Perspectives on the AIDS Epidemic: The Experience within the United States

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As of 13 June 1988 a cumulative total of 64,896 AIDS cases and 36,480 AIDS-related deaths had been reported to the United States Centers for Disease Control (CDC). Of the 63,880 adults afflicted, 63% were homosexual or bisexual men; 19% were intravenous drug users; 7% were homosexual men who were also I.V. drug users; 4% were heterosexuals; 3% were blood transfusion recipients; 1% were hemophiliacs; and 3% were people for whom risk factor information was incomplete. Of the 1,016 children with AIDS, 77% were born to a parent who had or was at risk for AIDS, 13% were blood transfusion recipients, 6% were hemophiliacs, and 4% were children for whom risk factor information was incomplete. Serologic surveys have provided information regarding the extent of HIV infection in high-risk groups. The number of AIDS cases projected through 1992 using the methods of extrapolation and back-calculation are 310,000 and 380,000 cases, respectively.

S hortly after initial recognition of the acquired immunodeficiency syndrome (AIDS) in the United States in 1981, additional cases were reported from Europe with similar clinical, immunologic, and epidemiologic features. By 1983–1984, it was apparent that AIDS was also present in some areas of Central Africa, the Caribbean, and South America (1, 2). Since then AIDS has become a global pandemic, with 96,433 cases of AIDS from 136 countries being reported officially to the World Health Organization as of June 1988 (Table 1).

Over 70,000 of these cases had been reported from 40 countries of the Americas, over 12,000 cases from 28 European countries, and over 11,500 from 43 African countries. The fact that slightly fewer than 900 cases had been reported from

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Oceania and only 254 cases had been reported from 21 Asian countries makes it appear possible that AIDS was introduced into these areas at a later time. In that case, given the right epidemiologic conditions, these areas could witness the same exponential increases in AIDS cases that other areas experienced during the first five years of the epidemic.

In some areas of the world, such as Africa, the official figures may be gross underestimates of the actual number of AIDS cases, due to inaccurate reporting arising from secondary weaknesses in health infrastructure and from difficulties with the CDC/WHO case definition of AIDS (3) that typically requires sophisticated diagnostic equipment. However, using the limited serologic surveys and selected AIDS surveillance studies available, the World Health Organization estimated in 1988 that there had been over 150,000 cumulative cases of AIDS worldwide, approximately 500,000 cases of individuals with AIDS-related conditions, and five to ten million people asymptomatically infected with the etiologic agent

Table 1. Numbers of countries reporting AIDS cases to the World Health Organization and the numbers of cases reported, by continent.[a,b]

Continent	No. of countries reporting one or more cases	No. of cases
Africa	43	11,530
The Americas	40	71,343
Asia	21	254
Europe	28	12,414
Oceania	4	892
Total	136	96,433

[a] As of June 1988 (World Health Organization, Global Program on AIDS).
[b] See updated case numbers (through 31 January 1989) on pp. 144–145.

of AIDS, the human immunodeficiency virus (HIV) (2). It is from this latter pool of asymptomatically infected individuals that additional cases of AIDS will eventually develop, and from which thousands of additional individuals will be infected with HIV through sexual or parenteral exposure.

Unfortunately, it appears that the vast majority of infected individuals reside in developing countries, where the economic and social impact of this disease will be greatest. Furthermore, in the absence of any curative drug or effective vaccine, it is likely that the AIDS epidemic will continue to spread, killing 80% of the diagnosed AIDS patients within two years of diagnosis and exerting its effects on the people of all countries.

Many issues have been raised concerning the future of the AIDS epidemic. There are uncertainties about how many people within a given population are infected with HIV, how many will progress to symptomatic AIDS, whether drug intervention will delay AIDS fatalities, and whether educational efforts aimed at prevention and control of HIV infection will have a dramatic impact on slowing the spread of HIV and AIDS. There are also questions as to whether the epidemiologic features of HIV witnessed over the past several years will change, and what effect such changes might have on the overall distribution of AIDS cases.

