

Perspectives

The HIV Pandemic: Worldwide Perspective and Focus on the United States

At the International AIDS Society–USA course in Atlanta in February, 2001, Harold W. Jaffe, MD, discussed current worldwide HIV disease epidemiology, several aspects of disease trends in the United States, and prevention goals of the Centers for Disease Control and Prevention for 2000 to 2005.

Global Burden of Disease

The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that approximately 36.1 million persons worldwide were living with HIV/AIDS as of the end of 2000. Disease in Sub-Saharan Africa and South and Southeast Asia accounts for approximately 85% of the total global burden; disease in North America is estimated to account for less than 2.5% of the worldwide total. There were approximately 15,000 new HIV infections per day in 2000. More than 95% of these infections occurred in developing countries. Approximately 1700 per day occurred in children under age 15 and approximately 13,000 per day occurred in persons in the 15 to 49 year age group, with 47% of these infections being in women and more than half occurring in individuals aged 15 to 24 years.

According to 1999 World Health Organization data, HIV/AIDS was tied with chronic obstructive pulmonary disease as the fourth leading cause of mortality for 1998 (4.2%), after ischemic heart disease (13.7%), cerebrovascular disease (9.5%), and acute lower respiratory infection (6.4%). In Africa, HIV/AIDS accounted for 19% of deaths in 1998, making it the leading cause of mortality on the continent. It is estimated that 13.2 million HIV-seronegative children had lost their mother or both parents to

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AIDS before the age of 15 years as of the end of 1999 (UNAIDS, 2000), with AIDS orphans in Sub-Saharan Africa accounting for the vast majority of this number. Life expectancy at birth has decreased markedly in many African nations; experts project that life expectancy in Botswana, which has one of the highest infection rates worldwide, will be approximately 29 years by 2010.

Heterogeneity of Infection Rates in Africa and International Disease Trends

Areas of Sub-Saharan Africa exhibit a wide variation in estimated HIV infection rates, ranging from less than 0.5% to greater than 36% in young adults. Factors that contribute to this heterogeneity likely include (1) between-region differences in sexual behavior (eg, age at first intercourse, number of partners, frequency of contact with commercial sex workers); (2) frequency of other sexually transmitted diseases (eg, ulcerative genital diseases such as chancroid, syphilis, and herpesvirus infection); (3) frequency of other infections that may increase susceptibility to HIV infection by acting as immune activators (eg, tuberculosis, schistosomiasis); and (4) circumcision practices. With regard to circumcision, recent data from a study in Uganda indicate that lack of circumcision is associated with increased risk of genital ulcer disease and may constitute an independent risk factor for HIV infection. In addition, there is some evidence to indicate that biologic differences among HIV-1 subtypes may be associated with differences in transmissibility. Although definitive evidence is lacking, there is some speculation that subtype C, the predominant subtype in southern Africa, is more readily transmissible than other subtypes.

Although the highest HIV/AIDS prevalence rates are in the countries in

Sub-Saharan Africa, the most rapid increase in infection rates currently is observed in the former Soviet Union. Data on cumulative HIV infections in Russia through 1999 indicate an increase from approximately 1000 in 1995 to approximately 15,000 in 1999, with most infections being attributed to injection drug use.

One example of prevention program success comes from experience documented by Centers for Disease Control and Prevention (CDC) and Thai investigators in Chiang Rai, a province of northern Thailand with a population of 1.2 million (Kilmarx et al, AIDS, 2000). Although the first cases of HIV disease were not reported in Thailand until 1988, an explosive spread of infection, particularly in northern Thailand, resulted in rates that were the highest in Asia within a short time. Epidemiologic investigation indicated a central role of commercial sex in transmission in Chiang Rai. Data from 1992 showed that there were 1177 female sex workers in 169 brothels in the province, with these women having high rates of sexually transmitted diseases. Data from 1991 indicate that 75% to 81% of male Thai army conscripts in the region had had sexual contact with female sex workers.

