REPORTS FROM AROUND THE WORLD

AIDS in the Developing World: An Epidemiologic Overview

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The pandemic of human immunodeficiency virus (HIV) infection is rapidly becoming a tropical disease. Sub-Saharan Africa alone currently accounts for ~60% of the estimated >11 million infections worldwide. In Africa the virus is transmitted heterosexually and in many areas is now widely dispersed in the general population. Spread of HIV in Asia has been more recent, with current estimates of 2 million infections, but has been very rapid in South and Southeast Asia. In Thailand extensive transmission of the virus has occurred over the last 5 years. Initially, infections were seen in users of intravenous drugs and in commercial sex workers; now, however, HIV has spread to the general population. Recent, although incomplete, data from India suggest an epidemic curve reminiscent of the early epidemic in Africa and Thailand. With this rapid spread of the infection, there may be as many as 26 million infections—most in developing countries—by the year 2000.

The report in 1981 of a few cases of *Pneumocystis carinii* pneumonia (PCP) in otherwise healthy young men in the United States began the era of recognition of the worldwide pandemic of human immunodeficiency virus (HIV) infection. It soon became clear that HIV, initially associated with homosexuality, could be transmitted by both homosexual and heterosexual contact, through contaminated blood and blood byproducts, and from mother to child. Perhaps the most important lesson we have learned in the first decade of the AIDS epidemic is that no group or region is immune to the threat. Furthermore, there is not one uniform AIDS epidemic. Rather, within each society, a set of epidemics coexist with different risk groups and rates of transmission. This report will provide a broad overview of the epidemic in the world, will cover Africa briefly, and will then concentrate on Thailand and India—two countries that have only recently been documented to have extensive spread of the infection.

Patterns of Spread

Although AIDS was initially recognized in the United States and shortly thereafter in Europe, researchers soon determined that the HIV epidemic was, in fact, global and that the infection had spread most widely in sub-Saharan Africa. As of July 1992, cases of AIDS have been reported in 168 countries [1]. To assist in understanding the epidemiology of the epidemic, the World Health Organization (WHO) developed a broad international classification of the different patterns of transmission worldwide [2]. Pattern I included the industrialized world and some countries in Latin America, where spread began in the late 1970s or early 1980s and transmission was primarily between intravenous drug users (IVDUs) and between homosexual men. Pattern II included sub-Saharan Africa and some countries in the Caribbean, where transmission began about the same time as in countries with pattern I transmission but was almost exclusively heterosexual. Spread occurred rapidly and heterosexual transmission appeared to occur more efficiently than that observed in the heterosexual communities in pattern I countries. Finally, pattern III countries were those where HIV was introduced in the mid to late 1980s and spread of the virus was limited.

Although these separate epidemic classifications were helpful at the time, with the continued spread of the epidemic, these patterns are no longer clearly segregated and have, therefore, lost their usefulness. For example, as late as 1988 Asia was classified as an area with pattern III transmission with few infections (most of which had been acquired from those living outside of the region) [1]. The preliminary assumption that the epidemic pattern of spread in this region might be less acute turned out to be wrong. Some pattern III countries, such as Thailand and India, have recently seen an explosive spread of the virus. Furthermore, in pattern I countries, the most rapid increase of HIV transmission is currently through heterosexual, not homosexual, intercourse. In some impoverished inner-city populations of the United States with a high incidence of cofactors such as sexually transmitted diseases (STDs), the pattern of heterosexual transmission resembles that seen in sub-Saharan Africa. These findings raise the disturbing question of whether any pathways of introduction of the virus will ultimately lead to an epidemic among heterosexuals in the vulnerable population of the country. If so, it becomes important to identify the factors

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Table 1. Geographical distribution of human immunodeficiency virus infections

Region	Estimated HIV prevalence	Estimated cumulative infections to date
Australasia, North America, and Western Europe	> 1.2 million	> 1.5 million
Latin America and the Caribbean	> 1.3 million	1.5 million
Sub-Saharan Africa	> 6.5 million	> 8 million
Asia	2 million	2 million
Global total	**> 11 million**	**> 13 million**

NOTE. WHO/Global Programme on AIDS estimates for 1993.

that will determine the magnitude of that epidemic. Although some of these potential factors have been studied, such as the number of partners and the rate of partner change and cofactors such as STDs and male circumcision practices, others remain to be elucidated.

