THE INCIDENCE of human immunodeficiency virus (HIV) in the United States during the 1990s has fallen to levels below the peak of the mid-1980s, but much of this decline reflects trends in white homosexual men older than 30 years. Because high-risk sexual behaviors and drug use are usually initiated in adolescence or young adulthood, the epidemic continues to be propagated in young people.

Until now, trends in the number of young people who become infected remained unknown. Surveillance of HIV incidence based on direct testing for HIV is currently limited to small cohorts at risk. There have been numerous surveys of HIV prevalence in selected populations but the results are difficult to generalize. Prevalence estimates from the National Health and Nutrition Examination Survey (NHANES) III may be relatively representative overall, but that survey excludes persons younger than 18 years and samples too few persons aged 18 to 25 years to provide reliable estimates specifically for this age group.

To assess national HIV incidence trends in young people, we used a statistical method known as back-calculation to estimate the incidence of infection by working backward from acquired immunodeficiency syndrome (AIDS) surveillance data on the basis of the natural history. We used this approach to re-construct the HIV epidemic among successive birth cohorts who have entered adolescence and young adulthood since the onset of the HIV epidemic in 1978. Previous reports that used this technique provided no estimates of trends in HIV incidence since 1987. The estimates of HIV incidence trends derived in this article are, to our knowledge, the most current estimates because they exploit new methods developed by the Centers for Disease Control and Prevention (CDC) to control for the effects of the 1993 revised AIDS surveillance case definition that limited previous analyses. Therefore, we are now able to estimate incidence trends by age, sex, race/ethnicity, and HIV exposure category through 1993. In the present analysis, we estimate HIV incidence and prevalence in 1988 and 1993 in persons aged 20 and 25 years in each of those years and identify the significant changes that have occurred.

**METHODS**

Back-calculation was used to estimate the past incidence of HIV infection that best predicts the observed epidemic of AIDS cases on the basis of the distribution of the incubation period between HIV infection and AIDS diagnosis. Knowledge of the incubation distribution is derived from natural history cohort studies that use the 1987 AIDS surveillance case definition promulgated by the CDC. To ensure consistency between AIDS incidence and the incubation distribution, we define AIDS according to the 1987 definition. All analyses exclude persons infected by perinatal transmission or transfusion of blood or blood products. We assumed that the study population was free of HIV infection before the age of 13 years.

In 1993, the CDC expanded the AIDS surveillance case definition to include HIV-infected persons with severe immunosuppression. To track AIDS using a consistent definition, the CDC has recently developed statistical methods.
to estimate the incidence of AIDS-defining opportunistic illnesses listed in the previous 1987 definition. The method distributes forward in time cases diagnosed solely on the basis of severe immunosuppression according to the likelihood of an AIDS opportunistic illness, accounting for death before the onset of an AIDS opportunistic illness as defined in 1987 (competing mortality) and for delays in the reporting of new AIDS diagnoses.

Using the CDC estimates of 1987-defined AIDS opportunistic illnesses, AIDS epidemic curves were tabulated for January 1982 through December 1995 using all cases reported to the CDC through December 1996. Cases with no identified risk of infection as of December 1996 were redistributed to established categories of HIV transmission according to estimates of the proportions who were eventually reclassified on the basis of more complete information.7 AIDS epidemic curves were truncated after December 1995 because new highly active combination therapies11 may have reduced AIDS incidence and mortality since then12 and available estimates of the incubation distribution might no longer apply. Because the hazard of AIDS is low during the first few years after HIV infection, back-calculation cannot provide reliable estimates of HIV incidence during the recent past. For this reason, the estimated HIV incidence curves are presented only through January 1993.

Subgroups of adolescent and adult cases aged 13 years or older were analyzed according to birth cohort (1960-1964, 1965-1969, and 1970-1974), sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and other), and hierarchical mode of HIV transmission (heterosexual contact, injection drug use, men with homosexual contact who also reported injection drug use, and heterosexual contact). Persons were classified as infected via heterosexual contact if they reported no male-male sex or injection drug use but did report heterosexual contact with a person with AIDS or HIV infection or belonging to an established HIV risk group.

