

HIV and Infant Feeding – ICAP Approach to Improving HIV-free Survival



ICAP

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Care and Treatment Programs

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Glossary of terms

Complementary feeding- the addition of any food, whether manufactured or locally prepared, to breast milk or formula when breast milk/formula becomes insufficient to satisfy all the nutritional requirements of the infant. This usually occurs around 6 months of age.

Early cessation of breastfeeding- the mother stops all breastfeeding including suckling before she would have otherwise done. This can occur as early as the first weeks of life and anytime before 12 months of age.

Exclusive breastfeeding (EBF)-infant receives only breast milk and no other liquids or solids including water, tea, and commercial formula, except prescribed medications such as vitamins, mineral supplements or medicine.

Formula feeding (FF)- use of commercial infant feeding which is formulated industrially in accordance with applicable Codex Alimentarius standards to satisfy the nutritional requirements of the first months of life until the introduction of complementary foods.

HAART- highly active antiretroviral therapy

HIV-free survival- child is alive and does NOT acquire HIV infection.

Home-modified animal milk- a breast milk substitute prepared at home from fresh or processed animal milk by diluting with water and adding sugar and micronutrients.

Mixed feeding or partial breastfeeding- feeding breast milk and other liquids and or solids prior to six months of age.

MTCT-mother-to-child-transmission (of HIV infection).

PMTCT- prevention of mother-to-child-transmission (of HIV infection).

Postnatal transmission (PNT) – mother-to-child-transmission of HIV occurring after delivery through breastfeeding.

Replacement feedings- feeding infants with commercial infant formula or home modified animal milk instead of breastfeeding until the child is fully fed on family food.

Weaning-period when the child is transitioned from breastfeeding to a diet completely devoid of any breast milk.

WHO-World Health Organization.

Introduction

Breastfeeding is the optimal food for all infants. It provides complete nutrition for infants and protects against a wide array of infectious and non infectious diseases.¹ Breastfeeding can contribute markedly to improved infant health and child survival.² Breastfed infants have decreased morbidity and mortality when compared to non breastfed infants. It is estimated that exclusive breastfeeding in the first 6 months of life can prevent 13% of under-5 mortality in the 42 countries which contributed 90% of child deaths world wide in 2000. This makes it the single most important contribution to improved child health and survival.³ Even in well developed countries breastfeeding has advantages when compared to formula feeding. In a large study of 15,890 children in the UK, infants who were breastfed had fewer hospitalizations for diarrhea and respiratory illnesses compared to non breastfed children.⁴ It was estimated that 53% of all hospitalizations for diarrhea and 27% for lower respiratory tract infections could be prevented in the UK each month if infants were exclusively breastfed. In the US breastfeeding has been associated with a decreased incidence of otitis media, gastroenteritis, and lower rates of obesity and asthma.⁵

However, breastfeeding poses a substantial risk for MTCT of HIV. The risk of acquiring HIV during breastfeeding is approximately 10-12%. Therefore, for infants who escape infection during pregnancy and delivery, 1 in 8 will become infected during breastfeeding. Overall, breastfeeding accounts for 40% of all MTCT transmission.⁶ In other words, of 100 infants born to HIV infected mothers, between 25 and 40 are likely to acquire HIV infection and 10-16 infections can be attributed to breastfeeding in the absence of any interventions. The risk of drinking 1 liter of breast milk is equivalent to the risk of one episode of unprotected sex.⁷ In Europe and the US, the rate of perinatal transmission of HIV has been reduced to < 2% due to use of combination antiretrovirals, obstetrical interventions and complete avoidance of all breastfeeding. However, apart from highly developed countries where deaths throughout infancy are low, i.e. less than 10 births per 1000 live births, replacement feeding often proves to be unsafe. In resource-limited settings where the risk of death during infancy due to malnutrition and infectious disease is high, i.e. 50 to greater than 100 per 1000 live births, sustainable alternatives to breastfeeding have been difficult to implement. The reasons are varied and complex and involve challenging logistical and cultural factors including lack of sanitation, safe water, poor health infrastructure for treating and preventing common causes of infant morbidity and mortality, expense, cultural practices and norms. Balancing the risks of possible HIV transmission against the risks of not breastfeeding remains a major public health dilemma for programs providing PMTCT and HIV care and treatment services to children and their families in resource-limited settings.

In 2000 WHO released guidelines on infant feeding in the context of HIV. At the time there were very few data documenting the benefits of breastfeeding for HIV-exposed and infected infants or the risks of replacement feeding and early weaning. Since that time several studies have examined these important issues. In October of 2006 WHO convened a meeting to review the latest data and make new recommendations on infant feeding in the context of HIV infection. This report

summarizes these new data, reviews new WHO guidance⁸ and outlines ICAP’s approach to improving HIV-free survival in infants born to HIV–infected women.