HIV in the World

WHO estimates that by mid 1993, the prevalence of HIV infection worldwide was >11 million, with a cumulative total of >13 million persons infected since the beginning of the epidemic [2a]. Of these, ~1 million are children. The rate of increase is such that ~1 million persons were infected in the first 6 months of 1993. By 1993, >75% of the new infections were occurring through heterosexual intercourse. Table 1 demonstrates the geographical distribution of infections. Developing countries account for >85% of the infections. Perhaps even more striking is the distribution of infection by gender. Although >40% of the infections are occurring in females, the geographical distribution of infection by gender is very skewed: infected female adults in Africa account for >80% of the overall number of infected female adults in the world.

There have been reports of >600,000 cases of AIDS in adults. WHO estimates, however, that when delays in reporting, underdiagnosis, and under-reporting are considered, the real total is likely to be 2.5 million [2a]. Close to 70% of these cases have occurred in sub-Saharan Africa.

Sub-Saharan Africa

WHO estimates that as of June 1993 there were >6.5 million HIV infections in sub-Saharan Africa, making over one-half of the total number of infections in the world attributable to this region. Although all countries in sub-Saharan Africa have now documented HIV infections, rates vary by country, with the highest rates seen in East, Southern, and Central Africa. In contrast, most West African communities have low but rising rates of infection. Although the vast majority of HIV infections on the continent are due to HIV-1, areas of West Africa and Portuguese-speaking countries in Africa have substantial numbers of HIV-2 infections. Even in these areas, HIV-1 infection seems to be spreading rapidly and will probably surpass HIV-2 infection as a public health problem.

High infection rates in Africa were first recognized among commercial female sex workers (CFSWs). These women, often working in urban areas and along trucking routes, rapidly became infected (core transmitters), which in turn led to large numbers of secondary infections. Over time, however, in countries with the highest infection rates, HIV has become so widely distributed in the general population that the concept of core high-risk groups for transmission has lost meaning [3].

In Africa, heterosexual transmission accounts for the vast majority of infections (>80%), with perinatal (<10%) and parenteral transmission (<10%) accounting for smaller percentages. Most parenteral transmission is through blood transfusion. Although some transmission is undoubtedly from contaminated injection equipment and instruments used for scarification, such a mode accounts for only a small percentage of cases [4]. Numerous studies have demonstrated that homosexuality or use of intravenous drugs as a risk factor for transmission in sub-Saharan Africa is rare.

In African populations, rates of infection begin to rise with the onset of sexual activity in teenagers and the incidence peaks in women 20–24 years old and ~5 years later for men. Surveys in a number of countries have demonstrated a higher infection rate in females than in males [5]. Although urban areas bore the brunt of infections during the first half of 1980, infection rates in rural areas are rising. Given the population distribution of Africa—with 70%–90% of the population living in rural areas—rural areas will soon have the highest absolute numbers of HIV infections.

Asia

Asia is home to one-half of the world's population. In this region, the last decade has brought an improvement in living conditions and substantial economic growth. Unfortunately, it also contains the area with the fastest growing HIV epidemic. Due to the explosive spread of HIV infection in Southeast and South Asia, recent estimates suggest that 2 million persons in Asia may be infected with HIV and that the number of new infections will surpass that in Africa before the end of the decade [6].

Thailand

In 1986, only 1 year after a male prostitute in Bangkok became the first HIV-infected person identified in Thailand, thousands of Thais were tested for HIV as part of a clearance

procedure for their becoming visiting laborers in the Middle East: none were positive [7]. This provided support for the optimistic and hubristic arguments proffered by some senior Thai health experts that Asians might be immune to the disease. In a few years, complacency was replaced by fear as the epidemic exploded through all sectors of the country.