For use in back-calculation models, the distribution of incubation times between HIV infection and 1987-defined AIDS was estimated from follow-up through December 1995 of 481 seroconverters in the Multicenter AIDS Cohort Study (MACS).13 The subjects were homosexual men who became infected between 1984 and 1994 (median year of infection, 1986). In these men, the median age at infection was 33 years and one quarter of the subjects were aged 28 years or younger. As in other natural history studies,14-16 a younger age at HIV infection was associated with slower progression to AIDS. The estimated median time to AIDS was 9.4 years for persons infected at age 25 years. The observed progression rates in this cohort are well characterized by a Weibull distribution with a scale parameter of 0.003 and a shape parameter of 2.448 for persons aged 25 years at seroconversion. Similar to other studies, the hazard of AIDS increased by the factor 1.025 for each 1-year increase in age at infection. It is likely that the hazard of AIDS levels off about 8 years after infection.17 The incubation distribution appears to be similar in men who have sex with men and in men and women infected through injection drug use.16,18 Hence, these age-adjusted estimates of the incubation distribution derived from the MACS were applied to each subgroup of AIDS cases determined from CDC surveillance data.

The HIV incidence curve was modeled as a flexible cubic spline to obtain smooth estimates without making strongly parametric assumptions.19 Variance calculations used a bootstrap procedure to incorporate uncertainty about AIDS hazard rates intrinsic to the MACS seroconverter cohort, as well as random variation of AIDS incidence.20 Injection drug users who are infected with HIV are at high risk of death from causes that are not AIDS-defining, such as suicide, drug overdose, and bacterial endocarditis.21 To avoid underestimating HIV incidence, the back-calculation models for this group incorporated a competing non-AIDS mortality rate of 1.5% per year from the time of HIV infection, a figure consistent with findings from cohorts of HIV-infected injection drug users.21

Prevalence of HIV as of January 1983, January 1988, and January 1993 were estimated for persons aged 18 to 22 years (midpoint, 20 years) in each of those years by summing the monthly incidence of infection through those dates in the successive birth cohorts and subtracting the corresponding number of persons with AIDS who died. The number of deaths among HIV-infected injection drug users was increased to reflect the number expected to die before the onset of an AIDS opportunistic illness. Similar calculations determined the prevalence in persons aged 23 to 27 years (midpoint, 25 years) in 1988 and 1993 in each of those years. All estimates were multiplied by the factor 1.18 to adjust for AIDS cases that never get reported to the CDC.22

Because the number of persons engaging in HIV-transmission risk behaviors is unknown, the number of persons in the general population23 served as the denominator to calculate comparative incidence rates, such as for the incidence of HIV infection attributed to heterosexual contact or injection drug use in men compared with the corresponding incidence in women. Point estimates are provided in the text and 90% confidence limits are provided in the figures.

RESULTS

Among the 38 million persons in the United States born between 1965 and 1974, 42,240 persons had developed AIDS opportunistic illnesses as of January 1996. On a per capita basis for this birth cohort, black men and women had the highest incidence of AIDS, with 124 per 100,000 black men and 60 per 100,000 black women developing AIDS during 1995. Hispanic men and women had AIDS incidence rates of 56 and 20 per 100,000, respectively, and white men and women had AIDS incidence rates of 23 and 5 per 100,000, respectively.

Homosexual contact was the leading HIV exposure category in young white, black, and Hispanic men with AIDS (Figure 1, A-C). In 1995, the incidence of AIDS attributed to homosexual contact was 4-fold higher in black men and 2-fold higher in Hispanic men than in white men. Injection drug use was the next largest exposure category in men with AIDS, followed by heterosexual contact. Heterosexual contact was the leading HIV exposure category in young white, black, and Hispanic women with AIDS (Figure 1, D-F). During 1995 the incidence of AIDS attributed to heterosexual contact was 36 per 100,000 in black women, 12 per 100,000 in Hispanic women, and 3 per 100,000 in white women.

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Estimates of HIV incidence are derived from trends in AIDS cases. Compared with men born between 1960 and 1964, HIV incidence attributed to homosexual contact in the younger cohorts was substantially higher during the teenage years but declined to lower levels as these men entered young adulthood (Figure 2). This pattern was observed in white, black, and Hispanic men. Similarly, HIV incidence was statistically significantly lower in 1993 than in 1988. In white men aged 20 years, the rate fell from about 56 to 24 per 100,000, a reduction of 57%. Statistically significant declines were also apparent in black and Hispanic men. Similarly, HIV incidence was lower among men aged 25 years in 1993 than in 1988. Among white men aged 25 years, about 110 per 100,000 became infected via homosexual contact in 1988, compared with 27 per 100,000 in 1993, a reduction of 75%. A similar decline over time was observed in successive birth cohorts of young white, black, and Hispanic men and women infected via injection drug use (Figure 3, A-F). For example, in men
aged 20 years in 1988, HIV incidence attributed to injection drug use was about 7, 55, and 68 per 100,000 white, black, and Hispanic men, respectively. Corresponding rates in 1993 were about 3, 33, and 35 per 100,000, respectively, a reduction of about 50%.

