WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults Aged 15 years or Older

World Health Organization
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WHO Case Definition for HIV Infection In Adults

Diagnosis of HIV infection is based on laboratory criteria

- Positive HIV antibody testing (rapid or laboratory-based enzyme immunoassay). This is usually confirmed by a second HIV antibody test (rapid or laboratory-based enzyme immunoassay) relying on different antigens or of different operating characteristics

OR

- Positive virological test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virological test obtained from a separate determination

HIV cases diagnosed and not previously reported in the country should be reported according to a standard national case definition.

WHO Case Definition for Advanced HIV Infection (Including AIDS) in Adults

Diagnosis of advanced HIV infection (including AIDS) is based on clinical or immunological criteria in an individual with confirmed HIV infection

- Confirmed HIV infection AND presumptive or definitive diagnosis of any stage 3 or stage 4 condition

OR

- Confirmed HIV infection AND CD4 count less than 350/mm^3

Cases diagnosed with advanced HIV infection (including AIDS) not previously reported in the country should be reported according to a standard national case definition.

WHO Case Definition for AIDS in Adults

AIDS is defined clinically or immunologically in an individual with confirmed HIV infection

- Confirmed HIV infection AND clinical diagnosis (presumptive or definitive) of any stage 4 condition

OR

- Confirmed HIV infection AND first ever documented CD4 cell count of less than 200/ mm^3

AIDS case reporting for surveillance is no longer required if HIV infection or advanced HIV infection is reported.

WHO Clinical Staging of HIV/AIDS for Adults with Confirmed HIV Infection

CLINICAL STAGE 1

- Asymptomatic
- Persistent generalized lymphadenopathy

CLINICAL STAGE 2

- Unexplained moderate weight loss (<10% of presumed or measured body weight)[i]
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

CLINICAL STAGE 3

- Unexplained[ii] severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhoea for longer than one month
- Unexplained persistent fever (above 37. 5°C intermittent or constant, for longer than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (current)
- Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × 10^9 per litre) and/or chronic thrombocytopaenia (<50 × 10^9 per litre)

CLINICAL STAGE 4[iii]

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis (with diarrhoea)
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis or coccidiomycosis)
- Recurrent septicaemia (including non-typhoidal *Salmonella*)
- Lymphoma (cerebral or B-cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

[i]Assessment of body weight in pregnant woman needs to consider the expected weight gain of pregnancy.
[ii]Unexplained refers to where the condition is not explained by other causes.
[iii]Some additional specific conditions can also be included in regional classifications (such as reactivation of American trypanosomiasis [meningoencephalitis and/or myocarditis]) in the WHO Region of the Americas and penicilliosis in Asia).

Presumptive and Definitive Criteria for Recognizing HIV Related Clinical Events in HIV Infected Adults

(Aged 15 years or older with confirmed HIV infection)

