

not readily available in many developing countries, and toxic side effects remain problems. The advent of these drugs raises its own tragic concern; because more people are living with HIV, the risk of spreading the infection will increase if vigilance is relaxed.

The enormous medical and social burden of AIDS has led to an explosion of research aimed at understanding HIV and its remarkable ability to cripple host defenses. The literature on HIV and AIDS is vast. Here we summarize the currently available data on the epidemiology, pathogenesis, and clinical features of HIV infection.

### Epidemiology

Epidemiologic studies in the United States have identified five groups of adults at high risk for developing AIDS. The case distribution in these groups is as follows:

- **Homosexual or bisexual men** constitute the largest group, accounting for more than 50% of the reported cases. This includes about 5% who were intravenous drug abusers as well. Transmission of HIV in this category appears to be on the decline: in 2009 about 60% of new cases were attributed to male homosexual contacts.
- **Intravenous drug abusers** with no previous history of homosexuality are the next largest group, representing about 20% of infected individuals and 9% of new cases in 2009.
- **Hemophiliacs**, especially those who received large amounts of factor VIII or factor IX concentrates before 1985, make up about 0.5% of all cases.
- **Recipients of blood and blood components** who are not hemophiliacs but who received transfusions of HIV-infected whole blood or components (e.g., platelets, plasma) account for about 1% of patients. (Organs obtained from HIV-infected donors can also transmit the virus.)
- **Heterosexual contacts** of members of other high-risk groups (chiefly intravenous drug abusers) constitute about 20% of the patient population. About 30% of new cases in 2009 were attributable to heterosexual contact. Heterosexual transmission, although initially of less numerical importance in the United States, is globally the most common mode by which HIV is spread. In the past few years, even in the United States, the rate of increase of heterosexual transmission has outpaced transmission by other means. In sub-Saharan Africa, where the infection rate is estimated to be about 10,000 new cases every day, more than half the infected individuals are women. Spread of the virus is occurring most rapidly in female sex partners of male intravenous drug abusers. As a result, the number of women with AIDS is rising rapidly. In contrast to the experience in the United States, heterosexual transmission has always been the dominant mode of HIV infection in Asia and Africa.
- **HIV infection of the newborn.** The epidemiology of AIDS is quite different in children younger than 13 years. Close to 2% of all AIDS cases occur in this pediatric population, and worldwide more than 500,000 new cases and almost 400,000 deaths were reported in children in 2006. In this group, the vast majority acquired the infection by transmission of the virus from mother to child (discussed later).
- In approximately 5% of cases, the risk factors cannot be determined.

It should be apparent from the preceding discussion that transmission of HIV occurs under conditions that facilitate exchange of blood or body fluids containing the virus or virus-infected cells. **The three major routes of transmission are sexual contact, parenteral inoculation, and passage of the virus from infected mothers to their newborns.**

- **Sexual transmission** is clearly the dominant mode of infection worldwide, accounting for more than 75% of all cases of HIV transmission. Because the majority of infected people in the United States are men who have sex with men, most sexual transmission has occurred among homosexual men. The virus is carried in the semen, and it enters the recipient's body through abrasions in rectal or oral mucosa or by direct contact with mucosal lining cells. Viral transmission occurs in two ways: (1) direct inoculation into the blood vessels breached by trauma and (2) infection of dendritic cells or CD4+ cells within the mucosa. In addition to male-to-male and male-to-female transmission, there is evidence supporting female-to-male transmission.

**Sexual transmission of HIV is enhanced by coexisting sexually transmitted diseases**, especially those associated with genital ulceration. In this regard, syphilis, chancroid, and herpes are particularly important. Other sexually transmitted diseases, including gonorrhea and chlamydia, are also cofactors for HIV transmission, perhaps because in these genital inflammatory states there is greater concentration of the virus and virus-containing cells in genital fluids, as a result of increased numbers of inflammatory cells in the semen.

- **Parenteral transmission** of HIV has occurred in three groups of individuals: intravenous drug abusers, hemophiliacs who received factor VIII and factor IX concentrates, and random recipients of blood transfusion. Of these three, intravenous drug users constitute by far the largest group. Transmission occurs by sharing of needles, syringes, and other paraphernalia contaminated with HIV-containing blood.

Transmission of HIV by transfusion of blood or blood products, such as lyophilized factor VIII and factor IX concentrates, has been virtually eliminated. This fortunate outcome resulted from increasing use of recombinant clotting factors and from three public health measures: screening of donated blood and plasma for antibody to HIV, stringent purity criteria for factor VIII and factor IX preparations, and screening of donors on the basis of history. However, an extremely small risk of acquiring AIDS through transfusion of seronegative blood persists, because a recently infected individual may be antibody-negative. Currently, this risk is estimated to be 1 in more than 2 million units of blood transfused.

- As alluded to earlier, **mother-to-infant transmission** is the major cause of pediatric AIDS. Infected mothers can transmit the infection to their offspring by three routes: (1) in utero by transplacental spread, (2) during delivery through an infected birth canal, and (3) after birth by ingestion of breast milk. Of these, transmission during