Despite the opportunity for transmission of HIV through Thailand's well-known sex industry, the first groups to show extensive spread were the IVDUs. A series of surveys done of various groups in different areas during 1988 demonstrated abundant infections, including an unprecedented 3%–5% increase in the infection rate per month in Bangkok [8]. Recent studies (June 1992) show the median national provincial prevalence in IVDUs to be 36% (Thailand Ministry of Public Health, Epidemiologic Division) and demonstrate the extent of the infection in all areas surveyed in Thailand. Although the number of IVDUs in Thailand is unknown, recent estimates suggest that Bangkok has 36,600 IVDUs among a total population of 6 million [9]. This large number of IVDUs and their high infection rate demonstrate the potential for further spread within the country. Active educational campaigns, including campaigns promoting the non-sharing of equipment, use of bleach for the cleaning of shared equipment, and use of condoms for sexual encounters, have showed some limited success [10].

Dramatic spread in Thailand was next demonstrated in CFSWs. The initial surveys in the national sentinel surveillance system, which began in June 1989, demonstrated infection rates of 44% in CFSWs in brothels in Chiangmai province and of 1%–5% in brothels in 12 other provinces [11]. These striking findings in Chiangmai were confirmed by further studies in that province during August 1989, which demonstrated a prevalence of HIV infection of 36% among 238 CFSWs working in 14 brothels [12]. The demonstration of HIV seroconversion by those seronegative in the first survey and retested in the second reinforced this finding; 20% were seropositive—an astounding seroconversion rate of 10% per month. In 1990, the sentinel surveillance system was expanded to include all provinces. Further surveys have shown that the prevalence continues to rise in all provinces. The median infection rate for women working in brothels has increased from 3.5% in June 1989 to 23.8% in June 1992 (figure 1) [13].

These findings, disturbing in any society, are particularly worrisome for Thailand, however, because prostitution is common and the rates of turnover and migration within the profession are high. The annual census of prostitution by the Thai Ministry of Public Health in January 1990 recorded 86,494 CFSWs working in 6,160 establishments. It is certain, however, that this is an underestimate and that the actual number may be as high as 500,000 [7]. There is a thriving tourist trade in commercial sex, but despite the notoriety of this tourist trade, it is not this group that is responsible for the highest rates of transmission. In a variety of studies, less-

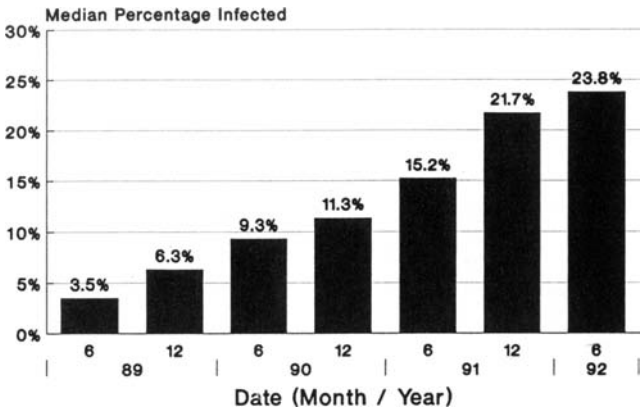

Figure 1. Number of infections with human immunodeficiency virus between June 1989 and June 1992 among commercial female sex workers in brothels in Thailand (data provided by the Epidemiology Division, Thailand Ministry of Public Health).

expensive CFSWs who serve blue-collar Thai workers, had higher rates of HIV infection than those serving white-collar Thais or tourists [14]. Thai males commonly employ CFSWs; studies have shown that from 43% to 97% have employed a CFSW at some time [15]. In a study to determine the sexual risk of adolescent Thais, a geographically stratified random sample composed of 2,801 persons were interviewed. The average age at first intercourse was 17.2 years for males, and 44.1% had their first sexual encounter with a prostitute [16]. There are significant gender differences in outcomes of the first sexual experience. Although 98% of the females married or developed a long-term relationship with their first sexual partner, even among those males whose first sexual contact was not with a prostitute, only 54% showed a similar behavior. As fewer than 1% of females report having sexual encounters outside of their regular relationships, most females other than CFSWs who are becoming infected are contracting HIV from their husbands or steady sexual partners [17]. Thus, programs that primarily target females without attempting to change the sexual behavior of males will do little to halt the spread of the epidemic among heterosexuals. This situation is reflected in other societies but has not always been acknowledged by those designing prevention programs. Innovative programs to change the sexual behavior of men are urgently needed.