In contrast, HIV incidence attributed to heterosexual contact was stable or increasing in the successive birth cohorts (Figure 4). Comparing the consecutive birth cohorts during their teenage years, there was a striking increase in HIV incidence attributed to heterosexual contact, especially in women (Figure 4).
Black women had the highest incidence of infection attributed to heterosexual contact. In 1993, about 1 in 1000 black women aged 20 years became infected via heterosexual contact, compared with 1 in 2800 Hispanic women and 1 in 15,000 white women.

Incidence of HIV was higher in young minority men than in white men from each route of transmission, including homosexual contact. Incidence of HIV was also higher in young minority women than in white women, both from injection drug use and from heterosexual contact.

During 1992, about 22,000 men and women born between 1965 and 1974 became infected with HIV. Of them, about 43% were homosexual men, 20% were injection drug users, and 34% were infected through heterosexual contact. Seventy-three percent were black or Hispanic persons and 28% were women.

Estimates of HIV prevalence are determined from cumulative HIV incidence minus deaths. Despite the declines in HIV incidence in young homosexual men and injection drug users, about 150,000 persons born between 1965 and 1974 were living with HIV as of January 1993, and, assuming that the incidence did not change from 1992, about 200,000 persons were living with HIV as of January 1996.

Prevalence of HIV as of January 1983, January 1988, and January 1993 is described in Figure 2. In men aged 18 to 22 years, HIV prevalence doubled between 1983 and 1988, from 14,900 to 30,300, but decreased by 27% between 1988 and 1993, to 22,100. The reduction in prevalence in young white men contributed most to this decline. Prevalence of HIV declined only slightly in black and Hispanic men. In contrast, in women aged 18 to 22 years, HIV prevalence increased by 36% between 1988 and 1993, from 8100 to 11,000, entirely because of the increasing heterosexual transmission to young women. Trends in HIV prevalence in persons aged 23 to 27 years were similar (Table 2). The prevalence of HIV decreased by 45% in white men, increased slightly in black men and decreased slightly in Hispanic men, and increased by 45% in women because of increasing heterosexual transmission. Overall, in men and women combined, prevalence in persons aged 18 to 22 years and 23 to 27 years (inclusive of persons aged 20 and 25 years) declined by 13.8% and 14.2%, respectively, between 1988 and 1993.

COMMENT

We have estimated HIV incidence in successive birth cohorts of persons who became adults since the onset of the HIV epidemic in 1978. The cohort born between 1960 and 1964 served as our comparison group. Persons in this cohort became 18 years old between 1978 and 1982, the period when the HIV epidemic was just starting but the virus was spreading rapidly. Few were infected before the age of 18 years but many became infected in their 20s. The younger cohorts (born between 1965 and 1969, and 1970 and 1974) became 18 years old between 1983 and 1987, and 1988 and 1992, respectively. For these cohorts, the pattern of HIV incidence reflects a balance between opposing factors. The increasing HIV prevalence meant that each risk-taking act conveyed a higher likelihood of exposure, while growing HIV awareness caused behaviors to change to reduce exposure.

We found 2 major trends in HIV incidence in young persons. First, compared with the cohort born between 1960 and 1964, younger cohorts more frequently became infected as teenagers. Incidence of HIV was higher in these younger cohorts of teenagers regardless of sex, race/ethnicity, or exposure group, an unfortunate consequence of engaging in risk behaviors at a time of high HIV prevalence. Second, in young adults aged 20 and 25 years, HIV incidence attributed to homosexual contact and injection drug use was lower in 1993 than in 1988, but the incidence attributed to heterosexual contact was stable or increasing.

Prevalence reflects both new infections and the number living with HIV. In young black and Hispanic men, the incidence in teenagers and heterosexual men offset reductions in incidence in homosexual men and injection drug users in their 20s. Consequently, prevalence was relatively stable between 1988 and

Figure 3.—Age-specific human immunodeficiency virus (HIV) incidence in the United States attributed to injection drug use, by sex and race/ethnicity, in persons born between 1960 and 1964, 1965 and 1969, and 1970 and 1974, as estimated by back-calculation. Incidence scale for white men and women (A, B) is one fifth that for black and Hispanic men and women (C-F). See Figure 2 legend for further information regarding interpretation of these data.
In 1993 in minority men aged 20 and 25 years. In contrast, declines in HIV incidence in young white men were so profound that HIV prevalence in this group declined by about 50% between 1988 and 1993, in both persons aged 20 years and persons aged 25 years. Occurring at a time of high overall HIV prevalence, this decline marks a notable prevention success. Unfortunately, HIV prevalence in women aged 20 and 25 years increased between 1988 and 1993, entirely because of increasing heterosexual transmission to women. Heterosexual transmission was the leading route of infection in young women.

