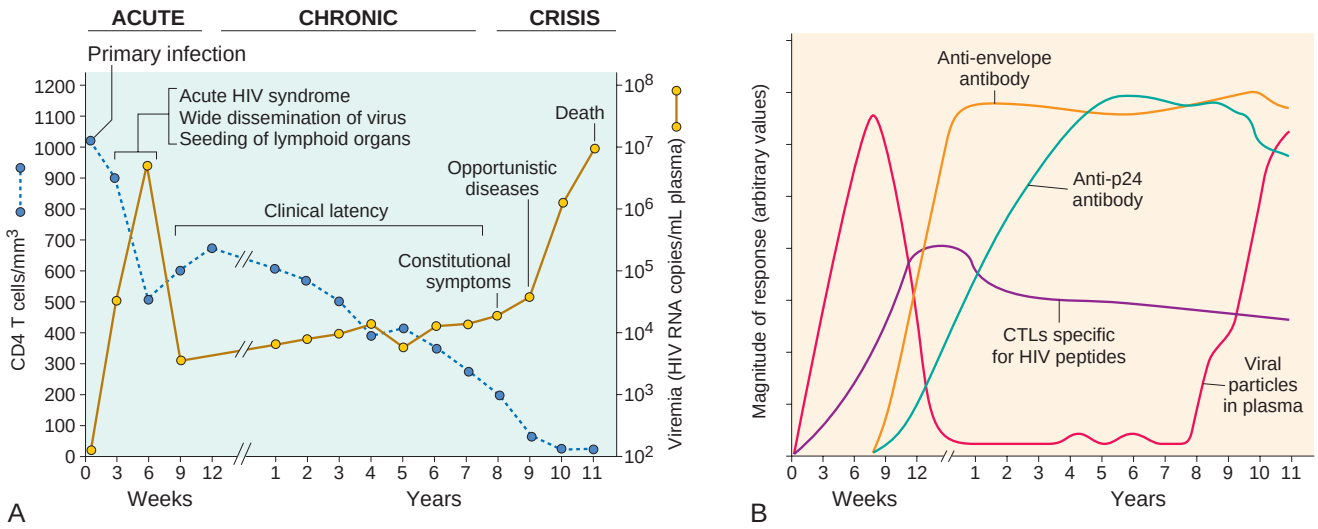

Figure 6-42 Clinical course of HIV infection. **A,** During the early period after primary infection there is dissemination of virus, development of an immune response to HIV, and often an acute viral syndrome. During the period of clinical latency, viral replication continues and the CD4+ T-cell count gradually decreases, until it reaches a critical level below which there is a substantial risk of AIDS-associated diseases. **B,** Immune response to HIV infection. A cytotoxic T lymphocyte (CTL) response to HIV is detectable by 2 to 3 weeks after the initial infection, and it peaks by 9 to 12 weeks. Marked expansion of virus-specific CD8+ T-cell clones occurs during this time, and up to 10% of a patient's CTLs may be HIV specific at 12 weeks. The humoral immune response to HIV peaks at about 12 weeks. (**A,** Redrawn from Fauci AS, Lane HC: Human immunodeficiency virus disease: AIDS and related conditions. In Fauci AS, et al (eds): Harrison's Principles of Internal Medicine, 14th ed. New York, McGraw-Hill, 1997, p 1791.)

the lymph nodes. This replication leads to viremia, during which high numbers of HIV particles are present in the patient's blood. The virus disseminates throughout the body and infects helper T cells, macrophages, and dendritic cells in peripheral lymphoid tissues.

As the HIV infection spreads, the individual mounts antiviral humoral and cell-mediated immune responses. These responses are evidenced by seroconversion (usually within 3 to 7 weeks of presumed exposure) and by the development of virus-specific CD8+ cytotoxic T cells. HIV-specific CD8+ T cells are detected in the blood at about the time viral titers begin to fall and are most likely responsible for the initial containment of HIV infection. These immune responses partially control the infection and viral production, and such control is reflected by a drop in viremia to low but detectable levels by about 12 weeks after the primary exposure.

The *acute retroviral syndrome* is the clinical presentation of the initial spread of the virus and the host response. It is estimated that 40% to 90% of individuals who acquire a primary infection develop this syndrome. This typically occurs 3 to 6 weeks after infection, and resolves spontaneously in 2 to 4 weeks. Clinically, this phase is associated with a self-limited acute illness with nonspecific symptoms, including sore throat, myalgias, fever, weight loss, and fatigue, resembling a flulike syndrome. Other clinical features, such as rash, cervical adenopathy, diarrhea, and vomiting, may also occur.

The extent of viremia, measured as HIV-1 RNA levels, in the blood is a useful surrogate marker of HIV disease progression and is of clinical value in the management of people with HIV infection. The viral load at the end of the acute phase reflects the equilibrium reached between the virus and the host response, and in a given patient it may remain fairly stable for several years. This level of steady-state viremia, called the *viral set point*, is a predictor of the rate of decline of CD4+ T cells, and, therefore, progression of HIV disease. In one study, only 8% of patients with a viral load of less than 4350 copies of viral mRNA per microliter of blood progressed to clinical AIDS in 5 years, whereas 62% of those with a viral load of greater than 36,270 copies developed AIDS in the same period.

Because the loss of immune containment is associated with declining CD4+ T-cell counts, the Centers for Disease Control (CDC) classification of HIV infection stratifies three categories on the basis of CD4+ cell counts: CD4+ cells greater than or equal to 500 cells/μL, 200 to 499 cells/μL, and fewer than 200 cells/μL (Table 6-15). For clinical management, blood CD4+ T-cell counts are perhaps the most reliable short-term indicator of disease progression.

Table 6-15 CDC Classification Categories of HIV Infection

Clinical Categories	CD4+ T-Cell Categories		
	1 ≥500 Cells/μL	2 200-499 Cells/μL	3 <200 Cells/μL
A. Asymptomatic, acute (primary) HIV, or persistent generalized lymphadenopathy	A1	A2	A3
B. Symptomatic, not A or C conditions	B1	B2	B3
C. AIDS indicator conditions: including constitutional disease, neurologic disease, or neoplasm			

Data from CDC. Centers for Disease Control and Prevention: 1993 revised classification system and expanded surveillance definition for AIDS among adolescents and adults. MMWR 1992;41(RR-17):1.