

Heterogeneity and Public Health in the Global HIV/AIDS Epidemic

At the opening session of the 2001 Conference on Retroviruses and Opportunistic Infections in February, Kevin M. De Cock, MD, reviewed global HIV/AIDS epidemiology, focusing on disease in Africa and response to the African epidemic from a public health perspective.

It is estimated that 36.1 million people were living with HIV/AIDS and that 21.8 million people had died with HIV disease by the end of 2000. In 2000, there were an estimated 5.3 million new HIV infections and 3 million AIDS deaths. The most important events in the second decade of the epidemic have been the introduction of new antiretroviral regimens, the advent of effective interventions to prevent mother-to-child transmission of HIV, and prolongation of healthy life in infected people in industrialized countries.

Trends in the United States

In the United States, abrupt declines in AIDS incidence and mortality began in 1996, with the introduction of potent antiretroviral regimens. However, incidence and mortality rates have stabilized since 1998. The range of AIDS rates per 100,000 population by state is wide, the rate in New York in 2000 being approximately 66 times that in North Dakota. Current major trends in disease include an increasing proportion of AIDS cases in women, now accounting for 24% of cases; a decreasing proportion of cases attributable to men having sex with men, now accounting for 40% of cases; and an increasing proportion attributable to heterosexual contact, now accounting for 25% of cases. Non-Hispanic blacks accounted for 48% of AIDS cases reported in 1999, and 54% of recently reported cases of HIV infection.

Potential causes of the stabilization of AIDS rates include reaching the limits to which therapy can extend survival, drug

resistance, treatment adherence failure, late HIV testing, lack of access to care, and increased HIV infection incidence. The Centers for Disease Control and Prevention estimates that up to one third of the approximately 900,000 people living with HIV infection in the United States do not know of their infection status. Data from several sources indicate that the national incidence of HIV infection has remained stable at approximately 40,000 new infections per year since the early

Science should determine public health policy. The scientific and philosophic underpinnings of public health are epidemiology and social justice; and surveillance is both the witness and judge in any epidemic. The Institute of Medicine defines public health as what we, as a society, do collectively to assure the conditions for people to be healthy. Social justice can be taken to mean the fair distribution to people of society's benefits and burdens and their consequences.—From Dr De Cock's prefatory remarks.

1990s. Approximately 70% of incident infections are in men, and more than half of all new infections are in African Americans. Men who have sex with men have the highest incidence rates, with most studies indicating a rate of approximately 2 per 100 person-years. Com-

pounding the failure to reduce the national incidence of HIV infection are increasing reports of unsafe behavior among men who have sex with men, including increased incidence of rectal gonorrhea, increased anal intercourse, and decreased condom use in San Francisco; and syphilis outbreaks in King County, Washington and elsewhere. Reports of increased risk behavior among men who have sex with men have also come from Canada, London, and Amsterdam.

Trends Elsewhere

In Latin America, HIV transmission among men who have sex with men and from injection drug use account for most AIDS cases, but heterosexual transmission of HIV is increasing, with a corresponding increase in proportions of infections in women. HIV epidemiology in the Caribbean is reminiscent of that in Africa, although currently the highest HIV-seroprevalence rate in the region, in Haiti, is considerably less than 10%.

The highest AIDS incidence in western Europe in 1999 was in Portugal, with the rate of 10 per 100,000 population being approximately 40% of that in the United States (Figure 1). In this region, the proportion of cases acquired heterosexually is now 31%, approaching the proportion

