VERTICAL TRANSMISSION OF HIV/AIDS IN SUB-SAHARAN AFRICA: AN EPIDEMIOLOGICAL REVIEW

By

Lucy Wanjiru Karanja

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ABSTRACT

VERTICAL TRANSMISSION OF HIV/AIDS IN SUB-SAHARAN AFRICA: AN EPIDEMIOLOGICAL REVIEW

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The Acquired Immuno-Deficiency Syndrome (AIDS), caused by the Human Immunodeficiency Virus (HIV), is one of the most catastrophic diseases in the world today. The disease has affected 50 million people and killed about 22 million of them in 20 years. The majority of those affected live in Sub-Saharan Africa (SSA). The majority of children who get infected with HIV do so through vertical transmission from their mothers before, during or after birth. The number of such children is increasing rapidly. So far, about 4-5 million children have been victims of the disease, and more than 3 million have died from it. In addition, the disease has orphaned another 13 million.

This study reviews the epidemiology of vertical transmission of HIV/AIDS and potential prevention strategies that can minimize its spread and effects in the SSA. Several interventions that are successful elsewhere are highlighted but unless these are tailored to prevailing social, economic, cultural and political constraints in the SSA, their effectiveness may be limited. There is need for more epidemiological research to understand specific circumstances of HIV/AIDS in the SSA. Community-based primary prevention strategies offer the best potential while greater political commitment, resources, and better collaboration is needed to face future challenges posed by this disease.

DEDICATION

This study is first dedicated to the Almighty God and Jesus Christ, my Lord and Savior! His mercy, love and healing enabled me to finish my degree program. Indeed, without Him, nothing would have been possible. But now I know that I can do all things through Christ who strengths me (Phil 4:13). *O Give thanks unto the Lord for He is good: because His mercy endures forever! (Psalms 118:1).* To Him alone belongs all the glory, praise and honor. Amen!

Secondly, to my dear husband, Daniel Karanja, whose strength, encouragement and faith in God fueled my determination. To him I say, "thank you and may God richly bless you for always being there for me". Thirdly, to my three incredibly wonderful children: Janet Karanja, Michael Karanja and Elyon Karanja. Their love and beauty, reflected in their honest smiles, encouraged me always. And finally, to my parents: John Muchina and Sarah Ngendo and my mother-in-law, Janet Wanjiru, for their tireless support and prayers all these years.

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KEY TO ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
CS	Cesarean Section
DNA	Deoxyribonucleic Acid
HIV	Human Immunodeficiency Virus
NVP	Nevirapine
PACTG 076	Pediatric AIDS Clinical Trials Group Protocol 076
PACTG 185	Pediatric AIDS Clinical Trials Group Protocol 185
PCR	Polymerase Chain Reaction
RNA	Ribonucleic Acid
SSA	Sub-Saharan Africa
STD	Sexually Transmitted Disease
USAID	United States Agency for International Development
UNAIDS	United Nations Program on AIDS
VCT	Voluntary Counseling and Testing
ZDV	Zidovudine
3TC	Lamivudine

Chapter 1

1.1 Introduction

Transmission of the Human Immunodeficiency Virus (HIV), which causes the Acquired Immunodeficiency Syndrome (AIDS), from mothers to their children has raised great concern for a number of reasons. The first reason is that the majority of children become infected through their mothers, a phenomenon referred to as vertical transmission. Secondly, the number of infected children has risen greatly in direct proportion to the increase in infection among women of childbearing age, who are the fastest growing segment of the HIV-infected population. Thirdly, the disease has reached levels that threaten all past achievements in child health. Therefore, there is an urgent need to understand the epidemiology of vertical transmission of HIV/AIDS and develop intervention strategies to curb the spread and effects of the disease, especially in Sub-Saharan Africa (SSA) where the majority of those infected live.

The United Nations Program on HIV/AIDS (UNAIDS) estimates that 36.1 million people had HIV or AIDS by the end of year 2000. Of these, 17 million were women and 1.4 million were children aged 15 years or less. So far, about 4-5 million children have been infected with the disease, and more than 3 million have died from it (Nourse and Butler, 1998; UNAIDS, 1998; WHO, 1995; Gabiano, 1992). In year 2000 alone, a total of 5.3 million people were newly infected; 600,000 of them were children, almost 1650 new infection every day (UNAIDS, 2000). There is something that can be done to prevent this, but it has to be expedited judiciously.

Vertical transmission of HIV/AIDS can take place before, during or after delivery (Borkowsky and Krasinski, 1992; Steihm and Vink, 1991). It accounts for 91 percent of all pediatric AIDS cases in the USA, 15-20 percent in Europe and 30-41 percent in the SSA (Chin and Mann, 1997; Salamon *et al*, 2000; Lindegren *et al*, 1999; Anderson, 1996). The transmission risk is attributed to many factors, which include maternal health and nutrition status, breastfeeding and mode of delivery, and the general prevalence of the disease in the population, especially among women of child-bearing age (Newell, 1998; Douglas and King, 1992). So far, efforts to combat the pandemic have been limited to the use of antiretroviral drugs, which have been found to cut transmission by 30-70%. However, the cost of these drugs remains prohibitive for most people in the SSA despite concerted efforts to reduce drug prices. Thus, the best hope in preventing vertical transmission of HIV/AIDS in the region lies with primary prevention strategies that reduce further infection and transmission, and the development of affordable vaccines.

To complement current prevention efforts in the SSA, there is an urgent need to carry out more systematic epidemiological research in order to understand the underlying factors influencing the spread and effects of the disease so that appropriate and effective prevention strategies can be developed. Very little of such information currently exists. This study makes its contribution by reviewing existing information on the epidemiology of vertical transmission of HIV/AIDS, highlighting the significance of the problem, outlining available prevention strategies and making recommendations on ways to minimize current levels of vertical transmission of HIV/AIDS in the SSA.

1.2 Significance of the Problem

Not since the Black Death devastated medieval Europe has humankind experienced infectious disease deaths on such a massive scale. Despite controversies about the origin of HIV/AIDS, there is no doubt that the disease is one of the greatest threats facing the world today. So far, it has infected more than 50 million people and killed about 22 million of them in 20 years. This translates to about 2 deaths per second worldwide. Moreover, what makes the disease even more devastating is the fact that it has no credible cure yet it is spreading at such an incredible rate. The numbers make this very clear: there were 22.6 million people living with the disease at the end of 1996. This number increased by 60% to 36.1 million in only 4 years! Consider the number of new HIV-infections: this has increased from 3.1 to 5.3 million between 1996-2000, an incredible 70% increase! Figure 1 illustrates these numbers.

That HIV/AIDS has ravaged the world is more clearly witnessed in the SSA, home to seven out of ten adults infected with HIV/AIDS, eight out of ten of all new HIV-infected people and nine out of ten deaths from the disease of children aged under 15 years (UNAIDS, 2000). It is estimated that infant and child mortality in east and southern Africa are now between one third and two thirds higher than they would be in the absence of HIV/AIDS. All these make the disease one of the greatest threats and cause of child mortality, and a significant reducer of life expectancy in the SSA (UNAIDS, 1998; Ryder *et al*, 1989; Nesheim *et al*, 1994; de Cock *et al*, 2000; de Martino et al, 2000).

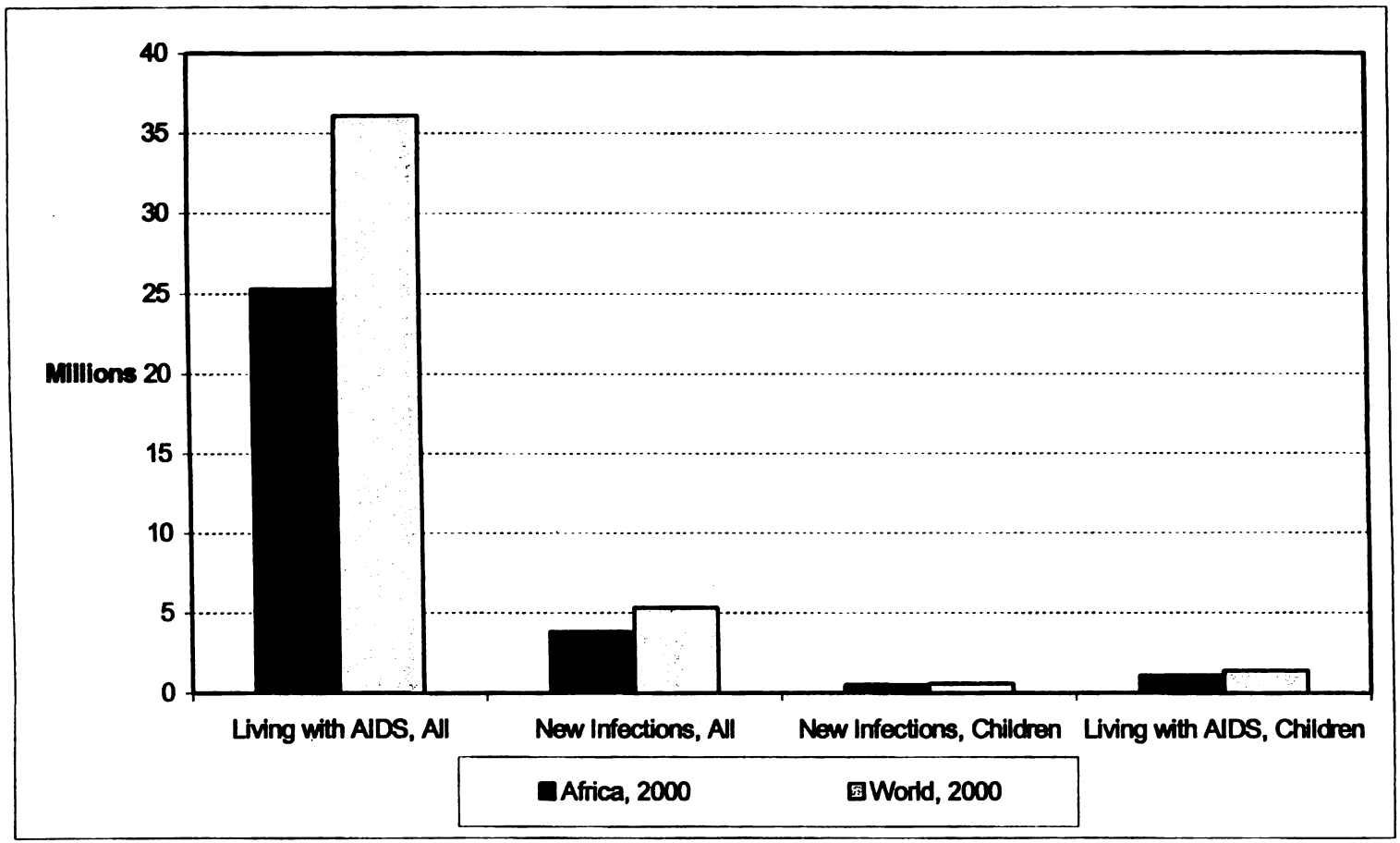

Figure 1: Global and Sub-Saharan Africa HIV/AIDS Burden, 2000

The prevalence of HIV infections among children in the SSA closely resembles the spread of the disease in the general population, especially among women of childbearing age. This, in turn, is influenced by rapid social, cultural, political and economic changes. Examples of these are poverty, migration of people as a result of wars or job-search, sexual domination of women by men and also cultural practices and traditions (Salamon et al, 2000). The situation has been further compounded by lack of political will and leadership, persistent denial and significant institutional and economic constraints facing many Africa countries. Given these issues, there is little hope for meaningful progress towards curtailing the spread and effects of the disease until there are drastic changes in response to the pandemic.

At least, the international community seems to have been jolted by the gravity of the situation. For the very first time, the 13th International Conference on HIV/AIDS was held in Africa, in Durban - South Africa in July 2000. More recently, in June 2001, the United Nations made an appeal for a $7-10 billion global fund to fight HIV/AIDS during a special session on HIV/AIDS dubbed "Global Crisis – Global Action" in which the international community made serious commitments to fight the pandemic (UN, 2001). Both meetings emphasized the need for collective effort and vigilance. It is noteworthy, though, that the global fight against HIV/AIDS in general, and infection among children in particular, will require more than rhetoric and grandiose conferences. Effective action needs a long-term global partnership in research and development, education and counseling, and support of complementary institutions that deliver needed information and treatment to the majority of affected people, especially in the SSA.

1.3 Objectives and Methodology

This study has four specific objectives. Firstly, the study provides a comprehensive update on vertical transmission of HIV/AIDS. Secondly, it describes the epidemiology of vertical transmission of the disease. Thirdly, the study highlights the magnitude of the problem and the factors affecting vertical transmission. Lastly, existing vertical transmission prevention strategies are reviewed and consideration made on the potential application in the SSA. In order to achieve the stated objectives, the study reviewed published materials on vertical transmission of HIV/AIDS mainly with reference the SSA.

Although the primary focus was on journal articles, credible institutional reports and books, such as those of the UNAIDS were considered. Standard search procedures were adopted to locate relevant studies. A MEDLINE search was used with keywords such as "Vertical Transmission of HIV/AIDS", "Prevention of Vertical Transmission of HIV/AIDS", "AIDS and STD", HIV and Antiretroviral Therapy", etc., as well as relevant section headings of this study. The inclusion criteria used were studies published between 1990-2000, those published in the English language and those dealing with vertical transmission of HIV/AIDS. Sources dealing with general HIV/AIDS topics, published before 1990 and written in other languages were excluded.

Chapter 2

2.1 Epidemiology of Vertical Transmission of HIV/AIDS

2.1.1 Rates and Incidence of Vertical Transmission of HIV/AIDS

The rates of vertical transmission range from 15-20% in Europe, 16-30% in the U.S. and 25-48% in SSA (Newell and Peckham, 1994; Wiktor et al, 1997; Thorne and Newell, 2000). The Ghent International Working Group standardized the range to between 25-35% globally (Working Group, 1995; Dabis *et al*, 2000). The difference in transmission rates is influenced by differences in the distribution of risk factors such as maternal disease status, mode of disease acquisition, mode of delivery, viral phenotype and genetic factors, whether breastfeeding or not and the frequency of breastfeeding, etc. Nearly 90% of new HIV-infections among children occur in the SSA, mainly due to a high HIV-prevalence in women of childbearing age, high fertility rate and high breastfeeding incidence (Saba, 1999; Peckham and Newell, 1997).

Vertical transmission is the primary route of HIV infection among infants and children below 15 years of age. In the case of the SSA, such transmission is closely correlated to the incidence of HIV/AIDS among women of childbearing age, the latter index becomes critically important in predicting the spread and potential impact of the disease in given populations. Figure 2 shows the HIV seroprevalence, which ranges between 5-45%, among pregnant women in selected SSA countries. The distribution of the disease reveals a geographical and demographic bias.