For example, there is some evidence that the HIV epidemic has slowed among homosexual men—due either to saturation of the susceptible population or adherence to preventive measures such as "safe sex" recommendations. Similarly, there is some evidence that HIV infection and AIDS have increased among intravenous drug abusers, raising yet another set of questions regarding heterosexual transmission of HIV to the sexual partners of these individuals, possible increases in the numbers of infected women spreading HIV infection to newborns via perinatal transmission, and eventual establishment of HIV infection as a sexually transmitted disease like syphilis, gonorrhea, or herpesvirus infection—thereby increasing the risk for promiscuous heterosexuals.

All of these issues have generated a great deal of debate and speculation that only time may be able to address. However, given nearly a decade of experience to date with this viral infection, it is possible to examine the available epidemiologic data from some countries with an eye to making some reasonably valid projections of epidemic trends over the next several years. These projections are needed to guide intensive educational and preventive control programs among selected high-risk populations, to plan financial assistance for medical research in some areas, and to conduct health planning designed to meet the AIDS-generated demand for medical care. Within that context, this article reviews the currently available data on HIV infection and AIDS in the United States, and presents some projections of the future of the AIDS epidemic there.

EPIDEMIOLOGIC FEATURES OF AIDS IN THE U.S.

As of 13 June 1988, a cumulative total of 64,896 AIDS cases had been reported to the U.S. Centers for Disease Control (CDC); of those afflicted, 36,480 (56%) had died. Also, 26,200 of these cases had been reported in the preceding 12 months, representing a 71% increase over the previous year. (AIDS ranked eighth among all diseases in 1986 with respect to years of potential life lost before age 65—4).

Most (63,880) of the 64,896 cases occurred among adults, 58,744 (92%) among men and 5,136 (8%) among women (Table 2). Homosexual and bisexual men accounted for 63% of these cases, intravenous drug users for 19%, and homosexual men who were also I.V. drug users for 7%. Three per cent of those afflicted had received blood transfusions contaminated with HIV, and 1% were hemophiliacs who had received infected factor 8 or factor 9 concentrates. Four per cent were heterosexuals who were either in sexual contact with people who had AIDS or were at risk for AIDS, or else were born in countries where heterosexual transmission of HIV is common. The remaining 3% were patients for whom risk factor information was incomplete—because they had died, refused to be interviewed, were lost to follow-up, were still under investigation, were men reported to have had only heterosexual contact with a prostitute, or were interviewed patients for whom no specific risk was identified.

Of the 1,016 children with AIDS, 77% were born to a parent who had AIDS or who was at risk of AIDS; 13% had received infected blood transfusions; and 6% were hemophiliacs who had received infected factor 8 or factor 9 concentrates. The remaining 4% included patients for whom risk information was incomplete.

Sixty-two per cent of the reported adult AIDS cases and 23% of the pediatric cases occurred among whites. Blacks accounted for 25% of the adult cases and 56% of the pediatric cases, while Hispanics accounted for 13% of the adult cases and 20% of the pediatric cases. Since blacks and Hispanics, respectively, ac-

Table 2. Cases of AIDS reported in the United States as of 13 June 1988, listed hierarchically.

| Transmission categories	Males		Females		Total	
Adults:						
Homosexual and bisexual males	40,228	(68%)	0	(0%)	40,228	(63%)
I.V. drug users	9,343	(16%)	2,650	(52%)	11,993	(19%)
Homosexual males and I.V. drug users	4,740	(8%)	0	(0%)	4,740	(7%)
Hemophiliacs	602	(1%)	18	(0%)	620	(1%)
Heterosexuals[a]	1,163	(2%)	1,482	(29%)	2,645	(4%)
Blood transfusion recipients	1,034	(2%)	567	(11%)	1,601	(3%)
Undetermined[a]	1,634	(3%)	419	(8%)	2,053	(3%)
Subtotal	58,744	(100%)	5,136	(100%)	63,880	(100%)
Children:						
Hemophiliacs	55	(10%)	3	(1%)	58	(6%)
Parents with or at risk of AIDS	397	(71%)	385	(84%)	782	(77%)
Blood transfusion recipients	85	(15%)	52	(11%)	137	(13%)
Undetermined[a]	20	(4%)	19	(4%)	39	(4%)
Subtotal	557	(100%)	459	(100%)	1,016	(100%)
Total	59,301		5,595		64,896	

