

A REVIEW OF HIV-1 IN AFRICA*

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HISTORICAL PERSPECTIVES

THE exact geographic origins of the human immunodeficiency virus type 1 (HIV-1) are unknown. The acquired immunodeficiency syndrome (AIDS) is a sufficiently dramatic disease that it is unlikely to have occurred with any frequency anywhere in the world and not been recognized. A retrospective serologic search for antibodies to the virus in repeatedly frozen and thawed stored sera produced nonspecific reactions initially interpreted as probable serologic evidence for widespread disease among African populations during the early 1970s.^{1,2} More recent seroepidemiology from healthy individuals collected before 1975 do not substantiate the prevalence of this virus anywhere in Africa until recently.³

At present, the earliest serum with antibodies to HIV-1 confirmed in several laboratories by several methods was collected in Zaire in 1959.⁴ The earliest viral isolate was obtained from a serum sample collected in Northern Zaire in 1976.⁵ Other serologic studies suggest that HIV-1 was endemic in some regions of Zaire during the 1970s.⁶ At this same time, some individuals following blood transfusion or heterosexual contact in Zaire became ill with what, in retrospect, was AIDS.^{7,8}

Epidemiologic features of AIDS in Central Africa have markedly differed from those occurring in Western countries.^{9,10} Early clusters of AIDS cases were linked by heterosexual contact, and the incidence of AIDS is similar in both men and women.¹⁰ Multiple heterosexual partners was the only major

*Presented as part of the Fifth Annual SK & F/FSK Anti-Infective Conference, *Controversies in Infectious Disease*, held by the Division of Infectious Diseases of the College of Physicians and Surgeons of Columbia University and funded by a grant from Smith Kline & French Laboratories and Fujisawa SmithKline Corporation at Laguna Niguel, California, November 14-16, 1987.

Dr. Francis Plummer is a Scholar of the Medical Research Council of Canada and an Awardee of the Canadian Life and Health Insurance Association.

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risk factor identified during epidemiological studies. Early reports from several countries documented that many female patients with AIDS were prostitutes.¹¹

In 1980 investigators from the University of Manitoba were invited to participate with colleagues from the University of Nairobi in a series of studies to determine the etiology, epidemiology, and control of genital ulcer disease in Kenya.¹² These studies were extended to involve prostitutes who appeared to be a major epidemiologic reservoir for genital ulcer disease and other sexually transmitted diseases in Nairobi.¹³ Additional studies investigating the epidemiology and perinatal transmission of sexually transmitted pathogens were begun in 1982.¹⁴ Sera collected from patients in a number of studies were initially surveyed for HIV-1 antibodies in 1986, and demonstrated that an explosive epidemic of HIV-1 was occurring in Nairobi.¹⁵ In Zambia similar retrospective and prospective seroepidemiologic data also suggest that HIV-1 is spreading rapidly.¹⁶

THE EXTENT OF THE AIDS EPIDEMIC

As of October 31, 1987, 8,490 cases of AIDS had been reported from 37 of the 47 countries of Africa.¹⁷ Almost half of these cases were reported during 1987, and 2,369 of these originated from Uganda. Although surveillance for AIDS is occurring in many African countries, health care organization makes under-reporting unavoidable, and only an approximation of the actual number of cases is possible. It is probable that under-reporting has an order of magnitude of three to fivefold. In particular, some countries have reported few or no cases despite informal reports suggesting that numerous patients are ill or have died with AIDS.

Under-reporting occurs for many reasons. Opportunistic infections, particularly tuberculosis, and perhaps other diseases endemic to tropical areas may be the immediate pathogen responsible for the patient's illness and death. For instance, in Zaire 33% of patients with tuberculosis are seropositive for HIV-1.¹⁸ Failure to recognize that these patients are dying as a result of HIV-1 infection will continue to lead to underestimates of disease incidence until widespread serologic testing permits all ill or dying patients to be tested. Carefully selected samples of various populations, in both rural and urban communities, within hospitals and in the community, need to be carried out to ascertain the true prevalence. The initial case definition used by the Centers for Disease Control to diagnose AIDS was not as applicable in Africa, and recent changes in criteria to diagnose the disease should improve the diagnostic accuracy for AIDS in Africa. Health care workers must recognize

that AIDS presents in Africa in about one half of the patients as a wasting disease associated with low-grade fever and diarrhea (ie., "slim disease").¹⁹ The exact mechanism responsible for these features and the pathogens involved remains uncertain.

