Articles

AIDS: An International Perspective

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The acquired immunodeficiency syndrome (AIDS) and infection with the human immunodeficiency virus type 1 (HIV-1) constitute a worldwide public health problem. Whereas in Europe and in most of the Americas transmission of HIV-1 has occurred predominantly among homosexual men and intravenous drug abusers, in Africa a distinct epidemiologic pattern has emerged that indicates that HIV-1 infection is mainly heterosexually acquired. Heterosexual transmission appears to be increasing in some parts of Latin America and the Caribbean, and possibly in the United States. In addition to HIV-1, at least one other human retrovirus, namely HIV-2, has been implicated as a cause of AIDS in Africa and Europe. Factors that influence heterosexual transmission of HIV-1 include genital ulcerations, early or late stages of HIV-1 infection in the index case, and possibly oral contraception and immune activation. The rate of perinatal transmission is enhanced when the mother's illness is more advanced. AIDS and HIV-1 infection may have a significant impact not only on public health, but also on the demography and socioeconomic conditions of some developing countries. Programs for the prevention and control of AIDS should be an immediate priority in all countries.

SOON AFTER THE INITIAL DESCRIPTION OF PATIENTS WITH AIDS in the United States, cases were reported from Europe with similar clinical, immunological, and epidemiological features (*1*). Indirect evidence for foci of AIDS in the Caribbean and Central Africa was subsequently provided by the observation of Haitian and African patients with AIDS in North America and Europe (*2*). Several field surveys then confirmed the presence of a relatively large number of patients with AIDS in Haiti and in several countries in Africa (*3–5*). As of 1 January 1988, 129 countries had reported at least one AIDS case to the World Health Organization (WHO) (*6*). AIDS has rapidly emerged as a worldwide public health problem that requires a global approach for control.

Although the immunology and pathogenesis of infection with the human immunodeficiency virus type 1 (HIV-1) appear to be similar throughout the world, there are geographic variations in epidemiologic patterns and clinical expression of the disease, and in the distribution of different human retroviruses. We review here some epidemiologic and biological features of HIV-1 infection outside North America and show how the international study of AIDS has contributed to our understanding of this disease.

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Global Patterns and Prevalence

The large numbers of AIDS cases that are now being reported are due to the spread of HIV-1 in the 1970s before it was isolated and its pathogenesis and transmission were understood. Since HIV-1 infection in a population may precede the development of AIDS by several years, an optimal understanding of the current epidemiology of AIDS must be based on an analysis of both HIV-1 seroprevalence data as well as reported AIDS cases.

Definition and reporting of AIDS. The original definition of AIDS proposed by the Centers for Disease Control (CDC) and WHO (*7*) was not useful in developing countries because these often lack adequate facilities for the definitive diagnosis of the stipulated opportunistic infections and other associated diseases. In October 1985, at a WHO workshop in Bangui, Central African Republic, a clinical definition of AIDS was developed. Limited field evaluation showed that the definition was highly specific for adults with AIDS (90%) but relatively insensitive (60%) for HIV infection (*8*). This case definition is now being widely used in developing countries for AIDS surveillance.

AIDS cases have been reported from all major areas of the world (Table 1). Of the total, about 70% have been reported from the United States. Figure 1 shows the cumulative number of AIDS cases reported to WHO by year of diagnosis.

Studies of the completeness of reporting in the United States (*9*) show that about 90% of AIDS cases meeting the CDC/WHO definition are reported to national authorities. Reporting of AIDS cases from Africa has in general been delayed and incomplete. The reasons for this include the limited access of large segments of the population to health care facilities where the diagnosis of AIDS can

Table 1. AIDS cases reported to WHO as of 9 December 1987.

Continent	Number of cases	Number of countries reporting		
		Total	Zero cases	One or more cases
Africa	8,652	47	10	37
Americas	55,354	44	2	42
Asia	224	28	9	19
Europe	8,775	28	1	27
Oceania	742	14	10	4
Total	73,747	161	32	129

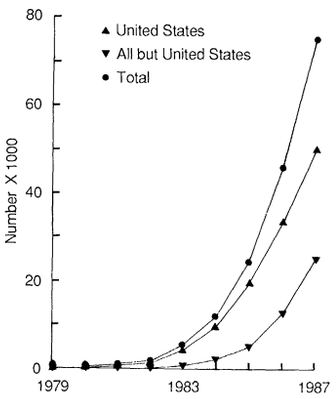

Fig. 1. Cumulative number of AIDS cases in the United States and other countries excluding the United States reported to WHO by year of diagnosis.

be established, the low efficiency of surveillance systems, the general lack of facilities for the diagnosis of AIDS, and the reluctance of some governments to officially acknowledge the existence of AIDS until 1987.

