

APPENDIX C: CAREC HIV/AIDS CASE DEFINITIONS AND CLASSIFICATION SCHEMES

Case definitions assist the clinician in making a diagnosis according to standardised criteria and are needed as a basis for management and reporting.

CAREC CASE DEFINITION FOR HIV INFECTION

ADULTS

The diagnosis of HIV infection is generally based on a positive HIV antibody test (ELISA, rapid test), confirmed by a second test using a different principle. In case of a discrepancy, a third test is done using another antibody test (ELISA, IFA, WB) or by demonstration of viral material (PCR, p24-Ag test).

The first test should be repeated in case of inconclusive results or of an initially nonreactive result in a patient with symptoms strongly suggestive of HIV-related disease.

CHILDREN

In cases of HIV-positive mothers, their children may carry maternal antibodies for up to eighteen months. In order to make a definitive diagnosis of HIV infection, viral material needs to be demonstrated by, for instance, PCR and p24-Ag test. Such a test should be carried out at least twice, at ages one month and four months. The HIV infection is confirmed by the PCR at age four months. In the absence of such facilities, HIV infection in infants born to HIV-infected mothers is defined as the persistence of HIV antibodies beyond age eighteen months. Antibody testing in the absence of breastfeeding should be carried out every three to six months until two consecutive negative results; or, infection is ruled out by two consecutive nonreactive antibody tests to age eighteen months. In the special case that a nonreactive infant has been exposed to breastmilk, testing of that child should be extended beyond the eighteen months.

CAREC CASE DEFINITION FOR AIDS

ADULTS AND ADOLESCENTS (AGE 13 YEARS AND OLDER)

A confirmed case of AIDS is defined as an individual, age thirteen years or older, who, in the absence of other known causes of immunosuppression (see *Table 10*) has a repeatedly positive screening test for HIV by an enzyme-linked assay (ELISA) together with at least **two major signs** and at least **one minor sign** or at least **one indicator disease**. Additionally, any HIV-infected adult or adolescent with an absolute CD4+ T cell count of <200 cells/mm³ is defined as having AIDS, even if that individual is asymptomatic.

Major Signs:

- Involuntary weight loss of $>10\%$ of baseline body weight
- Chronic diarrhoea with at least two loose stools per day for more than thirty days
- Intermittent or constant fever for more than thirty days

Minor Signs:

- Persistent cough for more than thirty days
- Generalised pruritic dermatitis
- Herpes zoster (HZV), multidermatomal
- Oropharyngeal candidiasis
- Generalised lymphadenopathy

Indicator Diseases:

- Bacterial pneumonia, recurrent (at least two episodes per year)
- Cancer, cervical, invasive

- Candidiasis of bronchi, trachea, or lungs
- Candidiasis, oesophageal
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptosporidiosis, chronic intestinal for more than thirty days
- Cytomegalovirus disease (CMV) (other than liver, spleen, or nodes)
- CMV (with loss of vision)
- Encephalopathy with no other cause
- Herpes simplex (HSV): chronic ulcer(s) for more than thirty days; or bronchitis, pneumonitis, or oesophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal for more than thirty days
- Kaposi's sarcoma (KS) if under age sixty
- Lymphoma, Burkitt's
- Lymphoma, immunoblastic
- Lymphoma, primary of brain under age sixty (or over age sixty)
- *Mycobacterium avium* complex (MAC) or *M. kansasii*, disseminated/extrapulmonary
- TB, any site (pulmonary or extrapulmonary)
- *Pneumocystis jirovecii* pneumonia (PCP)
- Progressive multifocal leukoencephalopathy (PML)
- Toxoplasmosis of brain (or of internal organ)
- Non-typhoid *Salmonella* septicaemia, recurrent
- Wasting syndrome (defined as ALL of major signs)
- Cryptococcosis, extrapulmonary
- Nocardiosis
- Strongyloidiasis, extra-intestinal

INFANTS AND CHILDREN (LESS THAN AGE 13 YEARS)

A confirmed case of AIDS is defined as an individual less than age thirteen years, who, in the absence of other known causes of immunosuppression (see *Table 10*), has a repeatedly positive screening test for HIV by ELISA together with at least **two major signs** AND at least **two minor signs** or at least **one indicator disease**.