Risk factors for postnatal transmission of HIV

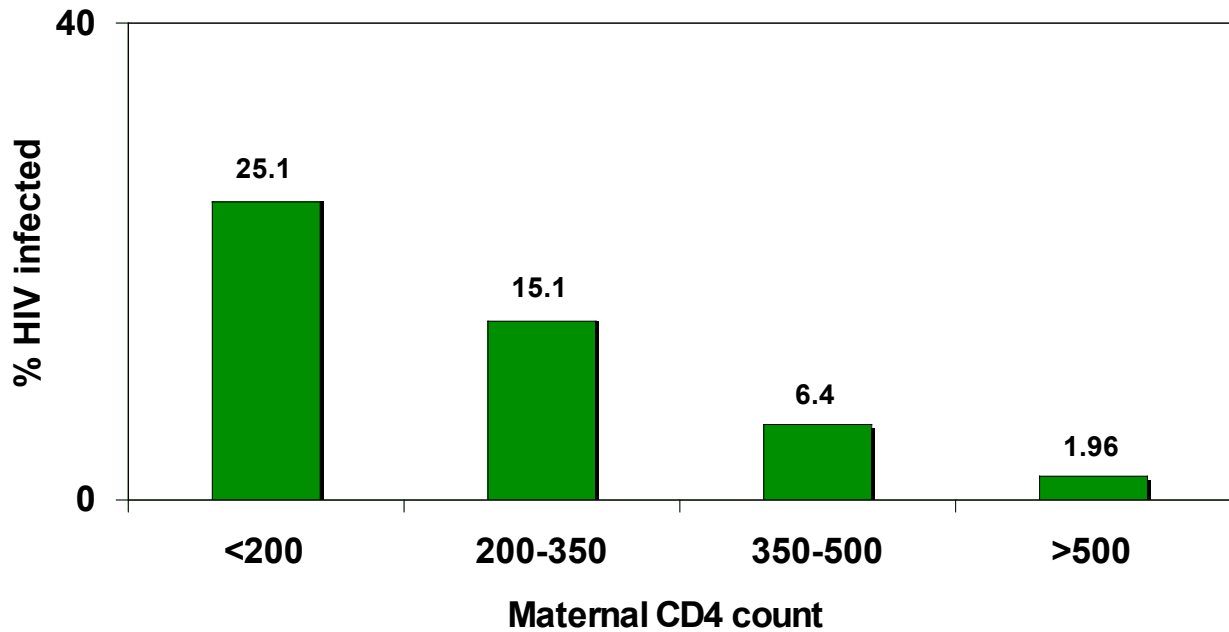
Several risk factors have been identified that influence the risk of postnatal HIV transmission (Table 1). Advanced maternal disease and increased maternal RNA viral load in plasma and breast milk are strongly associated with increased risk of transmission through breastfeeding.^{9, 10} Mothers with low CD4 counts are more likely to transmit infection to their infants postnatally. In the Ditrane Study, pregnant HIV-infected women in Côte d’Ivoire who met criteria for HAART (CD4 < 200) had a 2-4 fold greater risk of MTCT even when receiving short course ARV prophylaxis compared to those who were not HAART eligible.¹¹ In the Zambia Exclusive Breastfeeding Study, which is described in detail later, mothers with CD4 < 200 had a 2-5 fold increased risk of postnatal transmission compared to those with CD4 > 500 (Figure 1).¹² Acute maternal infection during pregnancy or lactation also increases the risk of postnatal transmission.^{13,14} Infant feeding patterns influence transmission: mixed feeding and prolonged breastfeeding can lead to higher risk of PNT. Breast problems such as cracked nipples, breast abscesses, clinical and subclinical mastitis have been shown to increase postnatal transmission.^{13,15,16} Other factors associated with PNT include prematurity as well as lesions in the infant’s mouth such as oral thrush.

Between 50-80% of postnatal transmission of HIV occurs in infants born to women with advanced disease (CD4 < 350).^{11, 12, 30, 33}

Table 1 Risk Factors for Postnatal Transmission of HIV Infection

Risk factors for <i>postnatal transmission</i> of HIV	
<u>Mother</u>	<u>Infant</u>
Advanced disease (low CD4 and high viral load)	Mixed feeding (breast milk with water, formula other liquids or solids)
Breast problems (cracked nipples, mastitis, breast abscess)	Breastfeeding duration
Recently acquired HIV infection	Oral lesions (mouth ulcers, thrush)
	Low birth weight

Figure 1 Rate of Postnatal HIV Infection by Maternal Baseline CD4 Count: Zambia Exclusive Breastfeeding Study (N=958)



Timing of HIV transmission postnatally

Postnatal transmission can occur anytime during breastfeeding; in the first days and weeks after delivery through colostrum/early milk and throughout all the later months through mature milk until all breast milk exposure ends. Currently, it is not possible to distinguish in a breastfed child whether an infection that is not detectable by PCR at birth but becomes detectable by PCR around 4-6 weeks was acquired during the intrapartum period or whether it was acquired through colostrum or early breastfeeding. Some studies have shown that colostrum and early milk have higher concentrations than later milk of cell-associated and cell-free virus.¹⁷ However, this is difficult to interpret since concentrations of other soluble immune factors are also higher in early milk, and the volume of milk consumed tends to increase as the child grows. Studies from Zimbabwe, Malawi and Tanzania have suggested that the risk of transmission per month is either constant or declines as the child gets older.^{18,19} However, all studies agree that there continues to be some risk of transmission throughout lactation. Therefore, cumulatively, the longer the child is breastfed the higher the transmission rate. A meta analysis of 9 studies performed in sub-Saharan Africa, Breastfeeding and HIV International Transmission Study Group (BHITS) that included 4085 infants born to HIV-infected women reported the cumulative probability of postnatal transmission at 18 months to be 9.3%. The estimated rate of postnatal transmission was constant at 0.8% per month or 8.9 transmissions per 100 child years of breastfeeding.²⁰ In other words if there are 1000 infants born to HIV-infected mothers, about 8 of them will acquire HIV through breastfeeding each month.

The rest of this update will review different approaches that have been suggested to decrease postnatal transmission. It will focus on new data, experiences in the field, and finally will outline ICAP's approach to reducing HIV-free survival.

Is avoidance of breastfeeding to decrease risk of MTCT safe?

Complete avoidance of breastfeeding is the only way to completely prevent postnatal MTCT. In resource rich countries HIV-infected mothers are advised not to breastfeed their infants. In the first randomized controlled trial in Africa to quantify the risks of postnatal transmission, 401 HIV-infected Kenyan women were randomized to breastfeed or formula feed their infants. The study was done in an urban setting, where all the mothers were provided with free formula, had access to clean running water in their homes, and their infants were closely monitored for intercurrent illness.²¹ None of the mothers or infants received any antiretrovirals (ARVs) for PMTCT. Transmission at 24 months was 20.5% in the formula feeding group compared to 36.7% in the breastfeeding group (efficacy of 44%). There was no significant difference in the overall two year mortality between the breastfed and formula fed infants (24 versus 20 percent) and the incidence of diarrhea was the same in both groups (149 versus 155 per 100 person years in the breastfed compared to the formula fed infants). However, there was an increased incidence of diarrhea and dehydration in the formula fed infants during the first 3 months of life.

