**Perspectives**

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


**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 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 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
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% 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 prototype 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 prev-

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**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.

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

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

<table>
<thead>
<tr>
<th>Geographic Area</th>
<th>Metropolitan Area &gt;500,000 Population (%)</th>
<th>Metropolitan Area 50,000-500,000 Population (%)</th>
<th>Nonmetropolitan Area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northeast: n=14,006*</td>
<td>91.1</td>
<td>5.8</td>
<td>3.0</td>
</tr>
<tr>
<td>North Central: n=433*</td>
<td>79.3</td>
<td>11.8</td>
<td>8.7</td>
</tr>
<tr>
<td>South: n=18,770*</td>
<td>71.6</td>
<td>15.0</td>
<td>11.7</td>
</tr>
<tr>
<td>West: n=7887*</td>
<td>90.0</td>
<td>6.2</td>
<td>3.8</td>
</tr>
</tbody>
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*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 population 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.

**Suggested Reading**