Major Signs:

- Weight loss of >10% of baseline or failure to thrive
- Chronic diarrhoea with at least two loose stools per day for more than thirty days
- Intermittent or constant fever for more than thirty days

Minor Signs:

- Generalised lymphadenopathy
- Oropharyngeal candidiasis
- Repeated common infections (otitis, pharyngitis, etc.)
- Persistent cough
- Generalised dermatitis
- Confirmed maternal HIV infection

Indicator Diseases:¹

- Chronic (persisting over two months) lymphoid interstitial pneumonitis
- Bacterial infections, unexplained, serious, recurrent (more than two in a two-year period), including sepsis, meningitis, pneumonia, abscess of an internal organ, and bone/joint infections
- Candidiasis of bronchi, trachea, or lungs

¹For diagnosis of these conditions, please refer to *Table 11*.

- Candidiasis oesophageal
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal for more than thirty days
- CMV infection with onset after six months
- HSV infection, disseminated, with onset after one month of age
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal for more than thirty days
- KS
- Lymphoma, Burkitt's
- Lymphoma, immunoblastic
- Lymphoma primary of brain
- TB, any site
- PCP
- PML
- Toxoplasmosis, disseminated, with onset after age one month

CAREC CLASSIFICATION OF HIV INFECTION IN ADOLESCENTS AND ADULTS

The determination of the stage of the disease and the monitoring of its progress over time are important to guide clinical management. Two classification systems have been proposed; the first can be applied in settings without facilities for measuring CD4+ T cell counts:

GROUP I: ACUTE HIV INFECTION

A mononucleosis-like syndrome, with or without aseptic meningitis, associated with seroconversion for HIV antibody. Antibody seroconversion is required as evidence of initial infection; current viral isolation procedures are adequately sensitive to be relied on for demonstrating the onset of infection.

GROUP II: ASYMPTOMATIC HIV INFECTION

The absence of signs or symptoms of HIV 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.

GROUP III: PERSISTENT GENERALISED LYMPHADENOPATHY (PGL)

Palpable lymphadenopathy (lymph node enlargement of ≥ 1 cm) at two or more extra-inguinal sites persisting for more than three months in the absence of a concurrent illness or condition other than HIV infection to explain the findings.

GROUP IV: OTHER HIV DISEASE

The clinical manifestations of patients in this group may be designated by assignment to one or more subgroups (A through 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 HIV infection, if needed for clinical purposes, research purposes, or disability determinations, may be achieved by creating additional divisions within each subgroup.

Subgroup A: Constitutional Disease. One or more of the following: fever persisting more than one month, involuntary weight loss of >10% of baseline, or diarrhoea persisting more than one month; and, the absence of a concurrent illness or condition other than HIV infection to explain the findings.

Subgroup B: Neurologic Disease. One or more of the following: dementia,

myelopathy, or peripheral neuropathy; and, the absence of a concurrent illness or condition other than HIV infection to explain the findings.

Subgroup C: Secondary Infectious Diseases. The diagnosis of an infectious disease associated with HIV infection and/or at least moderately indicative of a defect in cell-mediated immunity. Patients in this subgroup are further divided into two categories:

Category C-1. Includes patients with symptomatic or invasive disease due to one of twelve specified secondary infectious diseases listed in the surveillance definition of AIDS (this subgroup includes patients with one or more of the specified infectious diseases listed among the indicator diseases).

Category C-2. Includes patients with symptomatic or invasive diseases due to one of six other specified secondary infectious diseases: oral hairy leukoplakia, multidermatomal HZV, recurrent *Salmonella* bacteraemia, nocardiosis, TB, or oral candidiasis (thrush).