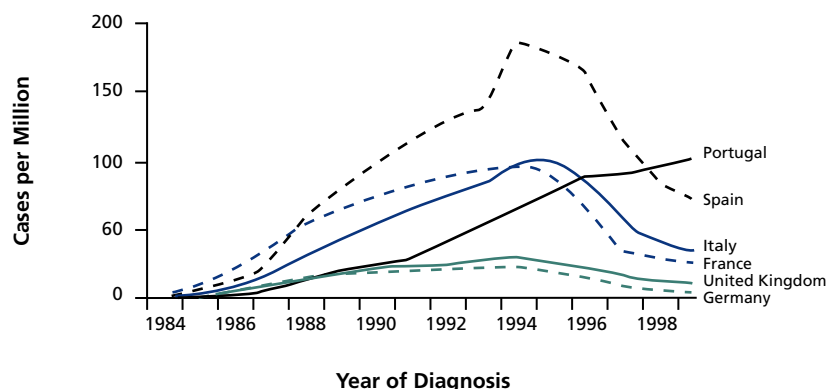


Figure 1. AIDS cases per million population in selected countries in western Europe, 1984 to 1999. Data are those reported by June 30, 2000, and are adjusted for reporting delays.

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attributed to injection drug use. Cases of perinatal infection have declined in most countries. Available data suggest that HIV incidence has stabilized in western Europe since the early 1990s, as in the United States. Large proportions of heterosexually acquired HIV infections in western European countries are in persons born in other countries where heterosexual transmission predominates, primarily African countries (Figure 2).

Rates of HIV infection have remained relatively low in much of central Europe. Rates have declined in Romania since the widespread infection of children with infected blood products in the early 1990s. HIV has spread explosively in many areas of eastern Europe since the mid-1990s. Reports of HIV infection in the Russian Federation increased by 410% between 1998 and 1999, and increases have also occurred in Latvia and Ukraine. Currently, most infections in this region are associated with injection drug use, ongoing epidemic syphilis, and increased commercial sex activity. Erosion of health infrastructure makes future trends in HIV infection unpredictable in this region of the world.

The spread of HIV/AIDS in Southeast Asia has been greatest in Cambodia, Thailand, and Myanmar (Figure 3), with the epidemic being driven by injection drug use and commercial sex. Infection rates remain relatively low in such countries as Japan, Indonesia, and the Philippines. An estimated 4 million people in India are HIV-infected, with a seroprevalence of 2% to 4% among pregnant women in Mumbai and Pune in the west contrasting with a seroprevalence of less than 1% in Calcutta and Delhi. Injection drug use drives the epidemic in the northeastern states near

Myanmar, where seroprevalence among drug users is more than 70%. Seroprevalence rates among injection drug users in Yunan Province in China increased to 70% or greater in the early 1990s, with the first appearance of HIV infection in sex workers in China occurring in this region. Yunan Province likely accounts for half of the estimated 500,000 to 1 million individuals with HIV infection in China.

Trends in Africa

Sub-Saharan Africa, with a population of approximately 600 million and 10% of the global population, accounted for 72% (3.8 million) of incident HIV infections and 80% (2.4 million) of AIDS deaths in 2000, and accounts for 70% (25.3 million) of the estimated total of HIV-infected people worldwide. Seroprevalence rates in pregnant women now exceed 40% in some areas of Zimbabwe and Botswana. Reductions in seroprevalence rates in pregnant women have been observed in some settings in Uganda and Zambia, possibly due to behavior changes, but trends in these areas are uncertain. In eastern and southern Africa, crude death rates are now 50% to 500% higher than expected, with increased mortality most evident in young adults and children under 5 years of age. Currently, 30% to 50% of Africans dying with AIDS have tuberculosis, with rates of this disease having doubled or tripled in many countries. The lifetime risk of dying with HIV disease now exceeds 60% for adolescents in southern African countries. Life expectancy will decrease by more than 30 years in some areas. By the end of 1999, more than 12 million African children had

lost their mother or both parents to AIDS, and there are now at least twice as many AIDS orphans in Africa as there are refugees and displaced persons (Table 1); perhaps no other aspect of HIV/AIDS has greater implications for social stability and security in Africa, yet there has been no organized international response to this crisis to date.

Epidemiologic Patterns

Current epidemiology indicates that, although vigilance regarding the spread of HIV is required everywhere, Africa is a world apart concerning HIV/AIDS. Only Africa is marked by high-prevalence, generalized population epidemics with equal or more women affected than men. With the exception of the lower-prevalence epidemic in the Caribbean, epidemics in other regions of the world are concentrated around specific risk groups, consisting of injection drug users, providers and consumers of commercial sex, and men who have sex with men.

