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Global Impact of Human Immunodeficiency Virus and AIDS

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INTRODUCTION

The human immunodeficiency virus (HIV)/AIDS epidemic has already devastated many individuals, families, and communities. The epidemic has left millions of children orphaned, has disrupted village and community life, and increasingly contributes to the erosion of civil order and economic growth. According to the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS), an estimated 34.3 million people worldwide were living with HIV/AIDS at the end of 1999 (see Table 3) and an estimated 15,000 people become infected each day (98). Of the global total of people who are living with HIV, 95% live in developing countries (93). As the epidemic evolves further, rates will continue to rise in communities and nations where poverty, social inequalities, and weak health infrastructures facilitate spread of the virus (93, 98).

Parallels can be seen in developed countries. For example, in the United States, communities of color, in which the poor, the undereducated, and those without regular access to health services are overrepresented, are increasingly at risk. In 1998, 45% of reported AIDS cases were among African-Americans and 20% were among Hispanics, yet these groups represent 12 and 13%, respectively, of the U.S. population (13). The epidemic in each region of the world is influenced by specific risk factors that are associated with the spread of HIV/AIDS and the responses that have evolved to address it. Factors that enhance the spread of HIV transmission include migration, economic instability, social and environmental factors, drug use, increased rates of sexually transmitted diseases (STDs), and poverty. In addition, subgroups of the virus may have different rates of transmission (12, 44, 61, 82).

In this article, we describe the trends in the global pandemic of HIV/AIDS outside the United States and discuss strategies to prevent further spread and to mitigate associated consequences. A great deal has been learned about the biological, behavioral, and environmental factors that influence HIV transmission and disease. However, a great deal still remains to be done to translate knowledge into action. It is critical to sustain current HIV prevention and care efforts so that further ground is not lost. However, it is also imperative that we work to expand these efforts, reaching individuals and communities with prevention and care programs that have been proven to work. To understand HIV/AIDS on a global level, prevention and care must address issues and conditions unique to different regions and communities.

The HIV/AIDS pandemic has taken on different forms in various parts of the world. In some areas, HIV infection has spread rapidly to the general population; in others, the spread has remained among higher-risk subpopulations, including sex workers and their customers, men who have sex with men, and injection drug users (IDUs). Worldwide, the adult prevalence rate is 1.07% of the population, and 47% of infections occur among women (98) (Table 1). AIDS is the fourth leading cause of death worldwide and the leading cause of death in sub-Saharan Africa. According to 1999 estimates, 18.8 million adults and children have died of HIV/AIDS since the beginning of the epidemic (98). Because the number of people infected with HIV continues to expand, the annual number of deaths worldwide can be expected to increase (93). In 1999, one-fifth of HIV-related deaths were among children and more than half of the adults who died of HIV-related causes were women. As of November 1999, a total of 2,201,461 AIDS cases had been reported to WHO. This total is an increase of 214,244 AIDS cases since November 1998.

Africa is the continent that has been most affected by the HIV/AIDS pandemic. Compared with other regions of the world, sub-Saharan Africa has the highest infection level, the lowest level of access to care, and the least economic stability. It accounts for almost 70% of the global total of HIV-positive people and 83% of cumulative AIDS deaths (93). Of all reported AIDS cases, 91% are estimated to have been heterosexually acquired (Table 2). Infections through blood transfusions and perinatal transmission from mother to child have also contributed to the spread of HIV across the continent. Tuberculosis (TB) is the most common opportunistic infection among AIDS patients in sub-Saharan Africa (94, 110). The contribution of the factors that facilitate transmission—high prevalence of STD, low rate of male circumcision, the unequal

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TABLE 1. Regional HIV/AIDS statistics and features, end of 1999[a]

Region	Start of epidemic	No. of adults and children living with HIV/AIDS	No. of adults and children newly infected with HIV	Adult prevalence rate[b] (%)	% of HIV-positive persons who are women	Main mode(s) of transmission[c]
Sub-Saharan Africa	Late 70s–early 80s	24,500,000	4,000,000	8.57	55	Hetero
North Africa & Middle East	Late 80s	220,000	20,000	0.12	20	Hetero, IDU
South & Southeast Asia	Late 80s	5,600,000	800,000	0.54	35	Hetero, IDU
East Asia & Pacific	Late 80s	530,000	120,000	0.06	13	IDU, hetero, MSM
Latin America	Late 70s–early 80s	1,300,000	150,000	0.49	25	MSM, IDU, hetero
Caribbean	Late 70s–early 80s	360,000	60,000	2.11	35	Hetero, MSM
Eastern Europe & Central Asia	Early 90s	420,000	130,000	0.21	25	IDU
Western Europe	Late 70s–early 80s	520,000	30,000	0.23	25	MSM, IDU
North America	Late 70s–early 80s	900,000	45,000	0.58	20	MSM, IDU, hetero
Australia & New Zealand	Late 70s–early 80s	15,000	500	0.13	10	MSM, IDU
Total		34,300,000	5,400,000	1.07	47	

[a] Data are from the UNAIDS report on the global HIV/AIDS epidemic: new HIV estimates, available at www.unaids.org/epidemic_update/report/epi_core.ppt. Accessed 16 November 2000.
[b] The proportion of adults (15 to 49 years of age) living with HIV/AIDS in 1999.
[c] Hetero, heterosexual transmission; IDU, injection drug use; MSM, sexual transmission among men who have sex with men.

status of women, migration, poverty, and patterns of social mixing—differs by country (58, 94).

At the start of the 21st century, 24.5 million adults and children in sub-Saharan Africa are estimated to have HIV infection or AIDS (Table 3) (98). UNAIDS/WHO estimated at the end of 1999 that 12.9 million women and 11.6 million men aged 15 to 49 in sub-Saharan Africa were living with HIV (prevalence, 8.57%). In this region, there were approximately 2.2 million HIV/AIDS deaths in 1999 (97, 98). Between 1986 and 1997, the mortality rate among men aged 15 to 60 increased significantly. Life expectancy in southern Africa rose to 59 years in the early 1990s but, because of AIDS, is likely to drop to 45 years between 2005 and 2010 (93). Unfortunately, AIDS kills people during their most economically productive years, making it the leading cause of potentially healthy years lost in sub-Saharan Africa as well as the leading cause of death.

Gains in child survival in sub-Saharan Africa are being reversed. By 2010, child mortality is projected to increase—to 150 per 1,000 population in Botswana, 120 per 1,000 in Kenya, 230 per 1,000 in Malawi, and 200 per 1,000 in Zambia (93).

In sub-Saharan Africa, the HIV/AIDS epidemic has had the greatest impact in urban areas. However, in countries with considerable mobility between urban and rural areas, the rates do not differ substantially.

A second HIV type (HIV-2) is found almost exclusively in West Africa, primarily in Senegal, Guinea, Guinea-Bissau, Burkina Faso, Ivory Coast, Gambia, and Cape Verde (42, 70, 71). The highest rates have been found in Guinea-Bissau: according to a community-based seroprevalence study, 10.1% of adults were found to be HIV-2 positive in 1989, compared with 8.9% in 1987 (71). The routes of transmission of HIV-2 are the same as those of HIV-1, and heterosexual contact is the route of most transmissions of both viruses. High rates of transmission are evident among people with STDs, female sex workers, and heterosexual partners of persons infected with HIV-2.

