The Centers for Disease Control (CDC) has developed a classification system for human immunodeficiency virus (HIV) infection in adolescents and adults that categorizes the clinical conditions associated with the broad spectrum of HIV infection—from no symptoms of HIV infection to severe manifestations of HIV infection. This classification system was created for epidemiologic and clinical purposes. Unlike the CDC’s case definition of AIDS, this classification system is not used for reporting purposes.

The CDC’s current HIV classification system, published in 1986, uses clinical disease states to divide HIV infection into four broad clinical categories. This system is described further in box E-1.

In November 1991, the CDC proposed revising its classification system for HIV infection. The proposed system would sub-categorize the clinical conditions associated with HIV infection on the basis of patients’ CD4+ lymphocyte counts.

As shown in box E-2, the proposed classification system includes three laboratory categories (i.e., ranges of CD4+ lymphocyte counts) and three clinical categories, resulting in a matrix of nine mutually exclusive categories. In incorporating CD4+ lymphocyte counts along with various clinical conditions, the CDC’s proposed classification system for HIV infection is similar to the CDC’s proposed case definition of AIDS (see app. B). The clinical categories in the proposed HIV classification system, however, differ from those in the CDC’s proposed case definition. As shown in box E-2, the clinical categories are as follows:

- **Clinical category A** includes asymptomatic HIV infection, persistent generalized lymphadenopathy, and acute primary HIV infection;
Clinical category B includes a variety of symptomatic conditions which are not included in the CDC’s 1987 surveillance case definition of AIDS, but which may be attributed to HIV infection or whose clinical course or management is complicated by HIV infection; and

Clinical category C includes any condition listed in the CDC’s 1987 surveillance case definition of AIDS.

Clinical category B of the proposed classification system for HIV infection includes some conditions which a physician judges to be HIV-related or the management of which is affected by HIV status. This category includes many of the conditions (e.g., bacterial endocarditis, pneumonia, sepsis, and pulmonary tuberculosis) that are noted to occur more commonly among HIV-infected injection drug users. Clinical category B also includes female-specific symptoms that are not included in the CDC’s 1987 case definition of AIDS. Cervical dysplasia or carcinoma and vulvovaginal candidiasis are included in category B.

The 23 AIDS-defining conditions in the CDC’s 1987 case definition of AIDS, included in clinical category C, have a much stronger relation to impairment of immune function caused by HIV-infection than do the conditions included in category B.
The CDC’s current classification system for HIV infection was published in 1986. At the time, HIV was known as human T-cell lymphotropic virus type III/lymphadenopathy-associated virus.

The current classification system classifies HTLV-III/LAV infection into four mutually exclusive groups, designated by Roman numerals I though IV and described further below. Classification in a particular group is not explicitly intended to have prognostic significance, nor to designate severity of illness. However, classification in the four principal groups, I to IV, is hierarchical, in that persons classified in a particular group should not be reclassified in a preceding group if clinical findings resolve, since clinical improvement may not accurately reflect changes in the severity of the underlying disease.

Group I (Acute HTLV-III/LAV Infection) includes patients with transient signs and symptoms that appear at the time of, or shortly after, initial infection with HTLV-III/LAV as identified by laboratory studies. All patients in Group I will be reclassified in another group following resolution of this acute syndrome.

Group I is defined as a mononucleosis-like syndrome, with or without aseptic meningitis, associated with seroconversion for HTLV-III/LAV antibody (15-16). Antibody seroconversion is required as evidence of initial infection; current viral isolation procedures are not adequately sensitive to be relied on for demonstrating the onset of infections.
Group II (Symptomatic HTLV-III/LAV Infection) includes patients who have had no signs or symptoms of HTLV-III/LAV infection. Patients in Group II may be subclassified based on whether hematologic and/or immunologic laboratory studies have been performed and whether test results are consistent with defects associated with HTLV-III/LAV infection.

Group II is defined as the absence of signs or symptoms of HTLV-III/LAV infection. To be classified in Group II, patients must have had no previous signs or symptoms that would have led to classification in Groups III or IV. Patients whose clinical findings caused them to be classified in Groups III or IV should not be reclassified in Group II if those clinical findings resolve.