Epidemiologic Heterogeneity: Why is Africa So Disproportionately Affected?

The global diversity of the HIV epidemic must be explicable through one of two models. Qualitatively, the epidemiology of any infectious disease reflects interactions among the agent, host, and environment. Numerically, epidemic growth depends on the basic reproductive rate, the number of secondary infections generated on average by 1 primary case. For a sexually transmitted infection, the basic reproductive rate depends on the rate of partner change, the transmissibility of the agent, and the duration of infectiousness. The effects of these parameters on transmission, however, are not linear and people with frequent partner change have a disproportionate impact on the spread of HIV.

With regard to the agent, HIV-2 illustrates the impact of inherently lower transmissibility compared with that of HIV-1, which probably explains why we face a pandemic of HIV-1 but not HIV-2 infection. HIV-1 is classified into 3 major subgroups, M, N, and O, with M being the pandemic form. In addition to 9 basic subtypes, other sub-subtypes and recombinant forms have been identified. The dominant global subtypes are: A, mainly in Africa; C, found in southern Africa and parts of India; and B, in Europe and the Americas; as well as the

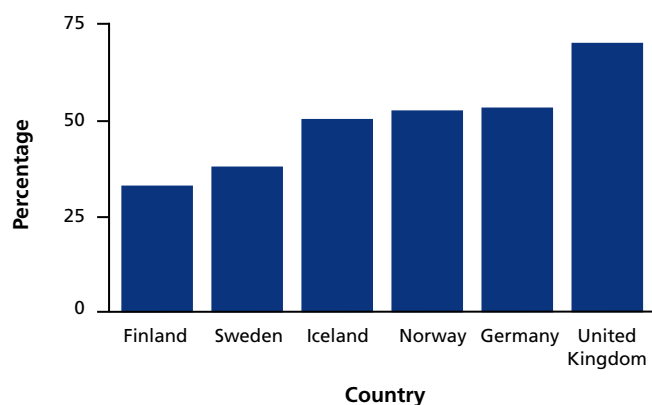


Figure 2. Percentage of cases of new heterosexually transmitted HIV infections in western Europe reported between 1997 and mid-2000 that originated in a country with a generalized epidemic, in most cases an African country.

recombinants A/E found in Asia and A/G found largely in West Africa. Indicative of the ancestry of HIV-1, all subtypes are found in Africa, with an astonishing diversity of subtypes in Central Africa, especially the Democratic Republic of the Congo. Biologic attributes of subtype C have been postulated to confer increased efficiency of transmission and replication, but epidemiologic proof of such effects is lacking. In summary, there is no firm evidence of biologic or virologic reasons for Africa's severe HIV/AIDS epidemic.

With regard to host factors, the presence of other sexually transmitted diseases and increased viral load in genital fluids and blood are associated with increased transmission; other data indicate that male circumcision is associated with a protective effect in acquisition of infection. One multicenter study compared low- and high-prevalence cities in east and west Africa, and concluded that prevalence differences are associated with transmission efficiency rather than behavior; key risk factors were lack of male circumcision and the presence of genital herpes. However, such conclusions need to be tempered by the awareness that it is difficult for epidemiology to capture certain factors relevant to disease transmission, including qualitative differences between groups. Types of sexual partners may be more important than absolute number of partners and mixing patterns (assortative vs nonassortative) may be important determinants of the spread of disease, with nonassortative mixing resulting in more efficient spread. There is also difficulty in assessing the effects of low-potency risk factors that are widely distributed