Prostitution, although technically illegal in Thailand, does not carry the same social stigma as in western countries. A survey of older primary- and secondary-school students from 55 schools in two northern Thai provinces found that although students were aware of commercial sex and of the overtly negative stigma it carried, they already had developed rationalizations for their future engagement in commercial sex [18]. They also felt that most men would be willing to marry a woman who had worked as a commercial sex worker, further indicating the lack of stigma in Thai society.

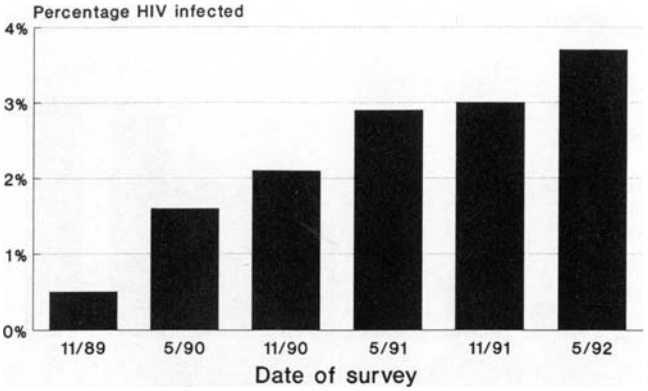

Figure 2. Infections with human immunodeficiency virus among randomly selected 21-year-old military recruits in Thailand.

The severity of the epidemic is reflected in recent data from the Thai military. Theoretically, all 21-year-old men in Thailand are required to participate in the draft lottery (although some are able to obtain exemptions, it is felt to be a representative sample). An HIV test is required as part of the registration process. The prevalence of the infection in these recruits has been rising steadily (figure 2) and has reached extremely high levels in the north, where the prevalence of infection among registrants from Chiang Mai and Chiang Rai was 10.5% and 15.3% in May 1991, respectively [19]. HIV infection is now also being seen among low-risk women in the general population. Rates of HIV infection in women using government antenatal clinics have risen from 0 in June 1989 to 1% in June 1992 (Thailand Ministry of Public Health, Epidemiologic Division).

Once the magnitude and seriousness of the problem had become clear in Thailand, various innovative programs were started to prevent transmission, and an active research program was instituted to evaluate the efficacy of these measures. In addition to education for the general population and health care workers, special targeted efforts were initiated for sex workers at brothels. Door-to-door engagement and training of brothel owners, often with the threat of police closure, has led to implementation of educational programs, including the use of peer educators, for the CFSWs [20]. Effectiveness has been monitored by researchers, and condom use has increased from 10% to 20% before the programs were instituted to 80% to 94% afterwards [20]. Nevertheless, focus group interviews have suggested that CFSWs still have difficulty negotiating with the men who refuse to use condoms, particularly when men offer more money for sex without a condom [21]. The Thais have realized pragmatically that a policy of condom use for 100% of sexual encounters needs to be developed for all CFSWs in Thailand [22]. In response, on 14 August 1991, the Thai national AIDS program approved such a mandatory condom policy [22], which dictates that services would be withheld from a customer who refuses to use a condom. This policy requires all establishments to comply to ensure that those who seek sex without a condom will not be able purchase services anywhere in the province. The success of this approach will need to be carefully monitored.

Because of the rapid spread of infection, it is estimated that 400,000–600,000 persons in Thailand have already been infected with HIV out of a population of 56 million (2% of the sexually active population). One model has suggested that there will be as many as 3.5 million HIV infections in Thailand by the year 2000 [23].

As part of the effort to prepare for the possible development of an HIV vaccine in the future, as well as to gain a better understanding of transmission, the molecular epidemiology of the infection in Thailand has recently been studied [24]. An intriguing finding has been of the presence of two genetically distinct strains that are too different to have diverged from the same precursor during the substantive spread of HIV in Thailand. Among those persons infected through heterosexual intercourse, 91% had the type A strain, and among IVDUs, 75% had the type B strain. This nonrandom mixing suggests that the epidemics are distinct and that spread of HIV infection to the heterosexual community did not occur through those using intravenous drugs or that these viruses exhibit some transmission tropism. Regardless, this important finding needs to be confirmed and further studied.