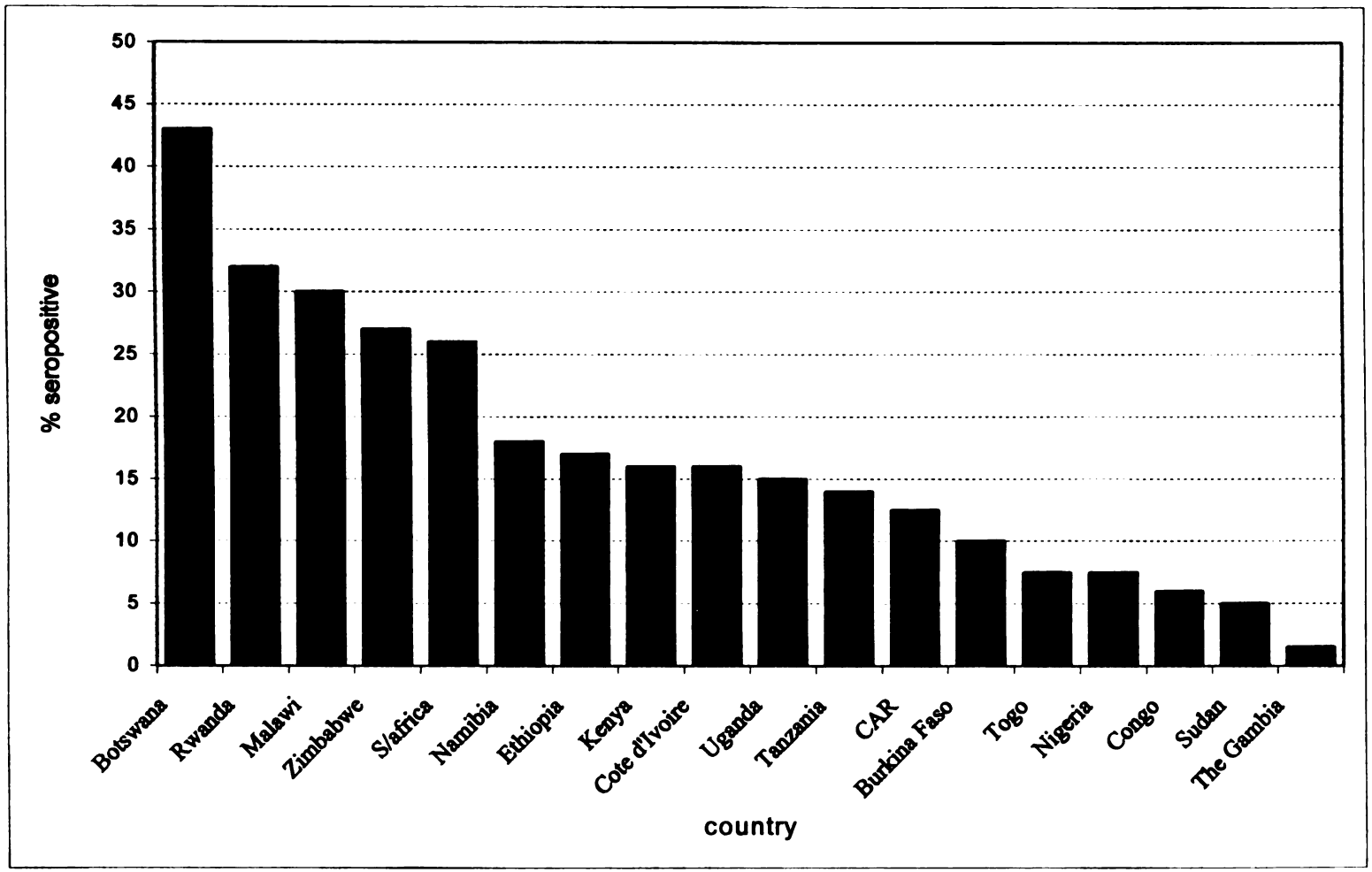

Figure 2: HIV Seroprevalence in Selected African Countries

Altogether, there are 12 countries in the SSA in which more than one-tenth of the adult population is HIV-infected. The highest infection rates are among men and women aged 15-49 years old, people with sexually transmitted diseases (STDs), long-distance truck drivers, military personnel, and female commercial sex workers. Women are more susceptible to infection than men. Meanwhile, the bulk of new infections are concentrated in Eastern and Southern Africa. Combined, one in five adults in Botswana, Namibia, Swaziland and Zimbabwe are living with HIV/AIDS. In fact, these four countries, together with South Africa, form the global epicenter for HIV/AIDS (UNAIDS, 1999). For instance, in Botswana and Zimbabwe, a shocking 43% and 20-50% of pregnant women have tested HIV-positive, respectively.

Admittedly, South Africa has the largest number of infected people in the whole SSA and its prevalence rate has increased alarmingly, from 13% in 1997 to 20% in 1999. In Malawi, Mozambique, Rwanda and Zambia, between one in seven and one in nine adults live with HIV infection. In Central African Republic, Cote d'Ivoire, Djibouti and Kenya, at least one in ten adults are HIV-infected. Although West Africa is relatively less affected by HIV infection, probably due to a low virulence of the strain found there, the prevalence rate in some countries is rising fast. Cote d'Ivoire is already among the 15 worst affected countries in the world while Nigeria, with a population of over 100 million people, has over 5% of its adults infected with HIV. Besides these two, most other West African countries have less than 3% HIV prevalence (UNAIDS, 2000).

2.1.2 Factors Affecting Vertical Transmission of HIV/AIDS

There is increasing evidence that the difference in observed HIV/AIDS incidences and transmission rates are due, in part, to differences in the distribution of risk factors (Peckman and Newell, 1997). Specific risk factors known to influence vertical transmission can be grouped into three major categories: maternal factors, mode of delivery and breast-feeding.[1]

2.1.2.1 Maternal Factors

Maternal factors that have been found to influence vertical transmission of HIV/AIDS include age of the mother, mode of infection, disease progression, maternal viral load, immunological and nutritional status, viral characteristics and genetic factors associated with immune response.

2.1.2.1.1 Maternal Age, Infection and Disease Progression

The rate of vertical transmission appears to be directly correlated with maternal age. Tovo *et al* (1996) found that the risk of infection increased with maternal age, from 16% for women <25 years to 30% for those >35 years. Progression of maternal infection was also directly related to increased transmission rate (Tovo et al, 1996; 1995; Mayaux et al, 1997; ECS, 1992; Kind et al, 1995; Lallemant et al, 2000). Primary infection during pregnancy is associated with a period of viremia, which poses increased risk of

[1] Factors that directly influence the incidence of HIV/AIDS in the general population, such as poverty, migration, etc. are not discussed here.

transmission to the fetus. Such infection is more likely to occur in populations with high HIV prevalence and heterosexual transmission, as is the case of the SSA. The more profound immunodeficiency and higher viral burden characterizing disease progression may explain greater infectivity of symptomatic women (Tovo et al 1997).

2.1.2.1.2 Maternal Viral Load and Immunological Status

Several studies suggest that there is a threshold of maternal viral load below which transmission would not occur (Dickover et al, 1996; Fang et al, 1995). However, clinical trials in the US, Europe, Thailand and Africa support a direct relationship between disease transmission and maternal viral load with the disease transmission occurring at all levels of maternal viral load (Cao et al, 1997; Mayaux et al, 1997; Shaffer et al, 1999; Sperling et al, 1996; Burns et al, 1999; Nogueira *et al,* 2001).

The mother's immunologic status during pregnancy and the duration of infection can influence the viral load and infectivity, which in turn affect vertical transmission. A low CD4 count or CD4/CD8 ratio, and p24 antigenemia are associated with increased transmission, as are other markers such as beta-2 microglobulin (Nogueira *et al*, 2001). In the French Prospective Cohort Study, using data from the first 3 months of life of 95 HIV-infected newborns, the greater the degree of maternal immunodeficiency or low CD4 count at delivery, the higher was the risk of *in utero* transmission (Rouzioux et al, 1993).

2.1.2.1.3 Maternal Nutritional Status and Genetic Factors

Vitamin A deficiency is common among HIV-infected pregnant women and is associated with high rates of vertical transmission of HIV (Semba, 1997). The biological mechanisms by which vitamin A deficiency could influence vertical transmission of HIV include impairment of immune responses in both mother and infant, abnormal placental and vaginal pathology and increased HIV viral burden in breast-milk and blood. In a study of 338 HIV-positive mothers in Malawi, the mean level of vitamin A in 74 mothers who transmitted HIV to their infants was $0.86\pm0.03\mu mol\ l^{-1}$. In the rest of the mothers, who did not transmit HIV to their infants, the level was $1.07\pm0.02\mu mol\ l^{-1}$ ($p < 0.0001$). Genetic factors such as human leukocyte antigens (HLA) or related immunogenic factors could also influence vertical transmission. A study to facilitate design of an HLA-based HIV vaccine investigated the distribution of the HLA class I antigen specificities in Botswana and found association between specific antigens with HIV resistance and others with its susceptibility (Novitsky et al, 2001).

2.1.2.2 Mode of Delivery, Pre-Maturity and Twin-Births

Exposure of infants to HIV-infected maternal fluids and blood in the genital tract is bound to affect the risk of vertical transmission. Therefore, delivery using elective cesarean section (CS) might reduce the risk of vertical transmission by avoiding contact with these infected fluids during the passage of infants through the birth canal. Obstetric factors such as rupture of membranes for over 4 hours, placental abruptions, amniocentesis, chorionic villus sampling, use of fetal scalp electrodes, episiotomy and the presence of vaginal lacerations during labor or pre-term delivery may increase exposure

of the fetus to maternal blood and body fluids and, therefore, are important risk factors in vertical transmission of HIV (Boyer *et al*, 1994; Landesman *et al*, 1996; Kuhn, 1999). The presence of chorioamnionitis or genital ulcers further increases peri-partum risk of transmission (Mofenson *et al*, 1999; Van Dyke *et al*, 1999; Wabwire-Mangen *et al*, 1999; Lee *et al*, 1998).

Results from a European Collaborative Study showed that infants of HIV-infected women delivered by elective CS had a lower risk of HIV-infection than infants delivered vaginally (ECS, 1992). Similar reductions in risk were reported from a Swiss perinatal study (Kind *et* al, 1995) and the Italian Pediatric Register (Gabiano *et al*, 1992). A subsequent analysis of a larger data set from the European Collaborative Study, after controlling for other risk factors such as prematurity and maternal clinical and immunological disease progression, showed that elective CS delivery significantly reduced the risk of vertical transmission by about 50 percent (ECS, 1994).

Extreme pre-maturity has been associated with increased vertical transmission. In the European Collaborative Study, a non-linear relationship was found between gestation age and vertical transmission, with children born before 34 weeks' gestation being three times more likely to be infected than children born after 34 weeks' gestation (ECS, 1992). Fawzi et al (2001) estimated the risk of vertical transmission during intrapartum and early breastfeeding periods to be 2.19 times higher for infants born before 34 weeks compared to those born after 37 weeks in Tanzania. This was probably the case since infants born before the transfer of adequate levels of maternal antibodies, which occurs

late in pregnancy, were likely to be more susceptible to infection during delivery. In the Italian Pediatric Register, by calculating the risk of infection at different weeks of gestation, the percentage of infected children was highest among very premature infants born before 32 weeks of gestation (Gabiano *et al*, 1992).

On twin-births, results from a large register of twins born to HIV-infected mothers showed that the first-born twin was more likely to be infected than the second-born twin, especially when the delivery was vaginal (Goedert *et al*, 1991; Goedert, 1997). This rendered credence to infection during passage through the birth canal, and occurrence of vertical transmission of HIV around the time of delivery (Newell, 1998). Duliege *et al* (1995) assessed the concordance, birth order, route of delivery, and other factors for vertical transmission of HIV in 115 prospectively studied twin pairs born to HIV-infected women.

The results showed that HIV infection occurred in 35% of vaginally delivered firstborn (A) twins, 16% of cesarean-delivered A twins, 15% of vaginally delivered second-born (B) twins, and 8% of cesarean-delivered B twins. The adjusted odds ratios for HIV infection were 11.8 (95% CI: 3.1-45.3) for concordance of infection with the co-twin, 2.8 (95% CI: 1.6-5.0) for A versus B twins, and 2.7 (95% CI: 1.1-6.6) for vaginally delivered versus cesarean-delivered twins. These results indicate that HIV infection of B twins occurs predominantly in utero, whereas infection of A twins (and, by implication, singletons) occurs predominantly intrapartum.

2.1.2.3 Breastfeeding

Breastfeeding provides nutritional, immunological and psychological benefits to infants. It protects them from mortality and morbidity associated with diarrheal diseases, pneumonia and other infections. Breast-feeding has also been shown to prolong the interval between births and thereby improve child survival and maternal health. It is therefore important that the risk of HIV infection through breastfeeding is weighed against the morbidity and mortality associated with alternatives to breastfeeding, such as formula feeding. Recent data from developing countries indicates that 30-50 percent of vertical transmission of HIV occurs through breastfeeding. The exact figure is, however, hard to determine with precision, both because of the difficulty of ascertaining time of HIV acquisition in individual infants and because of homogeneity of feeding practices in most cohorts (Kreiss, 1997). However, it has been estimated that the risk of HIV transmission through breastfeeding is 14% from mothers who were seropositive at the time of delivery and 29% from mothers who acquire HIV after birth (Dunn *et al*, 1992).

Several studies have evaluated the relationship between duration of exposure to breast milk and transmission risk. In a study done in Kenya, in which 42 percent of 239 children of seropositive women were infected, a pattern of antibody loss and reappearance, compatible with postpartum acquisition of HIV was observed in 44 percent of the infected children. Prolonged breastfeeding was significantly associated with approximately two-fold increased risk of HIV-1 transmission after adjusting for confounding factors (Datta et al, 1994).

Another randomized clinical trial conducted in the same country in 1992-98 determined the frequency of breast milk transmission of HIV and compared mortality rates and HIV-1-free survival in breastfed and formula-fed infants. Mother-infant pairs were assigned randomly to breastfeeding (n=212) and formula-feeding arms (n=213) at 32 weeks' gestational age. The two groups had similar pregnancy, labor, delivery and neonatal characteristics. The median follow-up time was 24 months for both groups (p=0.88). At the time of delivery, 408 women remained in the study and after excluding stillbirths and second-born twins, 401 infants remained.

Of these infants, 92 were HIV-infected, including 61 in the breastfeeding group and 31 in the formula-feeding group. Cumulative probability of HIV infection was significantly higher for infants randomized to breastfeeding than for formula feeding ($p<0.001$). At 24 months, the cumulative probability of HIV infection was 36.7% (95% CI, 29.4-44.0%) in the breastfeeding arm and 20.5% (95% CI, 14.0-27.0%) in the formula-feeding arm (p=0.001). Thus, the excess transmission occurring in the breastfeeding arm of the trial was 16.2% (95% CI, 6.5-25.9%), indicating that 44% of the transmission was attributed to breastfeeding (Nduati *et al*, 2000). Most of the transmission occurred early with 75% of the risk difference between breastfed and formula-fed arms occurring at 6 months, although the transmission continued throughout the duration of exposure. The 2-year mortality rates in both arms were similar but the rate of HIV-free survival was significantly lower in the breastfeeding arm than in the formula-feeding arm.