Two small demonstration projects in Mozambique and Rwanda have also successfully implemented formula feeding for HIV-exposed infants without increased morbidity.²² However, it is difficult and potentially dangerous to generalize results from these projects to large scale programs in settings where infant mortality rates are high, risk of infant death from not breastfeeding is substantial, and most women do not have access to safe water supply, good sanitation and preventive health services. The MASHI Trial in Botswana randomized 1200 women to breastfeeding (BF) plus prolonged infant prophylaxis (AZT for 6 months) or formula feeding (FF) plus short course prophylaxis (AZT for 1 month). Although infants who were formula fed were less likely to acquire HIV infection, early mortality (at 7 months of age) was significantly higher in the formula fed group: 9.5% compared to 4.9% in the breastfed infants.²³ The main causes of morbidity and mortality were malnutrition, diarrheal diseases and pneumonia. At 18 months there were more HIV-infected children in the BF group but more formula fed infants died thus HIV-free survival was the same at 18 months regardless of feeding method (14.2% in the FF compared to 15.6% in the BF group). Effects of early cessation on maternal health included increased risk of mastitis and breast abscess and loss of lactational amenorrhea.

The recent diarrheal disease outbreak in Botswana underscores the importance of carefully balancing the risk of HIV-transmission via breastfeeding against the risk of infant mortality from not breastfeeding; pitfalls of decision making that focuses only on the individual circumstances, not on the community health infrastructure and the critical importance of local factors. In Botswana, government provides free infant formula for 12 months to all infants born to HIV-infected women as part of the national PMTCT program. Between November 2005 and February 2006, heavy rains contaminated the public water supply resulting in an outbreak of diarrheal illness. A case controlled study compared children in the emergency room for diarrhea with those who had other illnesses. After adjusting for age and socioeconomic status, not breastfeeding was

associated with an 8.5 fold risk of mortality and formula feeding was the major risk factor for diarrhea (adjusted OR of 50).²⁴ Of note 90% of the women fed their infants formula; half showed evidence of poor growth prior to the illness, and half of the children who died did not receive adequate supply of infant formula. Mortality was significantly higher in the infants who developed Kwashiorkor. Not breastfeeding was associated with increased risk of hospitalization and subsequent death during the outbreak.

A study from Malawi reported on the effect of breastfeeding on maternal and infant mortality.²⁵ They analyzed longitudinal data from 2000 mothers and their infants enrolled in the nevirapine-zidovudine (NVAZ) trial. The median duration of breastfeeding was 18 months (interquartile range 9-22.5 months). Breastfeeding was highly protective against mortality among their infants, 55-60% decreased risk of child mortality: adjusted HR =0.44 (95% CI 0.28-0.70). This protective effect persisted regardless of the infants' HIV infection status. Breastfeeding was not associated with maternal morbidity or mortality after adjusting for maternal viral load and did not increase the risk of maternal HIV progression.

Although avoidance of breastfeeding has been successfully implemented in high and mid resource settings, the risks associated with formula feeding children living in resource-limited settings with high background rates of infant morbidity and mortality, outweigh the benefits of reduced HIV transmission as seen when implemented on a large scale as in Botswana. Breastfeeding has several advantages including improved nutrition, growth and development, anti-infective properties and improved child survival. Other benefits not well quantified include improved cognitive and psychosocial development, social and economic benefits to the mother and family. ICAP strongly recommends breastfeeding for infants and children living in resource-limited settings irrespective of maternal HIV status.

In resource-limited settings, use of replacement feeding has resulted in high rates of diarrheal diseases, malnutrition and increased mortality.^{12,23,24}

What about shortening the duration of breastfeeding?

WHO recommends that all pregnant HIV-infected women should be counseled about the risks and benefits of breastfeeding to enable them to make an informed choice using the AFASS (Affordable, Feasible, Assessible, Sustainable and Safe) criteria (Table 4). Women who choose to breastfeed are counseled to exclusively breastfeed and stop all breastfeeding when AFASS criteria are met. This practice of early weaning has been considered a potential means of reducing MTCT while providing some of the benefits of breastfeeding. The rationale for this is that infants can get the protective benefits of breastfeeding during the time when they are most vulnerable, < 6 months of age, and at the same time, HIV transmission can be reduced by early cessation of

breastfeeding since transmission is ongoing for the duration of lactation. However, several studies have now demonstrated that there are significant risks to early weaning.

In the Zambia Exclusive Breastfeeding Study (ZEBS) 958 mother-infant pairs were randomized to EBF until 4 months then wean rapidly or EBF with weaning as usual. The mean age of cessation of all breastfeeding was 16 months. It intended to measure whether early weaning would improve HIV-free survival by decreasing HIV transmission while providing some of the benefits of breastfeeding. The study found that there was no overall benefit to early weaning compared with continued breastfeeding (17 percent of infants in the early weaning group versus 19 percent of infants in the wean as usual group had HIV infection or had died by 24 months).¹¹ Early weaning was particularly harmful to HIV-infected children; survival was higher in HIV-infected children who continued breastfeeding compared to those who were weaned at 4 months (57% in the early weaning group compared to 29%, $p=0.01$). The ZEBS data also suggest that abrupt weaning may be particularly problematic. In a separate analysis, breast milk viral load was significantly higher in mothers who stopped breastfeeding abruptly. Median breast milk viral load was 7930 copies/ml in the early weaning group 2 weeks after cessation, compared to 904 copies/ml in the women who were still breastfeeding.²⁶ This may pose a risk to infants who resume breastfeeding after a period of cessation. This scenario is more common in women who abruptly wean their infants because of the increased likelihood of putting the child back to the breast after weaning to comfort or feed the crying hungry child.

Preliminary data from 3 other African studies presented at the 2007 Conference on Retroviruses and Opportunistic Infections (CROI) in Los Angeles, provide further evidence that early weaning is associated with serious health risks to the infants. In the Extended Infant Post-Exposure Prophylaxis study (PEPI), in Blantyre, Malawi, the frequency of diarrhea in 1,792 infants was compared to a historical cohort of 1,810 infants in the NVAZ Study conducted several years earlier at the same site. The mothers received counseling on exclusive breastfeeding and were advised to abruptly wean at 6 months (median duration of breastfeeding 183 days). Both mother and infant received cotrimoxazole (CTX) prophylaxis and education on hygienic preparation of replacements feeds. In the historical NVAZ cohort median duration of breastfeeding was 732 days and CTX was not widely used. Gastroenteritis frequency was highest in the period immediately following weaning in the PEPI trial. Diarrhea in the infants who were weaned early was more likely to be severe, resulting in hospitalization in the months immediately after abrupt weaning (3.1% at 7-9 months of age, compared to 0.1% in those who were weaned in the historic NVAZ cohort). Overall mortality and gastroenteritis related mortality was significantly higher in the early weaning group compared to the historical group that continued to breastfeed.²⁷

