 18%.^{14,15}

MODERATE EVIDENCE

- **Clinical chorio-amnionitis.** Observational clinical studies and histopathological studies on placental tissue have suggested that both placental and placental membrane inflammation are more common in HIV-infected mothers, irrespective of their immune status. In several studies this was shown to be associated with increased rates of

vertical transmission, 37% in women with evidence of inflammation and immunocompromise, 25.5% in women with normal immune parameters, and 11.3% in women without evidence of inflammation.¹⁶

- **Low birth weight.** A low birth weight (< 2 500 g) and/or gestational age < 34 weeks or > 38 weeks have all been associated with an increased risk of perinatal HIV transmission.¹⁷
- **Twin delivery.** Birth order has also been associated with differing risks of infection. The majority of twins are concordant in terms of HIV infection. However, there is a significantly increased risk of HIV transmission to the first-born twin as opposed to the second-born twin. In one report vaginally delivered first-born twins had an infection rate of 35% compared with 15% in second-born twins, while the rates with caesarean section delivery were 16% and 8%, respectively.¹⁸

SOME EVIDENCE

- **Unprotected sex with HIV-infected partner.** Sexual intercourse without condom use is presumed to expose the woman to higher quantities and mixed subtypes of the virus, which in turn may increase the maternal viral load, leading to increased transmission to the child.^{19,20}
- **Maternal cigarette smoking.** Cigarette smoking has been associated with a statistically significant, 3-fold increase in the risk of perinatal transmission in women with low CD4 counts.²¹
- **Intravenous drug use.** Injecting drug use, especially in the second and third trimester of pregnancy, may increase the risk of transmission. In the WITS study, heroin use in combination with cocaine use after the first trimester carried a 4-fold increase in the risk of MTCT.²⁰
- **Sexually transmitted infections.** Concurrent infection with other sexually transmitted infections may increase the risk of transmission.²²

5. RECOMMENDATIONS FOR THE CLINICAL ASSESSMENT AND CARE OF HIV-INFECTED PREGNANT WOMEN

First visit. Besides a comprehensive history and physical examination, special attention should be paid to sexual risk behaviour, current HIV-related symptoms, medication and care.²² We recommend a thorough genital tract examination to exclude any specific pathology (Pap smear, exclusion of sexually transmitted diseases). Financial, emotional and social support structures need to be assessed, and referrals organised as needed.

Maternal follow-up visits. Once a month until 28 weeks, then fortnightly until 34 - 36 weeks, then weekly till delivery. More frequent visits may be needed for medical or obstetric complications.

Fetal monitoring. Ultrasound should be done as indicated in uncomplicated pregnancies, with a baseline scan at 16 - 18 weeks for accurate dating and screening for anomalies. An earlier scan is indicated if the patient requests termination of pregnancy or is unsure of dates. Mothers with CD4 counts < 200/ μ l, and with evidence of substance abuse, should be monitored with special attention, since adverse outcomes such as preterm delivery and low birth weight are common.²³

Laboratory tests. The level of laboratory investigation will depend upon available resources. The following represents an optimal list:

- Full blood count with CD4 count, and hepatitis B screen at initial visit and to be repeated 6-monthly.
- Routine antenatal blood screening, e.g. blood group and Rh screen, rubella titre, RPR.
- Pap smear.
- HIV-RNA (viral load) at initial visit, repeat of 36 weeks.
- STD screening - vaginal wet preparation, gonococcus, bacterial vaginosis, chlamydia - at first visit and repeated at 32 - 36 weeks, as they are associated with increased risk of vertical transmission.
- Hepatitis B and C screening is indicated, where available.

Invasive procedures. Invasive procedures such as amniocentesis, chorion villus sampling and cordocentesis, and external cephalic version, should be avoided, as they may be associated with increased risk of transmission.

Counselling on sexual practices. At each visit the importance of safe sexual practices throughout the pregnancy should be emphasised.