To further understand the risk of HIV transmission through breast milk, a prospective cohort study was conducted in Malawi between 1994-97 (Miotti *et al*, 1999). A total of

672 infants participated in the trial. They were all born HIV-negative by HIV-positive women who had not received antiretroviral drugs during or after pregnancy. The infants and their mothers attended study clinics at 1.5, 3, 6, 9, 12, 15, 18 and 24 months after delivery. The time of infants' HIV-infection was estimated as the midpoint between the last negative and first positive DNA PCR results. Risk was assessed by Kaplan-Meier method. The median age of first visit with a negative HIV PCR result was 1.7 months. Thus, any postnatal infections did not involve colostrum. Infants uninfected at enrollment were followed up for 7155 person-months (596 person-years) while breastfeeding. No infant became infected after breastfeeding had stopped (268 person-months of follow-up), and none of the infants who were found to be PCR-positive had blood transfusions during the interval of infection. Thus, all of the new infections were attributable to breastfeeding.

The cumulative risk of infection for infants continuing to breastfeed after the first month was 3.5% at the end of 5 months, 7.0% at the end of 11 months, 8.9% at the end of 17 months, and 10.3% at the end of 23 months. The HIV-infection rates per person-month in the first 2 years of life were 0.7% (months 1-5), 0.6% (months 6-11), 0.3% (months 12-17), and 0.2% (month 18-23). This decline in HIV incidence was statistically significant. The trend showed a high risk of infection in early months of breastfeeding, which could be explained by the immaturity of the infant's immune system and by the large number of HIV-infected cells present in early breast milk.

In an Italian study of 793 children who were exclusively bottle-fed, the transmission rate was about 33 percent, but this doubled to 68 percent among 168 children who were

breastfed, and the rate increased with longer duration of breastfeeding (de Martino et al, 1992). In another study done in South Africa to assess whether the pattern of breastfeeding is a critical determinant of early transmission, infant-feeding practices of 549 HIV-infected women were prospectively assessed (Coutsoudis, 2000). The proportions of HIV infected infants at 3 months, estimated by use of Kaplan-Meier life tables were compared in the three different feeding groups: exclusively breastfed, mixed-fed, and formula-fed (never breastfed) infants. HIV infection was defined by a positive RNA-PCR test. At 3 months, 18.8% (95% CI, 12.6-24.9) of 156 never-breastfed children were HIV-infected compared with 21.3% (17.2-25.5) of 393 breastfed children (p=0.5).

The estimated proportion (Kaplan-Meier) of infants who were infected by 3 months was significantly lower for those exclusively breastfed to 3 months than in those who received mixed feeding before 3 months (14.6% [7.7-21.4] versus 24.1%[19.0-29.2], p=0.03). After adjustment for potential confounders, exclusive breastfeeding carried a significantly lower risk of HIV transmission than mixed feeding (hazard ratio, 0.52) and a similar risk to no breastfeeding (hazard ratio, 0.85).

2.2 Timing of Vertical Transmission of HIV/AIDS

The timing of vertical transmission of HIV/AIDS has great implications when planning prevention strategies (McGowan and Shah, 2001). Vertical transmission can occur *in utero*, during labor and after delivery through breastfeeding (Thorne and Newell, 2000). A number of studies suggest that between 50-80% of the transmission takes place at around the time of delivery (Mofenson, 1998; Stringer and Vermund, 1999; Bertolli *et al*, 1996; Chouquet *et al*, 1997; Thorne and Newell, 2000). This is why much of the current prevention effort is concentrated on interventions that aim to interrupt the disease transmission during delivery such as antiretroviral therapy and elective CS delivery.

The distinction of vertical transmission in the intrauterine, intrapartum and postnatally through breastfeeding is important because of the different approaches required for prevention. Neonates testing positive for HIV in the first 48 hours of life are considered to have acquired infection *in utero* (Bryson *et al*, 1992). However, current technologies cannot yet distinguish between late intrauterine, intrapartum and early postpartum transmission. In non-breastfeeding populations, about 30% of infant infections occur *in utero* and 70% during labor and delivery. In breastfeeding populations, as observed in most SSA countries, HIV transmission from breastfeeding is considerably high but also varies with the duration of breastfeeding.

A study by Bertolli *et al* (1996) estimated the timing of vertical transmission of HIV in a breast-feeding population in Kinshasa, Zaire. Breast-fed infants born to HIV-infected

mothers were monitored for a mean of 18 months. DNA-PCR test on venous blood drawn from children aged 0-2 days and 3-5 months old were used to estimate proportions of vertical transmission and transmission risks during the intrauterine, intrapartum/early postpartum, and late postpartum periods. The results indicated that among 69 HIV-infected children 23% (95% CI: 14-35%) were estimated to have had intrauterine infection, 65% (95% CI: 53-76%) intrapartum/early postpartum, and 12% (95% CI: 5-22%) had late postpartum infection. The estimated risks was 6% (16/261; 95% CI: 4-10%) for intrauterine infection, 18% (45/245; 95% CI: 14-24%) for intrapartum/early postpartum and 4% (8/189; 95% CI: 2-8%) for postpartum. Another study in Zimbabwe supported earlier studies indicating that most vertical transmission occurs during labor and delivery or in early postpartum period, and that the risk of transmission during breastfeeding was significant (Zijenah *et al*, 1998).

2.3 The Impact of Vertical Transmission of HIV/AIDS

The HIV/AIDS epidemic is not only the most important public health problem affecting large parts of SSA, but also an unprecedented threat to the region's development. The most disturbing long-term feature of the HIV/AIDS epidemic is its impact on life expectancy, making it an unprecedented catastrophe in the world's history. In about 16 countries with adult prevalence of 10 percent or more in the SSA, HIV/AIDS will erase 17 years of potential gains in life expectancy. This means that instead of reaching an average of 64 years, life expectancy in these countries will regress to an average of just

47 years in the next 10-15 years (World Bank, 1999). It is further estimated that HIV/AIDS related deaths among adults will increase from 8.6% in 1990 to 37.1% in 2020 (World Bank, 1997). Figure 3 represents a reversal of life expectance in 3 African countries as a result of HIV/AIDS.

The other glaring impact of the vertical transmission of HIV/AIDS is its effect on child mortality and morbidity. By 2005-2010, infant mortality in South Africa will be 60 percent higher than it would have been without HIV/AIDS (61 deaths per 1000 infants born rather than 38 per 1000 in the absence of AIDS). In Zambia and Zimbabwe, 25 percent more infants are already dying than would be the case without HIV. By 2010, Zimbabwe's infant and child mortality rates will have doubled (UNAIDS, 1998a). Figure 4 shows the reversal of long-term reduction in child mortality in Kenya, Zambia and Cameroon just as HIV/AIDS started to become prevalent in those countries. In fact, in most SSA countries, the disease is already the number one killer of children less than 15 years old.

HIV/AIDS is likely to profoundly disrupt the economic and social base of many families and countries. Many families will lose their bread-earners and end up exhausting their savings, and selling their assets, to pay health care and funeral costs, leaving families in debt or completely helpless. This impact is greatly felt by the children in the family. In 1997, approximately 1.5 million children in SSA were orphaned by the disease, losing one or both their parents to AIDS. This number grew to 13.2 million by 2000, and is projected to reach 28 million by 2010 (UNAIDS, 1998; UNAIDS, 2000).

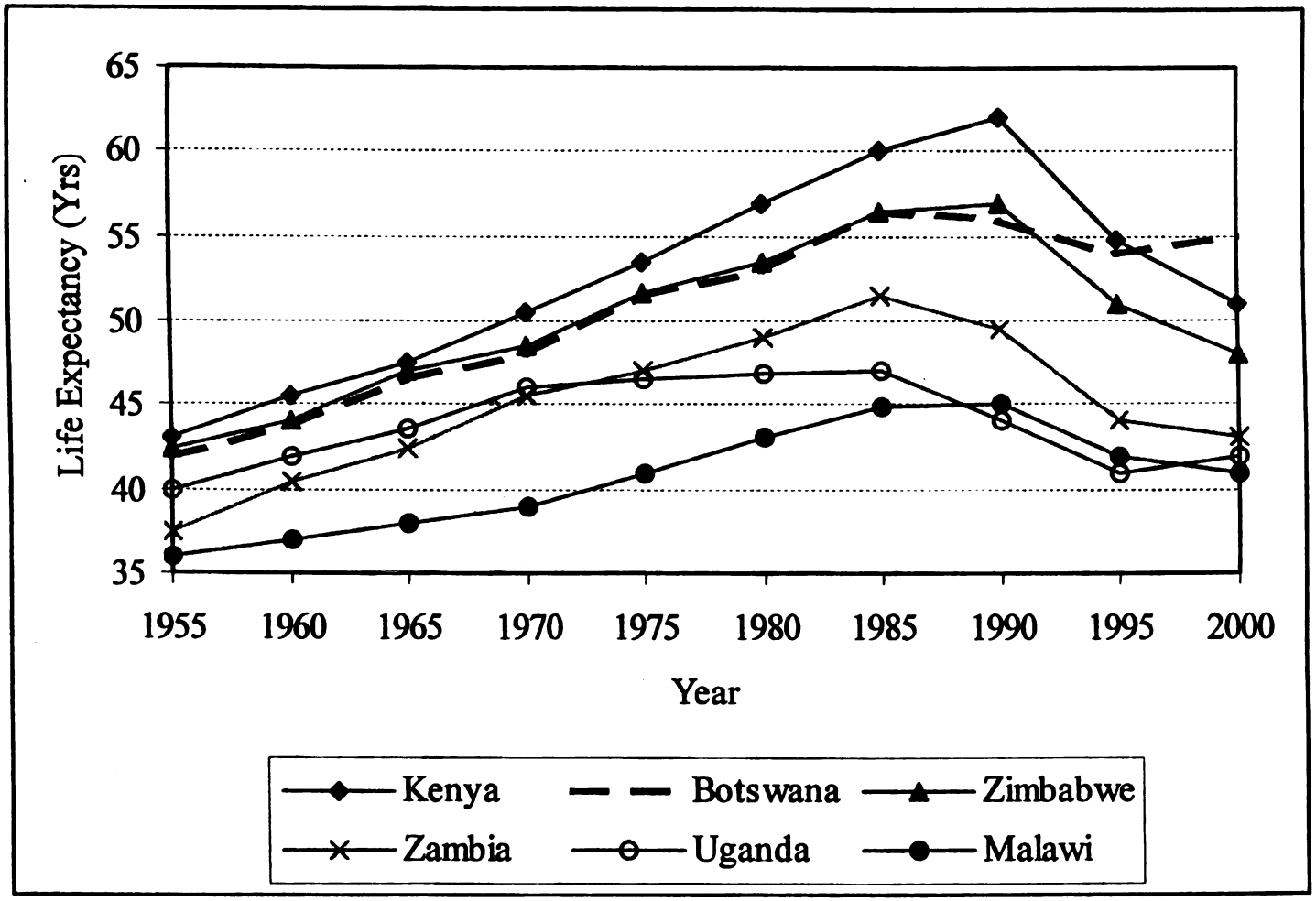

Figure 3: Estimated Life Expectancy at Birth in Selected African Countries, 1955-2000
Source: UNAIDS, 1998

These orphans are less likely to go to school or have access to adequate health care and are more likely to live in poverty, be malnourished, engage n hazardous labor including commercial sex and, in turn, be exposed to HIV infection (USAID, 1997).

The impact of the disease on the macro-economy, though remotely related to vertical transmission of the disease, is devastating. Illness and impending death of 10-25 percent of all adults in some countries will have a major impact on the social, political and economic well being of these countries. Labor productivity is likely to drop, the benefits of education lost, and resources that would have been used for investment elsewhere will be used for health care, orphan care and funerals. Savings rates will decline as more people drop off from productive work in society and become dependent on their families and communities.

Evidence already exists of losses in productivity and quality of life. For instance, Zambia lost 1300 teachers to HIV/AIDS in the first 10 months of 1998, an equivalent of about two-thirds of all new teachers trained annually. The Central Africa Republic already has a third fewer primary school teachers than it needs, which will cause about 71,000 children aged 6-11 years to lack primary school education by 2005. In Cote d'Ivoire, teachers are missing up to six weeks of classes before dying of HIV/AIDS compared to 10 days missed when they die of other causes. Moreover, increased demand for health services in many countries from people with HIV-related illnesses is heavily taxing public resources. In mid-1990s, treatment of people with HIV/AIDS consumed 66% of public health spending in Rwanda and a quarter of health expenditures in Zimbabwe (UNAIDS, 2000).

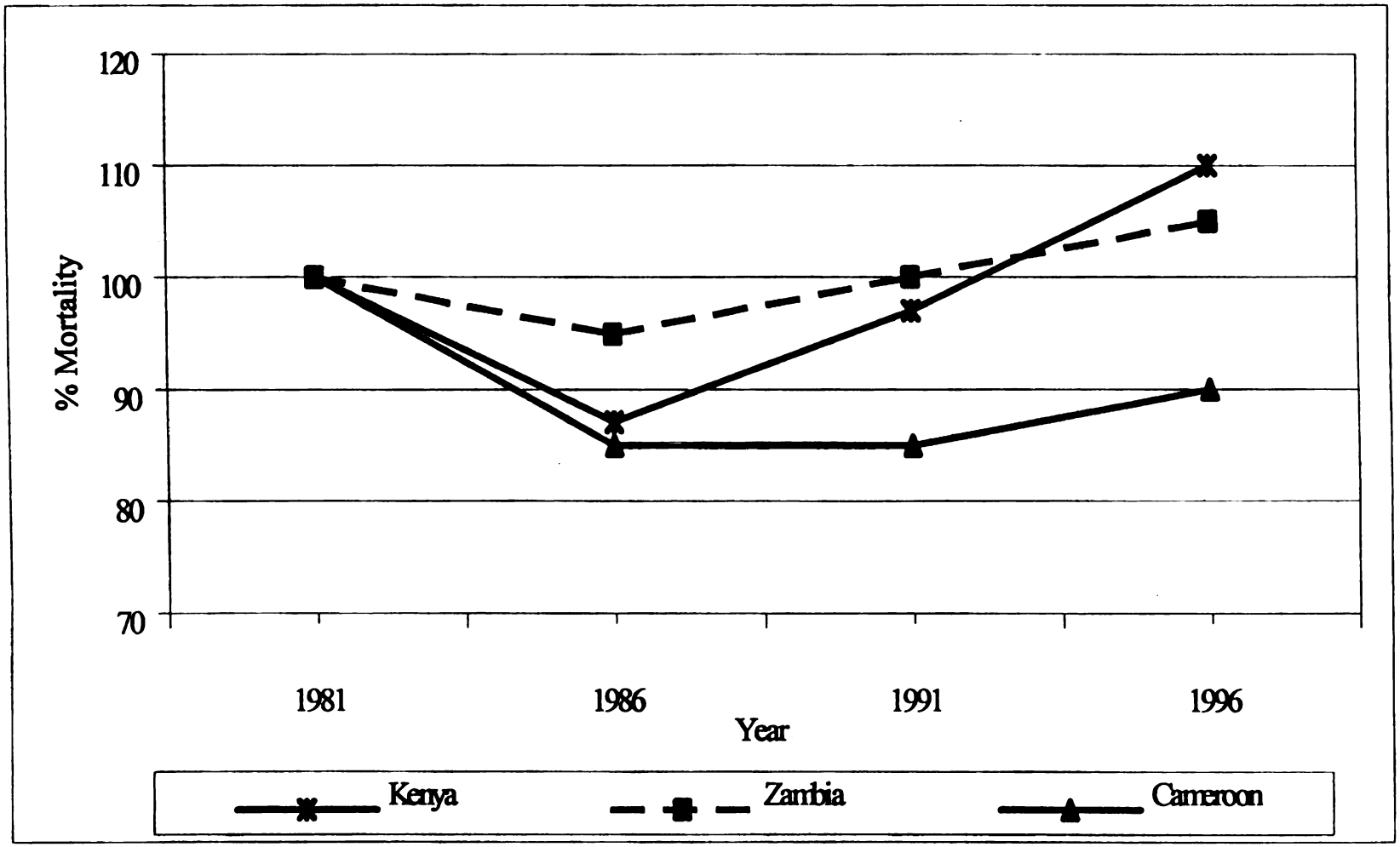

Figure 4: Child Mortality Rate in Kenya, Zambia and Cameroon, 1981-96.
Source: UNAIDS, 2000.