India

The situation in India is much less clearly defined than that in sub-Saharan Africa or Thailand. It is, however, the part of the world that has the international public health community most worried because of the enormous potential for transmission, given the size of the population, the prevalence of potential cofactors for transmission, and findings in early studies. Scattered and limited evidence shows disturbing trends that suggest India is following an epidemic curve similar to that seen in Thailand. The distribution of infection (21 of 23 states have detected at least one HIV infection), as well as the high infection rates in some risk groups, suggests a major epidemic. As the second most populous country in the world, with a population of 850 million, rapid unrestricted spread could quickly make India home to more HIV infections than any other country. The Indians are aware of this, and despite having officially reported only 238 cases of AIDS for the entire country as of September 1992, they have described India as a country sitting on top of an AIDS volcano waiting to erupt. WHO estimates that by late 1992, 1 million (600,000–3,000,000) individuals had already been infected in India, primarily in a few of the large cities [6]. The wide range of estimates reflects the almost complete absence of peer-reviewed published studies on HIV infections in India

that adequately describe the sampling methodology, a problem most likely related to the relatively late spread of HIV in this area and, as a result, the scarcity of researchers working on HIV. The studies available from conference proceedings and the news media are limited in their scope and methodology and, therefore, in their generalizability.

In India, high levels of infections have been determined to be present in three groups with risky behaviors: CFSWs, IVDUs, and professional blood donors. Results of studies of the prevalence of infection among CFSWs range from finding no infections to finding high rates in small samples. Regular samplings in the Bombay area have shown an increase from 1.1% in 1985–1986, to 18.1% in 1990, to 34.4% for the first half of 1992 [25, 26]. On the basis of these and other data, WHO has estimated that 20% of the estimated 100,000–300,000 CFSWs in the Bombay area are infected with HIV [27]. CFSWs in other areas have also been determined to have high rates of HIV infection. Rates have steadily increased among CFSWs in Madras from 2.8% in 1987 to 4.9% in 1989 [28]. Other authors have suggested that rates are much higher—30%–60% in major cities and towns—although these claims are not easily substantiated [29].

IVDUs in India also have experienced a rapid spread of infection. The number of IVDUs is unknown, although one author has suggested rates of use of 1%–2% in the general urban population in states in the northeast (Manipur, Mizoram, Nagaland) [30]. In this area, no infections were found in over 2,000 tests from 1986 to 1989. In October 1989 a prevalence of 2.9% was noted in a cross-sectional survey, and in 1992 HIV infection had increased to 50% to 60%. In a study to determine the role of transport and heroin tracking on IVDUs, the percentage of IVDUs in areas close to, distant from, and very distant from the national highway connecting Manipur to Myanmar (Burma) was determined. The prevalence of IVDUs was 1.3%, 0.9% and 0.2%, respectively, with HIV infection rates among IVDUs of 50%–51% in all three areas [31].

Infection rates in IVDUs in neighboring Myanmar also have risen dramatically, and although the available data are insufficient, a study has shown rates as high as 76% [29]. Studies of other risk groups in Myanmar have confirmed the high rate of transmission. In patients with STDs, rates of HIV infection have increased from 1.9% in 1990 to 15.9% in 1991 and in CFSWs, rates increased from 8% to 15.9% during the same period [6]. It is estimated that as of late 1992 a total of 100,000–150,000 persons had been infected with HIV [6].

The findings of screening studies of blood donors in India, although also limited, have varied by region, but most studies have shown higher rates of HIV infection among paid donors vs. unpaid donors [32, 33]. Paid donors in India tend to be extremely poor. In one study 93% of them had no fixed abode, 90% had been donating blood for money for >5 years, and most were HIV infected (86%) [34]. Limited studies of infection rates among patients at STD clinics and in the general population are showing steady increases, findings suggesting the beginning of wider spread to the heterosexual population [35].

There is also controversy about the spread of HIV-2 in India. Some studies have shown high rates of infection with HIV-2 as well as high rates of dual infection with HIV-1 and HIV-2. These claims were validated by testing blood samples from high-risk persons from the STD clinic in Bombay at the Georg-Speyer-Haus in Frankfurt; 49% were found to be infected with HIV-1, 6% with HIV-2, and 13% with both [36]. WHO has confirmed the presence of these infections (David Heymann, personal communication, 18 September 1992). Most of these infected individuals had not traveled outside of India, indicating that HIV-2 is being transmitted within India. Since transmission of HIV-2 in other areas has been linked to former Portuguese colonies, the role, if any, of Goa in the transmission of HIV-2 in India needs to be elucidated.