Patients in this group may be subclassified on the basis of a laboratory evaluation. Laboratory studies commonly indicated for patients with HTLV-III/LAV infection include, but are not limited to, a complete blood count (including differential with blood cell count) and a platelet count. Immunologic tests, especially T-lymphocyte helper (CD4') and suppressor (CD8') cell counts, are also an important part of the overall evaluation. Patients whose test results are within normal limits, as well as those for whom a laboratory-evaluation has not yet been completed, should be differentiated from patients whose test results are consistent with defects associated with HTLV-III/LAV infection (e.g., lymphopenia, thrombocytopenia, decreased number of helper (CD4') T-lymphocytes).

Group III (Persistent Generalized Lymphadenopathy) includes patients with persistent generalized lymphadenopathy, but without findings that would lead to classification in Group IV. Patients in this category may be subclassified based on the results of laboratory studies in the same manner as patients in Group II.
Group III is defined as palpable lymphadenopathy (lymph node enlargement of 1 centimeter or greater) at two or more extra-inguinal sites persisting for more than 3 months in the absence of a concurrent illness or condition other than HTLV-III/LAV infection to explain the findings. Patients in this group may also be subclassified on the basis of a laboratory evaluation, as is done for asymptomatic patients in Group II (see above). Patients with persistent generalized lymphadenopathy whose clinical findings caused them to be classified in Group IV should not be reclassified in Group III if those other clinical findings resolve.

Group IV (other HTLV-III/LAV) includes patients with clinical symptoms and signs of HTLV-III/LAV infection other than or in addition to lymphadenopathy. Patients in this group are assigned to one or more subgroups based on clinical findings: A) constitutional disease; B) necrologic disease; C) secondary infectious diseases; D) secondary cancers; and E) other conditions resulting from HTLV-III/LAV infection. There is no a priori hierarchy of severity among subgroups A through E, and these subgroups are not mutually exclusive.

The clinical manifestations of patients in this group may be designated by assignment to one or more subgroups (A-E) listed below. Within Group IV, subgroup classification is independent of the presence or absence of lymphadenopathy. Each subgroup may include patients who are minimally symptomatic, as well as patients who are severely ill. Increased specificity for manifestations of HTLV-III/LAV infection, if needed for clinical purposes or research or for disability determinations, may be achieved by creating additional divisions within each subgroup.
Subgroup A (Constitutional disease)--Defined as one or more of the following: fever persisting more than 1 month, involuntary weight loss of greater than 10 percent of baseline, or diarrhea persisting more than 1 month; and the absence of a concurrent illness or condition other than HTLV-III/LAV infection to explain the findings.

Subgroup B (Necrologic disease)--Defined as one or more of the following: dementia, myelopathy, or peripheral neuropathy; and the absence of a concurrent illness or condition other than HTLV-III/LAV infection to explain the findings.

Subgroup C (Secondary infectious diseases)--Defined as the diagnosis of an infectious disease associated with HTLV-III/LAV infection and/or at least moderately indicative of a defect in cell-mediated immunity. Patients in this subgroup are divided further into two categories.

--Category C-1--Includes patients with symptomatic or invasive disease due to one of 12 specified secondary infectious diseases listed in the surveillance definition of AIDS: Pneumocystis carinii pneumonia, chronic cryptosporidiosis, toxoplasmosis, extraintestinal strongyloidiasis, isosporiasis, candidiasis (esophageal, bronchial, or pulmonary), cryptococcosis, histoplasmosis, mycobacterial infection with Mycobacterium avium complex or M. kansasii, cytomegalovirus, chronic mucocutaneous or disseminated herpes simplex virus infection, and progressive multifocal leukoencephalopathy.
--Category C-2--Includes patients with symptomatic or invasive disease due to one of six other specified secondary infectious diseases: oral hairy leukoplakia, multidermatomal herpes zoster, recurrent *Salmonella* bacteremia, nocardiosis, tuberculosis, or oral candidiasis (thrush).