[a]See text for full description.

count for only 11.6% and 6.5% of the U.S. population, the percentages of AIDS cases among them are disproportionately high, particularly for black and Hispanic women and children with AIDS. Overall, the relative risk of AIDS for blacks and Hispanics is two to ten times greater than for whites, suggesting that AIDS is becoming an increasing health problem for minorities—especially among inner-city populations where intravenous drug abuse is common.

In 1986 the U.S. Public Health Service made a tentative projection of the number of AIDS cases that might occur between 1986 and 1991, a projection based on statistical extrapolation of trends and cases reported to the CDC through April 1986 (5). Specifically, it was predicted that a cumulative total of about 270,000 AIDS cases would be diagnosed by the end of 1991 using current surveillance criteria, and that these would have caused approximately 180,000 deaths (Figure 1). The actual number of cases diagnosed us-

ing the foregoing criteria in 1986 and 1987 was 15,900 and 20,600, after adjusting for reporting delays. The total of these figures amounted to 94% of the 15,800 and 23,000 cases that were foreseen by the projection (6). Incomplete reporting, reporting delays, and recent changes in the AIDS case definition all affect the accuracy of these projections, but it is clear that the projections closely approximated the actual number of cases reported through 1987. (Obviously, reporting delays, as well as changes in diagnostic practices and therapeutic regimens, must be carefully evaluated in interpreting future trends of reported AIDS cases.)

HIV INFECTION

While these AIDS case extrapolations are reliable for short-term projections, in seeking to make long-term projections it is important to understand the natural history of HIV infection and both the incidence and prevalence of HIV infection
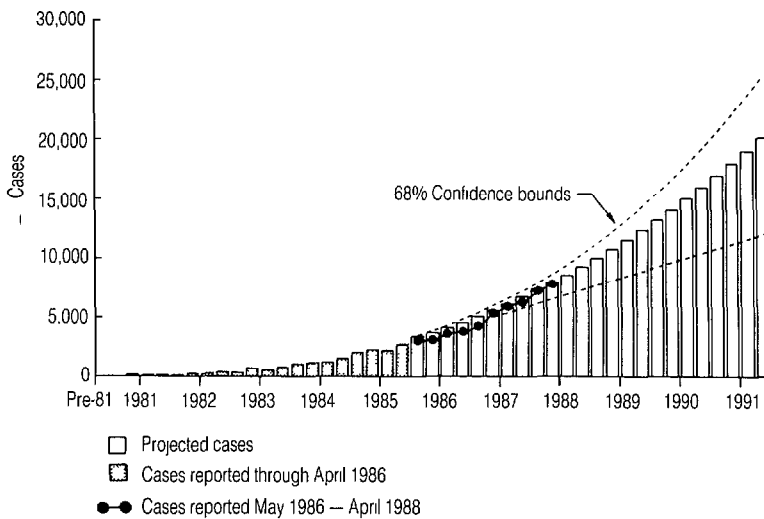
Figure 1. AIDS cases in the United States, showing projections through 1991 calculated from the known cases reported through April 1986 (adapted from ref. 6). Cases reported from May 1986 through April 1988 are shown for comparison.
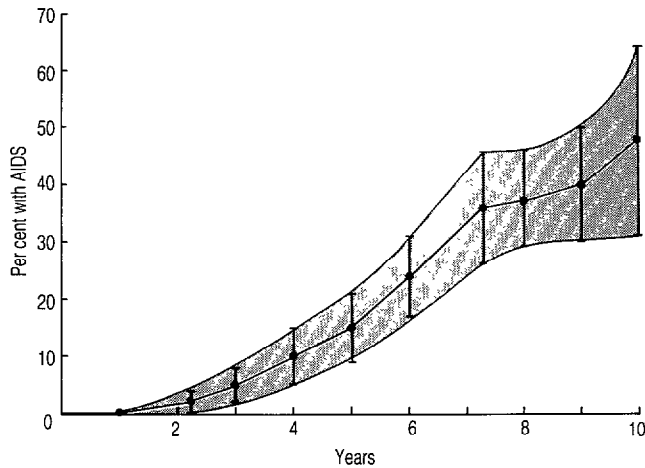
Figure 2. A Kaplan-Meier survival curve showing the proportions of homosexual men developing AIDS by estimated duration of HIV infection in the San Francisco City Cohort Study. The shaded area defines the 95% confidence interval (adapted from ref. 6).

