AIDS IN AFRICA: THE EXCRUCIATING DILEMMA OF BREAST FEEDING

LOUISE KUHN, PH.D.[1,2] AND EZRA SUSSER, M.D., DR.P.H.[1,3]
[1]Department of Epidemiology, Mailman School of Public Health, Columbia University
[2]Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Columbia University
[3]New York State Psychiatric Institute

INTRODUCTION

The explosive spread of HIV infection in sub-Saharan Africa carries in its wake urgent questions for science and society. In this paper, we address some of the complexities underlying one such issue: the dilemma of breast feeding by HIV-positive mothers. Central to the basic science of the dilemma are questions about mechanisms of mucosal transmission and of fetal and neonatal susceptibility to HIV infection. From an epidemiological perspective, we need accurate quantification of such parameters as rates of mother-to-child HIV transmission, the incidence of prevailing maternal and childhood illness, and the relative risks associated with feeding alternatives. Neither molecular nor epidemiological inquiries can proceed, however, without a firm grasp of the social context in which the dilemma originates and from which the solution will need to emerge.

EPIDEMIOLOGY OF HIV/AIDS IN AFRICA

The prevalence of HIV infection in sub-Saharan African countries now surpasses the most pessimistic projections made some 10 years ago when the epidemic was in its infancy. Statistics provided by the Joint United Nations Program on HIV/AIDS (UNAIDS) for the year 1999 indicate that an astonishing percentage of adults ages 15-45 years are infected with HIV in the southern African countries most severly affected by the epidemic: 36% in Botswana, 25% in Zimbabwe, 20% in South Africa, 19% in Namibia, and 20% in Zambia.[1a] As the leading cause of death in Africa, AIDS is reversing decades of improvement in life expectancy. For example, in Zimbabwe life expectancy in the mid-1980s exceeded 55 years, whereas in the new millennium it has fallen to less than 45 years.

In 1999 the World Health Organization, for the first time, ranked its 191 member countries' health systems. One of the major criteria used was the disability-adjusted life expectancy (DALE), which measures the equivalent number of years of life to be lived in full health. At the very bottom of the rankings were the 12 African countries with substantial HIV epidemics. These countries had DALEs of less than 35 years.[1b]

More than half of those infected are women in their childbearing years. In the absence of intervention, about 20%-30% of children born to HIV-infected women will acquire the infection, and at least a quarter of these infected children will die before their first birthday. Even if these children escape HIV infection, they may lose one or both of their parents to the disease before reaching adolescence.

This humanitarian emergency calls for a response from every sector of society in African nations. It also presents a challenge to the rest of the global community, particularly to the United States. While African nations must find the social and political will to mobilize against the epidemic, the immense material resources needed can come only from the United States and other developed nations.

PREVENTION OF MOTHER-TO-CHILD HIV TRANSMISSION

At least two relatively simple and inexpensive anti-retroviral drug interventions can substantially reduce the risk of pre- and perinatal HIV transmission. A short-course treatment of Zidovudine given late in pregnancy to the mother and a two-dose regimen of Nevirapine, one pill taken at the onset of labor and a syrup given to the infant shortly after birth, have been shown to reduce the risk of mother-to-child HIV transmission by more than half.[2-5] Encouragingly, Boehringer-Ingelheim, the manufacturer of Nevirapine, has promised to make the drug available free to any country wishing to implement prevention programs. Furthermore, the cost of Zidovudine has also fallen considerably in the last 5 years.

It should be noted, however, that the relative reduction in all transmission by these short-course regimens is less in breast-feeding than in non-breast feeding populations. This is because the drugs effectively reduce transmission only around the time of labor and delivery. HIV transmission during the postnatal period remains largely unaffected by the short-course treatment. Continued use of anti-retroviral drugs during breast feeding may or may not be effective for prevention of postnatal transmission, and regimens are being tested for this purpose. Even if successful anti-retroviral drug programs can be implemented in sub-Saharan African countries, transmission of HIV through breast milk will persist. Breast feeding-associated transmission may then become the predominant form of HIV transmission to the pediatric population.

