

of routes including sexual transmission, shared needles and syringes, and mother-to-child transmission intrapartum, perinatally, or via breast milk.

■ ESTABLISHMENT OF CHRONIC INFECTION

Persistence of Virus Replication HIV infection is unique among human viral infections. Despite the robust cellular and humoral immune responses that are mounted following primary infection (see “Immune Response to HIV,” below), once infection has been established the virus succeeds in escaping complete immune-mediated clearance, paradoxically seems to thrive on immune activation, and is never eliminated completely from the body. Rather, a chronic infection develops and persists with varying degrees of continual virus replication in the untreated patient for a median of ~10 years before the patient becomes clinically ill (see “Advanced HIV Disease,” below). It is this establishment of a chronic, persistent infection that is the hallmark of HIV disease. Throughout the often-protracted course of chronic infection, virus replication can invariably be detected in untreated patients by widely available molecular assays that measure copies of virion-associated HIV RNA in plasma (copies per milliliter). Levels of virus vary greatly in most untreated patients, usually ranging from fewer than 50 to greater than a million copies of HIV RNA per milliliter of plasma. Studies using highly sensitive molecular techniques have demonstrated that even in treated patients in whom plasma viremia is suppressed to below detection (lower limit, 20–50 copies of HIV RNA per milliliter depending on assay kit manufacturer) by ART, there is a continual low level of virion production in the majority of infected patients. In other human viral infections, with some exceptions, if the host survives, the virus is completely cleared from the body and a state of immunity against subsequent infection develops. HIV infection very rarely kills the host during primary infection. Certain viruses, such as HSV ([Chap. 192](#)), are not completely cleared from the body after infection, but instead enter a latent state; in these cases, clinical latency is accompanied by microbiologic latency. This is not the case with HIV infection as described above. Chronicity associated with persistent virus replication can also be seen in certain cases of HBV