in selected population groups. These statistics are often hard to derive due to the complexities of screening and testing large populations for HIV, as well as the difficulties involved in trying to follow these populations on an annual basis with repeated testing for HIV infection and AIDS case development.

However, properly conducted national seroprevalence surveys followed by seroincidence surveys could provide important information about many features relevant to the AIDS epidemic—including estimates of HIV infection rates and data on the relative importance of various kinds of transmission, types and frequencies of various sexual practices, and effects of various prevention and control efforts. More specifically focused serologic surveys could supplement these national surveys in order to more clearly define the natural history of HIV, the spread of HIV infection, and HIV risk factors in selected high-risk populations.

It is thought that retroviruses generally have long incubation periods between the time of infection and the development of symptoms. In the case of HIV, the mean incubation period following infection from a blood transfusion has been estimated at 8.23 years for adults and 1.97 years for children under five years old (7). Another study (6) has estimated the mean incubation period of AIDS in homosexual men to be 7.8 years.

Perhaps the best cohort study from which incubation times can be extrapolated is the San Francisco City Clinic Cohort Study. This investigation enrolled 6,700 homosexual and bisexual men in studies of hepatitis B virus infection between 1978 and 1980. Since 1983 these men have been followed for the development of AIDS, and sera collected from them as early as 1978 have been analyzed retrospectively for HIV infection (8). It was found that after 88 months of known HIV infection, 36% of the infected study subjects had developed AIDS and over 40% had other signs and symptoms of HIV infection; only 20% remained completely asymptomatic (Figure 2) (6).

It is clearly evident from this and other studies that the risk of disease progression increases with the duration of infection, and that a mean estimated incubation period of eight years is probably conservative, an estimate closer to 10 years being more realistic.

A large number of serologic surveys on selected populations have provided important information about the extent of HIV infection in these high-risk groups, and the CDC has recently reviewed the extent of HIV infection in the U.S. in an effort to estimate the number of infected individuals within the country (9). Many of the studies included in this CDC review differ in their sampling methods, inclusion and exclusion criteria for study subjects, the rigor with which they ascertain risk information, and the resulting bias. Consequently, the results cannot always be validly compared, and significant gaps exist in the information. However, the review did manage to develop a description of the patterns and trends of HIV infection.

For homosexual men, over 50 surveys in 22 cities in 15 states found HIV antibody prevalences ranging from under 10% to 70%, with most prevalence rates being between 20% and 50% (Table 3) (9). The highest prevalences of HIV infection were found in cohorts of homosexual men in San Francisco; otherwise, the prevalences varied geographically, without major peaks in any one region.

The prevalence of HIV antibodies among I.V. drug users varied markedly by geographic region. Overall, 90 studies in 53 cities in 27 states and territories found rates ranging from 50-60% of I.V. drug users in New York City, New Jersey, and Puerto Rico to less than 5% in most areas of the country not on the East Coast. Most data were obtained from surveys at drug abuse treatment facilities that treat mainly heroin addicts. Patients undergoing drug treatment are believed to represent only about 50% of the estimated 1.1 million I.V. drug users in the United States. While some evidence suggests that many of those not in treatment are habitual users who may have an even higher risk of HIV infection, an estimated

Table 3. U.S. Public Health Service estimates of HIV infection in the United States by population group, 1987.