Intrapartum care.

- There is no current indication for routine caesarean section (CS) in HIV-infected women, provided the HIV-RNA level is low. Elective CS, done before labour and rupture of membranes, reduces the risk of perinatal transmission, independent of zidovudine (ZDV) use. CS should rather be considered for standard obstetric indications and in women unable to achieve optimal suppression of viral replication. In all cases, the risks and potential benefits should be discussed with the mother in the course of the

antenatal care. Prophylactic antibiotics should be administered for all CSs in HIV-positive mothers.

- Universal precautions, including eye protection for midwife/obstetrician.
- Induction of labour should not involve artificial rupture of membranes.
- Artificial rupture of membranes should be avoided as there is increased risk of transmission, especially if the duration is > 4 hours.
- Invasive fetal scalp electrode monitoring and blood sampling should be avoided
- There is no current recommendation on use of prophylactic antibiotics in vaginal deliveries.
- Episiotomy should be used only where there is a strong obstetric indication.

Postpartum care.

- Where possible, breast-feeding should be avoided.
- Education about available methods of contraception should have started during antenatal care. A plan for the provision of contraception should be discussed before discharge.
- Safer sex practices should be encouraged.
- Necessary referrals for continuing HIV care for the mother.
- Paediatric postpartum care should include HIV diagnosis.

Prophylaxis for opportunistic infections (OI).

Recommendations for OI prophylaxis are based on studies in non-pregnant individuals. However, the progression of HIV disease and OI does not seem to be affected by pregnancy. Therefore, standard criteria for OI prophylaxis should be applied in pregnancy. Drugs should be chosen taking into consideration available information concerning safety during pregnancy. Initiation of treatment may be delayed until after the first trimester, balancing maternal and fetal benefit and risk.

- *PCP*. Co-trimoxazole 1 double-strength orally daily. Theoretical concerns regarding teratogenic effects in the first trimester and neonatal kernicterus have not been confirmed.
- *Toxoplasma*. Co-trimoxazole 1 double strength orally daily.
- *Fungal infections, oral thrush and vulvovaginal candidiasis*. Avoid systemic azole preparations. Use topical agents on an intermittent or continuous basis.
- *Herpes simplex virus*. Aciclovir has shown no increased risk or pattern for birth defects, and may be considered in patients who have frequent, severe recurrences of genital HSV.

- *Tuberculosis*. INH 300 mg + pyridoxine 50 mg daily orally for 9 months. Alternative is twice-weekly INH 900 mg + pyridoxine 100 mg for 9 months. Note drug interactions between TB treatment (especially rifampicin) and some antiretrovirals.

6. RECOMMENDATIONS FOR ANTIRETROVIRAL TREATMENT IN PREGNANCY

Several antiretroviral regimens have been shown to be effective in reducing MTCT of HIV. These vary in complexity, duration and cost. All the regimens include an intrapartum element, with varying antepartum and postpartum components. The choice of antiretroviral regimen will depend upon the practicality and effectiveness of the intervention, the safety of the drugs, the risk of drug resistance and the cost compared with available resources.²⁴

In all cases the decision on treatment should consider the treatment needs of the mother balanced against the potential risks and benefits to the baby. Although there is increasing experience with the use of antiretrovirals in pregnancy, the safety data are not complete for many compounds. The use of antiretroviral combinations for maternal treatment should be considered in the light of this. Table II lists the current state of knowledge on the safety of these drugs in pregnancy.

In settings where access to antiretroviral treatment is available, some women will be aware of their HIV status and on therapy, others will be known to be HIV-infected but not yet on treatment, and many more will be diagnosed for the first time at some stage of pregnancy. Treatment options vary for each of these groups. Several possible scenarios are given below:

KNOWN HIV-INFECTED WOMEN, WHO ARE RECEIVING ANTIRETROVIRAL THERAPY

Women who are already on antiretroviral therapy for their own health should continue on the therapeutic regimen during pregnancy, with the following considerations.