The other studies conducted in Kenya and Uganda compared health outcomes in HIV-exposed but uninfected infants before and after the WHO/UNICEF guidance was introduced that directed HIV-infected mothers to abruptly wean their infants after the first months of life. In both studies the rate of serious gastrointestinal infections was increased when compared to historical cohorts. In the Kisumu Breastfeeding Study (KiBS) the, rates of serious diarrhea requiring hospitalizations were much higher (1.8 versus 0.5 per 100 infant months) when compared to the historical cohort.²⁸ In the immunoglobulin/antiretroviral (HIVGLOB) PMTCT Trial early breastfeeding cessation was associated with increased risk of serious gastroenteritis amongst

HIV-negative infants. The rates of serious gastroenteritis doubled from the breastfeeding period to the 3 months after weaning, and infant deaths rose sharply during the 3 months immediately post weaning.²⁹

In the ZEBS study mastitis, engorgement and fever were all more common in the women who stopped breastfeeding early (4 months). At 6 months only 43% of women who stopped breastfeeding early were amenorrheic compared to 83% of those who continued to breastfeed, offering some protection against premature pregnancy.

HIV-free survival is not improved by early weaning.^{12,23,27,28,29}

What can be done to reduce MTCT during breastfeeding?

Promote exclusive breastfeeding

Several studies have shown that exclusive breastfeeding is associated with a decreased risk of HIV transmission when compared to non-exclusive breastfeeding or mixed feeding.^{30, 31, 32, 33} Two recent studies support this and, in addition, delineate the increased risk of transmission for women with advanced HIV disease. In the ZEBS study, discussed earlier, postnatal HIV transmission was 4% in the exclusively breastfed population compared to 10.1% in the non-exclusively breastfed group.

In the Vertical Transmission Study (VTS), 2722 HIV-infected and uninfected pregnant women attending the postnatal clinic in Kwazulu Natal were enrolled and self selected to either breastfeed or formula feed after counseling.³⁴ The rate of postnatal transmission in EBF infants who were negative at 6 weeks of age was 4.04% at 20-26 weeks of age. Infants who received mixed feeding (BF plus solids) were 10 times more likely to acquire HIV infection than those who were exclusively breastfed. The risk for infants who were fed both breast milk and formula was twice that of those exclusively breastfed at 26 weeks of age. Cumulative 3 month mortality was 6.1% in the EBF group compared to 15.1% in the infants given replacement feeds (HR 2.06, 1.00-4.27, p=0.051).

In the ZVITAMBO study, 4495 HIV-infected women, and their infants were followed for 2 years.³¹ Mothers were given counseling on infant feeding and HIV, and information was collected on infant feeding practices, infection and mortality. All women initiated breastfeeding at delivery. However, only 7.6% of women were exclusively breastfeeding at 3 months. Overall PNT (defined by a positive test after the 6 week negative test) was 12.1 %. Mixed breastfeeding was associated with a four fold increase in postnatal transmission of HIV compared to EBF during the first 6 months of life. In this study, EBF for as little as 6-12 weeks appeared to have conferred protection against PNT.

In a prospective study from South Africa looking at the mode of infant feeding on HIV transmission, 551 HIV-infected women who were enrolled in a vitamin a trial self-selected to

breastfeed or formula feed.³² Breastfeeders were encouraged to practice exclusive breastfeeding for 3-6 months. At 6 months, the risk of transmission was similar for women who reported EBF and women who used replacement feeds. At 15 months the cumulative probability of HIV infection remained lower amongst those who exclusively breastfed for 3-6 months compared to those with mixed feeding, with transmission rates of 25% vs. 36% respectively.

It is hypothesized that when infants are fed breast milk plus other solids or liquids, the immature gastrointestinal tract is exposed to pathogens which may cause inflammation and facilitate acquisition of HIV infection via the gastrointestinal tract. Solids may pose a greater hazard than liquids because large complex proteins may precipitate greater damage to the gut mucosa, thus facilitating entry of the virus. EBF may be healthier because it protects the integrity of the intestinal mucosa which presents a more effective barrier to HIV. Another possible mechanism is that mixed feeding results in suboptimal breastfeeding practices which predisposes to mastitis and cracked nipples, consequently increasing the risk of PNT.

Taken together these studies imply that any incremental amount in the duration of breastfeeding exclusivity is safer than mixed feeding. Mothers should be encouraged to exclusively breastfeed for as long as feasible, preferably until 6 months of age.

Exclusive breastfeeding reduces HIV transmission compared to mixed feeding. 12,30,31,32,33,34

Provide HAART for eligible mothers

Maternal health directly influences child survival; if a mother dies the risk of under 5 mortality triples.³⁵ Mothers with advanced disease are more likely to transmit infection to their children during pregnancy and lactation. In the ZEBs study, women with CD4 less than 350 accounted for 82% of postnatal transmissions. In the ZVITAMBO Study, women with CD4 of less than 200 were 5 times more likely to transmit postnatally, compared to women with CD4 count greater than 500. Women with CD4 count of less than 350 accounted for 46.9% of postnatal transmission (6 weeks to 18 months).³¹ So, women with advanced HIV disease who generally qualify for HAART for their own health account for the vast majority of transmissions during pregnancy and during breastfeeding.

Since maternal viral load, breast milk viral load and CD4 count are all independently associated with postnatal transmission, lowering maternal viral load, improving immune status by providing pregnant and lactating HAART eligible women with treatment will not only benefit the mother but may also decrease PNT. In the MASHI study described earlier, none of the 34 women in the breastfeeding plus zidovudine group who received HAART from delivery have yet transmitted HIV infection to their infants.²³ Four mothers who started HAART during lactation transmitted HIV to their infants; two each assigned to the formula fed and breastfed plus zidovudine groups.