CLINICAL EVENT	CLINICAL DIAGNOSIS	DEFINITIVE DIAGNOSIS
CLINICAL STAGE 1		
Asymptomatic	No HIV related symptoms reported and no signs on examination.	Not applicable
Persistent generalized lymphadenopathy (PGL)	Painless enlarged lymph nodes >1 cm, in two or more non-contiguous sites (excluding inguinal), in absence of known cause & persisting for ≥3 months	Histology
CLINICAL STAGE 2		
Unexplained moderate weight loss (<10% of body weight)	Reported unexplained involuntary weight loss. In pregnancy failure to gain weight.	Documented weight loss <10% of body weight.
Recurrent upper respiratory tract infections (current event plus one or more in last six-months)	Symptom complex, e.g. unilateral face pain with nasal discharge (sinusitis), painful inflamed eardrum (otitis media), or tonsillo-pharyngitis without features of viral infection (e.g. coryza, cough).	Laboratory studies where available, e.g. culture of suitable body fluid.
Herpes zoster	Painful vesicular rash in dermatomal distribution of a nerve supply does not cross midline.	Clinical diagnosis
Angular cheilitis	Splits or cracks at the angle of the mouth not attributable to iron deficiency, and usually responding to anti fungal treatment.	Clinical diagnosis.
Recurrent oral ulceration (two or more episodes in last six months)	Aphthous ulceration, typically painful with a halo of inflammation and a yellow-grey pseudomembrane.	Clinical diagnosis.
Papular pruritic eruption	Papular pruritic lesions, often with marked post-inflammatory pigmentation.	Clinical diagnosis.
Seborrhoeic dermatitis	Itchy scaly skin condition, particularly affecting hairy areas (scalp, axillae, upper trunk and groin).	Clinical diagnosis.
Fungal nail infections	Paronychia (painful red and swollen nail bed) or onycholysis (separation of the nail from the nail bed) of the fingernails (white discolouration, especially involving proximal part of nail plate – with thickening & separation of nail from nail bed)	Fungal culture of nail/nail plate material.
CLINICAL STAGE 3		
Unexplained severe weight loss (more than 10% of body weight)	Reported unexplained weight loss (>10% of body weight) and visible thinning of face, waist and extremities with obvious wasting or body mass index <18.5. In pregnancy weight loss may be masked.	Documented loss of more than 10% of body weight.
Unexplained chronic diarrhoea for longer than one month	Chronic diarrhoea (loose or watery stools three or more times daily) reported for longer than one month.	Not required but confirmed if three or more stools observed and documented as unformed, and two or more stool tests reveal no pathogens
Unexplained persistent fever (intermittent or constant and lasting for longer than one month)	Reports of fever or night sweats for more than one month, either intermittent or constant with reported lack of response to antibiotics or antimalarials, without other obvious foci of disease reported or found on examination. Malaria must be excluded in malarious areas.	Documented fever >37.5 °C. with negative blood culture, negative Ziehl-Nielsen (ZN) stain, negative malaria slide, normal or unchanged chest X-ray (CXR) and no other obvious focus of infection.
Persistent oral candidiasis	Persistent or recurring creamy white curd-like plaques which can be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender (erythematous form),	Clinical diagnosis
Oral hairy leukoplakia	Fine white small linear or corrugated lesions on lateral borders of the tongue, which do not scrape off.	Clinical diagnosis
Pulmonary TB (current)	Chronic symptoms: (lasting more than 2-3 weeks) cough, haemoptysis, shortness of breath, chest pain, weight loss, fever, night sweats, PLUS either positive sputum smear OR Negative sputum smear AND compatible chest radiograph (including but not restricted to upper lobe infiltrates, cavitation, pulmonary fibrosis and shrinkage). No evidence of extrapulmonary disease.	Isolation of *M. tuberculosis*
Severe bacterial infection (e.g. pneumonia, meningitis, empyema, pyomyositis, bone or joint infection, bacteraemia, severe pelvic inflammatory disease)	Fever accompanied by specific symptoms or signs that localize infection, and response to appropriate antibiotic.	Isolation of bacteria from appropriate clinical specimens (i.e. usually sterile sites).
Acute necrotizing ulcerative gingivitis or necrotizing ulcerative periodontitis	Severe pain, ulcerated gingival papillae, loosening of teeth, spontaneous bleeding, bad odour, and rapid loss of bone and/or soft tissue.	Clinical diagnosis.
Unexplained anaemia (<8g/dl), neutropenia (<0.5 ×10⁹/L or chronic (more than one month) thrombocytopenia (<50 ×10⁹/L)	Not presumptive clinical diagnosis.	Diagnosed on laboratory testing and not explained by other non-HIV conditions. Not responding to standard therapy with haematinics, antimalarials or anthelmintics as outlined in relevant national treatment guidelines, WHO IMCI guidelines or other relevant guidelines.
CLINICAL STAGE 4		
HIV wasting syndrome	Reported unexplained weight loss (>10% baseline body weight), with obvious wasting or body mass index <18.5. PLUS either unexplained chronic diarrhoea (loose or watery stools three or more times daily) reported for longer than one month. OR Reports of fever or night sweats for more than one month without other cause and lack of response to antibiotics or antimalarials. Malaria must be excluded in malarious areas.	Documented weight loss >10% of body weight; PLUS two or more unformed stools negative for pathogens OR Documented temperature of > 37.6 °C or more with no other cause of disease, negative blood culture, negative malaria slide and normal or unchanged CXR.