- Few data are available on the safety of antiretrovirals during the period of organogenesis in the first trimester. One option to reduce the risk would be to stop therapy for the duration of the first trimester. This decision should be taken in consultation with the patient, weighing the risks and benefits for both fetus and mother. If treatment is suspended, all drugs should be discontinued simultaneously.

TABLE II. SAFETY OF ANTIRETROVIRAL AGENTS IN PREGNANCY^{22,31}

ANTIRETROVIRAL DRUG	FDA PREGNANCY CATEGORY*	PLACENTAL PASSAGE, NEWBORN/MATERNAL DRUG RATIO	LONG-TERM ANIMAL CARCINOGENICITY STUDIES	RODENT TERATOGEN
Zidovudine (ZDV)	C	Yes (human) (0.85)	Positive (rodent, vaginal tumours)	Positive (near lethal dose)
Zalcitabine (ddC)	C	Yes (rhesus) (0.3 - 0.50)	Positive (rodent, thymic lymphomas)	Positive (hydrocephalus at high dose)
Didanosine (ddI)	B	Yes (human) (0.5)	Negative (no tumours, lifetime rodent study)	Negative
Stavudine (d4T)	C	Yes (human)	Not completed	Negative
Lamivudine (3TC)	C	Yes (human) (~1.0)	Not completed	Positive (anasarca and skeletal malformations at 1 000 mg/kg during osteogenesis)
Abacavir (ABC)	C	Yes (rats)	Not completed	Negative
Saquinavir (SQV)	B	Unknown	Not completed	Negative (but extra ribs in rats)
Indinavir (IDV)	C	Yes (rats)	Not completed	Negative (but cryorchidism in rats)
Ritonavir (RTV)	B	Yes (rats)	Not completed	Negative
Nelfinavir (NFV)	B	Unknown	Not completed	Negative
Amprenavir	C	Unknown	Not completed	Positive (thymic elongation, incomplete ossification of bones, low body weight)
Nevirapine (NVP)	C	Yes (human) (~1.0)	Not completed	Negative
Delaviridine (DLV)	C	Yes (rats)	Not completed	Ventricular septal defect
Efavirenz (EFV)	C	Yes (cynomolgus monkeys, rats, rabbits) (~1.0)	Not completed	Anencephaly; anophthalmia; microphthalmia (cynomolgus monkeys)

*FDA categories are: B — animal reproduction studies fail to demonstrate a risk to the fetus and adequate, well controlled studies of pregnant women have been conducted; C — safety in human pregnancy has not been determined, animal studies are either positive for fetal risks or have not been conducted, and the drug should not be used unless the potential benefits outweigh the potential risk to the fetus.

- There is concern regarding the safety of long-term combination use of didanosine (ddl) and stavudine (d4T) together for the duration of pregnancy. This combination has been implicated in idiopathic lactic acidosis and hepatomegaly with steatosis. **Women falling pregnant while on d4T and or ddl must discontinue these drugs immediately and change to another antiretroviral regimen.**
- There is evidence from animal studies of a potential teratogenic effect of efavirenz in early pregnancy. **Women who are on efavirenz-containing regimens should be changed to another combination regimen in pregnancy.**
- As there is very little information on the use and efficacy of antiretrovirals other than ZDV-containing regimens, consideration should be given to adding or substituting ZDV when the pre-existing therapeutic regimen does not contain it. However, ZDV must never be added to a combination containing d4T.
- Irrespective of the treatment regimen, the intrapartum and postpartum ZDV component of the PACTG 076 regimen should be instituted.