Provide effective PMTCT regimens for mothers and their infants

For mothers who are not HAART eligible, there are ongoing studies evaluating the use of maternal prophylaxis and infant prophylaxis during breastfeeding to decrease PNT while balancing the risk of toxicity, poor adherence and possible development of resistance. Data from single-dose nevirapine (sdNVP) studies suggest that sdNVP is also beneficial in decreasing PNT. In the HIVNET 012 trial in Uganda, sdNVP was compared to short course zidovudine. Postnatal transmission at 18 months (defined by a positive PCR test after a negative test at 6-8 weeks) was 15.7% in the sdNVP group compared to 25.8% in the zidovudine group at 18 months (efficacy of 41%).³⁶ In a follow-up to the NVAZ trial 1256 HIV-exposed infants who were uninfected at 1.5 months were followed for 2 years to determine the risk of late postnatal transmission.³⁷ The cumulative risk of HIV transmission at 24 months was 9.7%, similar to the meta-analysis from the BHITS study. The 1.5-6 month age interval was the one with the lowest risk of HIV transmission: 1.22%, compared to 4.05%, 3.48% and 1.27% at 6-12, 12-18, and 18-24 months respectively. Mothers who had received sdNVP were significantly more likely to have lower detectable breast milk viral load between 1.5-6 months. It is hypothesized that since nevirapine is lipophilic and has a long half-life it may decrease breast milk viral load. A small randomized trial in Kenya showed that breast milk viral load is suppressed by short course sdNVP.³⁸ Seventy-six mothers were randomized to zidovudine beginning at 34 weeks or sdNVP at the onset of labor. All the mothers' breastfed and breast milk samples were collected at regular intervals during the first 6 weeks postpartum. SdNVP was associated with significantly lower breast milk viral load during the first 21 days postpartum and HIV transmission at 6 weeks was significantly lower in the sdNVP group (6.8% compared to 30.3% in the zidovudine group). However, the study was not powered to detect the effect of sdNVP on postnatal transmission. This sustained suppression of breast milk viral load may contribute to the ability of sdNVP to decrease postnatal transmission. In the MASHI trial described earlier, provision of 6 months of zidovudine to infants while breastfeeding was not as effective as formula in preventing postnatal HIV transmission. There are several ongoing studies looking at providing 6 weeks of nevirapine to the infant to prevent PNT.

HAART to prevent postnatal transmission

Two studies recently presented at the 4th International AIDS Society meeting in Australia suggest that use of maternal HAART as prophylaxis to decrease postnatal transmission of HIV is safe and feasible. In the AMATA study from Rwanda, 572 HIV-infected pregnant women were given NNRTI based HAART starting after the first trimester regardless of CD4 count. 244 women chose to breastfeed and weaned at 6 months.³⁹ There were 6 HIV-infected children who tested PCR positive at birth (transmission rate of 1.4%). At 7 months no further transmissions had occurred in either group. In the MITRA PLUS study, all pregnant HIV-infected women were given HAART starting at 34 weeks or earlier if she was eligible.⁴⁰ Treatment was stopped at six months unless the mother required HAART for her own health. Mothers who chose to breastfeed were encouraged to wean at 6 months. The HIV transmission rate was 4.1% at 6 weeks and 5% at 6 months. However, full data from both studies still await peer review and further description of study design and cohort selection. While we await the results of these and

other studies to confirm these preliminary findings, keeping pregnant and lactating mothers healthy by providing them with care, and prioritizing eligible women for HAART may save two lives: those of the woman and her infant.

Breast health

Breast problems such as cracked nipples, breast abscess, subclinical and clinical mastitis have been associated with increased PNT. In the ZEBs study, abrupt weaning was associated with increased breast pathology. Amongst mothers who weaned early and abruptly, 11.5% developed mastitis compared to 0.8% in the continued breastfeeding group; breast engorgement 8.1% compared to 0.8%. In a study done in Nairobi, Kenya, the presence of nipple lesions or clinical mastitis during breastfeeding was associated with increased postnatal transmission.¹³ Subclinical mastitis and breast abscesses are also associated with increased postnatal transmission.^{14,15} Enhancing breastfeeding practices by promptly managing breast problems should protect infants from acquiring HIV postnatally.

How can we promote exclusive breastfeeding?

Unfortunately exclusive breastfeeding even in the first few weeks of life is not the norm in most cultures. Infants are given a variety of nutrient and non nutrient liquids/solids in the first few weeks of life because of cultural norms and practices, work outside the home, concerns regarding eventual food acceptance and the perception of insufficient milk production.⁴¹ However, several studies have shown that EBF can be improved by providing lactating women with intensive counseling and support. In the ZEBs study, EBF rates of 80% at 4 months were achieved with intensive counseling and support. In a randomized interventional study done in Mexico, EBF improved from 12% in the first 3 months of life to 67% by providing 6 sessions of supportive counseling.⁴² Another study from Bangladesh EBF improved from 6% at 5 months to 71% with 15 visits by trained peer counselors.⁴³ Neither of these two latter studies were amongst HIV infected-women. However, as shown by the ZEBs study, intensive supportive counseling that promotes initiation of breastfeeding immediately after delivery, on demand feeding, early identification and prevention of breast problems can improve EBF rates amongst HIV-infected women.

Providing baby-friendly environments in health care setting is also associated with breastfeeding uptake and exclusivity. In Belarus introduction of Baby-Friendly Hospital Initiative (BFHI) was associated with an increase in breastfeeding and exclusivity.⁴⁴ Thirty one maternity and public hospitals were randomized to receive an intervention based on the BFHI of the WHO/UNICEF or a control intervention of continuing usual infant feeding practices and policies. Infants from the BFHI sites were significantly more likely than control infants to be breastfed to any degree at 12 months, more likely to be exclusively breastfed at 3 months (43.3% vs 6.4%; $p<.001$) and 6 months (7.9% vs 0.6%; $p=.01$).

Counseling and support improves adherence to EBF.^{12,42,43,44}

Effect of breastfeeding on maternal health

The first randomized study on the effect of breastfeeding on maternal health reported a 3 fold increase in maternal mortality associated with breastfeeding compared to formula feeding.⁴⁵ In this study none of the mothers received antiretrovirals. Subsequent studies from Zambia, Tanzania, South Africa and Zimbabwe have disputed this finding.^{46, 47, 48, 49} In a recent study on maternal health and breastfeeding in Nairobi, Kenya, where mothers were provided with cotrimoxazole prophylaxis and eligible mothers received HAART, breastfeeding was not associated with increased viral load, disease progression or increased maternal mortality.⁵⁰ In the NVAZ study described earlier, breastfeeding by HIV-infected women was not associated with increased maternal morbidity or mortality.²⁶ There is currently no evidence that breastfeeding amongst HIV-infected women increases maternal morbidity and mortality.