Chapter 3

3.1 Prevention Strategies for Vertical Transmission of HIV/AIDS

Since studies indicate that the majority of infants are infected during delivery, the maternal plasma HIV viral load at delivery has been identified to be the most important predictor of vertical infection (MacDougall, 1997; McGowan and Shah, 2001). Thus, most of the current prevention strategies focus on use of antiretroviral therapy. Other options, such as elective CS, are also effective because they limit the time of fetal exposure to infected maternal body fluids at delivery, the time of greatest risk of transmission. Further, to avoid postnatal exposure and risk of transmission, HIV-infected mothers can be advised to limit or avoid breastfeeding their babies. Other strategies that are currently being researched on include use of antiseptic vaginal and cervical washes, screening and treatment of genital ulcers and other sexually transmitted diseases, voluntary counseling and treatment, and community education.

3.1.1 Antiretroviral Drug Intervention

So far, the most common prevention strategy against vertical transmission of HIV/AIDS has been the use of antiretroviral drugs. Table 1 shows a summary of selected studies on antiretroviral drug therapies in both breastfeeding and non-breastfeeding populations. The first comprehensive antiretroviral study was the Pediatrics AIDS Clinical Trials Group (PACTG) 076 protocol, which was carried out in the US in 1994 (Connors *et al*, 1994).

Table 1: Selected Prospective Antiretroviral Therapy Trials*

Study *(Site)*	Design	Breast Feeding	Arm (n)	Regimen			Transmission	
				Antepartum	Intrapartum	Postpartum	Rate (%)	*p*
PACTG 076 *(USA)*	Placebo-Control	No	A(205) B(204)	ZDV at ≥14 wk Placebo	ZDV Placebo	ZDV for 6 wk Placebo	8.3 25.5	0.00006
PACTG 185 *(USA)*	Placebo-Control	No	A(230) B(224)	Primary + HIVIG Primary + IVIG	ZDV ZDV	ZDV + HIVIG ZDV+ IVIG	6.0 9.4	NS
Bangkok *(Thailand)*	Factorial	No	A(198) B(199)	ZDV at ≥36 wk Placebo	ZDV Placebo	None None	9.4 18.9	0.006
ANRS *(Cote d'Ivoire)*	Placebo-control	Yes	A(140) B(140)	ZDV at ≥36 wk Placebo	ZDV Placebo	None None	15.7 24.9	0.07
DITRAME *(Cote d'Ivoire, Burkina Faso)*	Placebo-control	Yes	A(203) B(211)	ZDV at ≥36 wk Placebo	ZDV Placebo	ZDV to mother Placebo	18 27.5	0.028
HIVNET 012 *(Uganda)*	Placebo-control	Yes	A(302) B(307)	None None	ZDV NVP	ZDV to child NVP to child	25.1 13.1	0.0006
SAINT *(S. Africa)*	Randomized	Yes	N=1306	None	NVP ZDV+ 3TC	NVP to child + mother, 1-2 days ZDV+ 3TC to child + mother	13.3 10.2	>0.10
PETRA *(Uganda, S.Africa, Tanzania)*	Placebo-control	Yes	A(359) B(343) C(351) Placebo	ZDV+3TC at 36 wk Placebo Placebo Placebo	ZDV+3TC ZDV+3TC ZDV+3TC Placebo	ZDV+3TC 7days ZDV+3TC 7days Placebo Placebo	8.6 10.8 17.7 17.2	0.001

* Details of antiretroviral doses given are in the text. For drug names that are abbreviated, see page ix.

The study was a randomized, double-blind study that evaluated safety, efficacy and tolerance of ZDV given during pregnancy, at labor and to the infant after birth compared to an identically administered placebo. Since there was little knowledge concerning the mechanism and timing of transmission, the ZDV regimen was designed to provide maximal efficacy by targeting both potential periods of transmissions, that is, the intrauterine and intrapartum periods.

Participants in the PACTG 076 study were HIV-infected pregnant women between 14-34 weeks' gestation. Since the study involved a placebo, the women were asymptomatic or had minimal symptoms, with a CD4 lymphocyte count of more than 200/mm^3, and did not require therapy for their own health. The total women eligible for analysis were 409. The median maternal age was 25 years, the median CD4 lymphocyte count was 550/mm^3 and the median gestational age at the commencement of the study was 26 weeks. The racial/ethnic composition of the study group was similar to that of HIV-infected women in the US as a whole, with 81% of them being of minority race/ethnicity. Several other baseline characteristics were the same in both the placebo and non-placebo group.

The majority of the infants were full term, with 415 live births (206 in the ZDV and 209 in the placebo group). 403 of these were single births and six were sets of twins. The HIV-status was determined by the presence of one or more positive HIV cultures. Median gestational age at birth was 36 weeks and the median birth-weight was 3160g, and these were similar in both treatment groups. Low birth-weight occurred in 16% of the infants, with no difference between the two groups. Of the total, only 363 infants made the

interim efficacy analysis; the rest did not have HIV culture data. In the placebo group, 40/183 infants were infected compared to only 13/180 ZDV-group infants. The transmission rate at 18 months of age based on Kaplan-Meier analysis was 25.5% in the placebo group compared to 8.3% in the ZDV group, corresponding to a 67.5% reduction in the risk of transmission (p=0.00006). An updated analysis of 419 mother-infant pairs showed similar results, with estimated transmission rates of 24.0% in the placebo group and 7.8% in the ZDV group thereby confirming the interim findings. Follow-up of the PACTG 076 infants to 18 months indicated no significant differences in deaths, rates or types of congenital anomalies, physical weight, height or head growth between the ZDV-exposed and the placebo group. Further, developmental data revealed normal and similar mean mental and physical index scores for both groups, with no statistical difference.

After the study, recommendations on the use of ZDV to reduce vertical transmission of HIV were developed to provide a basis for non-coercive dialogue between infected women and their health providers. This included balancing the known benefits of treatment to the potential unknown risks of the regimen to the women and their infants. However, potential gaps still existed regarding the robustness of the ZDV efficacy in women with characteristics different from those of women enrolled in the trial, as well as on theoretical and unproven long-term risks of the regimen on both the mothers and infants. However, the taskforce made recommendations for different clinical scenarios on the basis of gestation of the pregnancy, maternal CD4 count, the mothers' clinical disease stage and prior history of antiretroviral history.

The PACTG 185 study followed the PACTG 076 and was designed to determine whether HIV-specific immunoglobulin administered prenatally with a single postpartum dose was more effective than ZDV alone (Mofenson *et al*, 1999). The study demonstrated no benefit from the addition of HIV-specific immunoglobulin, but the observed low transmission rate (5%) confirmed the efficacy of ZDV given as in the PACTG 076. This benefit was also observed in women with lower CD4 cell counts (median 306 cells/mm^3 in the PACTG 185 and 550 cells/mm^3 in the PACTG 076) and in the 24% of the mothers in the study who had ZDV exposure before pregnancy.

In 1996, the Center for Disease Control and Prevention (CDC) in collaboration with the UNAIDS began enrolling women in two placebo-controlled trials to determine the effectiveness of a shorter course ZDV treatment. One trial took place in Bangkok, Thailand and a similar one in Abidjan, Cote d'Ivoire. The Bangkok one was a randomized, double blind placebo-controlled trial (Shaffer *et al*, 1999). HIV-infected pregnant women at two Bangkok hospitals were randomly assigned placebo or one ZDV 300mg tablet twice daily from 36 weeks gestation and every 3 hours from onset of labor until delivery. The women were eligible if they were 18 years or older at delivery, were at 34 weeks or less gestation, lived in or near Bangkok, intended to deliver at the study hospital and not breastfeed and were willing and able to provide voluntary consent. Women included in the efficacy analysis in the two study groups did not differ significantly at enrolment. None of the women had previously used an antiretroviral drug, less than 1% had a history of injecting drug use, and the proportion with STD was low and was similar in the two groups.

The mothers were given infant formula and asked not to breastfeed. The main endpoint was babies' HIV infection status tested at birth, 2 months and at 6 months. Maternal plasma viral concentrations were measured. In total, 397 women were enrolled, 393 gave birth to 395 live-born babies. The median duration of antenatal treatment was 25 days and the median number of study drug doses was 53, and during labor it was 3. Adherence to the drug regimen was high and the study drug was well tolerated. Adverse effects were similar in the placebo and non-placebo groups. The results showed that of 392 babies, 55 tested positive by 2 months age; 18 in the ZDV group and 37 in the placebo group. The estimated transmission risks were 9.4% (95% CI 5.2-13.5) on ZDV and 18.9% (95% CI 13.2-24.2) on placebo (p=0.006; efficacy 50% [15.4-70.6]). Compared to PACTG 076 regimen which costed $800 per treatment, the shorter-course ZDV regimen in the Bangkok trial costed only $50 per treatment (Rutter, 1998).

The second study was a randomized trial done in a breastfeeding population in Abidjan, Cote d'Ivoire (Wiktor *et al*, 1999). All consenting, eligible HIV-infected pregnant women attending a public antenatal clinic in Abidjan were enrolled at 36 weeks' gestation and randomly assigned placebo or one ZDV tablet (300 mg) twice daily until the onset of labor, one tablet at onset of labor, and one tablet every 3 hours until delivery. DNA PCR test was used to determine infection status of babies at birth, 4 weeks and 3 months. A total of 280 women were enrolled, split equally between the placebo and the ZDV groups, with a median duration of the prenatal drug regimen of 27 days and median duration of labor of 7.5 hours. Treatment was well tolerated with no withdrawals because of adverse events and all babies were breastfed. Among babies with known infection

status at age 3 months, 30/115 (26.1%) babies in the placebo group and 19/115 (16.5%) in the ZDV group were identified as HIV-infected. The estimated risk of HIV transmission in the placebo and ZDV groups were 21.7% and 12.2% (p=0.05) at 4 weeks, and 24.9% and 15.7% (p=0.07) at 3 months, respectively. The efficacy was 44% (95% CI 1-69%) at age 4 weeks and 37% (95% CI 5–63%) at 3 months.

Another randomized double-blind placebo-controlled trial was carried out in public clinics of Abidjan, Côte d'Ivoire, and Bobo-Dioulasso, Burkina Faso and sponsored by *Agence Nationale de Recherche Scientifique* (ANRS) of France and the French Ministry of Cooperation (Dabis *et al*, 1999). Eligible participants were women aged 18 years or older, who had confirmed HIV-1 infection and pregnancy of 36-38 weeks duration, and who gave written informed consent. Exclusion criteria were severe anemia, neutropenia, abnormal liver function, and sickle-cell disease. Women were randomly assigned ZDV (n=214), 300 mg twice daily until labor, 600 mg at beginning of labor, and 300 mg twice daily for 7 days postpartum or matching placebo (n=217). The primary outcome was the diagnosis of HIV-1 infection in the infant on the basis of sequential DNA PCR tests at days 1-8, 45, 90, and 180.

The study analysis was based on 421 women and 400 life-births. Baseline demographic, clinical and laboratory characteristics were similar in the two groups. The Kaplan-Meier probability of HIV infection in the infant at 6 months was 18% in the ZDV group (n=192) and 27·5% in the placebo group (n=197). The efficacy of ZDV was thus estimated at 30%. Adjustment for center, period of recruitment, mode of delivery,

maternal CD4-cell count, duration of labor, prolonged rupture of membranes, and duration of breastfeeding did not change the treatment effect. The above trials showed that the use of ZDV resulted in consistently decreased HIV transmission risk. However, the issue of the cost was still nagging.

Therefore, a study was initiated in Uganda in 1997, the HIVNET-012, to compare the safety and efficacy of short course nevirapine (NVP) to ZDV during labor and the first week of life (Guay *et al*, 1999). NVP was selected because of its long half-life, potent antiviral activity, safety profile and lower cost compared to ZDV. 626 HIV-infected pregnant women were enrolled at Mulago hospital in Kampala, Uganda, and randomly assigned to either NVP or ZDV groups. The nevirapine group received 200mg orally at onset of labor and 2mg/kg given to babies within 72 hrs of birth. The ZDV group received 600 mg orally at onset of labor and 300mg every 3 hrs until delivery, and 4 mg/kg was given orally twice daily to babies for 7 days after birth.

The babies were tested for HIV infection at birth, 6-8 weeks, and 14-16 weeks by RNA PCR. HIV transmission and HIV-free survival was assessed using Kaplan-Meier analysis. The estimated risks of HIV transmission in ZDV and NVP groups were 10.4% and 8.2% at birth (p=0.354); 21.3% and 11.9% by age 6-8 weeks (p=0.0027); and 25.1% and 13.1% by age 14-16 weeks (p=0.0006), respectively. The efficacy of NVP compared with ZDV was 47% (95% CI 20-64) up to age 14-16 weeks. The two regimens were well tolerated and the adverse events were similar in the two groups. The NVP regimen cost was substantially lower, at about $4 per treatment.

In another trial, the South African Intrapartum Nevirapine Trial (SAINT), 1306 HIV positive women and their neonates were randomized to receive NVP or ZDV plus lamivudine (3TC) (Moodley, 2000). Women in the nevirapine arm received a single 200mg dose during labor then another 200mg dose 24-48 hours after delivery. Neonates in this arm received a single NVP 6mg dose 24-48 hours after birth. During labor, women in the combination arm received ZDV 600mg at the onset of labor then 300mg every 3 hours, plus 3TC 150mg twice daily.