Population	Estimated size of population	Approximate seroprevalence	Estimated total infected
People who are exclusively homosexual	2,500,000	20–25%	500,000–625,000
Others with homosexual contact, including highly infrequent contact	2,500,000–7,500,000	5%	125,000–375,000
Regular I.V. drug users	900,000	25%	225,000
Occasional I.V. drug users	200,000	5%	10,000
People with hemophilia A	12,400	70%	8,700
People with hemophilia B	3,100	35%	1,100
Heterosexuals without specific identified risks	142,000,000	0.021%	30,000
Others (heterosexual partners of people at high risk, heterosexuals born in Haiti and Central Africa, transfusion recipients, etc.)			45,000–127,000[a]
Total			945,000–1,400,000

Source: Centers for Disease Control (9). See text for more details.
[a]Five to ten percent of the total number infected in other groups.

200,000 intermittent users may have a lower prevalence of infection because of less frequent exposure to contaminated needles or equipment.

Regarding the estimated 15,500 persons with hemophilia, approximately 70% of the hemophilia A subjects tested and 35% of the hemophilia B subjects tested were seropositive.

Only a few studies have been performed that deal with people who are heterosexual partners of HIV-infected persons but who have no other identified risk factors for acquiring HIV infection. The prevalences of HIV infection observed among such groups range from under 10% to 60%. These wide ranges may reflect such things as different degrees of infectiousness of the index infected partner, differences in the frequency or type of sexual exposure, the duration of infection in the index partner, coexisting infections such as genital ulcers in one or both partners, or the clinical status of the index partner. Recent evidence suggests that infectiousness increases as the index partner's immune system deteriorates (10), and the relative efficiency of male-to-female versus female-to-male HIV transmission may also be an important factor in heterosexual infection. As yet there is insufficient information to definitively evaluate these differences (11).

Data from seroprevalence studies of the general U.S. population are even more limited, since these studies were only initiated in 1987. However, serologic screening of blood donors, civil applicants for military service, sexually transmitted disease (STD) clinic patients, newborn infants, women of reproductive age, and sentinel hospital patients has been under way for several years.

With respect to the highly selected population of blood donors, the prevalence of HIV infection was found to be 0.02% in 12.6 million American Red Cross blood donations made between April 1985 and May 1987 (9). (The overall level declined from 0.035% in mid-1985 to 0.012% in mid-1987, primarily as a result of eliminating previously identified seropositive people from the donor pool.) The overall prevalence among first-time donors in the period 1985–1987 was 0.043%.

Regarding military recruits, over 0.15% of 1,250,000 military applicants screened between October 1985 and September 1987 were HIV seropositive (12). As in other surveys, HIV seroprevalence varied considerably with the subjects' age, sex, race/ethnicity, and geographic area of residence.

Concerning patients attending STD clinics, review of 23 studies from 16 states indicated that 1,047 (4.6%) of 22,624 clinic attendees were HIV seropositive (9). In general, the seropositivity rate was higher among men (6.6%) than among women (1.6%). Seropositivity rates ranged from 0.5% to 15.2%, reflecting in part the proportion of attendees who were homosexual or bisexual, I.V. drug users, or heterosexual partners of bisexual men or I.V. drug users.

In these studies, nearly 90% of all HIV-seropositive persons belonged to recognized risk groups. Surveys conducted in six cities found the seroprevalence in heterosexual men and women without a history of I.V. drug abuse or known sexual contact with persons at risk to range from 0% to 2.6%, depending upon the population studied and the interview method used (6, 9, 13).

To sample a non-self-selected general population, the CDC developed a network of sentinel hospitals in collaboration with the participating institutions in September 1986. Based on the first 8,668 test results, the overall prevalence of infection was 0.32% (9). Higher rates were documented in selected areas such as

Baltimore, Maryland, where over 5% of the emergency room patients studied were HIV-positive (14).