In countries that have mounted aggressive prevention programs, seroprevalence rates have declined. The seroprevalence rates in 15 villages in rural Uganda declined from 8.2% in 1990 to 7.6% in 1994 (60). According to data from Rakai, Uganda, the HIV-1 seroprevalence rate among adults decreased from 23.4% in 1990 to 20.9% in 1992 (103). In Masaka, Uganda, HIV prevalence rates fell significantly from 1989 through 1997, from 4.5 to 1.5%, among girls aged 13 to 19 years. The rate among adolescent boys is much lower than that among adolescent girls and has remained stable (0.5%) (98). In Lusaka, Zambia, HIV rates among young women aged 15 to 19 exceeded 25% in 1993. These rates have dropped by almost half in the past 6 years because of effective HIV prevention efforts (98).

The South and Southeast Asia region and the East Asia and Pacific region, home to one half of the world's population, have experienced general improvement in living conditions and economic growth during the past several decades. Prevalence rates in the South and Southeast Asia region and in the East Asia

TABLE 2. Proportion of reported AIDS cases by mode of transmission by region from 1996 to 1999[a]

Region	% of cases					
	Heterosexual contact	Homo- or bisexual contact	Intravenous drug use	Transfusion/hemophilia	Mother to child	Other and unknown
Africa	91	0	0	1	7	0
Latin America/Caribbean	61	26	7	1	5	1
North Africa/Middle East	58	10	12	16	5	0
South and Southeast Asia	31	34	28	2	2	4
Europe	76	11	10	2	3	0
Western Pacific	58	20	15	2	4	0
Total	56	21	14	3	4	1

[a] Data are from reference 111.

TABLE 3. Adults and children estimated to be living with HIV/AIDS as of the end of 1999[a]

Region	No. of persons
Sub-Saharan Africa	24,500,000
South and Southeast Asia	5,600,000
Latin America	1,300,000
North America	900,000
East Asia and Pacific	530,000
Western Europe	520,000
Eastern Europe and Central Asia	420,000
Caribbean	360,000
North Africa and Middle East	220,000
Australia and New Zealand	15,000

[a] Data are adapted from the UNAIDS report on the global HIV/AIDS epidemic: new HIV estimates, available at www.unaids.org/epidemic_update/report/epi_core.ppt. Accessed 16 November 2000.

and Pacific region, 0.54 and 0.06%, respectively, continue to be relatively low (Table 1) (98). However, the number of people infected with HIV has increased steadily, to an estimated 6.1 million adults and children, and the cumulative total of AIDS deaths is 478,000 (98). The major modes of transmission in these regions are heterosexual transmission and, in some countries, injection drug use. In the South and Southeast Asia region, Cambodia has the highest prevalence rate for adults (4.04%).

India, where 3.7 million Indians were living with HIV/AIDS at the end of 1999, has the highest number of HIV-infected persons in Asia. However, given its large population, the overall HIV prevalence rate, 0.70%, is still low (98). Heterosexual contact with sex workers has been a major risk factor in HIV transmission. Surveillance studies have reported rates among sex workers of 51% in Bombay and 45% in Pune (25). Prevalence rates in 1997 among women attending antenatal clinics were 2.4% in Mumbai and 4.0% in Ponicherry (109).

Currently, China is estimated to have more than 500,000 HIV-infected persons (98). Most (70%) of the reported HIV infections and AIDS cases are among IDUs in Yunnan Province. In this region, HIV infection rates among IDUs range from 38% in Urumqi to 76% in Yining (51); however, transmission due to heterosexual contact is also increasing in southern China (93; Y. Shao, L. Su, X. H. Sun, H. Xing, P. L. Pan, H. Wolf, and J. Shen, Program Abstr. XII Int. Conf. AIDS, Geneva, Switzerland, abstr. 13132, 1998). Increases in other STDs are also an important risk factor for HIV in this region. In 1997, 462,000 patients were reported as having STDs, an increase of 16% since 1996. Given China's population of more than 1.3 billion, even small increases in prevalence will translate into large numbers of people affected by HIV.

Commercial sex is also responsible for a high proportion of cases in Cambodia, Myanmar, and Thailand. The epidemic of HIV in Thailand evolved from female sex workers to their male clients and subsequently to the female partners of the clients. It is estimated that 755,000 persons in Thailand have already been infected with HIV (overall prevalence rate, 2.15%) (98). Thailand has made considerable progress in the fight against HIV/AIDS. As condom use has increased and visits to female sex workers have decreased, sexual behavior has changed; as a result, HIV prevalence has decreased (63, 68). For example, HIV prevalence among young men in the military fell from 12.5% in 1993 to 6.7% in 1995. Also, the proportion of men who reported sex with female sex workers fell from 81.4% in 1992 to 63.6% in 1995. From 1991 through 1995, men's use of condoms with female sex workers increased from 61 to 92.5% (63).

In Latin America and the Caribbean, an estimated 1.6 million adults and children are living with HIV/AIDS (98). The HIV/AIDS epidemic in Latin America and the Caribbean differs greatly between and within countries. Latin America and the Caribbean consist of 44 countries, divided into six regions: the Andean Area, the Southern Cone, Brazil, Central America, Mexico, and the Caribbean. The modes of transmission differ considerably. Heterosexual transmission is predominant in the Caribbean (62%) and Central America (73%) (65). Male-to-male sexual contact is the largest single mode of transmission for the Andean Area, Mexico, and Brazil, accounting for 43, 38, and 32%, respectively, of infections (65). Injection drug use plays an important role in transmission in Brazil (responsible for 21% of HIV infections) and is the single largest transmission category for the Southern Cone (34%).

Rates of HIV infection among women are substantial and are increasing in some countries in Latin America and the Caribbean. The male-to-female ratio of AIDS cases in Brazil has decreased as HIV infection among women has increased due to spread through heterosexual transmission and injection drug use (10). In the Dominican Republic and Haiti, HIV prevalence rates among pregnant women who attend antenatal clinics range from 1 to 9% (65). Overall, regional rates among pregnant women are still low, but they have reached 3.5% in Bolivia and 2.7% in Brazil.

Until 1995, Eastern European countries, including the former Soviet Union, had reported few HIV cases, mostly among homosexual men. Screening of other groups, such as blood donors, pregnant women, STD patients, and IDUs, showed very low rates of infection from 1990 through 1994 (58). In the past few years, however, the rates have changed substantially. Since 1995, HIV has spread rapidly among IDUs in the Ukraine, Belarus, Moldova, Russia, Caucasus, the Baltic States, and in Kazakhstan, in Central Asia, where political, economic, and social transition has facilitated the spread of HIV.

Currently, 420,000 adults and children in the region comprising the former Soviet Union and Central and Eastern Europe are living with HIV/AIDS. Of the HIV-positive adults, 25% are women (98). The prevalence rate for adults in the Eastern Europe and Central Asia region is 0.21% (98). Rates among IDUs are increasing rapidly in some countries. In 1999, more than 5,000 IDUs in Moscow alone were HIV infected. HIV prevalence rates range from 2% among IDUs in Russia to about 30% in sentinel surveys in Ukraine and to more than 60% in Svetlogorsk, Belarus (54). In Ukraine, new HIV infections increased from 47 per year during 1992 through 1994 to 1,500 in 1995, 12,000 in 1996, and 15,000 in 1997. Recent estimates indicate that 80% of new infections are occurring among IDUs (10, 74, 87). Ukraine, the country in this region that has been most affected, accounted for approximately 90% of all AIDS cases reported in the region in 1998 and 1999 (87, 93).

There are signs that a sexually transmitted HIV epidemic could evolve rapidly in many areas of Eastern Europe, where rates of other STDs, specifically syphilis, have increased dra-

matically (2). In 1997, syphilis rates were as high as 262 per 100,000 population in some countries in the region (58). During 1998, WHO, having found a 50-fold increase in syphilis cases in Russia, estimated that 1 in 400 Russians were infected with syphilis, a rate that is 200 to 500 times greater than in Western European countries (41, 47).

