birth (intrapartum) and in the immediate period thereafter (peripartum) is considered to be the most common mode in the United States. The reported transmission rates vary from 7% to 49% in different parts of the world. Higher risk of transmission is associated with high maternal viral load and low CD4+ T-cell counts as well as chorioamnionitis. Fortunately, antiretroviral therapy given to infected pregnant women in the United States has virtually eliminated mother-to-child transmission, but it remains a major source of infection in areas where these treatments are not readily available.

Much concern has arisen in the lay public and among health care workers about spread of HIV infection outside the high-risk groups. Extensive studies indicate that HIV infection cannot be transmitted by casual personal contact in the household, workplace, or school. Spread by insect bites is virtually impossible. Regarding transmission of HIV infection to health care workers, an extremely small but definite risk seems to be present. Seroconversion has been documented after accidental needle-stick injury or exposure of nonintact skin to infected blood in laboratory accidents. After needle-stick accidents, the risk of seroconversion is believed to be about 0.3%, and antiretroviral therapy given within 24 to 48 hours of a needle stick can reduce the risk of infection eightfold. By comparison, approximately 30% of those accidentally exposed to hepatitis B–infected blood become seropositive.

Etiology: The Properties of HIV

HIV is a nontransforming human retrovirus belonging to the lentivirus family. Included in this group are feline immunodeficiency virus, simian immunodeficiency virus, visna virus of sheep, bovine immunodeficiency virus, and the equine infectious anemia virus.

Two genetically different but related forms of HIV, called *HIV-1 and HIV-2*, have been isolated from patients with AIDS. HIV-1 is the most common type associated with AIDS in the United States, Europe, and Central Africa, whereas HIV-2 causes a similar disease principally in West Africa and India. Specific tests for HIV-2 are available, and blood collected for transfusion is routinely screened for both HIV-1 and HIV-2 seropositivity. The ensuing discussion relates primarily to HIV-1 and diseases caused by it, but the information is generally applicable to HIV-2 as well.

Structure of HIV

Similar to most retroviruses, the HIV-1 virion is spherical and contains an electron-dense, cone-shaped core surrounded by a lipid envelope derived from the host cell membrane (Fig. 6-38). **The virus core contains (1) the major capsid protein p24; (2) nucleocapsid protein p7/p9; (3) two copies of viral genomic RNA; and (4) the three viral enzymes (protease, reverse transcriptase, and integrase).** p24 is the most abundant viral antigen and is detected by an enzyme-linked immunoabsorbent assay that is widely used to diagnose HIV infection. The viral core is surrounded by a matrix protein called p17, which lies underneath the virion envelope. Studding the viral envelope are two viral glycoproteins, gp120 and gp41, which are critical for HIV infection of cells.

The HIV-1 RNA genome contains the *gag*, *pol*, and *env* genes, which are typical of retroviruses (Fig. 6-39). The products of the *gag* and *pol* genes are large precursor proteins that are cleaved by the viral protease to yield the mature proteins. In addition to these three standard retroviral genes, HIV contains several other accessory genes, including *tat*, *rev*, *vif*, *nef*, *vpr*, and *vpu*, which regulate the synthesis and assembly of infectious viral particles and the pathogenicity of the virus. For example, the product of the *tat* (transactivator) gene causes a 1000-fold increase in the transcription of viral genes and is critical for virus replication. The functions of other accessory proteins are indicated in Figure 6-39.

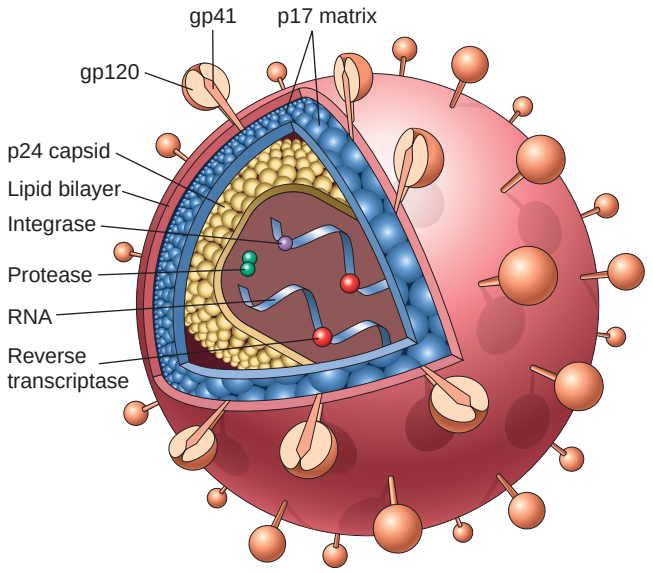

Figure 6-38 The structure of the human immune deficiency virus (HIV)-1 virion. The viral particle is covered by a lipid bilayer derived from the host cell and studded with viral glycoproteins gp41 and gp120.

Molecular analysis of different HIV-1 isolates has revealed considerable variability in certain parts of the viral genome. Most variations are clustered in particular regions of the envelope glycoproteins. Because the humoral immune response against HIV-1 is targeted against its envelope, such variability poses problems for the development of a single antigen vaccine. On the basis of genetic analysis, HIV-1 can be divided into three subgroups, designated *M* (major), *O* (outlier), and *N* (neither *M* nor *O*). Group M viruses are the most common form worldwide, and they are further divided into several subtypes, or clades, designated A through K. Various subtypes differ in their geographic distribution; for example, subtype B is the most common form in western Europe and the United States, whereas subtype E is the most common clade in Thailand. Currently, clade C is the fastest spreading clade worldwide, being present in India, Ethiopia, and Southern Africa.

Pathogenesis of HIV Infection and AIDS

While HIV can infect many tissues, **the two major targets of HIV infection are the immune system and the central nervous system.** The effects of HIV infection on each of these two systems are discussed separately.

Profound immune deficiency, primarily affecting cell-mediated immunity, is the hallmark of AIDS. This results chiefly from infection and subsequent loss of CD4+ T cells

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