Spectrum of Disease Associated with HIV

Untreated HIV infection usually results in a slow, nonlinear progression to severe immunodeficiency. However, the progression of disease varies greatly among individuals. Within 10 years after infection, approximately 50% of untreated individuals will develop AIDS, 30% will have milder symptoms, and fewer than 20% will be entirely asymptomatic (see Fig. 101-3). Children and adolescents progress to AIDS at a slower rate than older persons; fewer than 30%, in the absence of ART, will develop AIDS within 10 years after HIV infection. The rate of progression of immunodeficiency is not influenced by the route of HIV transmission and, in the long term, does not appear to differ by gender, although typically women with HIV infection tend to experience more rapid disease progression with lower levels of HIV in plasma.

First Impacts of HIV

Clinically recognized lymph node enlargement occurs in 35% to 40% of asymptomatic HIV-infected persons but is not significantly associated with either rate of progression of immunodeficiency or subsequent development of lymphoma. During early HIV infection, thrombocytopenia, probably caused by autoimmune platelet destruction, is common. Most HIV-infected individuals remain asymptomatic until their CD4 count falls to less than 200 cells/mm^3, a fact that contributes to the late diagnosis of disease. In parts of the world where tuberculosis is hyperendemic, persons with HIV with CD4 counts greater than 200 cells/mm^3 are at high risk for development of tuberculosis.

Early Immunodeficiency

Patients with moderate immunodeficiency (CD4 counts between 200 and 500 cells/mm^3) exhibit diminished antibody response to protein and polysaccharide antigens, as well as decreased cell-mediated immune function. These functional impairments are manifested clinically by a threefold to fourfold increase in the incidence of bacteremic pneumonias caused by common pulmonary pathogens (especially *Streptococcus pneumoniae* and *Haemophilus influenzae*) and by a marked increase in incidence of active pulmonary tuberculosis in endemic areas (Table 101-2).

Mucocutaneous lesions may be the first manifestations of immune dysfunction. These include reactivation of varicella-zoster (shingles), recurrent genital herpes simplex virus (HSV) infections, oral or vaginal candidiasis, and oral hairy leukoplakia (see later discussion). The earliest clinical manifestation of HIV infection in women may be frequent recurrence of *Candida* vaginitis in the absence of predisposing factors. Recurrent large, painful genital, perianal, or perineal ulcers caused by HSV type 2, are more frequent in women than in men. HIV-infected women show an increased prevalence of high-grade squamous intraepithelial lesions on Papanicolaou (Pap) smear. Both men and women may show similarly increased rates of dysplasia or neoplasia on rectal Pap smear.

Opportunistic Infections

With advanced immunodeficiency, indicated by CD4 counts lower than 200 cells/mm, patients are at high risk for development of OIs (see Table 101-2). Before the availability of effective antiretroviral drugs and use of prophylactic antibiotics, 60% of HIV-infected North American men developed *Pneumocystis* pneumonia (PCP). Incidence of *Toxoplasma* encephalitis before the availability of ART in the United States was estimated to be as high as 3.9 per 100 patient-years. CD4 counts lower than 50 cells/mm^3 indicate profound immunosuppression and, in the absence of effective ART, are associated with a high mortality rate within the subsequent 12 to 24 months.

Cytomegalovirus (CMV) retinitis, which can lead rapidly to blindness, and disseminated *Mycobacterium avium-intracellulare* (MAI) infection occur frequently in the absence of therapy. They respond adequately to specific therapy only if it is accompanied by effective control of viral replication.

TABLE 101-2 PROGRESSIVE COMPLICATIONS OF HIV INFECTION BY CD4 COUNT

CD4 COUNT (CELLS/MM^3)	OPPORTUNISTIC INFECTION OR NEOPLASM
>500	Herpes zoster
	Tuberculosis
200-500	Oral hairy leukoplakia
	Candida pharyngitis (thrush)
	Kaposi's sarcoma, mucocutaneous
	Bacterial pneumonia, recurrent
	Cervical or anal neoplasia
100-200	*Pneumocystis jirovecii* pneumonia
	Histoplasmosis capsulatum infection, disseminated
	Kaposi's sarcoma, visceral
	Progressive multifocal leukoencephalopathy
	Lymphoma, non-Hodgkin's
<100	*Candida* esophagitis
	Cytomegalovirus retinitis
	Mycobacterium avium-intercellulare
	Toxoplasma gondii encephalitis
	Cryptosporidium parvum enteritis
	Cryptococcus neoformans meningitis
	Herpes simplex virus, chronic, ulcerative
	Cytomegalovirus esophagitis or colitis
	Primary central nervous system lymphoma

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Identification of persons with HIV and support of linkage to effective care are critical public health priorities. Recent studies have demonstrated reduced transmission of HIV associated with ART. Despite the acknowledged priority of early diagnosis, the median CD4 count at diagnosis has remained fairly constant in the range of 175 cells/mm^3, indicating persistent delays in testing and treatment.

The CDC and the U.S. Preventive Services Task Force recommend that all persons between the ages of 13 and 64 years be tested for HIV once, with repeat testing and testing outside of this age group based on assessed risk for infection and reinfection. All pregnant women should routinely be offered HIV testing. The CDC, to meet this goal, further recommends that HIV testing be considered a part of routine medical care, without any requirement for written consent or formal pretest and post-test counseling. Pretest discussion is important to ensure that patients appreciate that they are being tested and that treatment is available if they are found to be HIV positive.

Standard testing for HIV infection begins with detection of antibodies to HIV in serum or in oral fluid. Positive antibody tests are confirmed by assessing for the presence of at least two