In response to the rapid spread of infection, the Thai government undertook an educational campaign through the mass media and in schools in the late 1980s. In 1991, it implemented the "100% condom" program, which included enlisting the cooperation of sex workers and brothel owners to enforce condom use in all sex acts, using police sanctions against establishments in which sexually transmitted diseases were detected (prostitution is technically illegal in Thailand), and distributing of 1.2 million free condoms per year. As a result of this initiative, rates of reported sexually transmitted diseases decreased by 59-fold between 1989 and 1999, from a high of 725.5 to 12.2 per

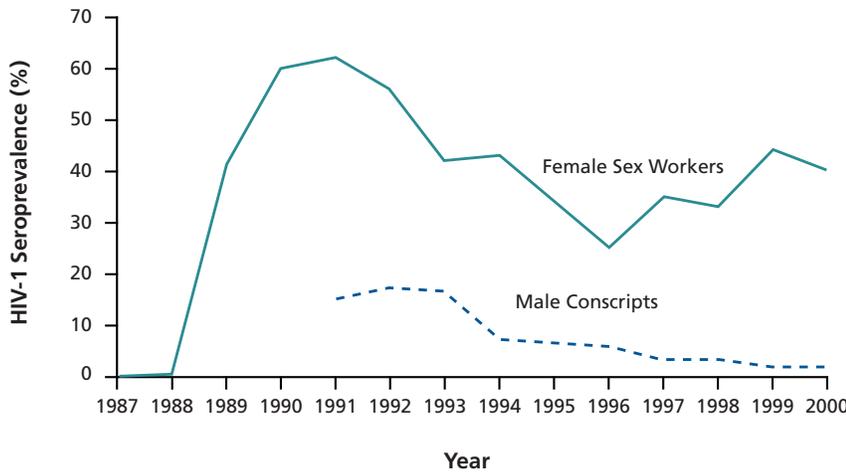


Figure 1. HIV-1 seroprevalence among female sex workers based in brothels (solid line) and among male army conscripts (dashed line) in Chiang Rai, Thailand, 1987 to 2000. (In 2000, prevalence was measured among conscripts in May only.) In 1991 the Thai government implemented its “100% condom” program. Adapted from Kilmarx et al, *AIDS*, 2000.

100,000 population. HIV-1 seroprevalence decreased from a high of 62% among female sex workers in 1991 to a low of 25% in 1996; the rate has subsequently increased to approximately 40% in 2000 (Figure 1). At the same time, HIV-1 seroprevalence among male army conscripts decreased from a high of 17.3% in 1992 to less than 2% in 2000. These findings should provide hope that it is possible to positively affect infection spread through the combination of science-based prevention and political initiative.

HIV-1 subtype B is the predominant virus in infection in North America. The potential for encountering HIV-1 infection with viral subtypes other than type B or HIV-2 infection raises some diagnostic and therapeutic issues for US physicians. Although HIV-1 antibody tests reliably detect antibody to all known subtypes of HIV-1, at least some of the commercially available tests do not reliably detect HIV-2 infection. Individuals with signs or symptoms suggestive of HIV infection who come from West Africa or who report sexual contact with someone from West Africa, the region to which HIV-2 infection appears largely confined, should undergo testing with a “Combi-test”; these tests, used in US blood banks, reliably detects antibodies to both HIV-1 and HIV-2. Commercial viral load assays do not reliably quantify HIV-2, although a pro-

totybe assay is available on a “research test only” basis (Roche Diagnostics, Indianapolis, Ind). For measurement of viral load of non-subtype B HIV-1, the Quantiplex version 3.0 (Bayer Diagnostics, Tarrytown, NY) is commercially available, although not approved by the US Food and Drug Administration. Also available on a “research test only” basis is Amplicor version 1.5 (Roche Diagnostics, Indianapolis, Ind).

With regard to therapeutic implications, limited available data indicate that response to potent antiretroviral therapy is similar in infections due to subtype B and those due to non-B subtypes; antiretroviral resistance mutations are generally similar among viral subtypes. Very few data are available on treatment of HIV-2 infection, in part because it is often untreated due to the low rate of disease progression. However, it is known that HIV-2 is intrinsically resistant to currently available nonnucleoside reverse transcriptase inhibitors, and these agents should thus not be used in attempts to treat HIV-2-infected patients.

US Disease Trends

Data from the CDC on reported AIDS cases and deaths in the United States through June 2000 indicate totals of 745,103 cases and 433,709 deaths in adults and adolescents and 8804 cases and 5086 deaths in children. Among 46,137 adult and adolescent AIDS cases reported in 1999, 66% occurred in black or Hispanic persons and 23% occurred in women; 44% of men with AIDS reported sex with men as their only risk factor. Figure 2 shows numbers of AIDS cases and deaths by quarter-year and preva-