Accurate data compilation and reporting to WHO will continue to be a problem until health care workers in all African countries are aware of the disease, serological confirmation is rapidly available, and notification is simple and straightforward.

APPROXIMATE EXTENT OF HIV-I SPREAD

In Kinshasa, Zaire, in 1986 the seroprevalance among adolescents and young adults in Kinshasa was 8%, declining to 6% among 30-49 year olds and 4% among those 50 years of age or older. Among infants 8% of those under one year of age were seropositive, compared to only 1% of healthy children ages one to 14 years. In Kinshasa from 1985 to 1986 the annual incidence of HIV-1 infection was estimated to be 1.0%.²⁰

Among 9,000 randomly selected individuals in the Central African French speaking countries, including the Cameroons, Central African Republic, Chad, Congo, Equatorial Guinea, and Gabon between 0-5% of individuals were seropositive in 1986.²¹

In Nairobi, Kenya, none of 118 men with chancroid and none of 111 pregnant women were seropositive for HIV-1 in 1980 and 1981 respectively,²² In 1981 five of 116 prostitutes were seropositive. By 1983 14% of 93 men with chancroid were seropositive. In 1985 174 of 286 (61%), 29 of 194 (15%) men with chancroid, and 22 of 1100 (2%) of pregnant women were positive for HIV-1.²² In these populations, serially followed for five years, the recent introduction of HIV-1 and its rapid spread among heterosexual populations was confirmed. In Nairobi HIV-1 appears to have had three routes of entry. It has spread by migration of prostitutes from Northwestern Tanzania and Uganda.¹⁵ The initial seropositive patients were prostitutes from this area, and many of these women periodically travelled back to their home regions where AIDS is widely prevalent. The second route of spread is travellers from other countries to Nairobi. Sexual exposure to men from Burindi, Rwanda, and Uganda were associated with increased HIV seropositivity.²³ A third route may be from contiguous spread from bordering western territories. Among men with sexually transmitted diseases and pregnant women, births in the most Western provinces of Kenya were associated

with increased risk of seroprevalence. Many of the men had recently migrated to Nairobi to seek work.²³

HIV-1 antibody prevalence is much less common in southern and western Africa. In surveys of antibody prevalence among migrant miners during 1986, seroprevalence was 3.7% in those from Malawi, 0.3% from Botswana, and 0.1% or less in those from Mozambique, Lesotho, Swaziland, and South Africa.²⁴

War, internal strife, migrating labor, and movements of refugees and population desolation for any reason are major routes that enhance the spread of HIV-1.

Only a few seroprevalence studies have been carried out in rural Africa, but the incidence of infection may be much lower. In rural Northern Zaire, sera collected in 1976 were positive for HIV-1 antibodies in 0.8% of 659 individuals.⁶ Ten years later a second serosurvey of 389 residents showed an identical prevalence of 0.8%.⁶ Traditional village life in rural Zaire carries a low risk of HIV infection.

From these very preliminary seroprevalence studies in sub-Saharan Africa, it is apparent that seroprevalence studies range from almost undetectable levels (<1:1000) to as high as 18% in otherwise unselected healthy individuals. Crude estimates of the number of infected individuals in sub-Saharan Africa have ranged from 3 to 10 million. Presumably in at least four, and perhaps in five or six countries, as many as 5% of sexually active adults (age group from 15-50) are infected. Additional well-done epidemiologic studies of the seroprevalence of HIV-1 are needed to determine the extent of the spread and to identify at risk populations for intervention strategies.