Appropriate care should be provided to all postpartum mothers since neither breastfeeding or avoiding breastfeeding will protect them from disease progression.^{46,47,48,49,50}

When can complementary feeds be safely introduced?

Exclusive breastfeeding is sufficient to provide optimal growth and development during the first 6 months of life.⁵¹ However, all infants whether they are breastfed or given replacement feeds, need additional nutrients usually beginning around 6 months of age. At this time, calories and nutrients from human milk are inadequate to provide all the energy needed for growth and development. The infant's gut is also more mature and better able to handle complex proteins and antigens. Additionally, infants are developmentally ready to start processing more complex foods because they can sit up, have teeth and have started mastering mastication skills. The introduction of foods at this age "complements" breast milk which continues to provide a valuable source of protein, vitamins, micronutrients through the second year of life. Feeding infants solids and liquids before 6 months of age is "mixed feeding" because exclusive breastfeeding alone provides all the nutrients required to support optimal growth and development for the first 6 months after birth.

In order to sustain growth and development and to promote health complementary foods rich in iron should be introduced gradually beginning at 6 months with continued breastfeeding until the infant can be safely fed on a diet devoid of any breast milk. This is usually around 12-18 months of age. Determining how to effectively discourage mixed feeding during the first 6 months of life and supporting complementary feeding after 6 months of age is an important challenge which needs to be addressed by PMTCT programs.

In summary, optimizing maternal health, promoting exclusive breastfeeding and introducing complementary foods at 6 months with continued breastfeeding is the public health approach to safe guard the health of HIV-exposed infants and to decrease postnatal transmission of HIV in resource-limited setting, while improving child survival.

ICAP approach to improving HIV-free child survival

The ICAP approach to improving HIV-free survival aims at balancing the risk of acquiring HIV from breastfeeding against the burden of infant morbidity and mortality from not breastfeeding. Using a public health approach we recommend the following to improve child survival in high prevalence resource limited settings:

Maternal

- All pregnant and lactating HIV-infected women should receive counseling on infant feeding during the antenatal and postnatal period (Table 3).
- All pregnant and lactating HIV-infected women should be screened for ARV eligibility and offered HAART according to national guidelines if they meet eligibility criteria.
- All pregnant HIV-infected women who are not eligible for HAART should be provided with optimal ARVs for prevention of MTCT.
- Lactating mothers who are not on HAART should have CD4 measurement at 6 months post partum. If they are found to be eligible; they should be prioritized to initiate HAART.
- Lactating mothers should be provided with counseling and nutritional support for themselves and their infants.
- Breast conditions which increase the risk of HIV transmission (mastitis, cracked nipples etc) should be prevented and treated promptly if they should occur.

Infant

- HIV-exposed infants should be exclusively breastfed for the first 6 months of life or as long as possible.
- Complementary feeds should be introduced at 6 months of life with continued breastfeeding.
- All infants should have growth monitoring, vaccinations, cotrimoxazole and counseling support for the first two years of life.
- Weaning is a vulnerable period as such infants should be closely monitored during that time.
- Infants who are determined to be HIV-infected by PCR should be encouraged to continue breastfeeding until 2 years of age.

Table 2 ICAP Approach to Improving HIV-Free Survival






The ICAP approach to improving HIV-free survival	
	Screen pregnant and lactating HIV-infected women for treatment eligibility
	Treat pregnant and lactating HIV-infected women with advanced disease and low CD4
	Actively support EBF for as long as possible until 6 months of life
	Complementary feeds should be introduced at 6 months with continued breastfeeding
	Keep mothers and infants engaged in care

Table 3 Infant Feeding Counseling

ICAP infant feeding counseling message
<ol style="list-style-type: none">1. Explain the risks of MTCT2. Explain the advantages and disadvantages of breastfeeding3. Encourage mother to exclusively breastfeed for the first 6 months of life4. Instruct how to practice safe breastfeeding (positioning, attaching, breast health)5. Reinforce adherence to care and treatment for mother. If mother is not on HAART, repeat CD4 at 6 months postpartum and reinforce adherence to care6. Encourage mother to continue breastfeeding irrespective of the early infant PCR result7. Provide nutrition counseling and growth monitoring for the first 2 years of life

Table 4 Recommendations from the WHO HIV Infant Feeding Technical Consultation, December 2006

The following recommendations for policy-makers and program managers are intended to supplement, clarify and update existing UN guidance and do not replace it. Based on this consultation, a technical update of the relevant UN guidance will be forthcoming.

- The most appropriate infant feeding option for an HIV-infected mother should continue to depend on her individual circumstances, including her health status and the local situation, but should take greater consideration of the health services available and the counseling and support she is likely to receive.
- Exclusive breastfeeding is recommended for HIV-infected women for the first 6 months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants before that time.
- When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected women is recommended.
- At six months, if replacement feeding is still not acceptable, feasible, affordable, sustainable and safe, continuation of breastfeeding with additional complementary foods is recommended, while the mother and baby continue to be regularly assessed. All breastfeeding should stop once a nutritionally adequate and safe diet without breast milk can be provided.
- Whatever the feeding decision, health services should follow-up all HIV-exposed infants, and continue to offer infant feeding counseling and support, particularly at key points when feeding decisions may be reconsidered, such as the time of early infant diagnosis and at six months of age.
- Breastfeeding mothers of infants and young children who are known to be HIV-infected should be strongly encouraged to continue breastfeeding.
- Governments and other stakeholders should re-vitalize breastfeeding protection, promotion and support in the general population. They should also actively support HIV-infected mothers who choose to exclusively breastfeed, and take measures to make replacement feeding safer for HIV-infected women who choose that option.
- National programs should provide all HIV-exposed infants and their mothers with a full package of child survival and reproductive health interventions with effective linkages to HIV prevention, treatment and care services. In addition, health services should make special efforts to support primary prevention for women who test negative in antenatal and delivery settings, with particular attention to the breastfeeding period.