With widespread underrecognition and underreporting of AIDS cases being taken into account, WHO estimates that approximately 150,000 cases of AIDS had probably occurred worldwide by the end of 1987.

Seroprevalence data. Hundreds of serologic studies of HIV-1 have been carried out throughout the world (*10, 11*). Although many of the early studies were flawed because of problems associated with the sensitivity and specificity of the enzyme-linked immunosorbent assay (ELISA), most of these problems have been resolved. Serosurveys are now also being conducted to determine the geographic distribution and prevalence of HIV-2 infection.

The data from all of these serologic surveys, in spite of methodologic limitations, provide a fairly reliable picture of the geographic and temporal spread of HIV infections throughout the world.

Historical perspective. Where and when HIV-1 first began to spread extensively cannot be determined. The first recognition and report of AIDS (California, 1981) occurred more than two decades after the earliest serologic reponse to HIV was found in stored blood (Zaire, 1959) (*1, 12*). However, similar studies on stored blood have not been reported from Europe or North America, and no conclusions can be drawn as to the origin of AIDS. The available data suggest that the spread of HIV-1 within urban areas of Central Africa began to increase markedly during the late 1970s (*11*). This scenario is consistent with retrospective studies demonstrating a marked increase of AIDS indicator diseases (cryptococcal meningitis, chronic diarrhea, and generalized Kaposi's sarcoma) in Central Africa in the late 1970s and early 1980s (*11, 13*). Isolated cases of AIDS in Africans were retrospectively diagnosed in Europe in the mid-1970s (*14*).

In contrast to the situation in the major cities, the prevalence of HIV-1 in most of rural Africa may not have changed significantly. For example, whereas a tenfold increase in HIV-1 antibody prevalence was documented in pregnant women in Kinshasa, Zaire, between 1970 and 1980, HIV seroprevalence remained low (0.8%) in one rural area in Zaire between 1976 and 1986 (*15, 16*). This observation suggests that the rate of HIV transmission may remain stable in the absence of conditions that enhance its spread. However, in some rural parts of Uganda the virus has spread rapidly (*5, 17, 18*). Social changes with disruption of traditional lifestyles may have promoted the spread of HIV infection in Africa and in other parts of the Third World (*19*).

Once introduced into populations where individuals are more likely to have multiple sexual partners and to be exposed to blood transfusions and unsterilized needles and syringes, HIV-1 may spread rapidly. The introduction of HIV-1 into the populations shown in Fig. 2 generally occurred in the late 1970s and early 1980s.

In the Caribbean, HIV-1 infection was introduced in the late 1970s, possibly by visitors from industrialized countries (*20*). The virus seems to spread at different rates in Latin American countries. Brazil had reported over 2000 cases of AIDS by the end of 1987 (*6*). In Haiti heterosexual transmission of HIV-1 infection appears to be responsible for a growing proportion of AIDS cases (*20*). Although information about AIDS in Asia is limited, HIV-1 seems to be of very recent introduction in that continent, where it is now beginning to spread in populations of males and females with multiple sex partners.

Global patterns. The available data on reported AIDS cases and HIV-1 seroprevalence provide a reasonable description of the current global patterns of infection and severe or fatal disease due to HIV-1 infection. Three distinct epidemiologic patterns of infection and disease can be distinguished. The relative frequencies and social features of the three types of transmission (sexual, parenteral, and perinatal) and the possible date of HIV-1 introduction or extensive spread account for these three patterns (Table 2 and Fig. 3).

Heterosexual and Perinatal Transmission

Heterosexual transmission. The initial assessments of the AIDS epidemic in African countries revealed a very different epidemiology from that in Western countries (*4*). Level of sexual activity with multiple partners, not sexual orientation, was the apparent risk factor. It has been difficult to reconcile a large heterosexual epidemic in Africa with data in Western countries that showed that the prevalence of HIV infection in regularly exposed spouses of men infected through blood transfusion or blood products was 7 to 23% (*21*). Over the past 2 years, evidence has emerged that partially elucidates the mechanisms of this dichotomy.