Subgroup D: Secondary Cancers. The diagnosis of one or more kinds of cancer known to be associated with HIV infection: KS, non-Hodgkin’s lymphoma (small, noncleaved lymphoma or immunoblastic sarcoma), or primary lymphoma of the brain.

Subgroup E: Other Conditions in HIV Infection. The presence of other clinical findings or diseases not classifiable above, which may be attributed to HIV infection and/or may be indicative of a defect in cell-mediated immunity.

CDC HIV/AIDS CLASSIFICATION SCHEME

Where CD4+ T cell count testing is routinely available, some clinicians may find it useful to classify HIV disease using the CDC classification system. Using this system, an HIV-infected individual’s status is designated by a letter (A, B, or C) that corresponds to his/her most advanced clinical status, followed by a number (1, 2, or 3) that corresponds to his/her nadir CD4+ T cell count, as outlined below:

NADIR CD4+ T CELL COUNT	Clinical Status*		
	A	B	C
>500 cells/mm ³	A1	B1	C1
200-500 cells/mm ³	A2	B2	C2
<200 cells/mm ³	A3	B3	C3

**Clinical Status Key:*

- A. Asymptomatic, PGL, or acute HIV infection
- B. Having had symptoms judged to be attributable to HIV infection, but not an AIDS indicator disease
- C. Having had an AIDS indicator disease, as outlined above.

The boxes highlighted in red denote individuals classified as having AIDS, based on the presence of an AIDS indicator disease or an absolute CD4+ T cell count of <200 cells/mm³.

Table 10: Other Known Causes of Immunosuppression

- Systemic corticosteroid therapy
- Other immunosuppressive or cytotoxic therapy
- Cancer of lymphoreticular or histiocytic tissue such as lymphoma (except for lymphoma localised to the brain, Hodgkin's disease, lymphocytic leukaemia, or multiple myeloma)
- Age under twenty-eight days (neonatal) at diagnosis
- Age under six months at diagnosis
- An immunodeficiency atypical of AIDS, such as one involving hypogammaglobulinaemia or angioimmunoblastic lymphadenopathy, or an immunodeficiency of which the cause appears to be a genetic or developmental defect rather than HIV infection
- Exogenous malnutrition (starvation due to food deprivation, not malnutrition due to malabsorption or illness)

Table 11: Diagnostic Methods for Indicator Diseases of AIDS

Cryptosporidiosis	Microscopy (histology or cytology)
Isosporiasis	Microscopy (histology or cytology)
KS	Microscopy (histology or cytology)
Lymphoma	Microscopy (histology or cytology)
PCP	Microscopy (histology or cytology)
PML	Microscopy (histology or cytology)
Toxoplasmosis	Microscopy (histology or cytology)
Candidiasis	Gross inspection by endoscopy or autopsy or by microscopy (histology or cytology) on a specimen obtained directly from the tissues affected, not from culture
Coccidioidomycosis	Microscopy (histology or cytology), culture, or detection of antigen in a specimen obtained directly from the tissues affected or a fluid from those tissues
Cryptococcosis	Microscopy (histology or cytology), culture, or detection of antigen in a specimen obtained directly from the tissues affected or a fluid from those tissues
CMV	Microscopy (histology or cytology), culture, or detection of antigen in a specimen obtained directly from the tissues affected or a fluid from those tissues
HSV	Microscopy (histology or cytology), culture, or detection of antigen in a specimen obtained directly from the tissues affected or a fluid from those tissues
MAC	Culture
Recurrent Bacterial Infection	<i>M. tuberculosis</i> or smear, histology
HIV Encephalopathy	Clinical findings of disabling cognitive or motor dysfunction interfering with occupation of activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection that could explain the findings. Methods to rule out concurrent illness and conditions must include cerebrospinal fluid (CSF) examination and either brain imaging (CT scan, MRI) or autopsy.