HIV-INFECTED WOMEN WITHOUT PRIOR ANTIRETROVIRAL TREATMENT, WHO PRESENT EARLY FOR ANTENATAL CARE

- The PACTG 076 regimen²⁵ can be started in all women who test positive in the first or second trimester, irrespective of immune status and viral load. It should be commenced between 14 and 34 weeks' gestation. It consists of ZDV, given orally antenatally and intravenously intrapartum to the mother, and postpartum to the baby for 6 weeks.
- When the criteria for commencement of highly active antiretroviral treatment (HAART) are present, triple therapy can be started. The current South African guidelines suggest commencing therapy when the CD4 count is below 350/ μ l and/or the viral load greater than 30 000 copies/ml. Initial treatment should be commenced with a ZDV-containing regimen. Regimens combining ZDV with d4T or ddl with d4T should not be used in pregnancy, because of potentially serious adverse effects on the mother.
- Therapy can be postponed until after the first trimester.

The PACTG 076 regimen. The use of ZDV in this regimen reduced the transmission of HIV from mother to infant by 68% (ZDV transmission rate 8%, placebo transmission rate 26%). Dosages are set out in Table III.

TABLE III. ZDV DOSAGES IN THE PACTG 076 REGIMEN

Antepartum: commence ZDV between 14 and weeks' gestation	ZDV 300 mg bd or ZDV 200 mg tds or ZDV 100 mg 5 x d
During labour	IVI XDV: loading infusion of 2 mg/kg for one hour followed by continuous infusion of 1 mg/kg h until delivery
Infant: initiate 8 - 12 hours after birth	ZDV 2 mg/kg every 6 hours for 6 weeks

HIV-infected women, without prior antiretroviral therapy, who present late (after 34 weeks) for antenatal care and /or in resource poor settings

Where an HIV-infected woman is identified late in pregnancy, there are several 'short course' antiretroviral regimens that have been shown to reduce transmission by 30 - 50%.²⁶ The choice of regimen will depend upon local availability and decisions on infant feeding.

The short course regimens shown to be effective in randomised controlled trials are shown in Table IV.

HIV-infected women who have received a sub-optimal antepartum regimen

The minimum duration of antepartum treatment necessary for protection in antiretroviral prophylaxis regimens that include an antepartum component is not defined. However, it is likely that a major mechanism for effective antepartum prophylaxis is reduction in maternal viral load, which probably requires at least 1 - 2 weeks of treatment. With relatively late antenatal clinic attendance and the uncertain timing of labour, the duration of antepartum treatment may be shorter than this for some women. In these cases, additional treatment may be recommended.²⁴

- Prophylaxis with 6 weeks of ZDV to the infant, intrapartum/postpartum ZDV + 3TC, or the two-dose nevirapine regimen may be considered for women receiving prophylactic regimens that include an antepartum component and who have received less than 2 weeks of ZDV antepartum treatment.

Use of antiretrovirals in treatment-naïve women who present at the time of labour

Where an HIV-infected woman is identified only at the time of labour, one of the intrapartum and postpartum regimens with either nevirapine or ZDV should be used.

- Single dose nevirapine (200 mg orally) at onset of labour and a single dose of nevirapine (2 mg/kg orally) to the infant at 48 - 72 hours (the HIVNET 012 regimen²⁷) or