Further, during post-delivery, women in the combination arm received ZDV 300mg twice daily plus 3TC 150mg twice daily, for 7 days. Neonates in this arm received ZDV 12mg twice daily plus 3TC 6mg twice daily for 7 days. Shortly after birth, the rate of HIV infection or death was 8.5% among NVP recipients and 7.4% among ZDV plus 3TC recipients. However, by day 56 this figure had increased to 14.3 and 12.5%, respectively, reflecting the transmission of HIV during breastfeeding. The rates of peripartum HIV infection, all HIV infections by Day 56 and HIV infection or death by Day 56 were not significantly different among the two groups, indicating that NVP was as effective as a combination therapy of ZDV and 3TC.

Another trial worth noting is the PETRA study carried out in three African countries: South Africa, Uganda and Tanzania (Saba, 1999). The aim of the trial was to assess the efficacy of ZDV + 3TC when given at different stages of probable transmission. 1457 HIV-infected women and their neonates were randomized to one of four treatment arms as follows:

A. ZDV + 3TC given at 26 weeks of pregnancy (prepartum), intrapartum, and 1 week postpartum for mother and neonate;

B. ZDV + 3TC intrapartum and 1 week postpartum for mother and neonate;

C. ZDV + 3TC intrapartum only; and

D. Placebo.

A 6-week assessment revealed that the combined neonatal HIV infection and mortality rate had been significantly reduced in arms A and B compared with D (8.2%, 12.3% and 19.1%, respectively). This showed a 52% efficacy for the full regimen (arm A) and 38% efficacy for intrapartum and postpartum treatment (arm B), and no efficacy for arm C. However, the treatment effect was lost after 18 months, maybe due to postpartum infection through breastfeeding.

Several studies have gone further and evaluated the cost effectiveness of various antiretroviral therapies in the SSA settings. One such study used a hypothetical computer model to simulate providing NVP to a cohort of 20,000 pregnant women. The model compared NVP treatment with no treatment and other short-term prophylactic regimens (Marseille *et al*, 1998). The analysis revealed that, in regions with 30 percent prevalence of HIV, universal application of the HIVNET-012 NVP regimen would avert 603 cases of infection in infants at a cost of $83,300 per year. At the same prevalence of HIV, targeted application of HIVNET-012 NPV regimen would avert 476 cases of infection and would cost $141,900. Therefore, the cost-effectiveness of the treatment was likely to be comparable to that of other well-accepted public health interventions in the high HIV-prevalence settings and about 70 times less expensive than even a shorter course of zidovudine (Alexander, 1999). Soderlund *et al* (1999), in a study based on South Africa,

also found the use of antiretroviral drugs to be cost-effective under different infant feeding regimes but the cost of implementing it at the country level would be out of reach for most SSA countries.

In summary, the PACTG 076, which was the pivotal vertical transmission study, demonstrated that use of ZDV could reduce vertical transmission of HIV by 68%. The treatment was effective but considered expensive at $800 per treatment and impractical where drugs cannot be delivered to remote communities due to lack of appropriate infrastructure and personnel. The cost of this treatment, combined with the probable timing of transmission indicated that a shorter course ZDV administered just before or during birth might be just as effective but far less expensive. The studies in Bangkok, Cote d'Ivoire and Burkina Faso showed that the short-course ZDV therapy was still efficacious and more affordable, an issue that is increasingly important for effective preventive HIV intervention in the SSA. The HIVNET study in Uganda, which demonstrated the efficacy of NVP, was the simplest and least expensive regimen.

3.1.5 Elective Cesarean Section

Researchers and clinicians have been looking beyond drug therapy to surgical interventions targeted at the crucial period of labor and delivery. It has long been suggested that HIV-positive women who deliver by elective CS are less likely to transmit the virus to their newborns than women who deliver vaginally are. However, such CS must be performed prior to the rupture of the membranes (Cadman, 1999). Studies have shown that the risk of vertical transmission nearly doubles when the membranes rupture

more than 4 hours before delivery (Burns and Mofenson, 1999). As long as the membranes are intact, pathogens such as HIV may have a more difficult time entering the uterus and infecting the fetus. Elective CS, performed while the membranes are still intact, might prevent the infant from being exposed to maternal blood and secretions while passing through the birth canal.

Past studies have shown that the risk of vertical transmission may be reduced by 50% with elective CS compared to other modes of delivery and without antiretroviral drug treatment (IPHG, 1999). Elective CS and the three-part ZDV regimen combined reduced vertical transmission by more than 85 percent. CS performed after labor has not been shown to reduce vertical transmission, hence the suspicion that most transmission occurs during labor and delivery. For this reason, HIV positive women must decide what to do before labor so that the procedure is scheduled at an appropriate time before the onset of labor.

However, other factors also need to be considered. For women who are taking antiretroviral drugs, especially those on maximally suppressive multi-drug therapy, the additional reduction in transmission through CS may be outweighed by the added discomfort and potential complications associated with the procedure since maximum benefits from CS are experienced only in women also taking ZDV. Those not taking ZDV and have elective CS remain at elevated risk of transmitting HIV to their infants. Moreover, operative delivery is associated with substantial morbidity and mortality, especially when done under less than ideal conditions, and it is expensive and not easily

implemented in the developing countries with limited healthcare infrastructure, budgets and inadequate voluntary HIV counseling and testing (VCT) programs (Mansergh et al, 1998). In addition, HIV-positive women may have an increased risk of post-operative complications (Semprini, *et al*, 1995). Finally, the risk/benefit ratio of CS delivery may vary from woman to woman. For instance, the additional benefits for a woman with undetectable HIV load and a CD4 count of 500cells/mm^3, who was on ZDV or a combination therapy, may be so low that it is outweighed by the increased risk of post-operative complications.

A meta-analysis of 15 North American and European prospective cohort studies evaluated the relationship between elective CS and vertical transmission of HIV using 8533 mother-child pairs. Multivariate logistic-regression analysis was used to adjust for other factors known to be associated with vertical transmission. After adjustment for receipt of ZDV, maternal stage of disease and infant birth weight, the likelihood of vertical transmission of HIV was decreased by approximately 50% with elective CS as compared to other modes of delivery (adjusted odds ratio, 0.43; 95% CI: 0.33-0.56). The results were similar when the analysis was limited to those with membrane rapture shortly before delivery. However, the likelihood of virus transmission was reduced by about 87% with both elective CS and receipt of ZDV during prenatal, intrapartum and neonatal periods compared to other modes of delivery and absence of antiretroviral therapy (adjusted odds ratio, 0.13; 95% CI: 0.09-0.19). These results showed that elective CS reduced the risk of transmission independently of the effects of antiretroviral therapy (IPHG, 1999).

In a Swiss study of 494 six-months-old children, combined use of elective CS and ZDV resulted in 0% transmission rate compared with 8% after elective CS alone, 17% after ZDV alone, and 20% after no intervention (Kind *et al*, 1998). Similarly, in another prospective study involving 599 infants born to 520 women in Spain, CS was associated with lower rates of vertical transmission in the absence of ZDV. The crude rate of HIV transmission was 6% among CS births compared with 21% for infants born vaginally.

Data from a prospective study in Durban, South Africa was used to investigate the associations between vertical transmission of HIV/AIDS and mode of delivery. A total of 141 children of HIV-infected women were followed until the children were 15 months of age to determine their HIV status. Supplementary data was collected from obstetric records, masked to the HIV status of the children. In this predominantly breast-fed population, infants delivered vaginally were more likely to be infected (39.8% infected) than were infants delivered by elective CS (22.9% infected; odds ratio, 0.45; 95% CI: 0.20-0.99).

There were no significant differences between CS deliveries undertaken following prior rupture of membranes and those undertaken with membranes intact, but the numbers for this comparison were small. Singleton CS deliveries without concurrent obstetric complications had lower rates of transmission than did vaginal deliveries (odds ratio, 0.20; 95% CI: 0.04-0.94). These results suggested that certain intrapartum events might modify the risk of HIV transmission, highlighting the importance of collecting more detailed intrapartum information in order to clarify the route by which mode of delivery

may be associated with vertical HIV transmission (Kuhn *et al*, 1999).

3.1.3 Breastfeeding and Vitamin A Supplementation

Breastfeeding is partially blamed for the high rate of vertical transmission of HIV/AIDS experienced in developing countries. In Sub-Saharan Africa, several studies indicate that more than one-third of HIV-positive infants get infected through breastfeeding. The studies suggest an average risk of late postnatal transmission through breastfeeding of one in seven children. Data from eight prospective studies that included breast-fed and formula-fed infants in developed and developing countries showed that the risk of vertical transmission increased significantly when infants were breastfed, and also increased with the duration of breastfeeding ((Leroy et al, 1998; Cadman, 1999).

While the ability of cheaper short-course antiretroviral drugs to reduce vertical transmission may provide hope for women in developing countries, it is likely that it may provide more protection for infants who are not breastfed. Therefore, it is likely that the margin of difference in transmission rates between those treated and those not treated will narrow in cases where women breastfeed their infants. In such circumstances, then, the greatest reduction in vertical transmission can only occur when an integrated prevention program which combines antiretroviral therapy and safe alternatives to breastfeeding are implemented. However, according to UNAIDS, it may be impractical in some countries to simultaneously implement access to antiretroviral drugs and access to safe alternatives to breastfeeding. In such situation, the implementation of one component should not be delayed until the other is feasible.

Moreover, in the SSA, where breastfeeding is the established method of infant feeding, failure to breastfeed may be interpreted as an indication of a woman's HIV-positive serostatus. Mothers in such cultures will need support to overcome possible stigmatization effects if they choose not to breastfeed. Meanwhile, health workers in different countries have tried to tailor their advice to suit the particular circumstances prevailing in their countries. For example, in Thailand there is relatively wide access to safe water and infant death from infectious diseases is less common than it is in the SSA. Most pregnant women in the former are now tested for HIV at delivery. Those found to be positive are given free infant formula and encouraged not to breastfeed.

The current recommendations on breastfeeding in the SSA are less clear. There, childhood infectious diseases are common and HIV testing is often not available. Most women have been encouraged to breastfeed regardless of their HIV status. The UNAIDS now encourages as much information as possible on the relative risks of breastfeeding and formula-feeding to be made available to HIV-positive mothers, requiring that they be tested, to enable them to decide for themselves whether to breastfeed or not. It is recommended that efforts continue to promote and support breastfeeding by women who are HIV negative or of unknown status. Hence, all women should have access to voluntary HIV testing and counseling that includes information on vertical transmission and infant feeding. It is currently acknowledged that in most poor countries, however, most women still are not provided with sufficient information and support to make an informed choice (UNAIDS, 1998). Moreover, the increase in infant morbidity and

mortality associated with not breastfeeding could outweigh any reduction in the risk of HIV transmission through breastfeeding.

On Vitamin A supplementation, data from several studies have shown significant reduction in infant morbidity and mortality, and increased postpartum CD4+, CD8+ and CD3+ cell counts in mothers but non-significant effects on vertical transmission of HIV (Semba, 1998; Fawzi et al, 1998; Fawzi et al, 2000). A study in Tanzania found no significant effect of Vitamin A on HIV status. Of babies in the multivitamin arm 38, (10.1%) were HIV-positive at birth compared with 24 (6.6%) in the no-multivitamin arm (relative risk [RR] = 1.54; 95% CI, 0.94-2.51; p = .08). Of babies born to mothers in the vitamin A arm, 38 (10.0%) were HIV-positive at birth compared with 24 (6.7%) in the non-Vitamin A arm (RR, 1.49; 95% CI, 0.91-2.43; p = 0.11). Neither multivitamins nor vitamin A had an effect on HIV status at 6 weeks among those who were HIV-negative at birth (*RR*=1.04; 95% CI, 0.65-1.66; *p*=0.88) and (*RR*=1.30; 95% CI, 0.80-2.09; *p*=0.29, respectively). Similarly, neither supplement was associated with being either HIV-infected or dead at birth (*RR*, 0.98; 95% CI, 0.76-1.27; *p*=0.89 and *RR*, 1.01; 95% CI, 0.78-1.31; *p*=0.95, respectively (Fawzi et al, 2000).

In Durban, South Africa 728 pregnant HIV-infected women received either vitamin A (*n*=368) or placebo (*n*=360) in a randomized, double blind trial (Coutsoudis et al, 1999). The vitamin A treatment consisted of a daily dose of 5000 IU retinyl palmitate and 30 mg beta-carotene during the third trimester of pregnancy and 200000 IU retinyl palmitate at delivery. HIV infection results were available on 632 children. There was no difference

in the risk of HIV infection by 3 months of age between the vitamin A [20.3%; 95% CI: 15.7-24.9] and placebo groups (22.3%; 95% CI: 17.5-27.1), nor were there differences in fetal or infant mortality rates between the two groups.

Women receiving vitamin A supplement were less likely to have a preterm delivery (11.4% in the vitamin A and 17.4% in the placebo group; p=0.03) and among the 80 preterm deliveries, those assigned to the vitamin A group were less likely to be infected (17.9%; 95% CI: 3.5-32.2) than those assigned to the placebo group (33.8%; 95% CI: 19.8-47.8). Therefore, Vitamin A supplementation, a low-cost intervention, did not appear to be effective in reducing overall mother-to-child transmission of HIV. However, its potential for reducing the incidence of preterm births and the risk of mother-to-child transmission of HIV in these infants needs further investigation.

In a study of the effect of Vitamin A supplementation in the US, statistical analysis of the data indicated that low maternal serum retinol levels during the third trimester of pregnancy were not associated with mother-to-child transmission of HIV-1. None of the 95 women studied had retinol levels so low as to have clinical symptoms of vitamin A deficiency. The serum levels of alpha-tocopherol, beta-carotene, and lycopene, three micronutrients that act as antioxidants and enhance immune function, were also measured. Statistical analysis of the data revealed no association of the levels of these three micronutrients with vertical transmission of HIV-1. The data indicated that vitamin A deficiency was rare in the US, and serum retinol levels were not associated with risk of vertical HIV-1 transmission. In view of the teratogenic effects of vitamin A when taken

as a supplement during pregnancy, pregnant HIV-infected women living in nations where vitamin A deficiency is not a public health problem should not be advised to take extra vitamin A supplements. But those in the SSA would benefit from such supplements, especially those showing significant vitamin A deficiency during pregnancy.