Romania has the greatest number of pediatric HIV/AIDS cases in Europe. Of 7,000 HIV-infected persons, 5,000 are children (98). Of the AIDS cases, 90% are among persons aged 0 to 14 years (97). In 1998, less than 10% of current pediatric cases were due to mother-to-child transmission; most transmissions occurred in health care settings through infected blood products and the use of contaminated equipment and syringes (93, 97). According to a Romanian study, 1 in 5 in a population of 101 abandoned infants and children was infected with HIV (38). Transmission to children through these routes has been contained, but if HIV infections among women of childbearing age increase, HIV infection in children through mother-to-child transmission could again become a major problem.

Although the Middle East and North Africa region has not yet experienced a major spread of HIV, it is estimated that 220,000 adults and children are living with HIV or AIDS (adult prevalence, 0.12%) (98). In 1999, approximately 20,000 adults and children in this region were newly infected with HIV. In the areas for which data exist, transmission can be attributed to injection drug use, heterosexual contact, and contaminated blood transfusions (93). Injection drug use is responsible for more than one-third of the AIDS cases in Tunisia and one-tenth of the cases in Egypt. During 1996, HIV prevalence among STD patients rose from 1.3 to 5% in Sudan. This pattern has also been seen in Yemen, Pakistan, and the Syrian Arab Republic (85). Currently, 89% of persons living with HIV/AIDS in this region are from Algeria, Egypt, Israel, Morocco, Sudan, Tunisia, Turkey, and the United Arab Emirates (98). Given the diversity of economies, cultures, and social systems, the future size and trends of the epidemic in this region are difficult to predict.

SEXUAL TRANSMISSION

Although AIDS was first defined in homosexual men in the United States and male-to-male sex remains the predominant mode of transmission in most industrialized countries, the predominant mode of transmission worldwide continues to be heterosexual contact (75% of total spread) (64, 93). As epidemics of HIV infections fueled largely by heterosexual transmission have developed in resource-poor countries, the age at which transmission occurs has fallen: half of all transmissions are now believed to occur among people under the age of 25 (93). As heterosexual transmission increases, the impact of the pandemic on women is rising, even in countries where other routes of transmission are more prevalent (64).

Several risk factors have been associated with the heterosexual transmission of HIV, including lack of circumcision, high virus load and decreased $CD4^+$ cell count in an infected partner, presence of an STD (genital ulcer disease or nonulcerative STDs), and certain sexual practices (sex during menses, bleeding during intercourse, and receptive anal intercourse). According to several studies, uncircumcised men were eight times more likely to be HIV infected than were those who were circumcised, and men with foreskins were more likely to transmit HIV to their sex partners during unprotected sex (35, 59). In a study in Nairobi, Kenya, the risk for seroconversion was 8.2-fold higher for uncircumcised men who visited female sex workers than for circumcised men who did so (11).

Increasing evidence supports a direct association between heterosexual transmission and virus loads (67). A recent study of discordant couples in Uganda revealed that the HIV-1 RNA level in the HIV-infected partner was highly correlated with the risk for heterosexual transmission. For every 10-fold increase in virus load, the risk for transmission increased >2-fold (28, 72; T. C. Quinn, M. Wawer, N. Sewankambo, et al., Program Abstr. 7th Conf. Retroviruses Opportunistic Infect., San Francisco, Calif., abstr. 193, 2000). Persons with virus loads of fewer than 1,500 copies of HIV-1 RNA/ml did not transmit the virus to partners.

Strong epidemiologic, clinical, and laboratory data demonstrate the increased risk for HIV transmission and acquisition due to other STDs. The presence of ulcerative and inflammatory nonulcerative STDs may promote the infectiousness of HIV and susceptibility to it by (i) disrupting normal mucosal barriers, which allows HIV into the bloodstream; (ii) facilitating HIV shedding in the genital tract; and (iii) recruiting HIV inflammatory cells to the genital tract (24, 31, 33, 45, 47, 48, 102). The presence of genital ulcers, syphilis, genital herpes, or chancroid in men and women is associated with a 1.5- to 7-fold-increased risk for HIV infection. Researchers of studies of African female sex workers found a significant association between chlamydia and HIV (median odds ratio [OR], 4.5; range, 3.2 to 5.7). In another study, of men and women at an STD clinic in Pune, India, genital ulcers were associated with HIV (OR, 2.1; range, 1.2 to 3.7) (46, 69, 76).

Two intervention trials examined the effect of treating STDs to reduce the spread of HIV infection (24, 37). In a study in Mwanza, Tanzania, the treatment of symptomatic STDs reduced HIV incidence by 40% (30). In a study of adults in the Rakai district in Uganda to assess the effect of the mass distribution of STD medications (to persons with and without symptoms) on HIV incidence, the treatment did reduce the prevalence of some STDs, but it did not decrease HIV incidence (5). Although the different effects of these two regimens is not totally understood, the difference in the relative durations of the epidemics (longer term in Uganda) and the different intervention methods most likely contributed to the different results. The Rakai results do tell us that prevention and control of STDs are effective, affordable, and feasible in resource-poor settings. The Mwanza study clearly showed that integrating STD care into primary health care services can lead to a considerable reduction in HIV transmission (32, 33).

In many parts of the developing world, STDs are prevalent but treatment and services are inadequate (37, 45, 48). The reduction in STDs can prevent HIV transmission in populations at high or medium risk, and accessible and effective STD treatment services can lower the incidence of HIV infection (31–33, 44, 46). Studies around the world confirm that improving the management of STD care is an important HIV prevention strategy.

TABLE 4. Clinical trials to reduce perinatal transmission

Trial	Drug	Treatment			Efficacy (%)	Estimated cost (US$)
		Antepartum	Intrapartum	Postpartum (to infant)		
No breast-feeding						
PACTG 076	3-part ZDV	100 mg 5 times/day starting at 14 to 34 wk	Intravenous, 2 mg/kg loading, then 1 mg/kg per h	2 mg/kg every 6 h for 6 wk	68	800
Thailand, short-course ZDV	ZDV	300 mg twice a day starting at 36 wk	300 mg every 3 h	None	51	80–100
Breast-feeding						
Abidjan, Ivory Coast, short-course ZDV	ZDV	300 mg twice a day starting at 36 wk	300 mg every 3 h	None	44 (at 1 mo), 37 (at 6 mo)	80–100
PETRA[a] A	ZDV-3TC	Twice a day starting at 36 wk	ZDV every 3 h, 3TC[b] every 12 h	Every 12 h for 1 wk	52 (at 8 wk)	100
PETRA B	ZDV-3TC	None	ZDV every 3 h, 3TC every 12 h	Every 12 h for 1 wk	38 (at 6 wk)	50
PETRA C	ZDV-3TC	None	ZDV every 3 h, 3TC every 12 h	None	5 (at 6 wk)	
HIVNET 012 (Uganda)	NVP	None	Single dose (200 mg) of NVP[c] at onset of labor	None	47 (at 4 mo)	4

[a] PETRA, perinatal transmission.
[b] 3TC, lamivudine.
[c] NVP, nevirapine.

MOTHER-TO-CHILD TRANSMISSION

Mother-to-child, or perinatal, transmission is estimated to account for 15 to 25% of all new infections (95). Worldwide, more than 90% of HIV infections in children are acquired by transmission from mothers to their infants. An estimated 2.4 million HIV-infected women give birth each year, resulting in 600,000 new infections in infants annually; thus, 1,600 infants are infected with HIV each day (88, 93, 95, 96). To date, 9 of 10 babies with perinatally acquired HIV infection have been born in Africa, where more than 50% of HIV infections occur in women of childbearing age (96). In addition, the number of cases in children in India and Southeast Asia seems to be rising rapidly as more women become infected.