TABLE IV. SHORT COURSE ANTIRETROVIRAL REGIMENS FOR THE PREVENTION OF MTCT OF HIV

TRIAL	CITATION	REGIMEN	TRANSMISSION	% REDUCTION
CDC-Thai regimen	<i>Lancet</i> 1999; 353: 773	AP: oral ZDV 300 mg bd from 36 weeks	ZDV – 9% Placebo – 19%	51%
		IP: oral ZDV 300 mg 3-hourly		
		PP: formula feeding		
Ivory Coast	<i>Lancet</i> 1999; 353: 781	AP: oral ZDV 300 mg bd from 36 weeks	ZDV – 16% Placebo – 25%	37%
		IP: oral ZDV 300 mg 3-hourly		
		PP: breast-feeding		
DITRAME	<i>Lancet</i> 1999; 353: 786	AP: oral ZDV 300 mg bd from 36 - 38 weeks	ZDV – 18% Placebo – 28%	38% breast-feeding population
		IP: oral ZDV 600 mg stat		
		PP: Mother oral ZDV 300 mg bd for 7 days		
PETRA arm A	6th Conference on Retroviruses and opportunistic infection, 1999, Abstract S-7	AP: oral ZDV 300 mg bd + 3TC 150 mg bd from 36 weeks	Arm A – 9% Placebo – 17%	42% at 6 weeks, breast-feeding population
		IP: oral ZDV 600 mg stat + 300 mg 3-hourly 3TC 150 mg 12-hourly		
		PP mother: oral ZDV 300 mg bd + 3TC 150 mg bd for 7 days		
		PP baby: oral ZDV 0.4 ml/kg 12-hourly + 3TC 0.2 ml/kg		
PETRA arm B		IP: oral ZDV 600 mg stat + 300 mg 3-hourly 3TC 150 mg 12-hourly	Arm B – 11% Placebo – 17%	37% at 6 weeks, breast-feeding population
		PP mother: oral ZDV 300 mg bd + 3TC 150 mg bd for 7 days		
		PP baby: oral ZDV 0.4 ml/kg 12-hourly 3TC 0.2 ml/kg		
Lallemant short-short	XIII AIDS Conference, July 2000, Durban, SA (LbOr03)	AP: oral ZDV 300 mg bd from 35 weeks	Transmission rate 10.6%	
		IP: oral ZDV 300 mg 3-hourly		

		PP baby: oral ZDV 0.4 ml bd for 3 days		
Lallemant short-long	XIII AIDS Conference, July 2000, Durban, SA (LbOr03)	AP: oral ZDV 300 mg bd from 35 weeks	Transmission rate 8.4%	
		IP: oral ZDV 300 mg 3-hourly		
		PP baby: oral ZDV 0.4 ml bd for 6 weeks		
Lallemant long-short	XIII AIDS Conference, July 2000, Durban, SA (LbOr03)	AP: oral ZDV 300 mg bd from 28 weeks	Transmission rate 5.7%	
		IP: oral ZDV 300 mg 3-hourly		
		PP baby: oral ZDV 0.4 ml bd for 3 days		
Lallemant Long-long	XIII AIDS Conference, July 2000, Durban, SA (LbOr03)	AP: oral ZDV 300 mg bd from 28 weeks	Transmission rate 6.7%	
		IP: oral ZDV 300 mg 3-hourly		
		PP baby: oral ZDV 0.4 ml bd for 6 weeks		
HIVNET 012	<i>Lancet</i> 1999; 354: 795	IP: oral nevirapine 200 mg po stat	13.1%	
		PP: baby: oral nevirapine 2 mg/kg within 72 hours		
SAINT (South African Intrapartum Nevirapine Trial)	XIII AIDS Conference, July 2000, Durban, SA (LBOR1)	IP: oral nevirapine 200 mg po stat	14%	
		PP mother: oral nevirapine 200 mg before discharge		
		PP baby: oral nevirapine 2 mg/kg/po within 24 - 72 hours		
AP = antepartum; IP = intrapartum; PP = postpartum.				

- Oral ZDV/3TC during labour and then 1 week of therapy with ZDV/3TC for the infant (the Petra B regimen²⁸) or
- ZDV intravenously or orally during delivery followed by ZDV orally to the infant for 6 weeks (a partial PACTG 076 regimen).^{9,29}

Use of antiretrovirals in infants born to mothers who received no antiretroviral therapy during pregnancy and delivery

Where the mother's HIV status is not known until after delivery, treatment should be provided to the child as soon as possible. There has been little research in this area, and the only information available on efficacy comes from a retrospective study of infants who received the 6-week treatment regimen with ZDV.³⁰ A trial is in progress comparing this to a nevirapine dose to the infant.

- Treat the infant with the 6-week course of ZDV.