3.1.4 Vaginal Cleansing, STD Treatment and Circumcision

A study in Malawi was recently completed that evaluated whether chlorhexadine vaginal cleansing during labor followed by neonatal chlorhexadine wash at delivery was associated with a decrease in vertical transmission of HIV (Biggar et al, 1996). The study included evaluation of approximately 7000 infants: 3327 born to mothers who had conventional deliveries and 3637 born to mothers who received a 0.25 chlorhexidine wash. The overall results did not show any significant impact of the intervention on infant HIV-infection status (26.7% among the intervention group against 27.9% in the control group). However, a *post hoc* subset analysis suggested that among infants born to mothers with membrane rupture greater than 4 hour there was significant reduction in perinatal HIV transmission. Stray-Pedersen *et al* (1999) found that intrapartum vaginal douching with 0.2% chlorhexidine can significantly reduce vertical transmission of microbes and both maternal and early neonatal infectious morbidity.

A recent community-based clinical trial in Tanzania evaluated whether treatment of symptomatic STDs in sexually active adults had any impact on HIV sero-incidence rates. Results of the study did indicate a significant decrease in HIV sero-incidence among the intervention group that had received the anti-microbial intervention (Grosskurth et al,

1995). Quinn et al (2000) enrolled 15,127 persons in rural Uganda in a randomized, controlled trial designed to determine whether intermittent antibiotic treatment to reduce the prevalence of other STDs would also reduce the rate of transmission of HIV. This was not successful (Wawer et al, 1999). However, of 415 couples in which one was HIV-positive and the other HIV-negative, 21.7% seroconverted during a follow-up period of up to 30 months, despite provision of condoms and counseling.

A study in rural Zimbabwe evaluating effective HIV control strategies also considered the correlation between HIV and STD incidences. The HIV seroprevalence was 23.3% and was higher in females, divorcees, widows, working men, estate residents, and respondents reporting histories of STD symptoms. A third of sexually active adults had experienced STD-associated symptoms but there were delays in seeking treatment. The study found that local program promoting safer sexual behavior and fast and effective STD treatment among young women, divorcees and working men could reduce the extensive HIV transmission in rural communities (Gregson et al, 2001).

There is compelling evidence from over 40 studies that male circumcision provides significant protection against HIV infection. Circumcised males are two to eight times less likely to become infected with HIV (Halperin and Bailey, 1999). Moreover, circumcision also protects against other STDs, such as syphilis and gonorrhea, and since people who have STD infections are two to five times more likely to become infected with HIV (Fleming et al, 1999), circumcision may even be more protective. In 1994, a group of scientists in Kenya published a review of 30 epidemiological studies showing a

strong correlation between high rates of HIV infection in African populations that do not practice male circumcision.

In a study done among couples in Uganda with discordant HIV status, in which the women were HIV positive and the their male partners were not, no new infections occurred among any of the 50 circumcised men over 30 months whereas 40 of 137 uncircumcised men became infected (Quinn et al, 2000). This and other studies have focused attention on the role of the foreskin in HIV infection, on how the HIV enters the penis and why men who are uncircumcised are more susceptible to infection. It is believed that the keratinised, stratified squamous epithelium, which covers the penile shaft and outer surface of the foreskin, provides a protective barrier against HIV infection. In contrast, the inner mucosal surface of the foreskin is not keratinised and is rich in Langerhans' cells, making it particularly susceptible to the HIV virus (Szabo and Short, 2000; Hussain and Lehner, 1998). There is, however, controversy about whether the epithelium of the glans in uncircumcised men is keratinised or not (Barreto *et al*, 1997).

Cultural and religious attitudes notwithstanding, in the light of the evidence presented, circumcising males may be recommended, especially in countries with a high prevalence of HIV infection. Although neonatal circumcision is easier to perform, and has a low incidence of complications, it would be 15-20 years before a program of circumcision had any effect on HIV transmission rates. In the meantime, circumcision at puberty

would be the most immediate effective intervention for reducing HIV transmission since it would be done before young men become sexually active.

3.1.5 Community Education, Voluntary Counseling and Testing

Although the use of antiretroviral drugs has borne the greatest results in reducing vertical transmission of HIV/AIDS in developed countries, its effectiveness in the SSA may be hindered by lack of resources and appropriate infrastructure or by unavailability and high cost of the drugs (Dabis et al, 2000). Since the rate of vertical transmission is highly correlated with HIV/AIDS prevalence in the general population, a second strategy of minimizing vertical transmission is to minimize HIV incidences among adults, especially women of child bearing age, and the youth. It is becoming clearer that an effective strategy in the short to medium-term must involve community education and awareness campaigns to avert risky sexual behavior. In the long-term though, increasing resources for HIV/AIDS research, education and drugs, and building more effective infrastructure for delivering necessary public health care to people with, and those at risk of acquiring, HIV/AIDS will be prudent.

Two decades of experience have shown that sexual behavior and attitudes contribute to the spread of HIV/AIDS (UNAIDS, 2000). As a result, interventions using voluntary counseling and testing (VCT), condom marketing, community education and treatment of STDs can be used to influence change of human behavior and reduce the risk of infection. The following examples demonstrate the effect that such interventions can have

on changing behavior and reducing transmission of STDs and HIV/AIDS (World Bank, 1999):

a. A Rwandan study showed that the incidence of new HIV infections decreased from 4.1% to 1.8% due to preventive counseling and testing of women an and their sex partners. The average cost of VCT in Sub-Saharan Africa, based on this and other studies, was estimated at $4.40 per person counseled and tested.

b. In the Democratic Republic of Congo, an intervention targeting education, STD treatment and provision of condoms to commercial sex workers resulted in an increase in regular condom use from 10% to 68% in 3 years, and a decrease in HIV incidence from 11.7 to 4.4 per 100 person-years of observation. The cost of STD treatment was estimated at $2.33 per case.

c. A project in Kenya distributed condoms and educational materials to male truck drivers through a work-place intervention program. This led to a 13% decrease in extramarital sex, a 6% decrease in visits to commercial sex workers, a significant reduction in STD incidence and related reduction in the risk of acquiring HIV.

d. There were significant decreases in HIV prevalence among women attending prenatal clinics in certain regions in Uganda between 1990/93 and 1994/95. Strong leadership by President Museveni himself, and partnership with civil society facilitated the changes leading to the decrease.

e. The leadership of Senegal chose not to deny the existence of the epidemic but to face the challenge right from the start. A timely and aggressive prevention campaign has helped the country maintain one of the lowest HIV infection rates in the SSA at 1.8%. This allows the government to consider utilizing treatment schedules that otherwise would not have been affordable (UNAIDS, 1998).

f. In Thailand, concerted government prevention efforts at the national and regional levels led to a sharp decline in new HIV and STD infections as condom use among sex workers rose dramatically.

The key to these programs was influencing change in risky sexual behavior, provision of condoms to vulnerable populations, effective diagnosis and treatment of STDs, providing free VCT and resources to mitigate against adverse impacts of HIV/AIDS.

Supplemental efforts that may reduce the HIV burden include:

a. Improvement of economic opportunities and reduction of harmful and discriminatory practices against women, especially those at risk of infection.

b. Education of children, especially girls, to enhance their ability to avoid infection.

c. Reducing school fees for children from poor families and HIV/AIDS orphans and providing foster care for the orphans, food programs for children and support for educational expenses to help families and children survive consequences of AIDS.

d. Establishing outreach programs for street children and other out-of-school youth to reduce HIV infection from risky lifestyles.

e. Creating incentives for training to encourage firms to maintain worker productivity despite losses of experienced workers to HIV/AIDS.

f. Providing home care for HIV/AIDS patients and support for their families and providing social funds and support to help grassroots organizations cope with the pandemic.

Successful programs like the ones in Uganda and Senegal have shown that government commitment to creating an enabling environment is important. However, it seems strategic to intervene early and prevent infections among vulnerable groups to avert subsequent larger number of new infections (World Bank, 1997). Therefore, it is recommended that countries with higher HIV prevalence rates target interventions at vulnerable groups and move beyond prevention to provide health care and mitigate the impact of the epidemic. On the other hand, in countries with lower prevalence rates the disease is still predominantly localized among high risk groups and priority should concentrate on community education and awareness to change the behavior of those at high risk of contracting and spreading the disease.

3.1.6 Prospective HIV/AIDS Vaccines

While promising new drug therapies for HIV have recently improved the health and hope of many HIV-infected individuals in the United States and elsewhere, control of the epidemic worldwide may rely more on the development of an effective anti-HIV vaccine. Development of such a vaccine requires new approaches and techniques. This has been slow due to challenges posed by lack of sufficient research resources, technical difficulties such as presence of unique viral characteristics such as antigenic variability, lack of suitable animal models and lack of clear definitions for disease protection, and lack of political will. A greater involvement by the private sector is seen as a necessary step in the development of the vaccines (MacDougall, 1997).

In the past, the performance of vaccine efficacy trials in developing countries has been shown to expedite the introduction of the vaccines in such populations. However, undertaking these kinds of clinical vaccine trials presents a variety of unique hurdles. For instance, policies of informed consent in developing countries may conflict with those of industrialized countries. Oral consent may be considered sufficient in regions of low rates of literacy or where oral contracts are generally considered equivalent to written documentation. In some developing areas, community and village leaders may provide consent for entire groups, in contrast to the practice of individual autonomy more prevalent in industrialized regions. In addition, the composition of institutional review boards in developing countries may differ from those in industrialized regions, and such discrepancies may disallow some studies and curb transfer of funding in others. The responsibilities of sponsors of vaccine trials in developing countries may also differ from

those of sponsors of trials in industrialized countries. For instance, vaccine development trials in developing countries may incorporate health education, medical care, and vaccination with non-study vaccines as part of the study protocol. The willingness of sponsors to support vaccine trials in developing countries may depend in part on the balance between the costs and logistical obstacles associated with the location and the benefits in terms of epidemiology, population, and other local characteristics.

Despite the hurdles associated with conducting clinical vaccine trials in developing countries, it is doubtless that such trials are needed, and that such trials must provide benefits not only for participants but also for the population at large. The reduction in the incidence of vaccine-preventable diseases has been called one of the most significant public health achievements of the past 100 years, and a multitude of promising new vaccines are on the horizon. Currently, more than 35 clinical vaccine trials are going on around the world, but only a few are taking place in Sub-Saharan Africa. In Kenya, a new HIV vaccine developed by Kenyan and British scientists, has been in trial since March 2001. The vaccine is designed to combat the strain of HIV that is common in eastern Africa. The scientists, drawn from Britain's Medical Research Council and the University of Nairobi, have been working on the project for more than four years. Much of the research is based on a group of prostitutes in a Nairobi slum who seem to have particularly strong immune systems that fend off HIV infection. The researchers found that the prostitutes had significantly high levels of cytoxic T cells, which stimulate the immune system to kill the virus, and are believed to be key to the immunity. (Nation, 2001; CNN, 2001).

In summary, this chapter reveals that there are a number of interventions that can be used to reduce the rate of vertical transmission of HIV/AIDS in the SSA. Current knowledge on the different factors influencing HIV transmission and the timing and mechanism of transmission ought to enable a better determination of priority intervention strategies that would provide the greatest reductions in transmission and new infections. However, this is spells a major challenge in that before substantial effort and sums of money are spent on particular interventions, there is need for carefully-designed, comprehensive epidemiological studies to confirm major factors influencing the disease transmission in the SSA.

It is not, by any means, prudent to cut-and-paste interventions that seem appropriate in developed countries and apply them blankly over the SSA settings. The new interventions will need to be sensitive to differences in social, cultural, economic and political circumstances. A good example is the fact that nearly all women in the SSA breastfeed, unlike those in the developed countries. This poses a special challenge while designing alternative feeding options since the economic cost, loss of benefits derived from breastfeeding and a social cost of stigmatization must be taken into account.

Chapter 4

4.1 Prospects of Preventing Vertical Transmission of HIV/AIDS

The continuing spread of HIV/AIDS throughout the world demands that urgent measures be taken to reduce the spread of the disease and enhance the capacity of countries and communities to respond effectively to the imposed threat. Unfortunately, without a vaccine in sight, the challenge before the global community seems almost insurmountable. But one thing is clear and acknowledged: no single strategy will sufficiently address all the problems. Because of differences in disease strains, prevalence and factors influencing the disease spread, multiple strategies will be required to bring about significant reduction to the pandemic and alleviate the burden of the disease on society (Dabis et al, 2000).

Numerous studies have been conducted, and others are going on, in the search of a promising cure for HIV/AIDS. Consequently, a lot of information has been generated that is useful in evaluating the potential of different prevention strategies for the SSA. Such strategies may be typically divided into two categories: (1) primary intervention strategies, which are ideal for HIV-negative people; and (2) secondary intervention strategies, which are applicable to people with HIV/AIDS. A further category, tertiary intervention strategies, can consists of measures available to deal with long-term impairments, disabilities or sufferings caused by the disease, thereby, extending prevention into rehabilitation (Last, 1995).

4.1.1 Primary Intervention Strategies

Primary intervention strategies are the best hope for the SSA. The key word is *prevention*, which is better and often cheaper than *cure*. According to UN (2001), prevention must be the mainstay of any future intervention strategies. Ideally, primary strategies should be targeted to HIV-negative people and communities with low disease prevalence. One of the most effective strategies under this category is the prevention of further disease spread through community education and awareness campaigns (World Bank, 1997). This can also done in regions and communities with high HIV-prevalence by targeting those that are infected and trying, through counseling, to impart safe-sex practices that would minimize the level of new infections. In both cases, the idea is to educate and inform individuals and communities on the benefits of abating risky sexual behavior. This, in the SSA setting, is most effectively done where there exist a deeper understanding of the culture, traditions and customs of the people, and how these interact with undesired behavioral changes. Hence, there is need for comprehensive community-level studies.

Since the needs of individuals, families and communities affected by HIV/AIDS are diverse and complicated, the best way to respond to their needs is through integrated, community-based approaches. Such approaches provide a framework for close cooperation of all the concerned parties, including hospitals, home-care providers, hospices, religious groups, schools, communities, families and individuals that take advantage of close personal interactions and informal organizations based on mutual support, common interest and kinship (UNAIDS, 1998). The advantage of such

community-based programs is their ability to (1) provide comprehensive health care that meets basic nutritional, social, recreation and economic needs of those affected; (2) access basic health and social services within the community; and (3) relieve psychological stress that may result from possible discrimination and prejudice.

The UNAIDS (1998) documents successful, practical HIV/AIDS prevention programs that have had huge impacts using community-based strategies. One example is in Uganda where the government partnered with community-based HIV/AIDS service organizations (ASOs) through the National HIV/AIDS Control Program to provide community health education as a strong option that can make a difference in the war against the disease. This makes existing social and community-network groups powerful sources of information and education on HIV/AIDS, thus preventing ignorance and further disease infections. The president of Uganda, Yoweri Museveni, is credited with being personally involved in the campaign.