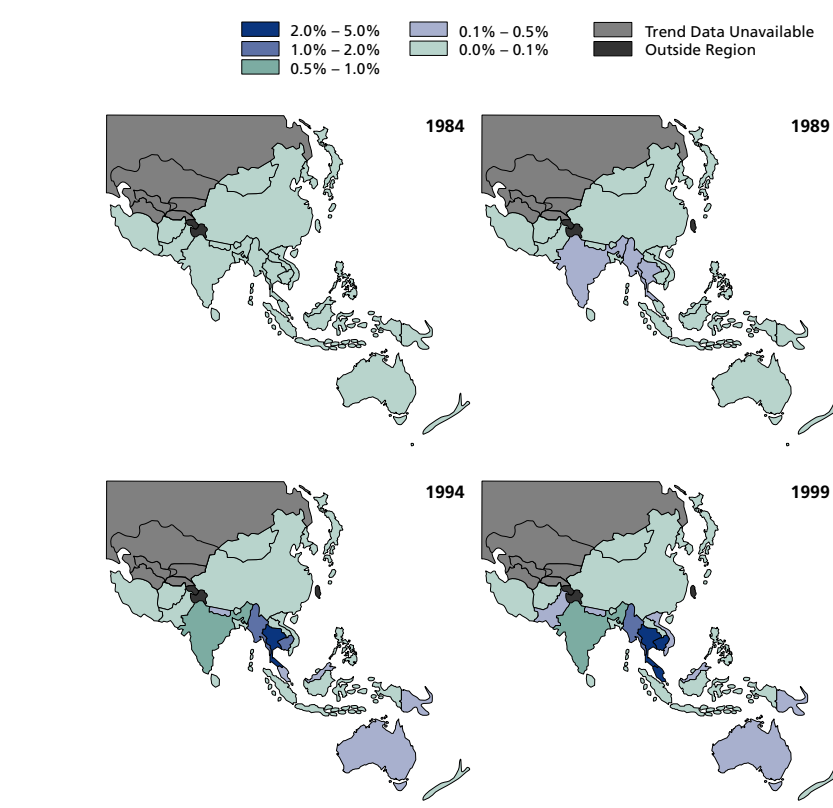


Figure 3. Spread of HIV over time in Asia, 1984 to 1999. Adapted from UNAIDS, June 2000. Available at: http://www.unaids.org/epidemic_update/report/index.html.

and thus may have important public health impact, and how risk factors can interact in a multiplicative rather than additive fashion, enhancing each others' impact.

Finally, effects of population level characteristics and norms are also difficult to assess. Although effects of individual risk

factors can be quantified, it is more difficult to determine population-attributable risks—for example, the proportion of people in a given population with levels of viral load likely to result in transmission. Early in an epidemic, many infected persons may have elevated viral loads in association with seroconversion; this could result in a wave of a new subtype washing over a population, falsely suggesting virus-specific enhanced transmissibility. It is possible (though unproven) that in a mature epidemic, enhancement of viral replication by intercurrent illnesses, such as malaria or tuberculosis, could result in a population with an increased prevalence of higher viral loads, thus creating an environment conducive to increased transmission efficiency. If added to this scenario are social risk factors such as poverty, conflict, and migration, which predispose to partner change and sexual disease transmission, then a high-risk environment can be envisaged in which a single act of unprotected sex carries risk of transmission substantially higher than that elsewhere, without implying major differences in the biology of the agent or in the behavior of most individuals.

Table 1. Estimated Cumulative Number of Children Orphaned by AIDS at Age 14 or Younger, End of 1999

Region	Estimated Cumulative Number
Sub-Saharan Africa	12,100,000
South and Southeast Asia	850,000
Latin America	110,000
Caribbean	85,000
North America	70,000
North Africa and Middle East	15,000
Western Europe	9000
East Asia and Pacific	5600
East Europe and Central Asia	500
Australia and New Zealand	<500

Adapted from UNAIDS, June 2000. Available at: <http://www.unaids.org/publications/graphics/index.html>.

Response to the Epidemic

Efforts to strengthen human rights in Africa and to combat stigma and discrimination against people with HIV infection need to be supported, but for successful efforts against the epidemic, the philosophic stance that pits human rights against public health needs to be abandoned. The response to the HIV epidemic in Africa is inadequate in character and intensity. The epidemic is unfolding imbedded in and inseparable from the context of collapsing public health and other social infrastructures; many of the public health issues surrounding the epidemic would need to be confronted even if an effective vaccine were available today.