7. INFANT FEEDING

Breast-feeding carries a considerable additional risk of HIV infection. Unfortunately replacement feeding may not be a feasible or acceptable option for some HIV-positive mothers. Current international guidelines recommend:²⁴

- When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breast-feeding by HIV-infected mothers is recommended.
- Otherwise, *exclusive* breast-feeding is recommended during the first months of life.
- To minimise HIV transmission risk, breast-feeding should be discontinued as soon as feasible, taking into account local circumstances, the individual woman's situation and the risks of replacement feeding (including infections other than HIV and malnutrition).

8. DIAGNOSIS OF PERINATALLY ACQUIRED HIV INFECTION

The diagnosis of HIV infection in children should form part of the package of care for HIV-infected women and their offspring. Diagnostic techniques are more complex in children owing to the persistence of maternal antibodies up to 15 months of age.

RECOMMENDED TEST METHODS

Infants < 1 year of age who are not breast-feeding:

The polymerase chain reaction (PCR) for detecting the DNA proviral form of the virus integrated into the genome of peripheral blood cells is the established laboratory investigation of choice for the diagnosis of perinatally acquired HIV-1 infection. Some laboratories have the capacity to detect RNA in the plasma of patients utilising a reverse transcription PCR (RT-PCR), but this test, which may have some advantages over DNA PCR, may not be routinely available. Quantitative methods (i.e. measuring viral load), should not be utilised in place of qualitative diagnostic methodologies. Comprehensive guidelines for the diagnosis of perinatally acquired HIV infection will be published in the next issue of this *Journal*.

Infants > 1 year of age and 3 months after breast-feeding has ceased: HIV-1 ELISA antibody test. A positive result must be confirmed at 15 months of age. Maternal antibodies disappear between 9 and 18 months, so a negative antibody test at 9 months of age or beyond where breast-feeding has ceased suggests absence of perinatally acquired HIV infection.