Moreover, integration of community-based education campaigns with voluntary counseling and testing (VCT) can be an important strategy to reach both the infected and non-infected individuals in the community. The VCT can be offered to all women visiting antenatal clinics and those that are at high risks. In addition, this may be much easily done if recommended and offered to all women at their first clinic visit, alongside other blood tests, so as to cause less anxiety and not affect successive follow-up visits. The bottom line is that it is critical to provide accurate information for all pregnant women explaining the benefits to themselves and their babies of making positive

diagnosis before delivery. Gibb et al (1998) suggests that any discussion of HIV transmission with a pregnant woman increased the likelihood of testing. However, concern about confidentiality must be addressed seriously and may require amendments to local policies and regulations. Mass screening, or compulsory testing, is considered undesirable and may risk deterring women from seeking antenatal care and couples from seeking joint screening. However, all screenings require sensitive equipment to reduce the number of false-positive results and stigmatization.

Condom use has been shown to be an effective means of reducing sexually transmitted diseases (STD) infection, and is positively correlated to decreases in HIV/AIDS infections, especially among high-risk groups. However, misconceptions about the effectiveness of condoms in protecting against the HIV still persist, and continue to be fueled by ethical, social and religious concerns. Scientifically, there is evidence that correct and consistent use of good quality condoms vastly reduce the likelihood of HIV transmission (UNAIDS, 2000). In fact, in many parts of the world, the use of condoms has increased substantially, especially among the youth. The same trend is observed in SSA countries but certain regions and communities shun condom use, citing religious and cultural conflicts. Nonetheless, there is evidence that targeted supply of condoms in high HIV/AIDS prevalent regions may reduce disease transmission and new infections.

4.1.2 Secondary Intervention Strategies

As suggested above, screening of HIV infection should be done as early as possible in pregnancy to allow women to make informed decisions about possible treatment options.

Use of antiretroviral drugs, although less effective in breastfeeding SSA populations than in non-breastfeeding populations in developed countries, is a viable option if the drugs are made accessible and affordable. Combination drug therapies and protease inhibitors, which are currently common in developed countries, are likely to be more expensive and outside the reach of the poor in the SSA. Use of any antiretroviral drugs must take into account their benefits and risks. Benefits may include undetectable HIV viral load, immunological improvements, reduced AIDS-related events, while potential risks may include adverse effects, interference with daily activities, teratogenic effects, drug resistance and incomplete viral suppression. As much as possible, HIV-positive pregnant women should be provided with as much information as possible on the use of antiretroviral drugs and counseled on its significance. It is recommended that HIV-infected women who are not currently on antiretroviral drugs start therapy after the first trimester (14 weeks gestation). This may not work very well in the SSA because most pregnant women start attending clinic many weeks after treatment should have started. In any case, if possible, the therapy should be given at least during labor and included in the regimen for the newborn.

Currently recommended drug therapies are considered expensive and somewhat complicated for many people in the SSA. Therefore, simpler and cheaper drug options may be more appealing. Making such drugs accessible, however, permeates beyond the cost issue. More effective drug delivery systems may be required and investments made in health systems to increase capacity to select and use drugs well, monitor patients' progress and side effects and manage the drug supply. At least, there are indications that

the cost of drugs will decline considerably as more and more countries allow importation of generic brands. Actually, through collaboration and mediation of the UNAIDS and World Health Organization (WHO), significant progress has already been made towards reducing the costs of drugs and making these available in many SSA countries. Effort made in Uganda and Cote d'Ivoire indicate that it is possible, with goodwill and determination, to negotiate significant reduction in drug prices and improvements in the delivery of health care (UNAIDS, 2000).

The challenge of breastfeeding is bound to be critical since this exposes babies to postpartum infection through the breast milk. This must be taken into account when evaluating and designing appropriate prevention strategies. Seemingly, the most sensible solution would be to provide alternative infant feeding options. However, this is no easy solution. Alternative feeding, such as formula feeding, can be very expensive and hard to constitute due to lack of proper sanitation. Given these constraints, perhaps the most feasible strategy for reducing breastfeeding-related transmission in the SSA settings would be to combine several weeks to months of postnatal antiretroviral drugs to HIV-exposed infants with early weaning at about 6 months. There is definitely need for more studies on how to exploit the benefits of breastfeeding but minimize the risk it entails in terms of postpartum disease transmission.

Elective CS has been mooted as another strategies that can reduce the risk of vertical transmission during labor and delivery, when the most of the transmission appear to occur. In fact, when combined with antiretroviral therapy, the reduction in vertical

transmission through elective CS has been increased, suggesting that CS provided additional benefits to the antiretroviral drugs. But for it to be useful, it needs to be done before the onset of labor and membrane rapture. This may be a great challenge since most pregnant women in SSA countries start their visits to the clinics late and few consent to HIV/AIDS screening. In most cases, it is also an expensive operation that is beyond the poor who are not likely to have health insurance to meet the cost incurred. Another problem is that HIV-women are more likely to have surgical complications than sero-negative women are, which is bound to be a serious factor in the SSA due to lack of good sanitation and guaranteed sterile environments. Therefore, post-operative infections are more likely to occur and result in increased morbidity and even mortality, so that the routine use of elective CS to prevent vertical transmission of HIV/AIDS may not be of overall benefit.

The use of antiseptic vaginal and cervical washes has been suggested as an inexpensive way to reduce potential viral exposure to newborns during delivery. Chlorhexidine has had widespread use as a disinfectant and can inhibit HIV viral replication *in vitro* at low concentrations. Several studies are still underway in the SSA to assess the benefit and acceptance of antiseptics as an option. Screening for genital ulcers, such as syphilis, and other STDs in HIV-infected pregnant women can be of dual benefit to the newborn by reducing the risk of acquiring the sexually transmitted diseases as well as transmission of HIV. However, there is very little research that has been done in this area, particularly in determining the relationship between various STDs and HIV/AIDS, and the effectiveness of treatment of the former in reducing both new infections and further transmission of

HIV. Similarly, more widespread research is needed on the effects of vitamin A supplementation and male circumcision. The former may be easily implemented through some form of nutritional programs while the latter, like condom use, may be tricky because it depends on cultural and religious norms.

All in all, there seem to be incredible opportunities from research done in developed countries, but for them to be exploited fully they must be adapted to the social, economic and political settings in the SSA countries. This cannot be done unless there is an effort made to understand these settings. Therefore, there is need for more epidemiological research cannot be over-emphasized. Moreover, ethical concerns raised about research on human subjects in developed countries must be upheld, appropriate data sampling strategies used and data accuracy ensured for the results to be credible and useful in designing better intervention strategies. It will be more effective to form interdisciplinary research teams that include epidemiologists, medical doctors, anthropologists, statisticians, econometricians, socio-economists, etc., who will present their results in public forums to local political, teachers, administrative and religious leaders to enhance ownership and educate the public. Articles in journals and books, unless they are translated into public policies, will do little to help end the current pandemic. The information generated must be communicated in a simple way to appropriate policy makers and the public. Governments, private sector and donors must all join hands and allocate more resources to research and to creation of an enabling environment that ensures more effective distribution and delivery of information and appropriate preventive options.

4.2 Constraints to Prevention of Vertical Transmission of HIV/AIDS

It is one thing to talk about the prospects of dealing with vertical transmission, but unless the many constraints limiting the capacity to deal with the problem are tackled, very little progress can be made against the spread of HIV/AIDS. A few of these problems were discussed in Section 4.1 while reviewing the prospects of HIV prevention. This section discusses a few more fundamental constraints and subtle issues that will require attention.

4.2.1 Silence, Denial and Lack of Political Will

One of the greatest tragedies about HIV/AIDS is that, despite being such a major threat to human existence, the disease has been given little attention and most commitments have remained rhetorical. Most tragic is the reception the disease received in the SSA, where more than two-thirds of its victims live. For a long time, most people saw the disease as a 'black and white' issue and insisted that it was Western media propaganda against the Africans. In fact, African government officials for years dismissed AIDS as a "racist conspiracy plot" invented by the West. The view became even more entrenched after the claim that the SSA was the origin of HIV.

For this reason, many African leaders failed to acknowledge the imminent threat of the disease in their countries mainly for political reasons. Accepting that the disease had made serious in-roads in their countries would have been equivalent to admitting their inadequacy and lack of commitment in protecting their people against the most serious disease in the world today. Unfortunately, even today, most of these leaders and their

governments have continued to give AIDS a half-hearted attention while millions of the people die helplessly. This is evident in that many government budgets remain skewed towards higher military and presidential spending but lower health, agriculture and education expenditures.

South African president Thabo Mbeki's denial that AIDS is caused by HIV, of course, stands out in this political malaise (Awofeso *et al*, 2001). His case was spotlighted during the 13th International AIDS Conference held in his own country in July 2000. His stand is, however, not unique. Many other leaders in the SSA portray the same attitude with their government priorities and budgets. Even though, in general, many countries in the region are economically hard-pressed, efforts must be made to ensure that public resources are allocated to prevention of HIV/AIDS, especially among women and children who bear the brunt of the disease.

In recent years, there has been greater and better access of HIV/AIDS information causing people throughout the world to appreciate the nature and magnitude of the problem. As more organizations mobilize resources and personnel, and as more research is done, many more people in the SSA are becoming aware of the problem and are taking appropriate steps to protect themselves and their communities against the disease. More leaders are taking the front seat in the fight against HIV/AIDS and are rationalizing their budgets, helped by donors, to reflect a greater appreciation of the problem paused by the disease. Uganda's president, Yoweri Museveni, is a gallant example of how much can be achieved when leaders take an active part in the fight. More exposure and messages

through the media are needed to inject the truth of the situation to more people. The process is slow and painstaking, mainly due to low literacy level, lack of training materials and budgets to support the effort. However, the effectiveness has been magnified as many more local people and institutions, such as churches and schools, take responsibility and openly discuss about the disease.

Recent advances in participatory approaches at community level have become successful in mobilizing local people to participate in events aimed at 'breaking the silence' about HIV/AIDS and encourage them to adopt various disease prevention strategies that limit their exposure to HIV/AIDS (World bank, 1999). Encouragingly, many governments have also formed community level HIV/AIDS consultative councils and allow HIV/AIDS education to be taught in schools. It is true that without strong political commitment on the part of African leaders, well-intentioned initiatives are doomed to fail. Hence, the current level of enthusiasm and support must be sustained and exploited. The United Nations has launched a massive global fund to fight the disease and urges all world governments to get involved.

4.2.2 Cultural Constraints and Lack of Awareness

Various traditions and cultural values have been found to influence, not only how people perceive and react to the AIDS pandemic, but also their predisposition to the disease. For instance, in Thailand, a study found that cultural constraints, such as the lack of visibility of the disease and traditional sexual practices, influenced communication about

HIV/AIDS prevention (Svenkerud and Singhal, 1998). Further, attitudes towards women and sex, have been intricately intertwined with the level and spread of HIV in the SSA to an extent that one cannot advocate effective HIV/AIDS prevention strategies without mentioning or tackling these issues. The subordination of African women on sex issues and lack of access to resources are cited as major reasons for the higher disease prevalence among women. The solution is increased empowerment of women so that they become more responsible in averting the disease threat.

Many of the same factors that have predisposed rural African women to ill health in the past now increase their vulnerability to HIV/AIDS, including poverty, malnutrition, uncontrolled fertility, and complications of childbirth. As men travel out from rural communities to urban centers in search of employment, their sexual contacts multiply; many acquire the HIV virus and infect their wives back at home. Women, too, are leaving rural areas for the promise of a better life in cities and commercial centers along the way. Their struggle for economic survival and personal autonomy has led many to form relationships with new sexual partners, with a consequent increase in HIV seroprevalence among them.

Ulin (1992) argued that HIV/AIDS prevention campaigns often do not take into account the cultural, social, and economic constraints on most African women's ability to limit sexual partners and use condoms. He proposed research to explore the meaning of HIV/AIDS and prevention choices in the socio-cultural context of the women's lives. A better understanding of how women, themselves, perceive and respond to current

attempts to prevent the transmission of HIV/AIDS is an increasingly critical factor in the intervention process. Most important, it is a necessary first step towards their effective participation, together with men, in the development of culturally relevant strategies for protecting themselves and their families.

A classic example of cultural values and norms that predispose people to HIV infection is the wife inheritance tradition among the Luo tribe of Kenya. Once an elderly married brother dies, of whatever cause, a younger brother inherits his household including his wife and children. Whereas this culture was well meaning and ensured sustenance of the deceased's household, in cases where the deceased died of HIV/AIDS the disease has been passed along unabated within households. Another example is the high level of disassortive mating between younger girls and older men in some cultures. In regions that have high HIV prevalence, and where older men are a high-risk group, younger women are placed at a greater risk than they would otherwise be.

A more explosive issue is the perception about use and issuance of condoms. Although research has shown that condoms are useful in preventing unnecessary infection by STD and HIV, the use of these among young adults in the SSA, who are most at risk of infection, has not picked up much. Many government and organizations working on HIV/AIDS provide free condoms but the majority of Africans, especially religious groups, regard condom use and sex education as inappropriate means of curbing the pandemic, and instead may encourage promiscuity and sexual immorality.

In spite of the presence of cultural "barriers" to prevention of HIV transmission, Gausset (2001) warns that the fight against AIDS should not be presented as a fight against such cultural barriers. This attitude is likely to be construed as part of a Western prejudice about sexuality in Africa, which tends to focus on its exotic aspects only (polygamy, adultery, wife-exchange, circumcision, sexual cleansing and the like). The study argued that many of the cultural aspects related to HIV/AIDS were not incompatible with safe sex behavior, and fighting against them may alienate the very people whose cooperation is necessary for sustained curbing of the spread of HIV/AIDS. However, the study argued that there is need to make behavior and practices safer in a way that is culturally acceptable to the people without replacing one culture (African) with another (Western).

4.2.3 Lack of Funds and Basic Infrastructure

The number one reason why most governments in the SSA are unable to effectively respond to the HIV/AIDS pandemic, is lack of funds and basic infrastructure. Most of these economies in the continent thrive on agriculture, which has suffered greatly in the past two decades as a result of world market instability, poor weather and low inputs, and now under attack from HIV/AIDS. Such economies can only afford to allocate between $3-20 per capita to health care. Beyond that, health care has to compete strongly against investment in agriculture, education and other important budgetary needs. With per capita Gross Domestic Product levels of less than $500, such economies would be hard pressed to provide for the necessary HIV/AIDS education campaigns, cheaper anti-retroviral drugs, basic health care and infrastructure that facilitates these.

Currently, most governments are at the mercy of donor agencies and international drug companies in their fight against HIV/AIDS. Very little additional funding is available from their treasuries to stem the spread of the disease. A study of total spending needed on the campaign against HIV/AIDS found that expenditures averaged about 150% of per capita Gross Domestic Product (GDP). Based on 1997 prices, the provision of triple combination therapy to all people with HIV in SSA was estimated to consume between 9-67% of total GDP. The care and support needed by people with HIV/AIDS will depend on the ability to mobilize human, infrastructure and financial resources. Since the ability to secure adequate financing of health systems in SSA is limited, determining priority investment using limited resources will require judicious decision-making and a firm commitment to start in the right direction even with limited resources.