Initial studies in Zaire and Rwanda showed nearly equal sex ratios among AIDS patients, and the major risk factor appeared to be multiple heterosexual partners (*4*). Subsequently, asymptomatic prostitutes in Rwanda, Kenya, and Zaire were shown to have HIV-1 prevalence rates of 25 to 88% (*22*). Retrospective seroepidemiologic studies of Nairobi prostitutes and men with chancroid documented a dramatic epidemic of HIV-1 infection in these populations (*23*). The prevalence in selected prostitutes in a lower socioeconomic area rose from 8% in 1981 to 61% in 1985, and in men with chancroid increased from 0% to 1980 to 17% in 1985. In these and similar studies in Africa, a major role for blood transfusion, injections, or anal intercourse could not be shown.

From a report of women infected with HIV-1 by artificial insemination from a single HIV-1–infected donor, it became clear that exposure of the cervix or endometrium to infected semen is sufficient to transmit the virus (*24*). However, a role for other factors was suggested by the low frequency of HIV-1 infection among the regular sex partners of American patients with hemophilia and blood transfusion recipients (*21*).

Transmission thus appears to be influenced both by factors that increase a person's susceptibility to HIV-1 and factors that increase a person's infectivity. These factors can operate locally or systemically, or can be inherent or immunogenetic.

Genital ulcers and other sexually transmitted diseases (STDs) were hypothesized to facilitate HIV-1 transmission in early studies (*23*). In case-control studies of prostitutes in Nairobi, the presence of genital ulcers was correlated with HIV-1 infection (*25*). A causal role for genital ulcers in increasing HIV-1 susceptibility could not be inferred from these cross-sectional studies because of the likeli-

hood that both ulcers and HIV-1 infection are related to sexual activity and that immunodeficiency can result in the frequent occurrence of genital ulcerations. In a prospective study of seronegative prostitutes from the same cohort, the presence of genital ulcers was associated with a greatly increased risk of acquiring HIV-1 infection (*26, 27*). *Chlamydia trachomatis* infection was also associated with an increased risk of HIV-1 infection, whereas gonococcal infection had no relation to infection with the virus, suggesting that genital ulcers and *C. trachomatis* may not be acting as covariants of sexual activity. Genital ulcers and *C. trachomatis* could permit penetration of HIV-1 by causing epithelial disruption or perhaps could increase the population of HIV-1 target cells at the site of infection by recruiting lymphocytes to the genital tract.

Oral contraception is another factor that may increase susceptibility of women to sexually acquired HIV-1 infection. In the prospective study of prostitutes described above, an increased risk of HIV-1 seroconversion was observed among oral contraceptive users independent of sexual activity, intercurrent sexually transmitted diseases, and condom use (*27*). Biologically plausible mechanisms for an increased susceptibility to HIV-1 among oral contraceptive users include: (i) increased area of cervical ectropion, (ii) increased concomitant *C. trachomatis* infection, and (iii) direct immunosuppressive effects of oral contraceptives (*28*). However, this study requires confirmation before oral contraceptives can be considered as a potential factor for increasing the risk of HIV-1 acquisition.

In men, local factors that influence susceptibility to HIV-1 are less clear. Genital ulcers may provide a portal of entry for the virus in men, but this effect on susceptibility may prove difficult to separate from a probable effect on increasing the infectivity of women. Recently, in a case-control study from Nairobi, uncircumcised men were found to have an increased risk of HIV-1 infection compared to circumcised men (*29*). In this study although genital ulcers were associated with HIV-1 infection and uncircumcised men were known to have an increased risk of chancroid (*30*), uncircumcised men had a higher HIV-1 seroprevalence independent of genital ulcers and indices of sexual behavior. If confirmed, the occurrence of balanitis or maceration of the glans penis or enhanced viral survival under the foreskin could increase susceptibility to HIV-1.