Epidemiology is unforgiving, even in industrialized countries. In the United States, resurgence of unsafe behaviors, the absence of a reduction in HIV infection incidence, and the flattening of the decline in AIDS cases emphasize the need for improved surveillance to understand trends in the epidemic. The current uncertainty regarding HIV trends in high-transmission areas in the United States is unnecessary. Yet, support for HIV surveillance, including financial support, is weak.

The CDC recommended in 1999 that HIV reporting be conducted by name, allowing integrated tracking of HIV diagnoses, AIDS, and AIDS deaths across the population, and permitting linkage of infected mothers and their exposed infants for evaluation of programs that could eliminate mother-child transmission. In addition, studies on behavior and disease morbidity, seroprevalence and seroincidence surveys in particular groups, and drug resistance and toxicity monitoring are needed.

Focusing efforts to prevent sexual and drug injection-associated transmission on HIV-infected persons is made easier in industrialized countries by the availability of effective antiretroviral therapy. Overall, greatly increasing voluntary testing to diagnose all infected persons, treating all infected persons medically according to guidelines, focusing prevention efforts on and around those with HIV infection, and implementing effective surveillance may constitute the most effective approach to HIV/AIDS prevention in industrialized countries today. Such an approach would also address the unacceptably large proportion of persons unaware of their serostatus, who may transmit HIV unknowingly and who are not benefiting from care; for more than 40% of persons with AIDS in

the United States, preventable illness was the first indication of HIV infection.

AIDS exceptionalism, the practice of confronting the HIV/AIDS epidemic in ways different from how other lethal or sexually transmitted infections are confronted, contributes to suboptimal response to the epidemic in this country and internationally. The fundamental question regarding HIV/AIDS in Africa is whether the epidemic will simply run its course or public health and biomedical interventions are capable of interrupting transmission and alleviating disease. If the answer is to be the latter, public health, social justice,

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and medical ethics offer a better preventive framework than does AIDS exceptionalism. As stated by New York State's Commissioner of Health, Herman Biggs, in 1913: "Public health is purchasable. . . . A community can determine its own death rate. . . . No duty of society . . . is paramount to this obligation to attack the removable causes of disease."

In much of Africa, the public health infrastructure has eroded and what is taken for granted elsewhere, such as blood supply safety, cannot be assumed. In the mid-1990s, a survey of donations in 6 hospitals in 1 country showed that, with seroprevalence among donors ranging from 2% to 20%, only 72% of seropositive units were correctly identified, with 17% being misdiagnosed and 10% not being recorded; 2% of apparently screened transfusions may have transmitted HIV.

In rural western Kenya, deaths in children under 5 years of age have increased 2- to 3-fold since the 1980s, with 1 in 4 children now dying before age 5. With the adult HIV prevalence of approximately 25%, it is likely that at least one third of the

pediatric mortality is HIV-related, but these appalling mortality rates also reflect high-level, stable malaria and its ineffective treatment due to chloroquine resistance; an overall decline in vaccination rates to only 50%; diarrheal diseases and malnutrition; and an eroding health care system. In such a context, measurable benefit from perinatal HIV prevention may not be achieved unless we simultaneously address traditional health problems that aggressively compete for mortality.

Public health measures that must be put into place in Africa include HIV testing. There is an unmet demand for voluntary counseling and testing for people who are well, as a prevention service and to help people facing life decisions. When services are convenient and inspire confidence, demand and uptake are greater than usually anticipated. Voluntary testing and counseling aims to keep those who are HIV-seronegative uninfected and to link those who are infected with prevention, care, and support services. The availability of rapid tests using whole blood should increase access to and uptake of testing. Seronegative persons in HIV-discordant relationships, who have been shown to have an infection incidence of 12 per 100 person-years in one study in Uganda, may constitute the largest vulnerable group on the continent. Keeping such persons uninfected is a priority for prevention of orphanhood.

