

### 3. HIV-1 Infection

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## Epidemiology

### Origin

The human immunodeficiency virus entered into human populations in central Africa. Although it is not known how recently this occurred, it is clear that the emergence of HIV into wider populations was the result of urbanization and modern transportation (e.g., truck drivers). Retrospective analyses of stored sera have documented the presence of HIV infection in Africa as early as 1959. The veracity of a report documenting AIDS in a British sailor in 1959 has been questioned. Several studies have documented seroprevalence rates of approximately 1 percent in ordinary populations in Zaire by the early to mid-1970s.

### Industrialized Nations

The AIDS epidemic in the United States and Europe, first recognized in 1981, has focused on several "high-risk" groups: homosexual and bisexual males, intravenous drug users and recipients of blood products. More recently, the female sexual partners of these individuals and their children have been the groups with the greatest rate of increase of HIV infection. In the general population, seroprevalence rates are approximately 0.01 to 0.1 percent.

### Developing Nations

The characteristics of the AIDS epidemic in developing nations are considerably different from those in industrialized nations. Heterosexual transmission and much more rapid spread are the norm. High-risk groups, including commercial sex workers and IV drug users, exist within the general population and have spread HIV infection. Although HIV infection is focused in urban areas, infection is rising most rapidly in rural areas.

**Africa.** HIV infection spread most rapidly in Africa during the 1980s. By 1990, as much as 20 percent of the general population and 30 percent of the urban population was HIV-infected in some countries, including Malawi, Rwanda and Uganda.

**Asia.** During the past decade, HIV infection has exploded in Asian countries. At present, Thailand and India have large populations of HIV-infected individuals, while China and Burma are lagging several years behind but showing virtually identical patterns of infection. Figures in Thailand demonstrate the spread of infection: in 1988 there were approximately 12,000 HIV-infected individuals and 18 reported cases of AIDS; by 1993 the figures were 700,000 HIV infections and 8000 AIDS cases. In India, seroprevalence among clients at a STD clinic has risen from less than 5 percent in 1988 to 40 percent in 1993. The epidemic in India may have several foci (e.g., CSWs in Bombay and Goa, IV drug users in NE India).

**Latin American and the Caribbean** Haiti was one of the original foci of the HIV epidemic, and seroprevalence is estimated at 10 percent in urban areas and 4 percent in rural areas. Brazil is the most severely affected country in South America.

### Viral Variation and Tracking the Spread of the Epidemic

HIV isolates can be broken down into different families, or clades, based on degrees of similarity of genetic sequence. Using these relationships as an epidemiological tool, one can determine how the infection spread. All HIV types are found in Africa. Types of HIV prevalent in Europe and North America are closely-related. The HIV found in India is different from that in Thailand.

## **Transmission**

HIV is an extremely fragile virus—it is killed by drying, for example. Thus, transmission requires intimate contact. The major modes of transmission include sexual intercourse, systemic inoculation through IV drug use or transfusion, and vertical transmission from mother to child. There is no evidence for aerosol or insect-borne transmission. Rare reports of transmission among household members who were not sexually intimate suggest that shared toilet items (e.g., toothbrushes and razors) can transmit infection.

Heterosexual transmission can occur from both male to female and female to male. Male to female transmission is 2 to 10 times more likely to occur than the reverse. In North America and Europe male to female transmission frequency has been estimated at .001 per act of intercourse, although a recent Thai study of female to male transmission gave the frequency of transmission as .03 to .05 per act.

Factors known to increase the likelihood of sexual transmission of HIV infection include:

- other sexually transmitted diseases, particularly those that lead to open lesions;
- lack of circumcision;
- intercourse during menses;
- anal sex; and
- stage of disease and virus load.

Sexual transmission can be limited by condom use and, to a lesser degree, by extravaginal ejaculation. Sexual transmission via oral routes has been reported, but is probably extremely infrequent.

The biological mechanism underlying the sexual transmission of HIV is not completely understood. In particular, the question of whether the mucosal epithelium is directly infected or whether infection traverses the epithelium to underlying lymphoid cells needs to be answered.

Vertical transmission of HIV can occur antenatally, perinatally and perhaps following birth through breastfeeding. (HIV has been shown to be present in breast milk.) Transmission occurs in 20 to 30 percent of births to infected mothers. Most transmission appears to occur perinatally. Maternal viral load is the major factor associated with transmission. Administration of anti-viral drugs to infected mothers may significantly reduce mother to child transmission.

Viral factors may influence the transmission of HIV. In Thailand, the epidemic initially involved viruses of two different clades (B and E) in roughly equal proportions. At the present time, more than 80 percent of new infections are due to clade E. The question of whether these viruses are more infectious has not been determined.

## **Diagnosis**

Laboratory diagnosis of HIV infection is performed by testing for anti-HIV antibody. Initial screening is by ELISA assay, with confirmation made by Western blotting. Confirmation is critical, since false positives can occur. The US Army has estimated the cost of HIV screening at \$1.50 per individual. There is generally a window of 1 to 3 months following infection before antibody develops.

There are a number of assays for measuring the degree of viremia. Such assays measure either viral antigens or determine the presence of viral nucleic acids. These are research tools and not of diagnostic use.

## **Management of HIV Infection**

Supportive care and management of opportunistic infections through treatment and prophylaxis are the most effective strategies. Anti-viral therapy is expensive and of limited value due to the ability of HIV to evolve drug resistance rapidly.

## **Prevention**

### **Education**

At the present time, the only means of preventing the spread of HIV infection is to educate populations at risk regarding high-risk behaviors. The difficulties of this are illustrated by a recent study of couples with stable heterosexual relationships with one HIV-infected partner. In this very high-risk situation with couples who received active education and counseling, less than half the couples used condoms consistently and more than 10 percent continue to have unprotected anal intercourse. Intravenous drug users are even less amenable to education.

### **Vaccines**

The development of vaccines to prevent HIV infection has been a major goal of AIDS research. A number of important unanswered questions exist, the primary concerning whether there is any form of protective immunity as result of exposure to HIV:

- Does one HIV infection protect against subsequent infections?
- Are there people who have been exposed to HIV, but never seroconvert or develop disease?
- Can spontaneous recovery from HIV infection occur?

Other issues, such as the ability of HIV to vary and our ability to induce mucosal immunity, pose additional problems.

A first round of testing of subunit vaccines, based on recombinant forms of the HIV envelope protein, has been performed. Large doses and multiple immunizations have been required to induce antibody responses. These vaccines have produced low levels of antibodies that cross-react with other strains of HIV. Some vaccine recipients have become infected with HIV. Although results have been discouraging, it is likely that a second round of testing with some of these vaccines will evaluate their efficacy in preventing disease.

Additional generations of AIDS vaccines are being created that have broader targets and use newer methods, such as replicating vectors and DNA immunization. Such vaccines will soon be undergoing phase I clinical trials.

While there is hope for the development of an AIDS vaccine, it is unlikely that an effective one will be available for use within the next decade.

## **Physical and Chemical Barriers to Infection**

Several approaches are being taken. Making condoms more acceptable depends on the development of newer materials that will better transmit tactile sensation, be less likely to cause allergic reactions and maintain their ability to act as a barrier to HIV. Vaginal microbicides also may be useful.

## **Prevention of Other STDs**

Since the presence of other sexually transmitted diseases has been shown to be a risk factor for the spread of HIV infection, it stands to reason that decreasing the incidence of these infections may slow the spread HIV.

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