Multiple factors influence the likelihood that an HIV-infected pregnant mother will transmit the infection to her child. Some of these risk factors include high maternal virus load, low $CD4^+$ count, decreased maternal cell-mediated immunity, premature rupture of membranes during labor, premature delivery, low birth weight, mode of delivery, untreated STDs, and prolonged labor (15, 24, 80). Mother-to-child transmission can occur in utero, intrapartum, or postpartum during breast-feeding. Risk factors in breast-feeding include high plasma virus load, mixed feeding practices, mastitis, and abscesses. The factors that determine the timing of transmission are still not well understood.

In industrialized countries, advances in the prevention of mother-to-child transmission have substantially reduced the number of children who acquire HIV. Pediatric AIDS Clinical Trial Group 076 (PACTG 076) showed that zidovudine (ZDV) administered to the mother during pregnancy and intrapartum and to the neonate could reduce perinatal transmission by 68% (Table 4) (13, 83). In developing countries, where HIV prevalence among pregnant women is higher than in industrialized countries but the health resources are limited, the cost and complexity of the 076 regimen hinder applicability (8).

Several studies have been conducted in developing countries to develop simpler and less expensive antiretroviral regimens to reduce perinatal transmission. Three studies—one in Thailand and two in the Ivory Coast—were conducted to look at shorter courses of ZDV (15, 78, 105). The trial in Thailand showed a 50% reduction in transmission from women who did not breast-feed and who took a shorter course of ZDV (78). Both of the studies in the Ivory Coast were of mothers who primarily breast-fed their infants (15, 105). One demonstrated a 37% reduction in transmission to the child at 3 months of age (105), and the other showed a 38% reduction at 6 months of age (15). In a multicenter trial in South Africa, Uganda, and Tanzania, three regimens of ZDV and lamivudine (3TC) were evaluated: prepartum, intrapartum, and postpartum; intrapartum and postpartum; and postpartum only (95). At 6 weeks, the reduction was greatest (52%) for the three-part course, followed by 38% for the intrapartum and postpartum regimen and no reduction in transmission for the postpartum-only regimen. The HIVNET 012 trial (Table 4) in Uganda compared the efficacy of an ultrashort course of ZDV versus nevirapine: vertical transmission in the nevirapine group compared with the ZDV group was reduced 47% at 4 months (34).

The need for cost-effective interventions in resource-poor settings is an immediate public health concern. The PACTG 076 regimen costs more than US$800 (Table 4). This high treatment cost is not cost-effective for countries with annual health expenditures of $2 to $40 per person (55, 106). Despite nevirapine's efficacy and low cost (approximately US$4), challenges still remain for prevention (34, 55).

Unlike the industrialized countries, where HIV-infected mothers are counseled not to breast-feed and safe alternative breast-feeding practices are available, breast-feeding is prevalent in most developing countries. Breast-feeding, the cornerstone of child health and survival strategies, plays an important role in reducing infant mortality in many countries. In developing countries, one-third to one-half of all HIV infections in young children are acquired through breast milk (23, 26, 84). Risk factors for transmission through breast milk include high maternal virus load and mastitis (8, 16, 77). In the presence of

mastitis, inflammatory cells, such as HIV-infected lymphocytes, could raise the virus load in breast milk and increase HIV transmission (28, 30, 36, 77; N. A. Galvaao, C. L. Silva, P. S. Naud, E. B. Chaves, S. A. Zachia, M. Larangeira, F. Dubina, and F. M. Hartman, Program Abstr. XII Int. Conf. AIDS, Geneva, Switzerland, abstr. 12155, 1998). According to a meta-analysis of 10 reports, the risk for transmission through breast-feeding is 7 to 22% for mothers who have established HIV infection when they give birth (30). Another investigation found a high risk for HIV transmission (0.7% incidence per month) from breast-feeding during 2 to 6 months postpartum; the findings also reflected a low but continuous risk for transmission during late breast-feeding (0.3% incidence per month during 12 to 24 months) (57). In a randomized clinical trial in Kenya, breast-feeding transmission was 16.1%, and most of the infections occurred during early breast-feeding. The use of alternatives to breast milk prevented 44% of infant infections (62).

A variety of approaches to prevent transmission during breast-feeding have been proposed. The early cessation of breast-feeding can still prevent some infections when artificial feeding is impractical because of cost, lack of clean water, or stigma (3, 62). To be effective, programs to reduce transmission by providing artificial feeding must minimize the likelihood of decreasing breast-feeding by uninfected women (43).

PARENTERAL TRANSMISSION

Transmission through blood transfusions, once a concern in many countries, has been nearly eliminated in developed countries by the routine screening of blood donations (9, 64, 107). In developing countries, transmission through the blood supply has yet to be eliminated, especially where HIV prevalence rates among blood donors are high and where screening of blood for HIV has not become routine (9, 38, 64, 88, 107). This situation is particularly a problem in places where blood transfusions are a commonly used treatment. It is believed that nearly a quarter of the estimated 2.5 million blood transfusions in Africa in 1995 had not been screened for HIV antibodies (64, 88). Studies among blood donors in India have shown that 50% of the blood is screened but that 10% of paid donors are HIV positive (50). During the period from 1989 through 1991, 10% of all orphans in Romania became infected with HIV through unsafe injections in hospitals and institutions (38, 81).

Injection drug use plays a critical role in the HIV epidemic in various regions, particularly Asia and southern Europe. According to studies in Southeast Asia, HIV prevalence among IDUs rose to 40% within 1 to 2 years after the first positive HIV test result. This was true in Bangkok, Thailand; Yunnan Providence, in southwestern China; Myanmar; and Minipur, in northeast India. HIV infection among IDUs has also spread in Malaysia and Vietnam (74, 75). The increase has coincided with new patterns of drug use, particularly the shift from smoking opiates to injecting drugs (influenced by the increased availability and affordability of injectable heroin), and increased migration and population mixing (74, 75, 81). HIV transmission among IDUs is also associated with drug distribution routes and patterns of migration. In Manipur, India, HIV infection through injection drug use is concentrated along the main trading road (6, 74, 75). Increased migration precedes the spread of HIV infection among IDUs. Similar associations were found among migrant mining laborers in Myanmar, fishing laborers in Thailand, and truck drivers in Russia and the Ukraine (7, 80, 81).

Well-documented HIV prevention strategies that have reduced HIV transmission among IDUs in developed countries are now being adopted in developing countries (Asia and Latin America) and transitional countries (Eastern Europe and the Newly Independent States) (18, 19, 74, 75). Interventions include needle exchange and distribution, condom and bleach distribution, outreach to IDUs, peer education programs, and social network interventions (6, 18, 93).

Programs that distribute condoms and bleach and provide advice on syringe cleaning are being implemented in Manipur (in northeastern India), Malaysia, Vietnam, Thailand, and Nepal (6). Other outreach programs for IDUs provide HIV prevention information in Belarus, Ukraine, Kazakhstan, the Russian Federation, China, Myanmar, Brazil, and Argentina (6).