Another technique for determining levels of infection among sexually active women consists of filter-paper blood testing of newborns to measure maternal antibody passively transferred to the child. One study in Massachusetts found the weighted average prevalence of infection among 30,078 childbearing women to be 0.21% (9, 15), the prevalence varying from 0.09% for women delivering at suburban and rural hospitals to 0.80% for those delivering at inner-city hospitals. Additional information has been provided by 27 studies of women in female health and childbearing settings. Among other things these studies (conducted in 19 cities in 12 states and territories) documented infection in anywhere from 1% to 2.6% of study subjects in the New York City area and Puerto Rico.

Obviously, the epidemic of HIV infection and AIDS cases is a composite of many individual, overlapping, smaller epidemics, each of which has its own dynamics and time frame (6). Whereas the overall incidence of new infection as well as the incidence among certain subgroups such as homosexual men and Red Cross blood donors may have declined slightly, in the absence of specific information incidence rates cannot be assumed to have declined among all subgroups or in all geographic areas. In fact, HIV infection rates among I.V. drug users and heterosexually active people appear to be increasing in localized areas such as inner cities, especially on the East Coast. (Two studies among originally seronegative I.V. drug users in the New York City area showed seroconversion in 3% and 19%, respectively, between 1985 and 1986.)

On the basis of the available data presented in its review, the CDC estimated that the number of HIV-infected Americans ranged from 945,000 to 1,400,000 (Table 3) (6). The major factors limiting the precision of this estimate are the unknown size of the population of homosexual and bisexual men, the unknown distribution by frequency and type of various risk-related practices within this population, and the unknown overall seroprevalence rate among the general heterosexual population without any specific identified risk (a rate estimated at 0.021% based on the rate of infection in military applicants with no identifiable risk factors).

While there is no substitute for carefully obtained HIV antibody incidence and prevalence data, certain inferences can be derived from these past studies.

Table 4. AIDS case projections by year, 1988–1992.[a]

| | Extrapolation method | | |
| | Estimated no. of cases | Interval (68% confidence) | Back-calculation method |
Years			
1981–1987	69,000		66,000
1988	39,000	32,000–41,000	41,000
1989	46,000	32,000–56,000	52,000
1990	60,000	28,000–73,000	63,000
1991	71,000	21,000–94,000	74,000
1992	80,000	13,000–111,900	84,000
Cumulative total	365,000	205,000–440,000	380,000

[a]Data provided by Mead Morgan, Ph.D., at the CDC (personal communication); and Ronald Brookmeyer, Ph.D , at Johns Hopkins University (personal communication).
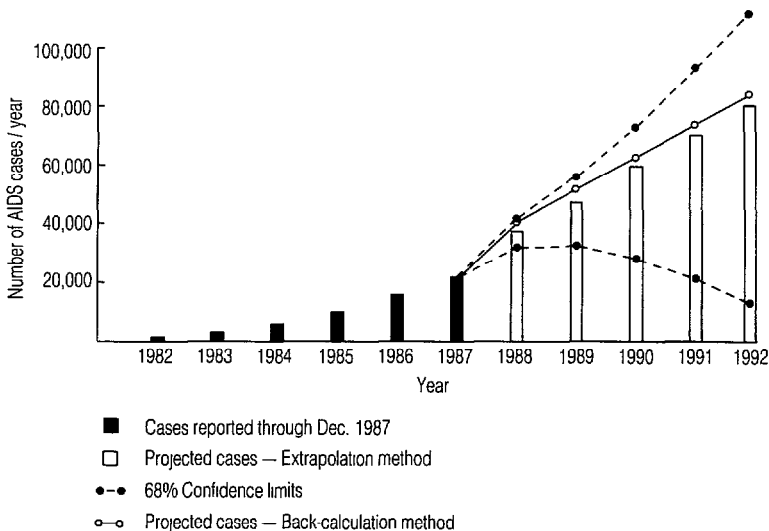
Figure 3. Revised projection of the number of AIDS cases anticipated in the United States through 1992, calculated from the known reported cases through 1987. The two projections shown were obtained using extrapolation and back-calculation (68% confidence limits for the projection based on extrapolation are also shown). The expected numbers of cases predicted by the two methods are remarkably similar.