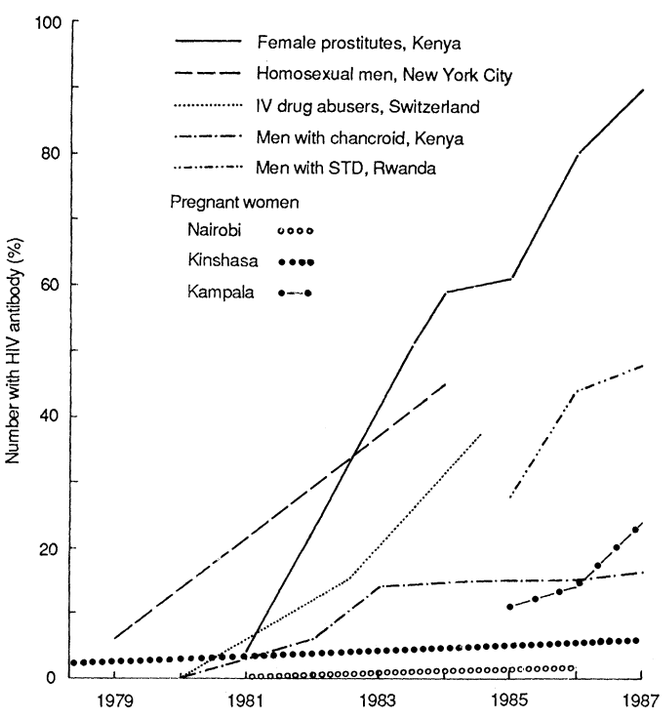

Fig. 2. Cohort and periodic cross-sectional studies of HIV seroprevalence in different population groups in Africa, Europe, and the United States [from (*16, 23, 64*)].

Factors operating at a systemic level to increase susceptibility to HIV-1 could include immunosuppression or immunologic activation occurring as a result of concomitant infections with viruses or protozoan parasites, for example. Chronically activated immune systems occur more frequently among African adults than American heterosexual men (*31*).

Evidence of a role for genetic factors in mediating susceptibility to HIV-1 is inconclusive. A reported association between certain phenotypes of a serum protein (group-specific component and susceptibility to HIV-1 infection) has not been confirmed in subsequent studies (*32*). Some attention has focused on variability of the epitopes on the CD4 molecule (T4 receptor, the binding site of HIV-1) as a factor mediating HIV-1 susceptibility. These results are also inconclusive (*33*).

One local factor that increases the infectivity of women has been identified. In a prospective study of men who acquired an STD from a group of prostitutes with a high prevalence of HIV-1 infection, Cameron *et al.* (*34*) found that men who acquired genital ulcers had a fivefold increased risk of subsequent HIV-1 infection compared to men who acquired urethritis. The actuarial risk of seroconversion at 6 months in men acquiring a genital ulcer was 25% compared to 7% in men acquiring urethritis. Since the men did not have genital ulcers at the time of intercourse with the prostitute, it seems probable that the acquisition of HIV-1 infection by men with genital ulcers is an index of the infectivity of the female sex partner rather than related to the susceptibility of the male partner. In addition, in this study a single sexual exposure was apparently associated with a female-to-male transmission risk of 5 to 10%, provided particular cofactors were present. This is considerably higher than previously estimated in other population groups.

One systemic factor that may influence infectivity is the clinical stage of HIV-1 infection. In a small number of patients with hemophilia, the risk of transmission of HIV-1 to an uninfected spouse was inversely related to the CD4/CD8 ratio, and among 62 heterosexual couples in Belgium a low CD4/CD8 ratio in the index case was the single most important risk factor for HIV-1 infection in the partner (*35*). Goedert *et al.* (*35*) hypothesized that declining immune function is associated with increased virus replication, resulting in enhanced infectivity. A further implication is that the overall rate of HIV-1 transmission may accelerate as an infected population progresses to immunodeficiency.

Perinatal transmission. In populations where HIV-1 infection is mainly heterosexually transmitted, a substantial proportion of women of childbearing age may now be infected with the virus. Between 2 and 15% of pregnant women in some areas of Central and East Africa are seropositive, and seroprevalence rates of up to 3% have been reported from West Africa (*36–38*). In Europe, women using intravenous drugs are the major source of perinatal infection with HIV-1 (*39*).

The time at which HIV-1 infection of the fetus or infant occurs is not yet known; potential opportunities for transmission occur in utero, during labor and delivery, and postnatally through breast milk or other vehicles. Limited studies from North America and Europe have documented HIV-1 infection in 30 to 65% of infants of HIV-1 seropositive mothers (*40*). Acquisition in utero appears to be the most frequent mechanism of HIV-1 transmission from mother to child.

Currently, several large studies of perinatal transmission are underway in Africa. In Nairobi, immunoglobulin M (IgM) antibody to HIV-1 was detected in the cord blood of 51% of 100 infants born to virus-infected mothers. Similarly, 46% of 600

infants of infected mothers in Kinshasa had IgM antibodies to HIV-1 in cord blood (*36, 37*). In both studies, the presence of IgM antibody to HIV-1 in cord blood was associated with the stage of HIV-1 infection in the mother, and suggested that mothers with immunodeficiency transmit HIV-1 more efficiently to their offspring during pregnancy than postnatally. Striking differences in clinical and obstetric correlates of perinatal transmission of HIV-1 were noted between populations recruited from two different hospitals in Kinshasa, one mainly serving an economically deprived population and one being attended by a more middle-class population (*37*). This suggests that such studies should be performed in different settings, and that results from one study should not be extrapolated without carefully considering all the characteristics of the population involved.