- Governments should ensure that the package of interventions referenced above, as well as the conditions described in current guidance^a, are available before any distribution of free commercial infant formula is considered.
- Governments and donors should greatly increase their commitment and resources for implementation of the Global Strategy for Infant and Young Child Feeding and the UN HIV and Infant Feeding Framework for Priority Action in order to effectively prevent postnatal HIV infections, improve HIV-free survival and achieve relevant UNGASS goals.

^a See http://www.who.int/child-adolescent-health/NUTRITION/HIV_infant.htm.

Bibliography

- ¹ Labok M, Clark D, Goldman AS. Breastfeeding: maintaining an irreplaceable immunologic resource. *Nature Reviews* 2004; 4:565-572.
- ² WHO Collaborative Study Team on the role of breastfeeding on the prevention of infant mortality. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet* 2000; 355:451-455.
- ³ Jones G, Steketee RM, Black RE, Bhutta ZA, Morris SS. How many child deaths can we prevent this year? *Lancet* 2003;362:65-71.
- ⁴ Quigley MA, Kelley YJ, Sacker A. Breastfeeding and hospitalization for diarrhea and respiratory infection in the UK millennium cohort study. *Pediatrics* 2007; 119:e837-e842.
- ⁵ Ip S, Chung M, Raman G, Chew P, et al. Breastfeeding and maternal and infant health outcomes in developed countries. Evidence Report/Technology assessment No 153(Prepared by Tufts New England Medical Center Evidence based Practice Center under Contract No.290-02-0022) AHRQ Publication No. 07-E007.Rockville, MD Agency for Healthcare Research and Quality .April.2007.
- ⁶ De Cock KM, Fowler MG, Merceier E, et al. Prevention of maternal-to-child transmission in resource poor countries-Translating research into policy and practice. *JAMA* 2000; 283:1175-1182.
- ⁷ Richardson B, John- Stewart GC, Hughes JP, et al. Breast milk infectivity in Human Immunodeficiency Virus-type 1 infected women. *J Infect Dis* 2003;187:736-740
- ⁸ WHO HIV and infant feeding Technical Consultation: Consensus Statement. Geneva, Switzerland. October 25-27 2006. Accessed on August 23, 2007.
http://www.who.int/child-adolescent-health/New_Publications/NUTRITION/consensus_statement.pdf
- ⁹ Moodley D, Moodley J, Coovadia H et al. The South African intrapartum nevirapine trial(SAINT): a multicenter, randomized , controlled trial of nevirapine compared to a combination of zidovudine and lamivudine to reduce intrapartum and early postpartum mother-to-child transmission of human immunodeficiency virus type-1. *J Infect Dis* 2003;187:725-736.
- ¹⁰ John-Stewart G, Mbori-Ngacha D, Ekpini R, et al. Breastfeeding and transmission of HIV-1. *J Acquir Immune Defic Syndr* 2004; 35:196-202.
- ¹¹ Leroy V, Karon JM, Alioum A et al. Postnatal transmission of HIV-1 after a maternal short-course zidovudine peripartum regimen in West Africa. *AIDS* 2003;17:1493-1501.
- ¹² Sinkala M, Kuhn L, Kasonde P et al. and the Zambia Exclusive Breastfeeding Study Group. No benefit of early cessation at 4 months on HIV-free survival of infants born to HIV-infected mothers in Zambia: the Zambia Exclusive breastfeeding Study. Fourteenth Conference on Retroviruses and Opportunistic Infections, Los Angeles, abstract 74, 2007.
- ¹³ Dunn DT, Newell ML, Ades AE, et al. Risk of human immunodeficiency virus type-1 transmission through breastfeeding. *Lancet* 1992;340:585-588.
- ¹⁴ Embree J, Njenga S, Datta P, et al. Risk factors for postnatal mother-to-child transmission of HIV-1. *AIDS* 2000;14:2535-2541
- ¹⁵ Semba R, Kumwenda NM, Hoover D, et al. Human immunodeficiency virus load in breast milk, mastitis and mother-to-child transmission of human immunodeficiency virus type-1. *J Infect Dis* 1999;180:93-98.
- ¹⁶ Willumsen J, Filteau S, Coutoudis A et al. Subclinical mastitis as a risk factor for mother-to-child transmission. *Advances in Experimental Medicine and Biolo* 2000;478:211-223.
- ¹⁷ Rousseau CM, Nduati RW, Richardson BA, et al. Longitudinal analysis of human immunodeficiency virus type 1 RNA in breast milk and its relationship to infant infection and maternal disease. *J Infect Dis* 2003;187:741-746.
- ¹⁸ Fawzi W, Msamanga GI, Spiegelman D, et al. Transmission of HIV-1 through breastfeeding in women in Dar es Salaam, Tanzania. *J Acquir Immune Defic Syndr* 2002;31:331-338.
- ¹⁹ Miotti PG, Taha TE, Kumwenda NI, et al. HIV transmission through breastfeeding. A study in Malawi. *JAMA* 1999;282:744-749.
- ²⁰ The Breastfeeding and HIV International Transmission Study (BHITS) Group. Late postnatal transmission of HIV-1 in breastfed children: an individual patient data meta-analysis. *J Infect Dis*. 2004;189:2154-2166.
- ²¹ Nduati RW, John G, Mbori-Ngacha D, et al. Effect of breastfeeding and formula feeding on transmission of HIV-1: a randomized clinical trial. *JAMA* 2000;283:1167-1174.
- ²² Marazzi MC, Gremano P, Liotta G, et al. Safety of nevirapine containing triple antiretroviral regimen to prevent vertical transmission in an African cohort of HIV-1 infected pregnant women. *HIV Med.* 2006 ;7 :338-344.
- ²³ Thior I, Lockman S, Smeaton L, et al. Breastfeeding plus infant zidovudine prophylaxis for 6 months vs formula feeding plus infant zidovudine for 1 month to reduce mother-to-child HIV transmission in Botswana. A Randomized trial: the MASHI Study. *JAMA* 2006; 296:794-805.