During 1992, about 22,000 persons born between 1965 and 1974 became infected with HIV. We estimate that about 43% were men infected via homosexual contact vs about half of the entire population living with HIV at that time. We also found that a higher proportion of HIV-infected young people had acquired the infection heterosexually than in the entire HIV-infected population, about 1 in 3 young people vs about 1 in 7 in the entire population. Furthermore, about two thirds were black or Hispanic, although these minority groups constitute only 27% of the US population born during those years.

Previous studies based on back-calculation estimated the average incidence of infection between 1987 and 1992 and provided no information about trends during this period. The current study was able to identify these trends because of the use of more recent AIDS surveillance data. However, 3 potential biases may have affected our results. First, ascertainment of mode of HIV transmission is subject to misclassification of unknown extent. In particular, heterosexual transmission may have become increasingly recognized over time. If so, our estimates of HIV incidence attributed to heterosexual contact may be too high. Second, CDC data for 1987-defined AIDS opportunistic illnesses are estimates and may be imprecise. Third, natural history could vary across risk groups or in adolescents and young adults. If AIDS progression rates are faster than we estimated, back-calculated HIV incidence will be too high.
Table 2.—Trends in HIV Prevalence in the United States in Persons Aged 23 to 27 Years*

<table>
<thead>
<tr>
<th>Race/ethnicity</th>
<th>No. of Men</th>
<th>No. of Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>61 100</td>
<td>33 700</td>
</tr>
<tr>
<td>Black</td>
<td>32 000</td>
<td>33 500</td>
</tr>
<tr>
<td>Hispanic</td>
<td>21 300</td>
<td>19 400</td>
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</table>

<table>
<thead>
<tr>
<th>Mode of HIV transmission</th>
<th>Homosexual contact</th>
<th>Injection drug use</th>
<th>Homosexual contact and Injection drug use</th>
<th>Heterosexual contact</th>
</tr>
</thead>
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<tr>
<td></td>
<td>77 500</td>
<td>19 600</td>
<td>13 300</td>
<td>2800</td>
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<tr>
<td></td>
<td>(3770)</td>
<td>(1040)</td>
<td>(7500)</td>
<td>(200)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mode of HIV transmission</th>
<th>Injection drug use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>86 500</td>
</tr>
<tr>
<td></td>
<td>(2630)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mode of HIV transmission</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>116 200</td>
</tr>
<tr>
<td></td>
<td>(4080)</td>
</tr>
</tbody>
</table>

*Data are expressed as mean (SD). HIV indicates human immunodeficiency virus.

Totals are adjusted for other race classifications and for persons with identified mode of HIV transmission.

Uncertainty about the effects of pre-1996 therapy on time to AIDS probably had only a minor impact on our analyses for 3 reasons. First, changes in the incubation period have been subtle and hard to detect in natural history cohort studies. The benefits of zidovudine mono-therapy are greatest in persons with AIDS or with severe immunosuppression, and prophylaxis against Pneumocystis carinii pneumonia does not prevent other AIDS-defining opportunistic illnesses from occurring. Second, our natural history estimates derived from MACS seroconverters. This cohort has therapy effects incorporated into the incubation distribution because these men have had good access to treatment from early in the course of infection. Third, the younger cohorts we studied could not have had HIV infection for many years and their experience is determined by AIDS events occurring within the first decade after infection. This part of the natural history curve is well estimated from the MACS and probably has been less affected by therapy.

The main limitation of our study is that back-calculation cannot identify HIV incidence trends during the most recent several years. Prevalence of HIV in young people could be lower or higher today than in 1990. Favoring a lower prevalence, HIV incidence was slowing by 1995 in young cohorts of homosexual men and injection drug users; it is hoped that this trend has continued. Furthermore, new combination therapies that lower the viral level may reduce the infectiousness of treated persons who expose others. Prevention can be strikingly effective in young persons, as demonstrated by the marked decline in HIV prevalence in young white men. However, complacency about exposure risks could have led to a resurgence of the epidemic since 1993. Despite some prevention successes, the rate of heterosexual transmission in young minority persons is a particular cause for concern. To guide current prevention efforts and to help plan future vaccine trials, we urgently need new studies that provide consistently obtained, up-to-date data on HIV incidence, prevalence, and risk behaviors, especially among youth.

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References