The contribution of breast-feeding in perinatal transmission of HIV-1 is unclear, yet HIV-1 has been isolated from breast milk, and reports of postnatal transmission, most probably through breast milk, have been reported (*41*). However, breast-feeding probably represents only a small incremental risk of mother-to-infant transmission compared to in utero transmission.

As a result of perinatal infection, Africa faces a rapidly growing problem of HIV-1 infection in infants and children. Results from the studies in Nairobi and Kinshasa suggest that infants born to HIV-1–infected mothers do not present more congenital abnormalities—in contrast to findings among newborns of infected intravenous drug abusers in the United States—but that they more frequently have generalized lymphadenopathy at birth than control infants (*36, 42*). The morbidity and mortality in the newborn associated with perinatal HIV-1 infection appears high. For example, in Kinshasa, infants born to HIV-1 seropositive mothers had a lower mean birth weight and shorter mean gestational age than infants in a control group, and at a hospital attended by a poor socioeconomic group, the death rate among infants of HIV-1 seropositive mothers within a few months after birth was nearly 20 times higher than among infants born to HIV-1 seronegative mothers (*37*).

Natural History of HIV-1 Infection

Studies on the natural history of HIV-1 infection in homosexual men in Europe and North America have shown annual progression rates to disease of approximately 2 to 5% (*43*). However, data are not available on HIV-1 progression among nonintravenous drug-abusing heterosexuals. Disease progression in HIV-1–infected African heterosexuals approximates the rate observed in Caucasian homosexual men (*44*). Among HIV-1 seropositive female prostitutes in Nairobi, 6% developed severe illness during 12 months of follow-up (*30*). Among African men and women with lymphadenopathy syndrome or AIDS-related complex (ARC) followed in Brussels, the annual progression rates to AIDS were 1.1 and 20.7%, respectively (*45*). In Zaire, 6.3% of 56 individuals who had seroconverted between 1984 and 1986 had developed ARC by the end of 1986 and 5% had developed AIDS (*46*). Among 91 men and women who were already seropositive at enrollment in the cohort in 1984, 16.3% had ARC in 1986, 3.3% had AIDS, and 11.9% had died from suspected AIDS over this 2-year period.

Prognostic factors for disease progression were originally identified in European cohort studies (*47*). A specific loss of immunoglobulin G antibodies against the *gag* gene and *gag* gene products of HIV-1 (p24) has been identified during clinical progression of HIV-1 infection, while antibody to the viral envelope glycoprotein remains stable. It is intriguing that free viral antigen as detected in an antigen-capturing assay is found less often in serum from African

Table 2. Patterns of HIV-1 infection in the world.

Pattern 1	Pattern 2	Pattern 3
Homosexual/bisexual men and intravenous drug abusers (IVDA) are the major affected groups	Heterosexuals are the main population group affected	More recent introduction with spread among persons with multiple sex partners
	Period when introduced or began to spread extensively	
Mid-1970s or early 1980s	Early to late 1970s	Early to mid-1980s
	Sexual transmission	
Predominantly homosexual. Over 50% of homosexual men in some urban areas infected. Limited heterosexual transmission occurring, but expected to increase	Predominantly heterosexual. Up to 25% of the 20- to 40-year age group in some urban areas infected, and up to 90% of female prostitutes. Homosexual transmission not a major factor	Both homosexual and heterosexual transmission just being documented. Very low prevalence of HIV infection even in persons with multiple partners, such as prostitutes
	Parenteral transmission	
Intravenous drug abuse accounts for the next largest proportion of HIV infections, even majority of HIV infections in southern Europe. Transmission from contaminated blood or blood products not a continuing problem, but existing cohort of tens of thousands of persons infected by this route before 1985	Transfusion of HIV-infected blood is major public health problem. Nonsterile needles and syringes account for undetermined proportion of HIV infections	Not a significant problem at present. Some infections in recipients of imported blood or blood products
	Perinatal transmission	
Documented primarily among female IVDA, sex partners of IVDA, and women from HIV-1 endemic areas	Significant problem in those areas where 5 to 15% of women are HIV-1 antibody-positive	Currently not a problem
	Distribution	
Western Europe, North America, some areas in South America, Australia, New Zealand	Africa, Caribbean, some areas in South America	Asia, the Pacific Region (minus Australia and New Zealand), the Middle East, Eastern Europe, some rural areas of South America

patients with AIDS than in serum from European patients (*48*).