THE BREAST FEEDING DILEMMA

A challenging dilemma arises from the risk of postnatal HIV infection posed by breast feeding for HIV-infected women in sub-Saharan Africa where the HIV epidemic co-exists with dependence on breast feeding. Failure to breast feed substan-

tially increases morbidity and mortality from other diseases in early childhood, including gastrointestinal and pulmonary infections. In many circumstances, breast milk substitutes are unavailable, are prohibitively expensive, or cannot be prepared hygienically. In many sub-Saharan African societies, breast feeding is culturally entrenched and deeply valued, and failure to breast feed may be an unwanted disclosure of HIV status.

Modeling of the competing risks has demonstrated that decisions between infant feeding options to minimize HIV transmission and non-HIV-related mortality are highly sensitive to background infant mortality rates and to the expected risks associated with avoidance of breast feeding.[7-9] In populations with high background infant mortality rates, even small to moderate increased risks associated with avoidance of breast feeding, can wipe out gains achieved by avoiding breast feeding-associated HIV transmission (Figure 1).[7-9] A consistent observation from mathematical models is that shifts away from breast feeding, if not confined to HIV-infected women, can result in substantial increases in child mortality in the population.[7-9] This underscores the need for promoting breast feeding among uninfected women and also the importance of HIV testing.

Weighing the competing risks of infant feeding alternatives requires accurate quantification of the magnitude of transmission via breast feeding. The widely quoted estimate of 14% (95% CI: 7-22%) as the excess risk of HIV-infection associated with postnatal exposure to breast milk is based on a meta-analysis[10] with serious methodological flaws. In the meta-analysis, the excess risk was calculated as follows: [transmission rate among HIV-infected women who had breast-fed their infants] minus [transmission rate among HIV-infected who had never breast-fed]. However, none of the studies included in the meta-analysis had recruited substantial numbers of both breast-fed and non-breast-fed infants: in studies conducted in Africa the vast majority of infants were breast-fed; in studies conducted in the U.S. and Europe the vast majority were not. Possible confounding factors associated with feeding choice were not considered. Despite these methodological weaknesses, the meta-analysis estimate was remarkably similar to that obtained in a randomized clinical trial. The trial conducted in Nairobi, Kenya, observed an excess postnatal transmission risk of 16% (95% CI: 7-26%).[11]

Figure 1

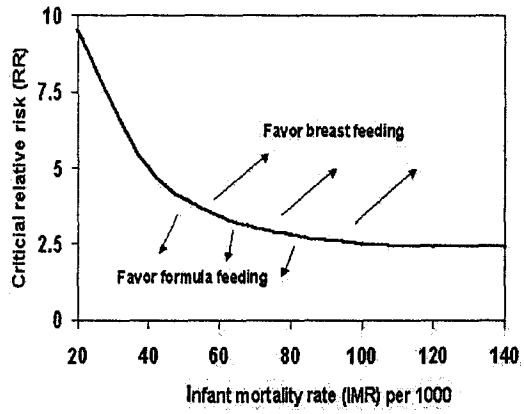

Figure 1. Decision-analysis model comparing the risk of HIV-infection or death among breast- fed versus formula-fed infants of HIV-infected women at different background infant mortality rates. When the relative risk of mortality associated with formula feeding exceeds the line shown on the graph, breast feeding results in fewer adverse outcomes than formula feeding assuming an excess transmission rate of 14%; when the relative risk is lower than the line shown the graph, formula feeding results in fewer adverse outcomes than breast feeding. Adapted from reference 9.

NOT ALL BREAST FEEDING IS CREATED EQUAL

The search for a single estimate of the risk of post-natal HIV transmission assumes homogenous exposure and lumps together all breast feeding—a simplification that neglects important consequences of the quality and duration of breast feeding. Cohort studies which have tested infants repeatedly to detect newly acquired HIV-infections over the full duration of breast feeding have observed that new infections continue to accrue while breast feeding continues.[12-16] This observation has led to the recommendation for early cessation of breast feeding. Such an approach is attractive since protection afforded by breast feeding from severe and life-threatening conditions is greatest in the first few months of life. Relative benefits of breast feeding decline as the child ages.[17,18] Despite many practical advantages, early cessation of breast feeding has not garnered sufficient enthusiasm to date to spur an evaluation of its capacity to reduce mother-to-child HIV transmission. This may be because early cessation alone cannot reduce postnatal HIV transmission in the first few months of life, and it is during these first few months of life that infants appear to be most vulnerable to breast feeding transmission.