REFERENCES

1. UNAIDS. *Report on the Global HIV/AIDS Epidemic – June 2000*. Geneva: UNAIDS 2000.
2. UNAIDS. *Mother-to-Child Transmission (Technical Update)*. Geneva: UNAIDS, 2000.
3. Cooper ER, Charurat M, Burns DN, Blattner W, Hoff R. Trends in antiretroviral therapy and mother-infant transmission of HIV. The Women and Infants Transmission Study Group. *J Acquir Immune Defic Syndr* 2000; **24**(1):45-47.
4. *National HIV and Syphilis Sero-prevalence Survey of Women Attending Public Antenatal Clinics in South Africa*. Pretoria: Department of Health, 2000.
5. De Cock KM, Fowler MG, Mercier E, et al. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. *JAMA* 2000; **283**: 1175-1182.
6. UNAIDS. *HIV and Infant Feeding: A Review of HIV Transmission through Breastfeeding*. Jointly issued by UNICEF, UNAIDS and WHO. (WHO/FRH/NUT/CHD 98.3, UNAIDS 98.5, UNICEF/PD/NUT(J) 98-3). Geneva: UNAIDS, 1998.
7. Ioannidis JP, Contopoulos-Ioannidis DG. Maternal viral load and the risk of perinatal transmission of HIV-1. *N Engl J Med* 1999; **341**: 1698-1700.
8. 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**: 539-545.
9. Bhadrakom C, Simonds RJ, Mei JV, et al. Oral zidovudine during labor to prevent perinatal HIV transmission, Bangkok: tolerance and zidovudine concentration in cord blood. Bangkok Collaborative Perinatal HIV Transmission Study Group. *AIDS* 2000; **14**: 509-516.
10. Mayaux MJ, Blanch S, Rouzioux C, et al. Maternal factors associated with perinatal HIV-1 transmission. French Cohort study: 7 years of follow-up observation. The Paediatric HIV Infection Study Group. *J Acquir Immune Defic Syndr Hum Retroviral* 1995; **8** (2): 188-194.
11. Caesarean section and risk of vertical transmission of HIV-1 infection. The European Collaborative Study. *Lancet* 1994; **343**: 1464-1467.
12. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1—a meta-analysis of 15 prospective cohort studies. The International Perinatal HIV Group. *N Engl J Med* 1999; **340**: 977-987.
13. Minkoff H, Burns DN, Landesman S, et al. The relationship of the duration of ruptured membranes to vertical transmission of human immunodeficiency virus. *Am J Obstet Gynecol* 1995; **173**: 585-589.
14. Dunn D, Newell ML. Mother-to-child transmission of human immunodeficiency virus type 1 in Nairobi. *J Infect Dis* 1995; **172**: 1418-1419.
15. Newell ML. Breastfeeding and HIV infection: a global perspective. *Hosp Med* 1999; **60**: 778-779.
16. Wabwire-Mangen F, Gray RH, Mmoro FA, et al. Placental membrane inflammation and risks of maternal-to-child transmission of HIV-1 in Uganda. *J Acquir Immune Defic Syndr Hum Retroviral* 1999; **22**: 379-385.
17. Newell ML. Mechanisms and timing of mother-to-child transmission of HIV-1. *AIDS* 1998; **12**: 831-837.
18. Duliege AM, Amos CI, Felton S, Biggar RJ, Goedert JJ. Birth order, delivery route, and concordance in the transmission of human immunodeficiency virus type 1 from mothers to twins. International Registry of HIV-Exposed Twins. *J Pediatr* 1995; **126**: 625-632.
19. Bulterys M, Chao A, Dushimimana A, et al. Multiple sexual partners and mother-to-child transmission of HIV-1. *AIDS* 1993; **7**: 1639-1645.
20. Bulterys M, Landesman S, Burns DN, Rubinstein A, Goedert JJ. Sexual behavior and injection drug use during pregnancy and vertical transmission of HIV-1. *J Acquir Immune Defic Syndr Hum Retroviral* 1997; **15**: 76-82.
21. Burns DN, Landesman S, Muenz LR, et al. Cigarette smoking, premature rupture of membranes, and vertical transmission of HIV-1 among women with low CD4+ levels. *J Acquir Immune Defic Syndr Hum Retroviral* 1994; **7**: 718-726.
22. McIntyre JA. *HIV in Pregnancy: a Review* (Occasional Paper No. 2). Geneva: World Health Organisation, 1999.
23. Lambert JS, Watts DH, Mofenson L, et al. Risk factors for preterm birth, low birth weight, and intrauterine growth retardation in infants born to HIV-infected pregnant women receiving zidovudine. Pediatric AIDS Clinical Trials Group 185 Team. *AIDS* 2000; **14**(10):1389-1399.
24. World Health Organisation. *New Data on the Prevention of Mother-to-Child Transmission of HIV and their Policy Implications: Conclusions and Recommendations* (WHO Technical Consultation on Behalf of the UNFPA/UNICEF/WHO/UNAIDS Inter-Agency Task Team on Mother-to-Child Transmission of HIV). Geneva: World Health Organisation, 2001.
25. 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.
26. Mofenson LM, McIntyre JA. Advances and research directions in the prevention of mother-to-child HIV-1 transmission. *Lancet* 2000; **355**: 2237-2244.
27. Guay LA, Musoke P, Fleming T, et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *Lancet* 1999; **354**: 795-802.
28. Saba J, PETRA Study Group. Current status of the PETRA Study. 2nd Conference on Global Strategies for the Prevention of HIV Transmission from Mothers to Infants, Montreal, Quebec, 2 September 1999.
29. US Public Health Service. Public Health Service Task Force 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. Revised January 24 2001. <http://www.hivatis.org> (accessed 1 April 2001). 2001.
30. Wade NA, Birkhead GS, Warren BL, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med* 1996; **339**: 1409-1414.
31. US Public Health Service. Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy. <http://hivatis.org/trtdgins.html#Perinatal> (Accessed 1 April 2001). 2001.