In the setting of medical care, routine, universal, confidential testing offers the best chance for rational medicine, whatever the resources available for treatment. Due to emphasis on pretest counseling and anonymity as well as lack of organized and systemic AIDS care in health care settings, untested HIV-infected patients fill hospital wards and tuberculosis clinics without their underlying condition being formally diagnosed or communicated to them. Some HIV-seronegative patients are misdiagnosed with AIDS on clinical grounds and abandoned.

A maternity hospital in Nairobi, the largest in Africa, performs almost 25,000 deliveries per year, approximately 4000 involving HIV-infected women. The women receive antenatal care in clinics outside the hospital that do not test for HIV; even if they did, tracking and transmittal of laboratory results would not be feasible. The pragmatic solution in this case would be routine, universal, rapid testing in labor, with provision of nevirapine to HIV-seropositive mothers and their infants. However, such a practice is controversial,

and currently no services are provided; the result is that approximately 1000 perinatal infections occur annually in this single hospital, a number several times greater than the annual number of perinatal infections in the entire United States.

In an ambitious perinatal program in Botswana, fewer than 10% of HIV-infected mothers receive zidovudine because of low voluntary test uptake. Short-term zidovudine treatment has an efficacy rate considerably less than 50%, and such programs will have little or no impact on pediatric HIV infection without universal testing of pregnant women.

More widespread testing is needed to allow such relatively inexpensive therapies as prophylaxis with isoniazid and cotrimoxazole to be provided, with the spectrum of disease in Africa being such that considerable benefit would be derived from their use. As it stands, few people in the health care setting are tested, target populations are difficult to identify, and service delivery is challenging. The same constraints would apply to use of antiretroviral drugs even if they were provided free of charge, quite apart from the challenges inherent in managing long-term therapy (adherence, toxicity, drug resistance) and countering the potential weakening of prevention practices that attends availability of treatment.

On the other hand, antiretroviral drugs are sold in every major city in Africa, and

pilot programs in Uganda and Côte d'Ivoire have shown that they can be used safely. It is inevitable that as benefits of treatment in rich, low-prevalence northern areas become ever more evident, the loud-

From Dr De Cock's closing remarks: In closing, I ask myself what we as a society would do to assure conditions for people to be healthy if the United States faced African HIV prevalence. Have underfunding, AIDS exceptionalism, and the 'individual rights' approach to the US epidemic unwittingly reinforced a deep cultural reluctance in Africa to deal with the taboos of sex and death, and promoted, rather than prevented, silence, stigma, and HIV transmission? Are we accepting this African holocaust in a way we never would if it were here? If so, then at some time, epidemiology will be heard and we will have to account for public health passivity in what is unquestionably Africa's greatest catastrophe since slavery. . . . For those to whom Africa may seem far away and who may legitimately wonder 'am I my brother's keeper?' I think we should acknowledge debts to the continent for all it has taught us about HIV/AIDS, and remember the African proverb: 'I am because of what I see of me in your face; I am because you are.'

er will be the call for access to antiretrovirals in the poor, high-prevalence south. International donors and technical agencies will face critical questions regarding drug implementation and the structures

needed to support it: will they be willing to initiate necessary programs and to build and maintain necessary infrastructure? Operational research questions abound with the inevitability of drug access and demand for treatment: When to start? What to start with? When to switch and what to switch to? What is minimum safe monitoring? What populations should be targeted? How can adherence be promoted? What opportunistic infection prophylaxis is to be used? Outside of the private practice setting, treatment approaches will have to be standardized, simple, generalizable, confidential, but not anonymous, and treatment will probably have to be delivered by dedicated clinics. If the international experience with programs for tuberculosis is to serve as a historical analogy, it is clear that the road ahead is a difficult one.

Presented in February 2001; reviewed and updated by Dr De Cock in June 2001.

Grant Support and Financial Disclosure: Dr De Cock has no affiliations with commercial organizations that may have interests related to the content of this article.