Whether microbial infections act as cofactors to enhance HIV-1 expression remains unresolved. Frequent exposure to a wide variety of infections in the developing world (for example, malaria, mycobacterial infections, STDs, and other viral infections) has been hypothesized to increase viral replication, thereby enhancing disease progression (*31*). Co-infection with human T cell leukemia virus (HTLV-1), which occurs in many tropical areas, may also influence the natural history of HIV-1 infection (*49*).

HIV-2

Isolates of HIV-1 from Africans appear more heterogeneous genetically and antigenically compared with isolates from Europeans and Americans (*50*). However, aberrant reactions of sera from West Africans to HIV-1 and simian immunodeficiency virus (SIV) led to the identification of another human retrovirus, HIV-2, in 1985 (*51, 52*).

Isolates of HIV-2 are antigenically and genetically more closely related to SIV than to HIV-1. The genomic sequence of HIV-2 is approximately 40% identical to that of HIV-1 and 70% identical to that of SIV (*52, 53*). HIV-2 is further related to HIV-1 in terms of morphology, cell tropism, in vitro cytopathic effect on $CD4^+$ cells, and in overall genetic organization. Experimental infection with HIV-2 has been achieved in baboons, but not in macaques (*54*). In baboons, a transient skin rash was associated with HIV-2 viremia. However, the virus could not be recovered after more than 4 weeks after inoculation, suggesting that chronic infection was not established.

The viral proteins of HIV-2 are highly divergent from those of HIV-1, with a 50% conservation for the *gag* and *pol* amino acids, and less than 30% for amino acids encoded by *env*, F (*orf*-2, *3'orf*), and Q (*orf*-1, *sor*) (*52, 53*). The envelope glycoproteins are also antigenically different from those of HIV-1. Thus, HIV-2 antibody-positive sera recognize the core proteins of HIV-1 but not the envelope glycoproteins, and vice versa (*52, 53*). Therefore, sera from individuals with antibody to HIV-2 may not react in currently used serologic assays for HIV-1.

That HIV-2 can cause disease in humans is indicated by isolation of the virus from blood and cerebrospinal fluid of patients with AIDS and ARC (*52, 55*). However, prospective studies on large cohorts are necesssary to fully define the clinical expression and natural history of HIV-2 infection.

On the basis of preliminary serosurveys and the identification of patients in Europe, HIV-2 transmission appears to be occurring principally in West Africa. In this area, seroprevalence rates for HIV-2 in the general population have ranged from 0.3 to 17%, and up to 64% of individuals at risk for STD, such as prostitutes, have been HIV-2 seropositive (*56*). In these same areas of Africa, infection with HIV-1 appears less or equally prevalent, perhaps because of its more recent introduction. Data suggest that HIV-2 infects populations similar to those infected by HIV-1, with heterosexual activity being the dominant mode of spread.

Like HIV-1, HIV-2 seems to spread rapidly and has been identified in Central Africa and in European patients in Europe (*57*). There is little doubt that HIV-2 will spread to other geographic areas, and active surveillance of HIV-2 infection is necessary in parts of the world outside West Africa. The simultaneous occurrence of HIV-1 and HIV-2 will have implications for diagnostic services, blood donor screening programs, and vaccine development.

Impact on Health and Society

In terms of morbidity and mortality, malaria, diarrheal diseases, and malnutrition may be more important than AIDS to individuals in Africa as well as other parts of the developing world. Nevertheless, the impact of HIV infection on health and society will be greater than that estimated on the basis of the current reported number of AIDS cases. Since AIDS mainly affects people in their most productive years, effects of this disease on society may be as pernicious as its effect on individuals.