■ Subgroup D (Secondary cancers) --Defined as the diagnosis of one or more kinds of cancer known to be associated with HTLV-III/LAV infection as listed in the surveillance definition of AIDS and at least moderately indicative of a defect in cell-mediated immunity:
Kaposi’s sarcoma, non-Hodgkin’s lymphoma (small, noncleaved lymphoma or immunoblastic sarcoma), or primary lymphoma of the brain.

■ Subgroup E (Other conditions in HTLV-IIILAV infection) --Defined as the presence of other clinical findings or diseases, not classifiable above, that may be attributed to HTLV-III/LAV infection and/or may be indicative of a defect in cell-mediated immunity. Included are patients with chronic lymphoid interstitial pneumonitis. Also included are those patients whose signs or symptoms could be attributed either to HTLV-III/LAV infection or to another coexisting disease not classified elsewhere, and patients with other clinical illnesses, the course or management of which may be complicated or altered by HTLV-III/LAV infection. Examples include patients with constitutional symptoms not meeting the criteria for subgroup IV-A; patients with infectious diseases not listed in subgroup IV-C; and patients with neoplasms not listed in subgroup IV-D.

Box E-2--The CDC’s Proposed Classification System for HIV Infection

The CDC’s proposed classification system for HIV infection divides HIV-infected patients into three laboratory categories and three clinical categories.

Laboratory Categories

[The three designated laboratory categories correspond to CD4⁺ lymphocyte counts per cubic millimeter (/mm³) of blood that guide clinical and/or therapeutic actions in the management of HIV-infected adolescents and adults. The laboratory categories are as follows]:

- **Category 1** -- A CD4⁺ lymphocyte count of more than 500 cells/mm³
- **Category 2** -- A CD4⁺ lymphocyte count from 200 through 499 cells/mm³
- **Category 3** -- A CD4⁺ lymphocyte count below 200 cells/mm³.

Clinical Categories

The clinical categories are defined as follows:

- **Category A** -- One or more of the conditions listed below occurring in an adolescent or adult with documented HIV infection. Conditions listed in categories B and C (below) must not have occurred.
  - Asymptomatic HIV infection;
  - Persistent generalized lymphadenopathy;
  - Acute (primary) HIV infection with accompanying illness or history of acute HIV infection.

- **Category B** -- Symptomatic conditions occurring in an HIV-infected adolescent or adult which are not included among conditions listed in clinical category C and which meet at least one of the following criteria: (a) the conditions are attributed to HIV infection and/or are indicative of a defect in cell-mediated immunity; or (b) the conditions are considered by physicians to have a clinical course or management that is complicated by HIV infection. Examples of conditions in clinical category B include, but are not limited to:
  - Bacterial endocarditis, meningitis, pneumonia, or sepsis;
  - Candidiasis, vulvovaginal; persistent (> 1 month duration), or poorly responsive to therapy;
  - Candidiasis, oropharyngeal (thrush);
  - Cervical dysplasia, severe; or carcinoma;
  - Constitutional symptoms, such as fever (> 38.5°C) or diarrhea lasting > 1 month;
  - Hairy leukoplakia, oral;
  - Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome;
  - Idiopathic thrombocytopenic purpura;
  - *Mycobacterium tuberculosis*, pulmonary;
  - Nocardiosis;
  - Pelvic inflammatory disease;
  - Peripheral neuropathy;
- **Category C** - Any condition listed in the CDC’s 1987 surveillance case definition of AIDS and affecting an adolescent or adult . . . . The conditions in clinical category C are strongly associated with severe immunodeficiency, occur frequently in HIV-infected individuals, and cause serious morbidity or mortality. HIV-infected persons should be classified based on both the lowest accurate (but not necessarily the more recent) CD4⁺ lymphocyte determination and the most severe clinical condition diagnosed, regardless of the patient’s current clinical condition (e.g., someone previously treated for oral or persistent vaginal candidiasis but who is now asymptomatic should be classified in clinical category B). The classification system is based on the absolute number of CD4⁺ cells but allows for the use of CD4⁺ percent when the counts cannot be obtained or are outdated in view of the patient’s current clinical condition . . . .