ECONOMICS OF HIV/AIDS CARE

The HIV/AIDS pandemic has profoundly affected the economy, the work force, individual workers and their families, health care expenditures, the cost of labor, and savings and investments (40, 100, 101, 107). AIDS is the second leading cause of death among adults in developing countries. It is projected that HIV will be responsible for almost 40% of all deaths from infectious diseases by 2020 (108). AIDS also has costly consequences, especially for the poor. Because AIDS affects people during their most productive years, it has negative consequences for worker productivity, family income, and national revenues (107, 108). As the pandemic evolves, it widens the gap between available resources and the needs for care. Annual medical costs in African countries during 1990 to 1993 ranged from US$210 (Malawi) to US$936 (Zimbabwe) per person (56). In industrialized countries during those years, costs ranged from US$20,000 (United Kingdom) to US$57,000 (Switzerland) per person (107). The overall cost of care in industrialized countries has increased steadily because of the increased number of AIDS cases, longer survival time, and increased use of expensive therapies.

The estimated cost of providing HIV treatment and care exemplifies the impact of AIDS on health budgets in the developing world (56, 107). For example, treatment costs in Tanzania accounted for 50% (US$26 million) of the country's 1991 health budget. By 2015, the total cost for HIV/AIDS treatment and care could reach US$155 million. By 2005, the estimated global cost of HIV/AIDS care and treatment is expected to account for more than a third of health spending by the government in Ethiopia, more than half in Kenya, and nearly two thirds in Zimbabwe (93, 101). Even countries with relatively low HIV prevalence will experience significantly increased health care costs because of HIV/AIDS.

In some middle-income countries, the cost of HIV/AIDS care is affected by the growing availability and use of antiretroviral medications for HIV-related illnesses. It is estimated that over a 1-year period (mid-1997 to mid-1998), Brazil averted US$136 million in hospital admission and treatment costs for people with HIV infection. However, Brazil's AIDS expenditure is 3.0 times the per capita gross national product

(107). In Argentina, antiretroviral medications are provided to HIV-positive persons. The result has been a 40% decrease in the rate of new AIDS cases (101, 107, 108). The effect of antiretroviral medications on the cost of HIV/AIDS care in most developing countries is limited because of high cost and the lack of a medical infrastructure to manage the distribution and use of these therapies (56, 107, 108). Overall, global HIV/AIDS spending will dramatically affect care in the future. The gap in new HIV infection rates and AIDS deaths between rich and poor countries, especially between Africa and the rest of the world, is likely to grow even larger in the next century.

HIV-ASSOCIATED ILLNESSES AND TREATMENT

TB is the most common opportunistic infection and the leading cause of mortality among people with HIV in developing countries, in contrast to industrialized countries, where *Pneumocystis carinii* pneumonia is the leading cause of HIV morbidity (53). According to studies in Uganda (53) and the Ivory Coast (52), TB caused or contributed to 30 to 40% of the deaths of HIV-infected persons. As of 1999, approximately 11 million persons were coinfected with HIV and TB (110). Most cases of clinical TB in HIV-infected persons are due to the reactivation of latent infections (20, 22). For persons with latent infection worldwide, the annual risk of developing clinical TB ranged from 5 to 8% for those with HIV infection, compared with 0 to 0.8% for those without HIV infection (4).

Recent randomized controlled trials showed that TB preventive therapy prevents TB disease in persons coinfected with HIV and TB. In a clinical trial in Haiti, 12 months of isoniazid prophylaxis decreased the incidence of TB from 10.0 to 2.2 per 100 person-years and slowed the progression to AIDS (66). A study in Uganda also showed the effectiveness of TB preventive therapy for HIV-infected persons. TB preventive therapy taken by HIV-infected persons after a positive tuberculin test result extended life expectancy 7.79 years, reduced the incidence of TB from 38,000 to 30,000 per 100,000, and reduced social and medical care costs (7). This study also showed that TB preventive therapy is cost-effective: it costs US$315 to US$636 to extend life by 1 quality-adjusted life-year.

Evidence suggests that TB speeds the progression of HIV, altering the course of HIV in areas of high TB prevalence (20, 22). Although TB preventive therapy should be incorporated into the care of HIV-infected persons, the prompt and complete treatment of people with active TB disease is essential for individual as well as public health purposes (4).

Highly active antiretroviral therapy reduces opportunistic infections and mortality, but it is not affordable for most persons in resource-poor countries. Before effective antiretroviral therapy was available in developed countries, the survival of HIV-infected persons depended upon preventing opportunistic infections by the use of antibiotic prophylaxis (104). In countries where antiretroviral therapy is not readily available, preventive therapy may reduce HIV-related morbidity and mortality among HIV-infected persons (17). Two studies in Abidjan, Ivory Coast, demonstrated that trimethoprim-sulfamethoxazole (co-trimoxazole) can reduce the frequency of opportunistic infections and death among HIV-infected people. In one study of HIV-infected patients with TB, the daily use of co-trimoxazole reduced mortality 46% (104). In the other study, co-trimoxazole reduced serious illness 43% (1). The results of these studies were the basis of a recent UNAIDS recommendation for the use of co-trimoxazole prophylaxis for people with HIV in developing countries to reduce the morbidity and mortality associated with opportunistic infections (99).

GLOBAL PANDEMIC: THE FUTURE

The examples of several countries show that it is possible to reduce the spread of HIV with existing technology and interventions. Strong prevention programs in Senegal, Thailand, and Uganda have caused the HIV-infected proportion of the population to drop to 1.8, 2, and 9.5%, respectively (86, 90, 92, 97). The prevention successes in these countries demonstrate the importance of aggressive national intervention programs that include key components such as behavior change communication, STD treatment, increased access to condoms, and increased access to HIV testing. Mass media, outreach, counseling, and peer education have been used to increase awareness and life skills among young people, those with high-risk behaviors, and the public at large (86, 90, 92, 97). Although the declines in HIV prevalence are modest, sound programs and political commitment can make a difference. Ultimately, it is the cumulation of these successes that will put an end to the spread of HIV and its pervasive impact on the global community.

Prevention is a cost-effective measure for fighting the disease and countering the economic effect of HIV/AIDS on individuals, families, and communities. Prevention interventions cost less than HIV/AIDS treatments and are economically sound investments (107, 108). The World Bank estimated that condoms, information, and STD treatment for female sex workers cost US$8 to US$12 per infection averted.

We have learned that no single approach will contain the epidemic and that we need all available resources. It is clear that making information and services available to young people is increasingly important in arresting the spread of the virus. Affordable barrier methods controlled by women, to complement the male condom, are also important (97). Women's biological vulnerability is compounded by their social status and economic status, both of which leave them at a disadvantage in demanding fidelity or the use of the male condom. Negotiating consistent condom use is not always feasible for many women. A microbicide will offer a preventive option that women can more easily control (89). A vaccine that is effective and affordable in developing countries would greatly improve the prospects for reducing the global pandemic (5, 37, 91).

As the pandemic proceeds, the global gap between the need for care and the available resources to provide care for people in countries most affected by this epidemic widens. To cope with these challenges, new models of care and cost-effective health care delivery systems are needed (53). Methods of making therapies, including antiretroviral therapies, affordable must be sought. As the HIV/AIDS epidemic continues to devastate the global community, increased prevention and care efforts must address strategies to prevent new cases of HIV and to help those who are infected.