Pneumocystis pneumonia	Dyspnoea on exertion or nonproductive cough of recent onset (within the past 3 months), tachypnoea and fever; AND Chest x-ray evidence of diffuse bilateral interstitial infiltrates AND No evidence of bacterial pneumonia. Bilateral crepitations on auscultation with or without reduced air entry.	Cytology or immunofluorescent microscopy of induced sputum or bronchoalveolar lavage (BAL), or histology of lung tissue.
Recurrent severe bacterial pneumonia (this episode plus one or more episodes in last 6 months)	Current episode plus one or more previous episodes in last 6 months, acute onset (<2 weeks) of severe symptoms (e.g. fever, cough, dyspnoea, and chest pain) PLUS new consolidation on clinical examination **or** CXR. Response to antibiotics.	Positive culture or antigen test of a compatible organism.
Chronic herpes simplex virus (HSV) infection (orolabial, genital or anorectal) of more than one month, or visceral of any duration	Painful, progressive anogenital or orolabial ulceration; lesions caused by recurrence of HSV infection and reported for more than one month. History of previous episodes. Visceral HSV requires definitive diagnosis.	Positive culture or DNA (by PCR) of HSV or compatible cytology/histology.
Oesophageal candidiasis	Recent onset of retrosternal pain or difficulty on swallowing (food and fluids) together with oral Candida.	Macroscopic appearance at endoscopy or bronchoscopy, or by microscopy/histology.
Extrapulmonary tuberculosis	Systemic illness (e.g. fever, night sweats, weakness and weight loss). Other evidence for extrapulmonary or disseminated TB varies by site: pleural, pericardial, peritoneal, -meningeal, mediastinal or abdominal lymphadenopathy, osteitis, or miliary TB (diffuse uniformly distributed small miliary shadows or micronodules on CXR). Discrete cervical lymph node *M. tuberculosis* infection is considered a less severe form of extrapulmonary tuberculosis.	*M. tuberculosis* isolation or compatible histology from appropriate site, together with compatible symptoms/ signs (if culture/histology is from respiratory specimen then must be other evidence of extrapulmonary disease).
Kaposi's sarcoma	Typical gross appearance in skin or oropharynx of persistent, initially flat, patches with a pink or violaceous (blood bruise) colour skin lesions that usually develop into plaques or nodules.	Macroscopic appearance at endoscopy or bronchoscopy, or by histology.
CMV disease (other than liver, spleen or lymph node).	Retinitis only: may be diagnosed by experienced clinicians. Typical eye lesions on fundoscopic examination: discrete patches of retinal whitening with distinct borders, spreading centrifugally, often following blood vessels, associated with retinal vasculitis, haemorrhage and necrosis.	Compatible histology or CMV demonstrated in CSF by culture or DNA (by PCR).
CNS toxoplasmosis	Recent onset of a focal neurological abnormality or reduced level of consciousness AND response within 10 days to specific therapy.	Positive serum toxoplasma antibody AND (if available)single/multiple intracranial mass lesion on neuro-imaging (CT or MRI)
HIV encephalopathy	Clinical finding of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks or months in the absence of a concurrent illness or condition other than HIV infection which might explain the findings.	Diagnosis of exclusion: and (if available) neuro-imaging (CT or MRI)
Extrapulmonary cryptococcosis (including meningitis)	Meningitis: usually sub acute, fever with increasingly severe headache, meningism, confusion, behavioural changes that responds to cryptococcal therapy.	Isolation of Cryptococcus neoformans from extrapulmonary site or positive cryptococcal antigen test (CRAG) on CSF/blood.
Disseminated non-tuberculous mycobacteria infection	No presumptive clinical diagnosis.	Diagnosed by finding atypical mycobacterial species from stool, blood, body fluid or other body tissue, excluding lung.
Progressive multi focal leukoencephalopathy (PML)	No presumptive clinical diagnosis	Progressive neurological disorder (cognitive dysfunction, gait/speech disorder, visual loss, limb weakness and cranial nerve palsies) together with hypodense white matter lesions on neuro-imaging or positive polyomavirus JC (JCV) PCR on CSF.
Chronic Cryptosporidiosis (with diarrhoea lasting more than one month)	No presumptive clinical diagnosis.	Cysts identified on modified ZN microscopic examination of unformed stool.
Chronic Isosporiasis	No presumptive clinical diagnosis.	Identification of Isospora
Disseminated mycosis (e.g. coccidiomycosis, histoplasmosis, penicilliosis)	No presumptive clinical diagnosis.	Histology, antigen detection or culture from clinical specimen or blood culture.
Recurrent septicaemia (including non-typhoidal salmonella)	No presumptive clinical diagnosis.	Blood culture.
Lymphoma (cerebral or B cell non-Hodgkin)	No presumptive clinical diagnosis	Histology of relevant specimen or for CNS tumours neuroimaging techniques
Invasive cervical carcinoma	No presumptive clinical diagnosis.	Histology or cytology.
Atypical disseminated visceral leishmaniasis	No presumptive clinical diagnosis.	Diagnosed by histology (amastigotes visualized) or culture from any appropriate clinical specimen.
HIV-associated nephropathy	No presumptive clinical diagnosis	Renal biopsy
HIV-associated cardiomyopathy	No presumptive clinical diagnosis	Cardiomegaly and evidence of poor left ventricular function confirmed by echocardiography.

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