Latin America and the Caribbean

Although Latin America is not covered in detail in this paper, a brief review of the characteristics of the epidemic is warranted for the sake of completeness. The epidemic of HIV infection in Latin America and the Caribbean is heterogeneous and is rapidly changing. As of September 1992, a total of 60,217 cumulative cases of AIDS had been reported, and it is currently estimated that >1.5 million persons in Latin America and the Caribbean have been infected [37]. Spread of HIV in Latin America probably began about the same time as in North America. The primary groups afflicted were homosexual or bisexual men and IVDUs, a pattern leading to a very high ratio of males to females infected. In some countries in the Caribbean, such as Haiti, however, epidemic patterns have been more similar to those in sub-Saharan Africa. In many countries in Latin America, heterosexual transmission has been on the rise since the mid- to late 1980s and may soon become the major mode of transmission.

Tuberculosis

One particular issue in the epidemiology of international AIDS that deserves special attention is the association between tuberculosis and HIV infection in the developing world. In many regions, tuberculosis is the most common opportunistic infection in those individuals with AIDS. Most cases of clinical tuberculosis in HIV-infected persons are due to reactivation of latent infections. The annual risk of development of clinical tuberculosis in those with latent infection has ranged from 5% to 8% in those with concomitant HIV

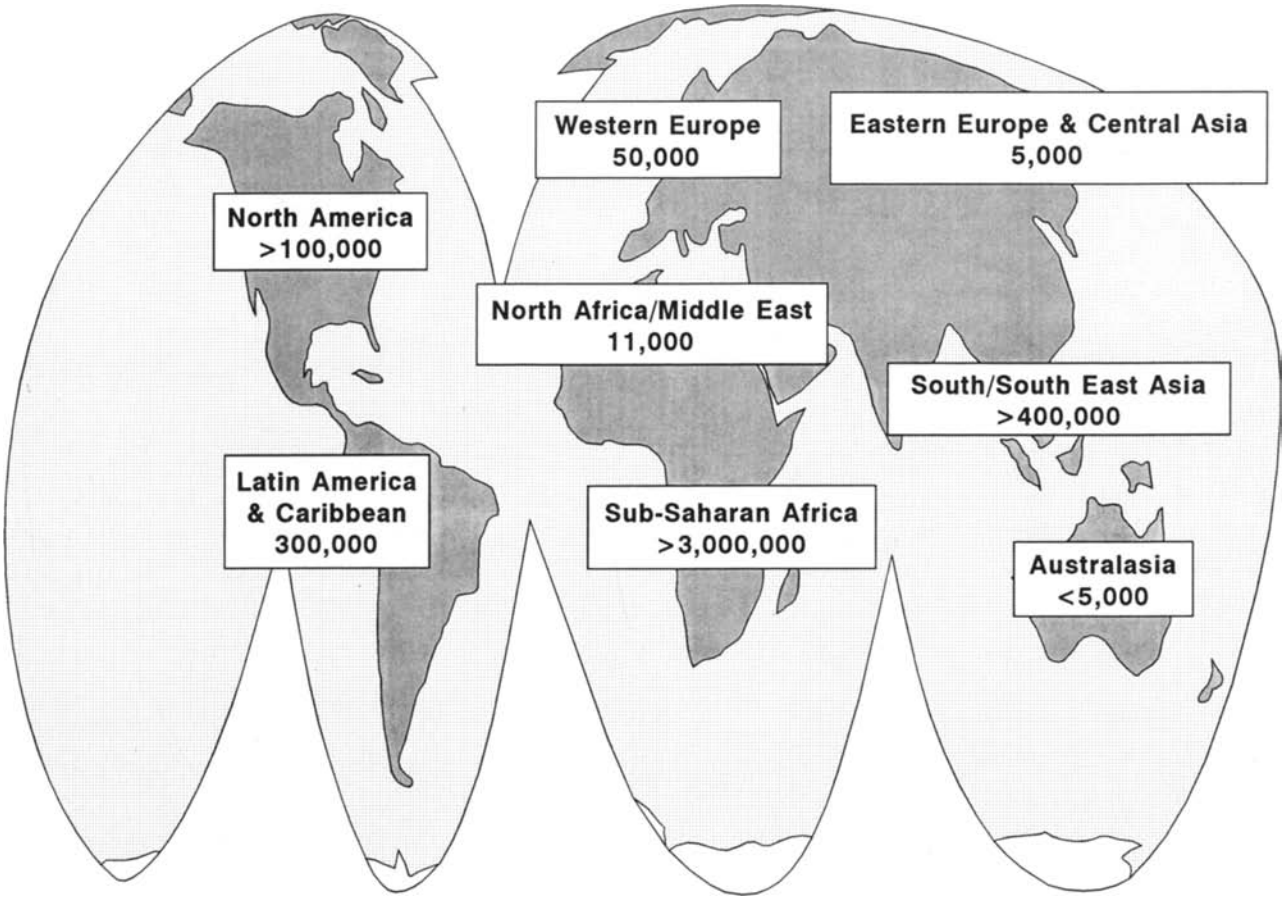

Figure 3. Estimated number of persons 15–49 years old coinfected with human immunodeficiency virus and the tubercle bacillus (global total, >4,000,000). Source: WHO, 1992.

infection vs. 0 to 0.8% in those without HIV infection [38]. The cumulative lifetime risk in those dually infected may be as high as 30%. It is estimated that currently 4 million persons are coinfected with HIV and the tubercle bacillus. As can be seen in figure 3, the vast majority of these are in sub-Saharan Africa. As an estimated 1.7 billion persons throughout the world are infected with the tubercle bacillus, the progression of the HIV epidemic will intensify the problem, in terms both of the role of tuberculosis as an early opportunistic infection in those infected with HIV and of increased spread to the general population [38]. In addition, there recently has been a large worldwide increase in multidrug-resistant tuberculosis strains [39]. Low compliance with tuberculosis therapy in some persons dually infected with HIV in combination with a weakened immunologic response have permitted the selection of some organisms resistant to virtually all drugs used for tuberculosis therapy. The case-fatality rate for these patients may be >80% [39]. Attention must be given to this problem before multiresistant strains become the norm. The implications for diagnosis, treatment, and prevention of this new tuberculosis epidemic are vast.