PROJECTIONS FOR THE NEXT FIVE YEARS

Extrapolations into the future of the consequences of HIV-1 in Africa are fraught with error. In Western societies, HIV-1 seroprevalence and seroincidence studies have been carried out more widely than in African countries and, despite this, projections of HIV-1 infections have varied widely. In Africa, where the risk factors for heterosexual and possibly other routes of transmission are still to be determined, projections of seroincidence are very speculative. However, the documentation of recent introduction and rapid spread of HIV-1 in Nairobi and urban Zambia is alarming. It seems that, at least in the early stages of HIV-1 entry into a population, seroprevalence can double each year. This estimate may be conservative if data for both perinatal and heterosexual transmission are combined.

These projections lead to alarming estimates for total numbers of infected individuals in sub-Saharan Africa during the next five years. If five million individuals are presently infected, arithmetic projection suggests that as many as 50 million Africans may be infected by 1993. These figures should not be used to project gloom and despair for Africa, but rather should be a global goad to increase our efforts to ensure that these projections do not occur.

A mathematical model of the dynamics of HIV-1 transmission in African countries is necessary, but epidemiologic data are at present inadequate to formulate accurate models. Information on the incubation period, the infectiousness of both men and women, the rate of progression to AIDS, knowledge, attitude, and belief about sexuality and sexually transmitted diseases, the effectiveness of intervention programs, and factors that modify genetic susceptibility are all essential if we are realistically to determine the size of the anticipated epidemic.

The demographic implications for AIDS in Africa are staggering. If 50 million Africans are infected with HIV by 1993, this will be about 8% of the total population of the continent. However, in sub-Saharan Africa, seroprevalence of HIV-1 will vary between 15 and 40% among sexually active age groups (15-50 years of age). Assuming progression to AIDS is similar to what has been observed in Western countries, this will have a significant impact on the population of many African countries with a projection of more than one million deaths by 1991 and an additional 10 million in the five-year period from 1992 through 1996.

The impact of AIDS will fall most heavily on Uganda, Zaire, Zambia, Tanzania, Rwanda, and Burindi. Between one and 5% of sexually active adults will have died of AIDS by 1991. In the absence of effective programs to control virus spread or to treat disease, other nations including Kenya, Zimbabwe, Sudan, Angola, Congo, Mozambique, French Equatorial Africa, Cameroon, Chad, and the Central African Republic will have serious disease problems within 3 to 5 years. Ethiopia, Somalia, the countries of West Africa, and Southern Africa may not experience the major impact of the disease until 1995 or later. For all these countries it is essential that efforts to prevent the spread of HIV-1 receive the highest political and economic priority now.

The impact of AIDS on the health care system will be substantial. Health costs already are a major concern, and resources are very inadequate for anything more than basic services and disease prevention. Diseases related to HIV-1 will dramatically increase total health care costs and severely damage

much of the health infrastructure that has been established in most African countries.

The AIDS epidemic in Africa could potentially cause greater dislocation than any combination of famine, drought, or war that has occurred. As the disease primarily affects the age groups in society who are both parents and breadwinners, the number of dependents will rapidly increase relative to the providers. Whereas famine, drought, and poverty claim the very young and the aging, AIDS claims the most productive segment of society. Human resource development is a particular concern with regard to the AIDS epidemic. Managerial skills and a skilled labor force are essential to achieve developmental objectives. HIV-1 incidence seems to be particularly high among individuals in responsible positions.¹⁶

Diseases such as tuberculosis and perhaps measles may cause increased problems because of the effect of HIV-1 on the immune system.

Gains in social development made by many African countries over the past three decades will undoubtedly be jeopardized by the AIDS epidemic.

Overall, the economic and social impact of AIDS at present can only be crudely extrapolated from very imprecise projections of known and assumed seroprevalence studies. Good models for more exact projection of disease are urgently needed.