First, it seems clear that HIV infection is widely prevalent among selected high-risk groups in our society, such as homosexual and bisexual men, intravenous drug abusers, hemophiliacs, and heterosexual partners of these at-risk individuals. Second, while the incidence of HIV infection may be slowing in homosexual men, it is continuing to increase in intravenous drug users and their heterosexual partners. Third, HIV infection rates appear to be increasing among minority populations, particularly in the inner cities along the Eastern Seaboard. Fourth, the natural history of HIV infection suggests that the mean incubation period from the time of infection to the time of developing AIDS is at least eight to ten years.

Together, these facts indicate that the AIDS epidemic has not yet peaked, and that the number of AIDS cases is not likely to decline within the next several years. Rather, it appears that the number of AIDS cases will continue to increase for at least five years and possibly longer. For even if we were 100% successful in preventing further transmission today, the number of AIDS cases would continue to rise on an annual basis because of the large number of people already infected with HIV.

AIDS PROJECTIONS

At a recent meeting of the U.S. Public Health Service, the number of AIDS cases were projected by year for 1988–1992 using two methods. The first method, referred to as the extrapolation approach, statistically fit an empirical model to past trends and projected those trends into the future (5). This approach is reasonable because HIV's long and variable incubation time yields a distribution that will smooth trends and AIDS incidence even though the underlying

trends in HIV infection may be changing. The total number of cumulative cases projected through 1992 using the extrapolation method was 365,000 (Table 4, Figure 3).

A second method, known as back-calculation, estimates future AIDS cases from the historical trends in HIV infection, AIDS incidence data, and knowledge of the incubation time distribution assuming that those infected continue to develop AIDS according to that distribution (16). Although the method as originally proposed does not account for new infections (such as those occurring within two to three years), it gives reasonable near-term projections (two to three years) because of the long incubation time of HIV. (Additional adjustments can also be made to allow for new infections.) Utilizing the back-calculation method with the current estimate of infected people (Table 3), a cumulative total of 380,000 cases was estimated through 1992. It should be noted that the projected numbers of AIDS cases increased annually throughout the time period.

Each of these methods has certain limitations. The extrapolation model is purely empirical and assumes that diagnostic and reporting trends remain unchanged. The model does not depend upon or use quantitative data on the natural history of HIV infection. Despite these limitations, over the past three years the model has performed well in projecting relatively short-term AIDS trends (e.g., the number of future cases arising in two years—Figure 1, 6).

In contrast, the back-calculation method requires accurate information about HIV's incubation time distribution. Additional follow-up of selected cohorts is continually needed to more precisely estimate the shape of this distribution, and additional adjustments are required to account for new infections. While these matters have relatively little impact on short-term projections, they become increasingly important over time irrespective of the model used.

CONCLUSIONS

HIV infection and AIDS have become a major cause of morbidity and mortality in the United States. Since over a million U.S. residents are thought to be infected with HIV, morbidity and mortality can be expected to increase over the next few years, and the number of AIDS cases will continue to rise. While the social and medical impact of this disease will be profound, with medical care alone costing billions of dollars, the greatest tragedy will be the loss of thousands upon thousands of lives.

Although this article concerns itself with the HIV/AIDS problem in the United States, that problem is common to all nations; and it is only through a united international effort that we can hope to control the disease and prevent further transmission. Basic control actions—including professional and public education, risk-behavior reduction in the high-risk groups, and screening of blood supplies—can be implemented, but the obstacles to complete control remain pervasive in our political societies. Further information about the magnitude of HIV infection and HIV incidence rates within many populations, and updating of projections of infection, disease, and mortality by the use of updated mathematical models should help convince political and medical authorities, as well as the general public, about the overall impact of this disease on our society.

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