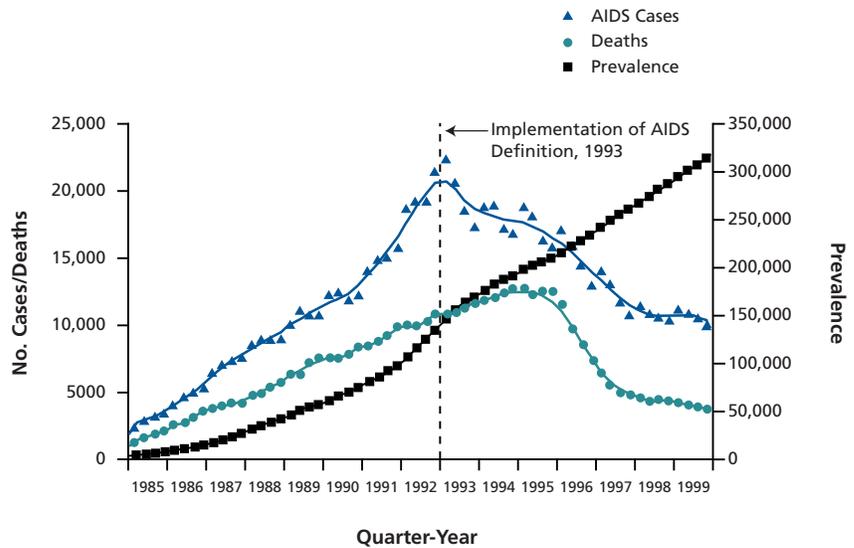


Figure 2. Estimated incidence of AIDS and AIDS deaths and number of persons living with AIDS (prevalence) by quarter year from 1985 to 1999 (adjusted for reporting delays). Adapted from Centers for Disease Control and Prevention, AIDS surveillance-trends L207 slide series, available at <http://www.cdc.gov/hiv/graphics/trends.htm>.

lence of AIDS (number of individuals living with AIDS) between 1985 and 1999. The trends in reported AIDS cases may be distorted because of an expansion in the AIDS case definition in 1993. Nonetheless, the number of cases per quarter has declined since 1993 and the number of deaths per quarter began declining around 1996, when potent antiretroviral therapy became broadly available. Rates have appeared to plateau at about 10,000 cases and 4000 deaths per quarter; with the reduction in mortality and continued accumulation of new infections, the number of persons living with AIDS continues to increase, reaching approximately one third of a million in 1999.

Cases of perinatally acquired AIDS have decreased from a peak of more than 200 per quarter in 1992 and 1993 to less than 200 per year in 1999. This decrease is associated with the dramatic increase in use of antiretroviral therapy in HIV-infected pregnant women or their infants. Data on rates of such use from 34 states indicate an increase from approximately 10% in 1993 to 80% or more in 1997 to 1999. Many of the cases of lack of treatment of the mother or infant are associated with not knowing the infection status of the mother. To aid in achievement of the goal of eliminating perinatal transmission in the United States, increased efforts at determining infection status of pregnant women are

needed. Although early identification of infection is optimal, such efforts may include use of new technology for rapid testing during labor.

Table 1 shows distribution of AIDS cases reported in 1999 in metropolitan and nonmetropolitan areas by geo-

The considerable number of AIDS cases in US rural populations indicates the need for special emphasis on HIV prevention in such settings

graphic region of the United States. HIV disease predominantly affects urban populations. However, the reporting of a considerable number of cases in rural populations indicates the need for special emphasis on prevention in such settings. One study by Beltrami and colleagues (*South Med J*, 1999) among 417 persons receiving HIV services in rural

Alabama between 1995 and 1997 indicates that the high-risk behaviors exhibited in rural settings are the same as those in urban settings. Slightly more than half of those with HIV infection were homosexual or bisexual men, with the remainder of the population consisting of equal proportions of heterosexual men and heterosexual women. During the period in which infection was presumed to occur (between last seronegative HIV test or 1981 and first seropositive HIV test), 45% of these persons resided only in nonurban Alabama; 19% used crack cocaine, 18% exchanged sex for money or drugs, and 13% injected drugs. The proportion of infected individuals who practiced such high-risk behaviors and who lived usually or exclusively in nonurban settings increased over time.

Findings in such studies suggest that individuals may have acquired infection in urban settings earlier in the epidemic and then returned to their more rural places of residence, establishing networks of HIV transmission in their communities with sex and needle-sharing partners. Figure 3 shows a sex network identified in a CDC investigation in a small community in Mississippi (MMWR, 2000). The investigation began in early 1999 with the diagnosis of HIV infection in 2 individuals as part of a routine sexually transmitted diseases evaluation, and eventually identified 44 involved individuals, all of whom were African American, including 7 with HIV infection. The infected men had an average age of 25 years and the median age among the 5 women in the cluster was 16 years. Only 2 of the infected individuals knew that treatment exists for HIV infection.