A cohort study of infants in Malawi breast-fed by their HIV-infected mothers revealed a trend of decreasing incidence of postnatally acquired HIV infection as the child aged.[19] The risk of "late postnatal" infection, a term used loosely to refer to post-natal transmission after approximately 6 months of age, may be as low as 3 HIV infections per 100 child-years of breast feeding.[20] Hence early cessation of breast feeding may come too late to confer much benefit if no modification is made to the risk of transmission in the early months. Early cessation of breast feeding is also not without disadvantages: longer-term breast feeding promotes early childhood growth and development, decreases morbidity and mortality from infectious disease, and extends post-partum amenorrhea, thereby reducing fertility.

EXCLUSIVE BREAST FEEDING MAY OFFER A NEW SOLUTION

Attention to the quality, not only the duration, of breast feeding may suggest a new solution to the dilemma of postnatal HIV transmission. Nutritionists make an important distinction between exclusive, partial, and predominant breast feeding. Exclusive breast feeding is defined as breast feeding in the complete absence of all other fluids and solids and is recommended for up to 6 months of age, during which time breast milk alone can satisfy all the infant's nutritional and fluid needs.[21] Exclusive breast feeding has long been known to be superior to partial and predominant breast feeding as a way to reduce infant morbidity and mortality in the first 6 months of life.[22-24] The protection afforded by exclusive breast feeding against gastrointestinal and respiratory disease is well-established. Exclusive breast feeding may also play a role in reducing the risk of postnatal HIV transmission since the practice exposes the child to fewer bacterial contaminants and to a more restricted range of food antigens. This in turn reduces immune activation in the gastrointestinal tract, a process necessary for HIV transmission by this route. Exclusive breast feeding also facilitates maturation of the infant's gut and may help maintain the integrity of the intestinal mucosal barrier.[25] However, prior to a study in Durban, South Africa, exclusive breast feeding had not been studied with respect to HIV transmission.

In the Durban study, infants of HIV-infected mothers were stratified into three groups: (1) those who were never breast-fed, (2) those who were exclusively breast-fed to 3 months or more, and (3) those who were breast-fed but who were also supplemented with other liquids or solids prior to 3 months of age. HIV transmission rates in these three groups were compared. At birth, transmission rates in the never, exclusive, and mixed breast feeding groups were similar. Exclusive breast feeding among breast-fed infants of HIV-infected mothers resulted in significantly lower rates of transmission than did breast feeding supplemented with liquids and/or solids.[26] Transmission rates among exclusive breast feeders and non-breast feeders were similar up to 6 months of age. At 6 weeks, non-breast feeders and exclusive breast feeders still had similar transmission rates (18% and 15%, respectively) but mixed breast feeders were starting to surpass both groups (22%). Up to 6 months of age, cumulative transmission rates were similar among non-breast feeders (19%) and exclusive breast feeders (19%), whereas the cumulative transmission rate increased steadily over this time period among the mixed breast feeders reaching 26% by 6 months (Figure 2).[27]

The results of the Durban study suggest that if breast feeding remains strictly exclusive, HIV transmission via this route can be prevented. However, exclusive breast feeding cannot persist indefinitely, and by 6 months of age the infant requires foods in addition to breast milk. The Durban study showed that, after 6 months of age, new HIV-infections began to accrue at older ages once breast feeding ceased to be exclusive.[27] These findings suggest that short-duration exclusive breast feeding, i.e., exclusive breast feeding followed by abrupt cessation of breast feeding when the addition of other foods becomes nutritionally necessary, may be best for infants of HIV-infected mothers in low resource settings. While this is a reasonable inference on the basis of the available data, it is essential that it be further evaluated so that public health practices based on good empirical evidence can be used to protect children born to HIV-infected women.