REFERENCES

1. **Anglaret, X., G. Chene, A. Attia, S. Toure, S. Lafont, P. Combe, K. Manlan, T. N'Dri-Yoman, and R. Salamon.** 1999. Early chemoprophylaxis with trimethoprim-sulphamethoxazole for HIV-1 infected adults in Abidjan, Côte d'Ivoire: a randomised trial. Lancet **353:**1463–1468.
2. **Anonymous.** 1997. AIDS and HIV infection worldwide. Communicable Dis. Rep. **7:**461–462.
3. **Anonymous.** 1998. Recommendation of the safe and effective use of short-course ZDV for prevention of mother-to-child transmission of HIV. Wkly. Epidemiol. Rec. **73:**313–320.
4. **Anonymous.** 1999. Preventive therapy against tuberculosis in people living with HIV. Wkly. Epidemiol. Rec. **74:**385–400.
5. **Attawell, K., and H. Grosskurth.** 1999. From knowledge to practice: STD control and HIV prevention. European Communities, Brussels, Belgium.
6. **Ball, A., S. Rana, and K. Dehne.** 1998. HIV prevention among injecting drug users: responses in developing and transitional countries. Public Health Rep. **113:**170–181.
7. **Bell, J. C., D. N. Rose, and H. S. Sacks.** 1999. Tuberculosis preventive therapy for HIV-infected people in sub-Saharan Africa is cost-effective. AIDS **13:**1549–1556.
8. **Burns, D., and L. Monfenson.** 1999. Paediatric HIV-1 infection. Lancet **354**(Suppl. II)**:**1–16.
9. **Buve, A., and M. Rogers.** 1998. Overview: epidemiology. AIDS **12:**S53–S54.
10. **Caceres, C., and N. Hearst.** 1996. Update in Latin America and the Caribbean: an update. AIDS **10**(Suppl.)**:**43–49.
11. **Cameron, D., J. Simonsen, L. D'Costa, A. Ronald, G. Maitha, M. Gakinya, M. Cheang, et al.** 1989. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. Lancet **ii:** 403–407.
12. **Carlos, M., Y. Yamamura, F. Diaz-Mitoma, and J. Torres.** 1999. Antibodies from HIV-positive and AIDS patients bind to an HIV envelope multivalent vaccine. J. Acquired Immune Defic. Syndr. **22:**317.
13. **Centers for Disease Control and Prevention.** 1999. HIV/AIDS surveillance report. **11**(2)**:**1–44.
14. **Connor, E., R. Sperling, and R. Gelber, for the Pediatric AIDS Clinical Trials Group Protocol 076 Study Group.** 1994. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. N. Engl. J. Med. **331:**1173–1180.
15. **Dabis, F., P. Msellati, N. Meda, C. Welffens-Ekra, B. You, O. Manigart, V. Leroy, A. Simonon, M. Cartoux, P. Combe, A. Ouangre, R. Ramon, O. Ky-Zerbo, C. Montcho, R. Salamon, C. Rousioux, P. Van de Perre, and L. Mandelbrot, for the DITRAME Study Group.** 1999. 6-month efficacy, tolerance, and acceptability of a short regimen of oral zidovudine to reduce vertical transmission of HIV in breastfed children in Côte d'Ivoire and Burkina Faso: a double blind placebo-controlled multicentre trial. Lancet **353:**786–792.
16. **De Cock, K., M. Fowler, E. Mercier, I. de Vincenzi, J. Saba, E. Hoff, D. J. Alnwick, M. Rogers, and N. Shaffer.** 2000. Prevention of mother-to-child HIV transmission in resource-poor countries. JAMA **283:**1175–1182.
17. **De Cock, K., A. Grant, and J. Porter.** 1995. Preventive therapy for tuberculosis in HIV-infected persons: international recommendations, research, and practice. Lancet **345:**833–836.
18. **Des Jarlais, D., H. Hagan, S. Friedman, D. Friedman, D. Goldberg, M. Frischer, S. Green, K. Tunving, B. Ljungberg, A. Wodak, et al.** 1995. Maintaining low HIV seroprevalence in populations of injecting drug users. JAMA **274:**1126–1131.
19. **Des Jarlais, D., G. Stimson, H. Hagan, et al.** 1996. Emerging HIV infectious diseases and the injection of illicit psychoactive drugs. Curr. Opin. Public Health **2:**130–137.
20. **Dolin, P., M. Raviglione, and A. Kochi.** 1994. Global tuberculosis incidence and mortality during 1990-2000. Bull. W. H. O. **72:**213–220.
21. **Dunn, D., M. Newell, A. Ades, and C. Peckham.** 1992. Risk of human immunodeficiency virus type 1 transmission through breast-feeding. Lancet **340:**585–588.
22. **Dye, C., S. Scheele, P. Dolina, V. Pathania, and M. C. Raviglione for the WHO Global Surveillance and Monitoring Project.** 1999. Global burden of tuberculosis. JAMA **282:**677–686.
23. **European Collaborative Study.** 1992. Risk factors for mother-to-child transmission of HIV-1. Lancet **339:**1007–1012.
24. **Fleming, D. T., and J. N. Wasserheit.** 1999. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex. Transm. Infect. **75:**3–17.
25. **Ford, N.** 1997. Conference report: response to the AIDS epidemic to Asia and the Pacific: report on the III International Conference on AIDS in Asia and the Pacific, Chiang Mai, Thailand, 17–21 Sept., 1995. AIDS Care **8:** 117–124.
26. **Fowler, M. G., J. Bertolli, and P. Nieburg.** 1999. When is breastfeeding not best? The dilemma facing HIV-infected women in resource-poor settings. JAMA **282:**781–783.
27. **Reference deleted.**
28. **Garcia, P. M., L. A. Kalish, J. Pitt, H. Minkoff, T. C. Quinn, S. K. Burchett, J. Kornegay, B. Jackson, J. Moye, C. Hanson, C. Zorrilla, and J. F. Lew.** 1999. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. N. Engl. J. Med. **341:**394–402.