There is also reason for concern regarding increased risk behavior among homosexual men, given a number of reports of increases in sexually transmitted diseases in this population in several locales. A marked increase of syphilis cases predominantly involving homosexual men in Seattle and King County, Washington, was observed in 1998 and 1999 (CDC, MMWR, 1999), at a time of a record low national incidence of syphilis; many of the affected individuals in this outbreak also have HIV infection. A similar outbreak of syphilis has been observed among homosexual men

Table 1. AIDS Cases Reported in 1999 by Size of Place of Residence and by Geographic Area

	Metropolitan Area >500,000 Population (%)	Metropolitan Area 50,000-500,000 Population (%)	Nonmetropolitan Area (%)
Northeast: n=14,006*	91.1	5.8	3.0
North Central: n=433*	79.3	11.8	8.7
South: n=18,770*	71.6	15.0	11.7
West: n=7887*	90.0	6.2	3.8

*Includes AIDS cases with unknown metropolitan area of residence. Unpublished data from Centers for Disease Control and Prevention.

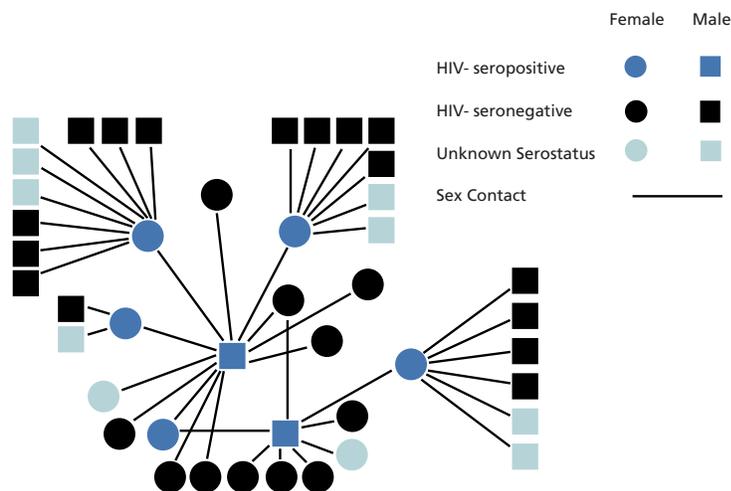


Figure 3. Sex networks of HIV-infected adolescents and young adults in a nonurban community in Mississippi. Shown are sex contacts among 44 individuals who were HIV-seropositive, HIV-seronegative, or had unknown HIV-serologic status. Adapted from Centers for Disease Control and Prevention, *MMWR*, 2000.

in Southern California. Cases of rectal gonorrhea and rectal chlamydia infection in homosexual men in Seattle and King County also increased by 2-fold or more between 1997 and 1999; a similar increase in cases of rectal gonorrhea in homosexual men in San Francisco occurred between 1994 and 1998 (CDC, *MMWR*, 1999). Increases in such sexually transmitted diseases have also been observed in such cities as Chicago and Washington, DC.

Although certainly worrisome, these trends in sexually transmitted diseases may not necessarily indicate increasing rates of HIV transmission. For example, the use of antiretroviral therapy may be reducing the infectiousness of persons engaging in high-risk behaviors. However, preliminary data from a study of almost 3000 young homosexual men from 6 American cities indicated an overall HIV prevalence of 13% and incidence of 4.4%. Infection rates in black and Hispanic participants were even higher (CDC, *MMWR*, 2001).

The factors underlying these trends are unclear, but may include the beliefs that HIV disease is now curable and that infected persons receiving treatment are not infectious, as well as fatigue with safer sex messages and practices. Whatever the reasons for these outbreaks, the possibility of a resurgence of the HIV epidemic in the male homosexual popu-

lation should be met with renewed prevention efforts.

CDC HIV Prevention Goals for 2000 to 2005

The CDC has established 3 domestic HIV prevention goals to be met by 2005. The first is to reduce the annual incidence of new HIV infection by 50% from the current level of approximately 40,000 per year. The second is to increase the proportion of infected persons who know of their HIV serologic status to 95% from the current estimated level of 70%; such new technology as rapid HIV tests may help in this regard. Finally, it is hoped that by 2005 the proportion of infected persons who are linked to appropriate health care can be increased to 80% from the current level of 50%. Although these goals may appear modest, their achievement will require a substantial increase in commitment to prevention on the parts of affected communities and their health care providers and both government and nongovernment agencies.

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Suggested Reading

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