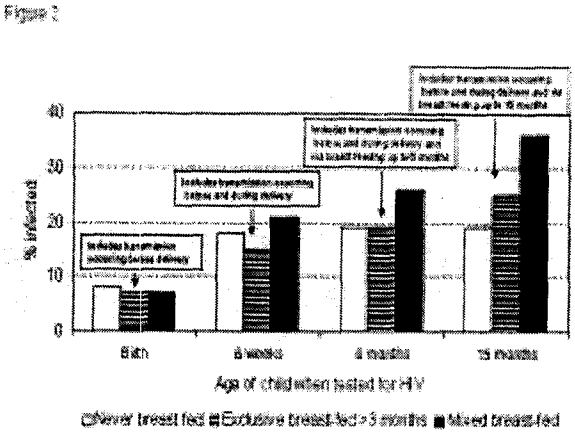

Figure 2. Summary of the results of the study conducted in Durban, South Africa, that compared the risk of HIV transmission among 157 children never breast-fed, 118 children exclusively breast-fed to 3 months, and 276 children mixed breast-fed. Shown in the figure are the cumulative percentages of the children born to HIV-infected mothers in the 3 groups testing positive at each age. Testing positive on the day of birth can be used roughly to signify that transmission occurred before birth and testing positive at later ages includes transmission occurring before or during birth as well as any post-natal breast feeding infections up until the age of testing. Adapted from references 26 and 27.

IS EXCLUSIVE BREAST FEEDING A PRACTICAL INTERVENTION?

If its efficacy is supported by further studies, short-duration exclusive breast feeding may help reduce postnatal HIV transmission while preserving the many other health benefits of breast milk for infants. Exclusive breast feeding, however, is very rare in most parts of the world, even in those areas where breast feeding is almost universal and of long duration. Many barriers to exclusive breast feeding have been identified, including cultural traditions, work outside home, and perceptions of insufficient milk production. An advantage of using exclusive breast feeding to reduce postnatal HIV transmission is that there is considerable experience in promoting the practice outside the context of HIV infection. Randomized trials have shown that simple community- and health service-based interventions can significantly increase adoption and prolongation of exclusive breast feeding.[28-30]

Exclusive breast feeding is unequivocally the most healthful form of infant feeding during the first 6 months of life even

in the absence of HIV infection; thus the potential public health benefits of widespread adoption of the practice could be substantial. Few would challenge the importance of research on methods to reduce postnatal HIV transmission through breast milk, yet conducting such research raises several practical and ethical difficulties. Allowing exposure of infants to any breast feeding by HIV-positive mothers, a practice strongly discouraged in the United States, poses some risk of transmission. Furthermore, much of the research on AIDS in Africa has been called to task for failing to enforce standards used in high-income countries for control treatments. This is even more complicated in the case of breast feeding, for which it is precisely the mutability of the associated risk that is in question. Applying standards used in high-income countries out of context introduces other risks to mother and infant. This dilemma shows how critical it is to consider local epidemiological and social issues in designing research programs in developing countries.

The way forward

Despite the many questions remaining about mother-to-child HIV transmission through breast feeding, there seems to be little doubt about the value and urgency of programs designed to reduce perinatal transmission pharmacologically. The known clinical benefits of antiviral regimens clearly outweigh theoretical risks. Surveillance of any emerging drug resistances and their clinical consequences should proceed concurrently. Although the drugs for prevention are relatively cheap, the infrastructure to deliver the intervention may cost considerably more. At the least, societies require rudimentary prenatal and obstetric services in which health workers can explain the risks and benefits of HIV testing and perform the actual tests. The glaring deficiencies in such systems in most parts of the world where the epidemic is most severe does not preclude a preventive approach. To the contrary, demonstrated means of preventing mother-to-child HIV transmission may well provide the impetus to strengthen prenatal and obstetric services, which in turn is likely to benefit other aspects of maternal and pediatric health. Continuing care postnatally would allow treatment and care of HIV-infected adults and children as needed. Moreover, HIV counseling and testing that becomes a fundamental component of prenatal care could have the secondary benefit of preventing sexual transmission of HIV in adults. Regardless of the approach, the dilemmas raised by the HIV epidemic involve both advocacy and science and require us to appreciate the experience of people grappling with this epidemic.

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