29. **Gibb, D.** 1998. Reduction of mother-to-child transmission of HIV infection: non-pharmaceutical interventions and their implementation. Int. J. STD AIDS **9:**19–21.
30. **Gibb, D. M., and B. H. Tess.** 1999. Interventions to reduce mother-to-child transmission of HIV infection: new developments and current controversies. AIDS **13**(Suppl.)**:**93–102.
31. **Gibney, L., P. Choudhury, Z. Khawaja, M. Sarker, N. Islam, and S. Vermund.** 1999. HIV/AIDS in Bangladesh: an assessment of biomedical risk factors for transmission. Int. J. STD AIDS **10:**338–346.
32. **Grosskurth, H.** 1999. From Mwanza and Rakai to Beijing and Moscow? STD control and HIV prevention. Sex. Transm. Infect. **75:**83–85.
33. **Grosskurth, H., F. Mosha, J. Todd, E. Mwijarubi, A. Klokke, K. Senkoro, P. Mayaud, J. Changalucha, A. Nicoll, G. ka-Gina, J. Newell, K. Mugeye, D. Mabey, and R. Hayes.** 1995. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. Lancet **346:**530–536.
34. **Guay, L. A., P. Musoke, T. Fleming, D. Bagenda, M. Allen, C. Nakabito, J. Sherman, P. Bakaki, C. Ducar, M. Deseyve, L. Emel, M. Mirochnick, M. G. Fowler, L. Mofenson, P. Miotti, K. Dransfield, D. Bray, F. Mmiro, and J. B. Jackson.** 1999. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. Lancet **354:**795–802.
35. **Halperin, D., and R. Bailey.** 1999. Male circumcision and HIV infection: 10 years and counting. Lancet **354:**1813–1815.
36. **Halsey, N., R. Boulos, E. Holt, A. Ruff, J. Brutus, P. Kissinger, T. Quinn, J. Coberly, M. Adrien, and C. Boulos.** 1990. Transmission of HIV-1 infections from mothers to infants in Haiti: impact on childhood mortality and malnutrition. The CDS/JHU AIDS Project Team. JAMA **264:**2088–2092.
37. **Hayes, R., M. Wawer, R. Gray, J. Whitworth, H. Grosskurth, and D. Mabey.** 1997. Randomised trials of STD treatment for HIV prevention: report of an international workshop. Genitourin. Med. **73:**432–443.
38. **Hersh, B., F. Popovici, L. Zolotusca, N. Beldescu, M. Oxtoby, and H. Gayle.** 1993. Risk factors for HIV infection among abandoned Romanian children. AIDS **7:**1617–1624.
39. **Hitchcock, P., and L. Fransen.** 1999. Preventing HIV infection: lessons from Mwanza and Rakai. Lancet **353:**513–515.
40. **International Labour Organization.** 2000. HIV/AIDS: a threat to decent work, productivity and development. International Labour Organization, Geneva, Switzerland.
41. **Kalichman, S., J. Kelly, K. Sikkema, A. Koslov, A. Shaboltas, and J. Granskaya.** 2000. The emerging AIDS crises in Russia: review of enabling factors and prevention needs. Int. J. STD AIDS **11:**71–75.
42. **Kanki, P., K. Traversm, S. Mboup, C. Hsieh, R. Marlink, A. Gueye-Ndiaye, T. Siby, I. Thior, M. Hernandez-Avila, J. Sankale, I. Ndoye, and M. Essex.** 1994. Slower heterosexual spread of HIV-2 than HIV-1. Lancet **343:**943–946.
43. **Kuhn, L., and Z. Stein.** 1997. Infant survival, HIV infection, and feeding alternatives in less-developed countries. Am. J. Public Health **87:**926–931.
44. **Kunamosont, C., H. Foy, J. Kreiss, et al.** 1995. HIV-1 subtypes and male-to-female transmission in Thailand. Lancet **345:**1078–1083.
45. **Laga, M., M. Diallo, and A. Buve.** 1994. Interrelationship of STD and HIV: where are we now? AIDS **8:**119–124.
46. **Laga, M., A. Manoka, M. Kivuvu, B. Malele, M. Tuliza, N. Nzila, J. Goeman, F. Batter, and M. Alary.** 1993. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. AIDS **7:**95–102.
47. **Laga, M.** 1995. STD control for HIV prevention—it works! Lancet **346:** 518–519.
48. **Laga, M., M. Alary, N. Nzila, A. T. Manoka, M. Tuliza, F. Behets, J. Goeman, M. St. Louis, and P. Piot.** 1994. Condom promotion, sexually transmitted diseases treatment, and declining incidence of HIV-1 in female Zairian sex workers. Lancet **344:**246–248.
49. **Latyshev, G., and D. Rechnov.** 1998. Drug use by young people in St. Peterburg: facts, causes, and ways to improve the situation. Russ. J. HIV/AIDS Related Problems **2:**94.
50. **Li, P., and E. Yeoh.** 1995. Update on epidemiology of AIDS in Asia. AIDS Clin. Rev. **96:**347–386.
51. **Liao, S., K. Hirabayashi, K. Tajima, K. Soda, Z. Yi, Z. Dong, C. He, and Y. Lin.** 1998. HIV in China: epidemiology and risk factors. AIDS **12**(Suppl. B)**:** 19–25.
52. **Lucas, S., A. Hounnou, and C. Peacock.** 1993. The mortality and pathology of HIV infection in a West African city. AIDS **7:**1569–1579.
53. **Mann, J., and D. Tarantola.** 1996. AIDS in the world II. Oxford University Press, New York, N.Y.
54. **MAP Network.** 2000. The status and trends of the HIV/AIDS epidemics in the world: provisional report, July 5–7, 2000. UNAIDS, Washington, D.C.
55. **Marseille, E., J. G. Kahn, F. Mmiro, L. Guay, P. Musoke, M. G. Fowler, and J. B. Jackson.** 1999. Cost effectiveness of single-dose nevirapine regimen for