Health services. The most visible impact of AIDS on the health system involves the direct cost of medical care for a disease that requires repeated hospitalization. Health care systems in some African cities are already overloaded with AIDS patients. For example, in one hospital in Central Africa over one-third of patients in internal medicine wards have AIDS (*58*). These patients occupy hospital beds and consume scarce resources (pharmaceuticals, per-

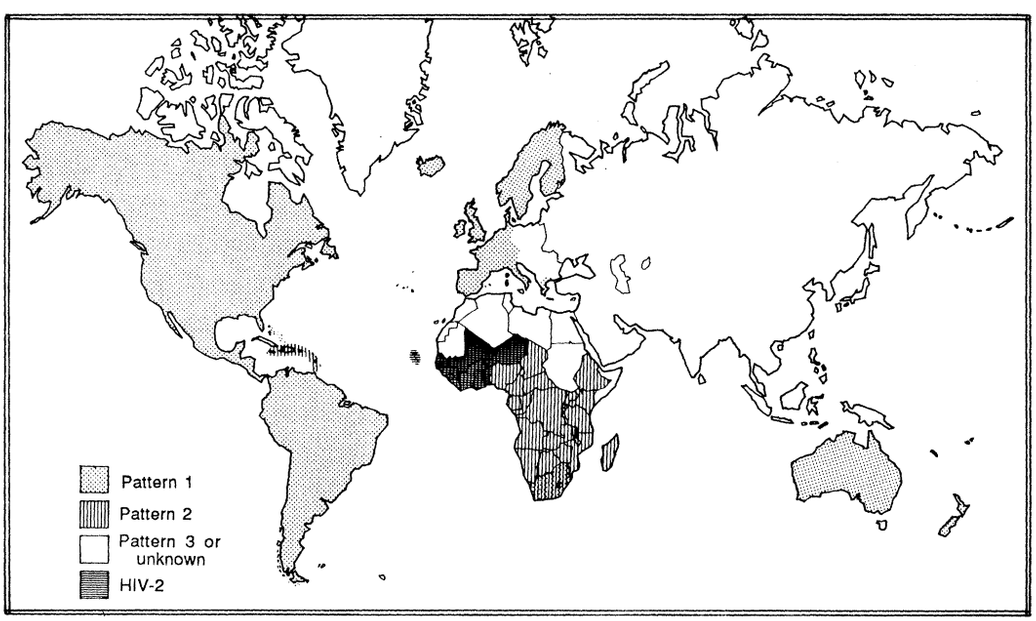

Fig. 3. Patterns of HIV-1 infection in the world (see Table 2). (Pattern 2 is occurring increasingly in parts of Latin America, where pattern 3 also occurs in some large rural areas.)

sonnel time) in palliative treatment that might be better used for illnesses that can be cured.

Infection with HIV-1 may have a negative impact on ongoing health programs. The natural history of endemic diseases such as tuberculosis and syphilis may be modified by concomitant HIV infection so that patients experience more fulminant disease or relapses after treatment. These effects may lead to higher rates of transmission of endemic diseases in the population (*59*). Consequently, standard management of common diseases may become less effective, and more expensive approaches may have to be used.

Questions concerning the effect of HIV-1 infection and the safety, immunogenicity, and efficacy of childhood immunizations (*60*) have not yet been fully answered. The decreased immunogenicity of both live and killed vaccines in HIV-1–infected children must be considered along with the risks and sequelae of vaccine-preventable diseases in the developing world (*60*). Other programs directly affected by the AIDS epidemic include diarrheal disease control, because of the strong association between HIV-1 infection and chronic diarrhea in Africa, and mother and child health programs, including family planning, because of the increased infant mortality as a result of perinatal transmission of the virus.

The AIDS epidemic illustrates dramatically the need for strengthening some of the weakest components of the health services, such as health education, laboratory services, blood banks, and the control of STDs.

Socioeconomic and political consequences. Because AIDS affects men and women in their procreative years, and their offspring, it may reduce the rates of population growth in certain urban populations of Central and East Africa where 5 to 25% of women of childbearing age are HIV-1 seropositive (*10, 11, 36, 37*). An annual AIDS incidence of 500 to 1000 cases per million adults, as documented in some African cities, may lead to an adult mortality rate attributable to HIV-1 infection of at least 0.1% per year (*58, 61*). The continuous decline in infant mortality rates over the last decades may cease. In addition, the rates of population growth in some areas may decrease as a result of premature deaths in adults, and of fatal HIV-1 infection in children.

Loss of skilled manpower as a result of HIV-1 infection may be important in countries where the educated elite have a higher incidence of HIV-1 infection (*19*). Estimates of the economic costs of HIV-1 infection in Africa are urgently needed. Determining the level of funds that should be allocated to AIDS as opposed to other health problems is an unresolved issue since the effectiveness of ongoing and planned interventions for AIDS is unknown.

Societal reactions to AIDS in African countries have been similar to reactions in Europe and North America, with denial, panic, and stigmatization occurring, often in response to sensational reports in the Western media or to discriminatory measures, such as compulsory HIV-1 screening for students or immigrants, implemented by other governments. The selective impact of HIV-1 on young and middle-aged adults, including members of the business and government elite, leads to a potential for economic and political destabilization in areas of the developing world most severely affected by the virus.