-
- ²⁴ Creek T, Arvelo W, Kim A, et al. A large outbreak of diarrhea among non-breastfed children in Botswana, 2006- Implications for HIV prevention strategies and child health. Fourteenth Conference on Retroviruses and Opportunistic Infections, Los Angeles, abstract 9, 2007.
- ²⁵ Taha TE, Kumwenda NI, Hoover DR et al. The impact of breastfeeding on the health of HIV positive mothers and their children in sub-Saharan Africa. *Bull WHO* 2006; 84:546-554.
- ²⁶ Thea D, Aldrovandi G, Kankasa C, et al. Post-weaning breast milk HIV-1 viral load, blood prolactin levels and breast milk volume. *AIDS* 2006 20;1539-1547.
- ²⁷ Kafulafula G, Thigpen M, Hoover D, et al. Post-weaning gastroenteritis and mortality in HIV-uninfected African children receiving antiretroviral prophylaxis to prevent MTCT of HIV-1. Fourteenth Conference on Retroviruses and Opportunistic Infections, Los Angeles, abstract 773, 2007.
- ²⁸ Thomas T, Masaba R, van Eijk A et al. Rates of diarrhea with early weaning among infants in Kisumu, Kenya. Fourteenth Conference on Retroviruses and Opportunistic Infections, Los Angeles, abstract 774, 2007.
- ²⁹ Onyango C, Mmiro F, Bagenda D, et al. Early breastfeeding cessation among HIV-exposed negative infants and risk of serious gastroenteritis: Findings from a Perinatal Prevention Trial in Kampala, Uganda. Fourteenth Conference on Retroviruses and Opportunistic Infections, Los Angeles, abstract 775, 2007.
- ³⁰ Coutoudis A, Pillay K, Spooner E, et al. Influence of infant feeding patterns on early mother-to-child transmission of HIV-1 in Durban, South Africa. *Lancet* 1999; 354:471-476.
- ³¹ Iliff PJ, Piwoz E, Tavengwa N, et al. Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival. *AIDS* 2005; 19:699-708.
- ³² Coutoudis A, Pillay K, Kuhn L et al. Method of infant feeding and transmission of HIV-1 from mothers to children by 15 months off age: prospective cohort study from Durban, South Africa. *J Acquir Immune Defic Syndr* 2001;15:379-387.
- ³³ Coutoudis A. Influence of infant feeding patterns on early mother-to-child transmission of HIV -1 in Duran South Africa. *Ann of the NY Academy of Science* 2000;918:136-144.
- ³⁴ Coovadia H, Rollins, N, Bland R, et al. Mother-to-child transmission of HIV -1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study. *Lancet* 2007; 369:1107-1115.
- ³⁵ Taha TE, Kumwenda NI, Broadhead RL. Mortality after the first year of life among human immunodeficiency virus type 1 infected and uninfected children. *Pediatr Infect Dis J* 1999;18:689-694.
- ³⁶ Guay LA, Musoke P, Fleming T, et al. Intrapartum and neonatal single dose-nevirapine compared to Zidovudine for the prevention of maternal-to-child transmission of HIV-1 in Kampala, Uganda:HIVNET 012 randomized trial. *Lancet* 1999;354:795-802.
- ³⁷ Taha TE, Hoover DR, Kumwenda NI, et al. Late Postnatal transmission of HIV-1 and Associated factors. *J Infect Dis* 2007; 196:10-14.
- ³⁸ Chung MH, Kiarie JN, Richardson BA et al. Breast milk HIV-1 suppression and decreased transmission: a randomized trial comparing HIVNET012 nevirapine versus short course zidovudine. *AIDS* 2005;19:1415-1422.
- ³⁹ Arendt V, Ndimubanzi P, Vyankandondera J et al. AMATA study: effectiveness of antiretroviral therapy in breastfeeding mothers to prevent postnatal vertical transmission in Rwanda. Presented at IAS 2007, Sidney Australia.
- ⁴⁰ Kilewo C, Karlsson K, Ngarina M, et al. Prevention of mother-to-child transmission of HIV-1 through breastfeeding by treating mothers prophylactically with triple antiretroviral therapy in Dar es Salaam, Tanzania-the MITRA PLUS study. Presented at IAS 2007 Sidney, Australia.
- ⁴¹ Cohen RJ, Brown KH, Rivera LL, Dewey KG. Promoting exclusive breastfeeding for 4-6 months in Honduras: attitudes of mothers and barriers to compliance. *J Hum Lact* 1999;15:9-18.
- ⁴² Morrow AL, Guerrero ML, Shults J, et al. Efficacy of home-based peer counseling to promote exclusive breastfeeding: a randomized controlled trial. *Lancet* 1999;353:1226-1231.
- ⁴³ Haier R, Ashworth A, Kabir I, Huttly SR. Effect of community-based peer counselors on exclusive breastfeeding practices in Dhaka, Bangladesh: a randomized controlled trial. *Lancet* 2000; 356:1643-1647.
- ⁴⁴ Kramer MS, Chalmers B, Hodnett Ed, et al. Promotion of Breastfeeding Intervention Trial (PROBIT). A randomized trial in the Republic of Belarus. *JAMA* 2001; 285:413-420.
- ⁴⁵ Nduati R, Richardson BA, John G, et al. Effect of breastfeeding on mortality among HIV-1 infected women: a randomized trial. *Lancet* 2001; 357:1651-1657.
- ⁴⁶ Coutoudis A, Coovadia H, Pillay H, Kuhn L. Are HIV-infected women who breastfeed at increased risk of mortality? *AIDS* 2001;15:653-655.
- ⁴⁷ Kuhn L, Kasonde P, Sinkala M, et al. Prolonged breastfeeding and mortality up to 2 years postpartum among HIV-positive women in Zambia. *AIDS* 2005; 19:1677-1681.
- ⁴⁸ Sedgh G, Spiegelman D, Larsen U, Msamanga G, Fawzi W. Breastfeeding and maternal HIV-1 disease progression and mortality. *AIDS* 2004; 18:1043-1049.

⁴⁹ Breastfeeding and HIV International Transmission Study Group. Mortality among HIV-1 infected women according to children's feeding modality. *J Acquir Immune Defic Syndr* 2005;39:430-438.

⁵⁰ Otieno PA, Brown ER, Mbori-Ngacha DA, et al. HIV-1 disease progression in breastfeeding and formula feeding mothers: a prospective 2 year comparison of T cell subsets, HIV-1 RNA, levels, and mortality. *J Infect Dis* 2007; 105:220-229.

⁵¹ Butte NF, Lopez-Alarcon MG, Garza C. Nutrient adequacy of exclusive breastfeeding for the term infant during the first six months of life. Geneva, Switerland:WHO;2002.