mothers and babies to decrease vertical HIV-1 transmission in sub-Saharan Africa. Lancet **354:**803–809.
56. **Martin, A.** 1996. The cost of HIV/AIDS care, p. 390–413. *In* J. Mann and D. Tarantola (ed.), AIDS in the world II. Oxford University Press, New York, N.Y.
57. **Miotti, P. G., T. E. Taha, N. I. Kumwenda, et al.** 1999. HIV transmission through breastfeeding: a study in Malawi. JAMA **282:**744–749.
58. **Monitoring the AIDS Pandemic Network.** 1998. The status and trends of the HIV/AIDS epidemic in the world. MAP, Geneva, Switzerland.
59. **Moses, S., F. Plummer, and J. Bradley.** 1994. The association between lack of male circumcision and risk for HIV infection: a review of the epidemiological data. Sex. Transm. Dis. **21:**201–210.
60. **Mulder, D., A. Dunn, and A. Kamali.** 1995. Decreasing HIV-1 seroprevalence in young rural Uganda cohort. Br. Med. J. **311:**833–836.
61. **Murray, M., J. Embree, S. Ramdahin, A. Anzala, S. Njenga, and F. Plummer.** 2000. Effect of human immunodeficiency virus (HIV) type 1 viral genotype on mother-to-child transmission of HIV-1. J. Infect. Dis. **181:**746–749.
62. **Nduati, R., G. John, D. Mbori-Ngacha, B. Richardson, J. Overbaugh, A. Mwatha, J. Ndinya-Achola, J. Bwayo, F. Onyango, J. Hughes, and J. Kreiss.** 2000. Effect of breastfeeding and formula feeding on transmission of HIV-1. JAMA **283:**1167–1174.
63. **Nelson, K., D. Celentano, S. Eiumtrakol, D. Hoover, C. Beyrer, S. Suprasert, S. Kuntolbutra, and C. Khamboonruang.** 1996. Changes in sexual behavior and a decline in HIV infection among young men in Thailand. N. Engl. J. Med. **335:**297–303.
64. **Nicoll, A., and O. N. Gill.** 1999. The global impact of HIV infection and disease. Communicable Dis. Public Health **2:**85–95.
65. **Pan American Health Organization (PAHO).** 2000. AIDS surveillance in the Americas: biannual report, February 2000. PAHO, Washington, D.C.
66. **Pape, J., S. Jean, J. Ho, A. Hafner, and W. D. Johnson, Jr.** 1993. Effect of isoniazid prophylaxis on incidence of active tuberculosis and progress of HIV infection. Lancet **342:**268–272.
67. **Pedraza, M., J. del Romero, F. Roldan, S. Garcia, M. Averbe, A. Noriega, J. Alcami, et al.** 1999. Heterosexual transmission of HIV-1 is associated with high plasma viral load levels and a positive viral isolation in the infected partner. J. Acquired Immune Defic. Syndr. Hum. Retrovirol. **21:** 120–125.
68. **Phoolcharoen, W.** 1998. HIV/AIDS prevention in Thailand: success and challenges. Science **280:**1873–1874.
69. **Plummer, F., J. Simonson, and D. Cameron.** 1991. Co-factors in female-to-male transmission of HIV. J. Infect. Dis. **163:**233–239.
70. **Popper, S., A. Sarr, K. Travers, S. Mboup, M. Essex, and P. Kanki.** 1999. Lower human immunodeficiency virus (HIV) type 2 viral load reflects the difference in pathogenicity of HIV-1 and HIV-2. J. Infect. Dis. **180:**1116–1121.
71. **Poulsen, A., P. Aaby, and A. Gottschau.** 1993. HIV-2 infection in Bissau, West Africa, 1987–1989: incidence, prevalence, and routes of transmission. J. Acquired Immune Defic. Syndr. Hum. Retrovirol. **8:**941–948.
72. **Quinn, T. C., M. J. Wawer, N. Sewankambo, D. Serwadda, C. Li, F. Wabwire-Mangen, M. Meehan, T. Lutalo, and R. Gray.** 2000. Viral load and heterosexual transmission of human immunodeficiency virus type 1. N. Engl. J. Med. **342:**921–929.
73. **Reference deleted.**
74. **Rhodes, T., G. V. Stimson, N. Crofts, A. Ball, K. Dehne, and L. Khodakevich.** 1999. Drug injecting, rapid HIV spread, and the 'risk environment': implications for assessment and response. AIDS **13**(Suppl. A)**:**259–269.
75. **Rhodes, T., G. V. Stimson, C. Fitch, A. Ball, and A. Renton.** 1999. Rapid assessment, injecting drug use, and public health. Lancet **354:**65–68.
76. **Risbud, A., K. Chan-Tack, D. Gadkari, R. Gangakhedkar, M. Shepherd, R. Bollinger, S. Mehendale, C. Gaydos, A. Divekar, A. Rompalo, and T. C. Quinn.** 1999. The etiology of genital ulcer disease by multiplex polymerase chain reaction and relationship to HIV infection among patients attending sexually transmitted disease clinics in Pune, India. Sex. Transm. Dis. **26:**55–62.
77. **Semba, R., N. Kumwenda, D. Hoover, T. Taha, T. Quinn, et al.** 1999. Human immunodeficiency virus load in breast milk, mastitis, and mother-to-child transmission of human immunodeficiency virus type 1. J. Infect. Dis. **180:**93–98.
78. **Shaffer, N., R. Chuachoowong, P. A. Mock, C. Bhadrakom, W. Siriwasin, N. L. Young, T. Chotpitayasunondh, S. Chearskul, A. Roongpisuthipong, P. Chinayon, J. Karon, T. D. Mastro, and R. J. Simonds.** 1999. Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. Lancet **353:**773–780.
79. **Reference deleted.**
80. **Shapiro, D.** 1999. Risk factors for perinatal human immunodeficiency virus transmission in patients receiving zidovudine prophylaxis. Obstet. Gynecol. **94:**897–908.
81. **Simonsen, L., A. Kane, J. Lloyd, M. Zaffran, and M. Kane.** 1999. Unsafe injections in developing world and transmission of bloodborne pathogens: a review. Bull. W. H. O. **77:**789–800.
82. **Soto-Ramirez, L., B. Renjifo, M. McLane, et al.** 1996. Langerhans' cell tropism associated with heterosexual transmission of HIV. Science **271:** 1291–1293.
83. **Stringer, J., E. M. Stringer, P. Phanuphak, P. Jetwana, D. Reinprayoon, E. M. Funkhouser, and S. H. Vermund.** 1999. Prevention of mother-to-child transmission of HIV in Thailand: physicians' attitudes on zidovudine use, pregnancy termination, and willingness to provide care. J. Acquired Immune Defic. Syndr. Hum. Retrovirol. **21:**217.
84. **Tess, B., L. Rodrigues, M. Newell, D. Dunn, and T. Lago, for Sao Paulo Collaborative Study for Vertical Transmission of HIV-1.** 1998. Infant feeding and risk of mother-to-child transmission of HIV-1 in Sao Paulo State, Brazil. J. Acquired Immune Defic. Syndr. Hum. Retrovirol. **19:**189–194.
85. **UNAIDS.** 1996. The status and trends of the global HIV/AIDS pandemic: July 1996. UNAIDS, Geneva, Switzerland.
86. **UNAIDS.** 1998. A measure of success in Uganda: the value of monitoring both HIV prevalence and sexual behavior. UNAIDS, Geneva, Switzerland.
87. **UNAIDS.** 1998. AIDS epidemic update: December 1998. UNAIDS, Geneva, Switzerland.
88. **UNAIDS.** 1998. Finding out one's HIV status; HIV and mortality; treatment; mother-to-child transmission. UNAIDS, Geneva, Switzerland.
89. **UNAIDS.** 1998. Microbicides for HIV prevention. UNAIDS, Geneva, Switzerland.
90. **UNAIDS.** 1998. Relationship of HIV and STD declines in Thailand to behavioural change. UNAIDS, Geneva, Switzerland.
91. **UNAIDS.** 1998. The public health approach to STD control. UNAIDS, Geneva, Switzerland.
92. **UNAIDS.** 1999. Acting early to prevent AIDS: the case of Senegal. UNAIDS, Geneva, Switzerland.
93. **UNAIDS.** 1999. AIDS epidemic update: December 1999. UNAIDS, Geneva, Switzerland.
94. **UNAIDS.** 1999. Global situation of the HIV/AIDS pandemic, end 1999. UNAIDS, Geneva, Switzerland.
95. **UNAIDS.** 1999. Mother-to-child transmission (MTCT) of HIV. UNAIDS, Geneva Switzerland.
96. **UNAIDS.** 1999. Prevention of HIV transmission from mother to child. UNAIDS, Geneva, Switzerland.
97. **UNAIDS.** 1999. The UNAIDS report. UNAIDS, Geneva, Switzerland.
98. **UNAIDS.** 2000. Report on the global HIV/AIDS epidemic: June 2000. UNAIDS, Geneva, Switzerland.
99. **UNAIDS.** 2000. UNAIDS/WHO hails consenus on use of cotrimoxazole for prevention of HIV-related infections in Africa. UNAIDS, Geneva, Switzerland.
100. **USAID.** 1999. HIV/AIDS briefs: the economic impact of AIDS. USAID, Washington, D.C.
101. **USAID.** 1999. The economic impact of AIDS in Africa. USAID, Washington, D.C.
102. **Wasserheit, J. N.** 1992. Epidemiological synergy: interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. Sex. Transm. Dis. **19:**61–77.
103. **Wawer, M., D. Serwadda, and R. Gray.** 1997. Trends in HIV-1 prevalence may not reflect trends in incidence in mature epidemics: data from the Rakai population-based cohort, Uganda. AIDS **11:**1023–1030.
104. **Wiktor, S., M. Sassan-Morokro, A. Grant, L. Abouya, J. Karon, C. Maurice, G. Djomand, A. Ackah, K. Domoua, A. Kadio, A. Yapi, P. Combe, O. Tossou, T. Roels, E. Lackritz, D. Coulibaly, K. De Cock, I. Coulibaly, and A. Greenberg.** 1999. Efficacy of trimethoprim-sulphamethoxazole prophylaxis to decrease morbidity and mortality in HIV-1 infected patients with tuberculosis in Abidjan, Côte d'Ivoire: a randomised controlled trial. Lancet **353:**1469–1475.
105. **Wiktor, S. Z., E. Ekpini, J. Karon, J. Nkengasong, C. Maurice, S. T. Severin, T. H. Roels, M. K. Kouassi, E. M. Lackritz, I.-M. Coulibaly, and A. E. Greenberg.** 1999. Short-course oral zidovudine for prevention of mother-to-child transmission of HIV-1 in Abidjan, Côte d'Ivoire: a randomised trial. Lancet **353:**781–785.
106. **World Bank.** 1993. World development report 1993: investing in health. Oxford Press, New York, N.Y.
107. **World Bank.** 1997. Confronting AIDS: public priorities in a global epidemic. World Bank, New York, N.Y.
108. **World Bank.** 1999. Investing in HIV/AIDS. World Bank, Washington, D.C.
109. **World Health Organization.** 1997. Global AIDS surveillance. Wkly. Epidemiol. Rec. **72:**357–364.
110. **World Health Organization.** 2000. Global tuberculosis. WHO/CDS, Geneva, Switzerland.
111. **World Health Organization.** 1999. Global situation of the HIV/AIDS pandemic, end 1999, p. 30. UNAIDS, Geneva, Switzerland.