Lessons from the Third World

Research on AIDS, HIV-1, and other retroviruses by African investigators and their international collaborators has contributed greatly to our understanding of the AIDS epidemic worldwide. Most important, studies in Africa have demonstrated that HIV-1 is primarily a heterosexually transmitted disease and that the main risk factor for acquisition is the degree of sexual activity with multiple partners, not sexual orientation.

Cofactors (genital ulcers, *C. trachomatis* cervicitis, and possibly the uncircumcised state and oral contraceptives) have been shown to alter susceptibility to HIV-1 or the infectivity of infected persons through sexual transmission. This information indicates that the control of other STDs could prove to be a means for indirect control of HIV-1 transmission.

African studies are showing that behavior can be changed and that such change can decrease HIV-1 transmission (*62*). Some African governments have shown the rest of the world how to rapidly develop strong national campaigns against AIDS.

Global Control and Prevention of AIDS

Although the prevention and control of AIDS are ultimately dependent on the decisions of individuals, these decisions are influenced by local, national, and even international customs. Educational programs must take these factors into consideration, and it will therefore be necessary for these programs to involve experts in the social and behavioral sciences. One urgent need in all countries affected by AIDS is to resolve the difficult issue of disclosure of information about HIV-infected individuals. This issue, like that of resource allocation, will require the participation of members of many professions as well as the public.

Programs to prevent STDs depend on the delivery of messages to specific audiences and the provision of support services (counseling, condoms) to maximize compliance. Because few data on sexual practices are available, surveys of knowledge, attitudes, and practices will be required to determine the culturally appropriate messages for defined segments of the population (prostitutes, adolescents, male homosexuals and bisexuals) in each country or for entire populations. Since programs to prevent STDs have been undertaken before, the success and failures of such programs should be examined so that mistakes made previously can be avoided in AIDS control programs.

To prevent transmission of HIV-1 and related viruses through blood transfusions it will be necessary to ensure that transfusions are given only when indicated, to use donor deferral or selection methods, and to screen blood for HIV antibody. In most areas of Africa and Latin America, the costs of screening and the general infrastructure requirements for blood banking have limited the implementation of such safety measures. Particularly in Africa, donor deferral or the screening of donors on the basis of clinical or epidemiological criteria is unlikely to protect the blood supply and could drastically reduce the available donor pool (*63*). A simple and inexpensive screening assay for HIV infection that can be used in the developing world is urgently needed (*63*).

The role of certain practices in traditional and Western medicine, such as the reuse of needles, razor blades, or other instruments, in the spread of HIV infection has not been well documented, even though the sharing of syringes and needles is known to put intravenous drug abusers at high risk for AIDS. Ensuring that instruments used once are properly discarded is difficult in disadvantaged circumstances, and transmission of the virus through needles and other skin-piercing instruments will be difficult to control.

The prevention of perinatal transmission depends primarily on protection of women of childbearing age from HIV infection. In women already infected with the virus it may be possible to prevent (or interrupt) pregnancy. However, issues of childbearing, contraception, and abortion are complex and require different approaches depending on the cultural background of the population.

International cooperation. The translation of these general approaches to HIV prevention into coherent national programs

requires political commitment, resources, planning, and technical guidance. Recognizing the global importance of AIDS, WHO has developed a Global AIDS Strategy. WHO's Special Program on AIDS has three objectives: (i) to prevent HIV transmission, (ii) to reduce morbidity and mortality associated with HIV infections, and (iii) to unify and unite national and international efforts to control and prevent AIDS.

National AIDS control programs are being rapidly established throughout the world with the technical and financial support of the international community. The World Health Organization is directing and coordinating the global effort against AIDS. Multinational organizations such as the European Economic Community have supported AIDS control in developing countries, as have many international assistance agencies, either through WHO's Special Program on AIDS or bilaterally in conformaty with WHO's global AIDS strategy. The goals of the programs in most countries are to (i) establish a national AIDS committee, (ii) assess the current rate of infection, (iii) establish HIV and AIDS surveillance, (iv) ensure adequate laboratory support, (v) educate health workers at all levels, (vi) develop, implement, and evaluate prevention programs, and (vii) establish programs to reduce the impact of HIV-associated infections on individuals and the community.

The control and prevention of AIDS will require a sustained, long-term commitment. There will be no easy answer.

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