RISK FACTORS FOR HIV-1 SPREAD IN AFRICA

It is now agreed that HIV-1 transmission among adults in Africa is sexual, involving bidirectional heterosexual spread. At least a dozen seroprevalence studies in various African countries have repeatedly reinforced the observation that promiscuity is the major risk factor. There is, at present, no epidemiologic evidence to suggest that HIV-1 is spreading by routes not already known through studies primarily carried out in Western countries.

Studies consistently show significantly higher numbers of heterosexual partners among persons with AIDS in Africa, as compared to controls. Male patients with AIDS have had more sexual activity with prostitutes than controls.²⁵ In particular, men attending sexually transmitted disease clinics and prostitutes are at highest risk of infection causing HIV-1.

Factors that facilitate heterosexual transmission are still being determined. In the United States available information suggests that HIV-1 is transmitted less readily than such other sexually transmitted diseases as *N.gonorrhoeae*, *C.trachomatis*, or *H.simplex*.²⁴ Transmission studies among HIV-discordant couples in long-term sexual relationships with hundreds of encounters suggest that most sexual partners remain uninfected. It has been estimated that

the risk of infection is less than 0.1% of unprotected episodes of heterosexual penile-vaginal intercourse.²⁴

On the other hand, in Africa several studies have shown that stable heterosexual couples are frequently infected.

What, if any, are the differences in heterosexual infectivity and susceptibility that account for the apparent increased risk of heterosexual transmission of HIV-1 in Africa?

Several recent studies have suggested that genital ulceration markedly increases infectivity of women for their male partners.^{14,23} Following a single sexual exposure with a seropositive prostitute, men who present with chancroid have a risk between 15-20% of acquiring HIV-1.²⁵ Among men presenting with gonococcal infection following sexual contact with an HIV-1 infected prostitute, the risk is approximately one third as great.²⁶ Although other explanations may account for this difference, we assume that it is due to the presence of an ulcer in the female partner.

No other factors to date have identified risk factors that increase infectiousness of women for their male partners. However, very preliminary studies suggest that men with foreskins have a significantly increased risk of HIV-1 seroconversion following intercourse with an infected prostitute.²⁶

Our studies have shown that the foreskin increases the risk of acquiring chancroid by about three-fold following intercourse with a prostitute with a genital ulcer.²⁶ However, independent of genital ulcers, we have observed that men with sexually transmitted diseases, both gonococcal urethritis and chancroid, are more likely to be infected with HIV-1 if they are uncircumcised. Ulcers and foreskins are independent risk factors. Among circumcised men, a recent history of ulcers within the past two years is the major epidemiologic association with HIV-1 seropositivity.²⁶ Among uncircumcised men, genital ulcers and foreskins both are major risk factors.

Any discussion about the biologic role of the foreskin in the transmission of HIV-1 is speculative. Perhaps mucosal lesions, following intercourse, are more common in males with foreskins. It is also possible that virus can persist for longer periods in the moist milieu of the preputial sac. These studies suggest that the urethra is probably not the route by which HIV-1 gains male access following heterosexual intercourse.

Risk factors for male-to-female transmission are equally poorly understood. In an initial study among Nairobi prostitutes, genital ulceration and oral contraceptives appear to be associated with increasing seroprevalence among at-risk groups.¹⁴ In a recent prospective study we have shown that genital ulceration is a major risk factor with an odds ratio of greater than 10

for seroincidence of HIV among prostitutes with ulcers compared to a cohort group who did not have ulcers.²⁷ In the same group of prostitutes oral contraceptives also appeared to increase the risk for acquisition of HIV-1 as did positive cervical cultures for *Chlamydia trachomatis*. A positive cervical culture for *N.gonorrhoeae* was not a risk factor for HIV-1 seroconversion.

Among prostitutes presumably with multiple opportunities to acquire HIV-1 from their infected male partners, this cohort study clearly identified risk factors for seroconversion. Whether these risks can be extrapolated to other populations, in which women have much less risk of seroconversion, is unknown. Perhaps ulcers may be a major portal of entry. Biologic mechanisms by which oral contraceptives or *C.trachomatis* may facilitate HIV-1 transmission are unknown.