Lack of funds also means that less research than is currently demanded can be expected. Because of the nature and extent of the current HIV/AIDS crisis, the tendency is to spend most effort and resources on adapting antiretroviral drugs that have been successful elsewhere to the situation in the SSA. There is nothing wrong with that. But because there exists little or no background information about the specific nature of the disease characteristics and transmission, factors influencing its spread and potential intervention options in the SSA, the results are bound not to be as useful as if they were complemented with detailed background information. Therefore, appropriate epidemiological research is needed to understand the specificity of the HIV/AIDS outbreak, spread and effects in the SSA, avoid "trial and error" research and focus attention on the most promising intervention strategies.

4.2.4 Lack of, and Constraints to, Comprehensive Epidemiological Studies

In the past 20 years, a lot of studies have been done on different aspects of HIV/AIDS, from the biology of the disease to factors influencing its transmission and spread. However, relative few of these studies have been done in the SSA. Of late, there has been a surge in such studies particularly in eastern and southern Africa, the regions deeply affected by the pandemic. But these are inadequate in providing the kind of comprehensive information that is desired for development of new and appropriate interventions for the SSA.

To realize this goal, there are significant constraints that will have to be overcome. First, the SSA study populations are homogenous, especially with respect to breastfeeding, making it difficult to compare treatment effects. Secondly, the populations are heterogeneous in relation to social, economic and cultural content, thus making it difficult to generalize treatment effects and increasing the complexity of study designs. Thirdly, there are problems with ethical standards and study consent (Smyth and Weindling, 1999). Fourthly, some of the studies are sponsored by drug companies and may not consider the purpose and complexity of the trials or the needs of the study countries (Varmus and Satcher, 1997). This assumes a greater dimension given the antiretroviral drug-price debate and the controversy over generic brands. Lastly, data collection, sampling procedures and analytical methods provide formidable challenges.

There is also concern about the use of placebo-controlled study design and justification of a no-treatment group. The justification for the latter has been that the trials address a

pressing need in these countries, they are being conducted according to widely accepted ethical standards and that there is enormous local support. There are also specific methodological difficulties with research in children include smaller and more heterogeneous populations, measuring clinically relevant outcomes and investigating rapidly evolving disease processes. In many areas of pediatric practice, therapies have been studied only in adults, and it becomes hard to generalize from adult to child, especially to newborns. The standard procedure is to test a treatment on adults, prove that it is safe and efficacious before applying it to children.

Future studies and methodologies need be less evasive and based on voluntary rather than mandatory testing and screening. However, more resources are needed for community education so that people appreciate the need to participate in such testing and counseling programs which have been shown to be very successful in certain communities. Such programs will need to be backed by realistic data and information from well designed and thought out epidemiological studies.

4.3 Conclusion and Recommendations

There is no doubt that HIV/AIDS is the most devastating disease in the world in recent times. So far, it has affected more than 50 million people and claimed more than 20 million lives in twenty years. The magnitude and rate of the disease spread is such that, unless strong measures are taken to slow it down, it will impose more severe burden on almost all communities and countries in the world. Currently, the most affected region is the SSA, home to nearly 70% of all HIV-positive adults and 80% of all HIV-positive children. This, together with increasing depths of poverty, deteriorating health care systems and unresponsive governments, have led to deep social and political problems that limit the ability of these countries to deal with the pandemic. As a result of years of denial and political inaction, the disease is ravaging SSA and threatens to reduce life expectancy by nearly two decades and reverse significant gains made in the past from better maternal and child health. For these reasons, all the nations of the world have no option but to collaborate and pool resources in order to act against this deadly disease.

Vertical transmission of HIV/AIDS in SSA, which is the focus of this study, has lately become a serious concern because it translates into a severe and credible threat to future generations. A high rate of pediatric HIV/AIDS infection in SSA is already threatening to destabilize demographic structure and dynamics in many countries leading to severe future economic and social burdens, including unsustainable levels of dependency. Since most pediatric infections are acquired from the mothers, the most effective means of preventing them is through primary prevention of the disease in women and reduction of

vertical transmission. Several past breakthroughs are encouraging in this regard. The most common one is the use of antiretroviral drugs administered to both mother and child. Many drug regimens have been tested in different countries and found to be effective, though some may require additional evaluation of efficacy, safety and development of resistance in the SSA setting.

However, high cost of the drugs and lack of adequate basic delivery and monitoring infrastructure limit the application of these drugs in the SSA. Therefore, the successful use and effectiveness of the drugs in SSA is contingent upon reduction of drug costs or availability of generic ones and complimentary investment in basic infrastructure and manpower necessary to ensure the efficient distribution and use of the drugs. This will require serious mobilization and re-allocation of resources by governments and donors commensurate with the enormity of the pandemic, a great potential challenge to many SSA governments that are already struggling to provide food, education and other necessities to their populations. Strategies to pool available resources and work in partnerships will greatly enhance financial, material and informational resources, as well as reduce duplication of efforts.

Use of antiretroviral drugs in SSA may also be greatly limited by the fact that most women breastfeed their babies, exposing their newborns to danger of late postnatal transmission of HIV/AIDS through the breast milk. Strategies to prevent transmission via breast milk include replacement feeding, early weaning after exclusive breastfeeding and postpartum antiretroviral prophylaxis during breastfeeding. Women with HIV/AIDS

infection should be assisted in choosing how to feed their infants by having complete and accurate information. Uninterrupted access to safely prepared, nutritionally adequate breast milk substitute would greatly lower the risks of infant diseases and deaths. However, artificial feeding in unhygienic conditions may be associated with increased child morbidity and mortality due to diarrhea and other related diseases. Since breastfeeding ordinarily confers infants with adequate nutrition and immunity, alternative feeding regimes must be nutritionally comparable, not overly expensive, and without adverse effects on child health and survival. Efforts to formulate alternate infant feeds from locally available materials and provision of simple water filters or water-treatment equipment to sanitize the water may be worthwhile in the long run.

Past studies indicate that treatment of symptomatic STDs may lead to significance reduction in vertical transmission of HIV/AIDS. Therefore, any strategies that reduce incidences of STD are likely to reduce the incidences of HIV/AIDS and hence vertical transmission. Provision of condoms, especially among high-risk groups and high-HIV-incidence communities, greatly reduce incidences of STD and may directly limit the level of HIV/AIDS transmissibility. Although this approach is controversial and strongly opposed by various community groups, it is important that the parties involved openly discuss the issues and reach an amicable solution that offers needed help and takes into account all the viewpoints expressed. Meanwhile, scientific tests carried out to prove the efficacy of using condoms in preventing the disease would shed more light on the topic. Other secondary interventions such as circumcision and vaginal cleansing will require

more research to establish their efficacy while acknowledging their sensitivity to different cultural and social norms.

Due to the significant problems associated with implementing secondary interventions in SSA, such as limited resources and manpower, the most effective means of minimizing the spread and effects of vertical transmission of HIV/AIDS is through primary interventions such community education and voluntary counseling and testing. Studies indicate that many local community-based initiatives aimed at reducing the adverse effects of the disease are under way and have shown good success. These initiatives include pooling labor to alleviating loss of labor from deaths, improving food security and supplementing family incomes to maintain household expenditure patterns.

Governments can be involved in enacting deliberate policies and build institutions that strengthen these coping strategies by improving access to resources such as capital, land, labor and management skills for affected families. Additionally, improving technology access to raise household productivity and economic welfare, and strengthening legal frameworks can facilitate community groups to step up the much needed local support. Programs and policy should aim at reinforcing indigenous responses, such as local credit and labor support groups, and promoting the effectiveness of community-based organizations and non-governmental organizations. Such organizations have made a difference in Uganda, one of the success stories on HIV/AIDS prevention using community outreach approaches.

One of the greatest potential challenges is how to influence people to shift from risky sexual behavior that predispose them to infection. Since such behavior tends to be culturally oriented, there is need to involve community leaders and social workers in such campaigns. Provision of basic information on what causes the disease, factors influencing the spread and how to best mitigate against the effects of the disease, preferably using simple, local language illustrations will be required to pass on an accurate picture of the reality and change current mythical views of the disease. Strategies that increase availability of such information to schools, churches and other community institutions and facilitate community-based awareness campaigns are likely to be productive in this respect.

More generally, interventions to prevent vertical transmission highlight weaknesses of allied services in resource-poor settings and offer incredible challenges to strengthen them. Most obvious is the poor quality of maternal health care services in many countries in SSA, illustrated by high rates of maternal and infant mortality and the general absence of treatment for HIV/AIDS. Identifying HIV-infected women and men offers an opportunity to introduce rational simple disease care and management strategies, including screening for opportunistic diseases. To this end, carefully designed voluntary counseling and testing programs can go a long way in not only identifying target groups but also providing a chance to reduce further infection. However, policies and practices need review to ensure that pre-test counseling requirements are not barriers to diagnosing HIV infection in women and preventing transmission to their children. In many countries, what is needed is incorporating simplified, but routine, HIV counseling and testing into

standard antenatal care while keeping it voluntary, confidential and supportive of HIV/AIDS prevention in women and their partners. Increased use of rapid testing may be useful in cases where women access antenatal care sporadically or only access care at delivery.

Preventing vertical transmission of HIV/AIDS in the SSA requires that the disease be addressed as a major potential threat to mankind. Since the world has become one large "global village", and what affects one community tends to affect the next, consideration must be made for joint bilateral and multilateral interventions, and shared information and outcomes. However, if international research is to serve any purpose now, then results from past successful studies must lead to public health action. In the meantime, more epidemiological research is needed to provide more specific information about the nature and effects of HIV/AIDS in the SSA. Such information will help tailor specific recommendation for the SSA to increase effectiveness and appropriateness of the interventions. For this to work, all countries must rally together to make this possible for the benefit of all children and future generations.

In summary, this review notes the following key issues:

1. HIV/AIDS is indeed the most catastrophic disease in the world today and it poses a serious and credible threat to future generations based on current rate of vertical transmission and infection and the level of incidence in the general population and among children under 15 years of age.

2. The HIV/AIDS threat is greatest in the SSA. The region has the largest share of adults and children living with the disease, and the highest rate of new infections. Several political, social, cultural and economic reasons are responsible for this state of affairs.

3. Transmission of HIV/AIDS from mothers to their children is a major concern that deserves greater attention and urgent interventions made to reduce the risk of transmission. Notably, the current pattern of infection among children tends to match that in women of childbearing age.

4. Several factors influence the rate of vertical transmission. These include the health and nutritional status of mothers, disease progression and viral load, viral characteristics, genetic characteristics associated with immune response, presence of other STDs, mode of delivery and breastfeeding.

5. So far, the greatest prevention strategy against vertical transmission of HIV/AIDS has been the use of antiretroviral drugs. These have been successful in developed countries but face specific challenges when applied to the SSA such as lack of access to the drugs due to their high cost and also lack of appropriate delivery infrastructure.

6. Other prevention strategies, such as alternative infant feeding, vaginal cleansing, cesarean section, vitamin A supplementation and STD treatment have shown good potential and are being investigated more extensively. Several vaccines are also under trial.

7. Most current research efforts in the SSA are concentrated on adapting measures that have been successful elsewhere, such as the use of antiretroviral drugs, with little epidemiological research done to support such measures. The disadvantage of doing this is that it may lead to ineffective and inappropriate intervention strategies for the SSA. Furthermore, variability in study methodologies, criteria, case definitions and trial settings, has made it difficult to generalize results and make better use of the information generated. Data gathering, sampling procedures and analytical techniques

need to be standardized to ensure comparable results. A further challenge is manifested through data incompleteness and inaccurate measurement.

8. Primary intervention strategies such as community education, voluntary counseling and testing offer the greatest potential for reducing vertical transmission in the SSA. Most of those having HIV/AIDS are unaware that they are infected due to ignorance, lack of counseling and testing services, and widespread stigma and fear attached to the disease which can result in rejection and even violence against people known to be HIV-positive.

9. There are significant constraints hindering progress of HIV/AIDS research in the world, and particularly in the SSA. Denial, silence and lack of political will by governments and communities are major contributors to the escalation of the disease problem. This has resulted in lack of adequate resource and international collaboration commensurate with the level of the disease problem, which is a significant barrier to progress towards developing effective prevention strategies.

In view of the findings noted above, this study makes the following recommendations:

1. The HIV/AIDS pandemic deserves greater attention from all governments since none of the countries is shielded from its effects. Political will expresses the national commitment and provides overall leadership to the nation in response to HIV/AIDS. Particularly, more attention is required to reduce the level of vertical transmission of HIV/AIDS in the SSA. Such increased attention demands greater responsibility and mobilization of resources by all parties involved. Truly, the magnitude of the HIV/AIDS problem in the world requires nothing short of total commitment, more action and less rhetoric, towards finding long-lasting solutions to the problem.

2. The SSA needs more assistance than has been given or acknowledged so far if the level of disease occurrence is to be drastically reduced. Bilateral and multilateral donors must be willing to give more resources for research and education. Effective

programs that offer both prevention and care, involving a wide range of actors (governments, civil society, private sector and donors) are needed. Such programs must work in synergy and not duplicate efforts, and be willing to share information and other resources. Political, religious and social leaders must openly advocate against the disease and avoid unnecessary controversies that send mixed signals to the people.

3. Current research is far between in terms of time and space, and seems rather uncoordinated. In order to make the information generated more useful, there is need for greater and better collaboration and partnership among all participating groups, establishment of an accessible global HIV/AIDS information network and standardization of data sampling, collection and analytical procedures. This will reduce duplication of research effort, increase the efficiency and effectiveness of research as well as improve the dissemination of outcomes. In addition, current research in SSA must seek to incorporate specific regional aspects that make the results more realistic and appropriate. For instance, alternative infant feeding regimes must be cheap and easy to formulate in water-limited conditions. Similarly, antiretroviral drug therapies need to be simple to use and affordable.

4. While secondary intervention strategies are being sought, such as antiretroviral therapy, more attention need be turned towards primary intervention strategies. The latter have been found to be effective in dealing with potential community challenges and are already being adopted while dealing with HIV/AIDS. Examples include community education and awareness campaigns and voluntary counseling and testing (VCT) programs. The primary objective of such strategies will be to sensitize the community about the existence of HIV/AIDS, how it is spread and its effects. Hopefully, this will minimize risky sexual behavior, reduce the rate of new infections, and encourage people to seek VCT. Particularly, women need encouragement to seek prenatal care early and get tested for HIV/AIDS.

5. In the meantime, since the cost of antiretroviral drug therapy is prohibitive to most people in SSA, there is need to work on lower cost drug options. In addition, the governments need to be encouraged to improve their health care infrastructure and train medical personnel on how to handle and administer these drugs while monitoring for unwanted side effects.

6. While every effort is going on to contain the spread of the disease, there is an urgent need to take care of those that have contracted the disease. Many local community organizations have been formed to provide support and education concerning HIV/AIDS. However, these groups need help and coordination. The government must enact policies that facilitate such roles that are best provided at the local level by such organizations.

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