The Future

It is difficult to predict the future course of the HIV epidemic. The assumptions necessary to construct a reliable model (baseline rates of infections; doubling time; efficacy of transmission; and the effect of transmission-enhancing risk factors such as STDs and their prevalence; incubation periods; and survival times) are not well quantified. Thus, how HIV will spread among future populations must be considered unknown, particularly in areas such as India, where even the current magnitude of spread is still relatively unknown. Perhaps even more important is our lack of knowledge about the extent to which risky behaviors will be changed over the next few years among different groups. Despite these difficulties, WHO has estimated that by the year 2000, there will be 26 million persons infected with HIV, representing a cumulative total of 30–40 million persons infected since the beginning of the pandemic. Because 90% of the HIV infections will be in developing countries, there is the disturbing possibility that HIV will begin to be seen as "another tropical disease" and will be ignored by the research and policy-making communities.

In addition to the continued spread of the virus, during the 1990s and beyond, countries will have to deal with the social and economic consequences of the infections that occurred in the 1980s. As infections spread through families and communities, coping mechanisms will be overwhelmed. WHO estimates that by the year 2000, there will be >10 million children orphaned by AIDS. It is not yet clear how society will deal with the increase in childhood mortality and the increase in dependency, as working-age infected persons become ill and die and leave the very young and old.

It should be clear from the previous discussions that HIV will have a dramatic effect in many countries for the foreseeable future. Epidemiological patterns are changing, and thus each country must have the capacity to monitor the infection and evaluate its interventions. Active prevention programs are under way in most countries, and successful strategies are beginning to be documented and replicated [40]. The extent to which the dramatic spread of the epidemic can be halted is not known. The international scientific and aid communities have responded to this epidemic with unprecedented resources, but many more are needed. More important, even if human and financial resources are made available, the political will to provide the leadership to attack this difficult and sensitive problem will be necessary. Only then will the world be truly prepared to provide what is needed to stop the spread of the epidemic and to assist communities to cope with the individual and societal consequences of infection.

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