Hidy recently reviewed cultural practices that might contribute to the transmission of HIV-1 in Africa.²⁸ Although female circumcision has been proposed as a mechanism whereby heterosexual transmission is enhanced, this does not appear to be epidemiologically important. Female circumcision is most intensively practised in West Africa, Ethiopia, and Sudan. It is less frequent in the area currently epidemic for HIV-1.

Homosexuality is not practised overtly in most regions of sub-Saharan Africa. Anal intercourse is denied by most heterosexuals.

Unsterilized shared needles may be a significant route of transmission for the transmission of HIV-1. However, needlestick injuries in Western societies are rarely responsible for virus transmission. Although Mann et al. reported a correlation between a history of injection and AIDS in Zaire, it was not possible to exclude the bias that treatment was sought for illness occurring in patients with HIV-1 infection.²⁸

Other African practices that result in possible exposure from bloody instruments include scarification and group circumcision. AIDS transmission is theoretically possible, but this does not explain the observed epidemiologic spread of HIV-1.

Insects have been investigated as a possible means of transmission of HIV-1. Any possible role does not fit with known epidemiological data. Insects do not selectively bite sexually active individuals. At present, no biologic evidence supports the idea that HIV-1 can survive in insects or suggests that they may have any role in transmitting this virus.

STRATEGIES FOR CONTROL OF HIV-I IN AFRICA

No easy solutions for the problem of HIV-1 are on the horizon. An effective vaccine for individuals at risk is at least five years away. Inexpensive

effective treatment regimens to diminish virus dissemination from infected individuals, to prevent initial infection or progression to disease, or to cure AIDS is also years in the future. An inexpensive penicillin-like panacea for HIV-1 is improbable.

The energy and resources of both African nations and the world must be directed toward control of heterosexual transmission of HIV-1. National committees to coordinate education, surveillance, research, and control strategies must be organized in each country in Africa. Most countries should also establish smaller regional committees based throughout the country.

The main thrust of control must be the education of sexually active young men and women. Presumably, in most instances in Africa this education should be incorporated into existing health education programs. The message must be factual and convey the risks for acquiring HIV-1 through sexual relationships. It must also emphasize the importance of limiting the number of sexual partners and of using condoms in sexual relationships.

In Western societies, attempts to change sexual behavior have met with variable success. Among homosexual men in the United States, the decline in HIV seroincidence and other sexually transmitted diseases has been dramatic. In Nairobi, among prostitutes the use of a condom has become widespread as a result of a program with limited funding and goals. Both prostitutes and their male clients are now requesting condom use and more than half of all sexual encounters involve condoms.³⁰ Among prostitutes, this has resulted in a dramatic fall in the risk of seroconversion.³⁰

Sexual behavior, including such determinants as knowledge, cultural and individual attitudes and practices, have not been adequately studied in most parts of the world, including Africa. As a result, we have limited information as to cultural or other determinants of sexual behavior. Research is urgently required to determine what may be major impediments to the control of HIV-1 through education and behavioral modification in Africa.

Recent evidence that genital ulcer disease and perhaps some other sexually transmitted diseases are major cofactors for HIV transmission provide an opportunity to develop control programs and to evaluate the effectiveness of decreasing the incidence of genital ulcers on the seroincidence of HIV-1. Control programs for all sexually transmitted diseases must be combined with control programs for HIV-1.

These programs will require a vast infusion of money and committed individuals. Bureaucratization and politicalization of AIDS programs must be avoided. It is essential that Africans with authority and managerial skills be given leadership roles in AIDS control programs. Money must be pro-

vided by such agencies as the World Health Organization and various Western countries through augmented allocations to health funds for Africa. AIDS has the potential to make it impossible for most African countries to achieve the goal of "health for all by the year 2000."

For most African nations there is theoretically time to embark on effective control programs. For others strategies to limit virus spread and disease impact may be the only option available. These are poor and incomplete solutions to what is rapidly becoming the most serious crisis for Africa during this century.

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