

Clinical Tract

Module on

Natural course of HIV disease and WHO staging in adults

LEARNING OUTCOMES FOR COUNSELLORS, SOCIAL WORKERS, DIETICIANS, LABORATORY TECHNICIANS AND DATA TYPISTS

After completion of this module the learner should be able to:

- Identify pertinent positive and negative in the history of an HIV patient.
- Know how to explain to a patient what happens if HIV is left untreated.
- Know how HIV staging is done according to WHO.
- Know how to explain to a patient what a doctor or nurse is checking on in the physical examination.

LEARNING OUTCOMES FOR DOCTORS AND NURSES

After completion of this module the learner should be able to:

- Identify pertinent positive and negative in the history of an HIV patient.
- Know how to explain to a patient what happens if HIV is left untreated.
- Conduct a focused physical examination on an HIV positive patient.
- Stage a patient according to WHO criteria.

1. INTRODUCTION

Ultimately the profound immune suppression resulting from HIV infection renders patients vulnerable to opportunistic infections and malignancies. The median time from infection to Acquired Immunodeficiency Syndrome (AIDS) is 8-10 years in developed countries, but there is individual variation with a small proportion of patients progressing very fast, and a smaller proportion of patients who remain clinically stable, the so-called non-progressors. There isn't good data available for developed countries on the duration from HIV infection to AIDS. We do however know that poor socio-economic circumstances and malnutrition can shorten the time duration from primary HIV infection to AIDS.

The CD4 count plays an important role in gauging damage to the immune system and cannot be left unmentioned in a discussion on the clinical staging of HIV, but was covered in the module on Laboratory diagnoses and monitoring of HIV.

2. STAGING OF HIV

The immunodeficiency that develops during HIV infection is a continuum, but several discrete clinical phases can be identified. Understanding the natural history of HIV infection allows the doctor to make treatment decisions based on the clinical presentation of the patient.

The World Health Organization (WHO) uses standardised criteria to clinically stage HIV infection. This staging accommodates facilities where CD4 testing is not freely available and thus only uses patient clinical determinates. The WHO staging is attached as an addendum to this module.

The Centres for Disease Control also has a staging system, but dependent on both the clinical picture and CD4 count of the patient.

Table 1. CDC AIDS Surveillance Case Definition for Adolescents and Adults

	A. Symptomatic/PGL/acute HIV infection	B. Symptomatic (not A or C)	C. AIDS-defining condition
CD4 ≥ 500	A1	B1	C1
CD4 200-499	A2	B2	C2
CD4 < 200	A3	B3	C3

WHO Stage 1

The acute retroviral syndrome is usually symptomatic. Patients mostly present with symptoms resembling "flu" or infectious mononucleosis. The symptoms are usually dismissed as a common cold or 'flu by the patient and physician; thus very few patients are diagnosed during seroconversion. Infrequently the patient may present with an opportunistic infection at this stage.

The so-called asymptomatic HIV stage may last for a number of years. Most of these patients are unaware of their status, and if sexually active, proceed to infect others. Persistent generalised lymphadenopathy (PGL) is the presence of lymphadenopathy in two sites other than inguinal for a period longer than six months.

WHO Stage 2

A number of clinical manifestations of autoimmune responses to HIV can be found in the patient even in early disease. These include arthritis, anaemia, glomerulonephritis, thrombocytopenia, neuropathies and disturbances of coagulation. This is due to the chronic and acute activation of the immune system by the HIV where immunoglobulins are not effectively cleared from the body.

At this stage patients may also develop a range of minor dermatological conditions of which some are immune related, for example prurigo or pruritis, acne and seborrhoeic dermatitis. Other skin conditions include fungal nail infections and recurrent oral ulceration. At this stage the patient may experience the first attack of herpes zoster shingles. This is a flare up of a previous herpes zoster infection (chicken pox as a child) and not a reinfection with the virus.

Upper respiratory tract infections are common, especially sinusitis.

Patients are also at an increased risk of idiosyncratic drug reactions. The most frequent drug reaction seen is co-trimoxazole allergy.

WHO Stage 3

Anorexia, significant weight loss, night sweats and malaise may occur as the disease progresses, even in the absence of opportunistic disease.

Chronic diarrhoea is a feature of this stage and should be investigated for other possible infective organisms before ascribing it to HIV. Systemic bacterial infections such as pneumonia and pyelonephritis are also more frequent.

Recurrent oral candidiasis and oral hairy leukoplakia can occur. Vulvovaginal candidiasis may be chronic or poorly responsive to topical therapy.

Pulmonary tuberculosis (PTB) can appear in patients at any CD4 count. The presentation is more typical in patients with higher CD4 counts, while in patients with very low CD4 counts it can be extremely difficult to confirm a diagnosis of PTB because of the atypical presentation of the disease.

WHO Stage 4

This stage includes all the Acquired Immune Deficiency Syndrome (AIDS) defining conditions. AIDS is diagnosed should any *one* of these conditions be present.

Molluscum contagiosum, although not included in the WHO stage 4 conditions, is a sign of advanced disease and is more extensive the more advanced the immune suppression is. It is caused by a poxvirus and presents as dome shaped papules with central dimpling.

PAP smears in female patients are very important since cervical intra-epithelial neoplasia (CIN) lesions quickly progress to invasive cervical cancer.

Extrapulmonary tuberculosis is regarded by the WHO as AIDS-defining. Extrapulmonary presentations of TB include TB pleuritis, TB lymphadenitis, TB meningitis and military TB. Mycobacterium avium disease, *Toxoplasma gondii*, Cryptosporidium and Cytomegalovirus infections usually present at CD4 counts

below 50 cells/ μ L. Some of the atypical fungi that may occur include histoplasmosis, coccidioidomycosis, aspergillosis and mucormycosis. Herpes simplex ulceration is frequently seen in earlier stages of HIV, but in Stage 4 it presents as chronic ulceration.

In patients with low CD4 counts a clinician would have a high index of suspicion and actively investigate for opportunistic infections should the patient be symptomatic.

An in depth discussion of opportunistic infections and cancers is discussed in a following module.

3. THE INITIAL CLINICAL EVALUATION OF THE PATIENT

The initial evaluation should include:

- A complete history and physical examination
- Full blood count
- Serum transaminases (AST and ALT)
- CD4 count
- Syphilis serology
- Papanicolaou smears for female patients

Mild cytopenia and mildly raised liver transaminases are frequently seen.

Additional investigation for a patient in whom ARVs are considered:

- HIV viral load

4. FREQUENTLY SEEN PHYSICAL SIGNS

Symptoms and signs are dependent on the stage of presentation. Patients with acute seroconversion will have different presenting symptoms and signs in comparison to patients with advanced HIV. These are non-specific generalised symptoms and signs that need interpretation in the light of a high index of suspicion. It is of particular importance to note that symptomatic disease can occur at any stage of HIV disease irrespective of CD4 cell counts.

A complete physical examination should always be done at follow-up, but special attention should be paid to the mouth, lymph nodes and the feet, as well as any signs that may point to systemic opportunistic infections.

Change in body weight

A patient should be weighed at every visit to the clinic and a loss of weight should trigger more intensive review of the history and a more focused physical examination for possible causes of lost of weight. Stable patients can also gain weight, as could patients starting on antiretrovirals.

The mouth

HIV infection is associated with a variety of oral lesions and oral manifestations are often the first clinical expression of HIV infection in an individual. Examination of the oral cavity can give some indication of the status of the immune system. The history should always include questions on appetite, taste and any oral pain or dysphagia.

Table 2. Common oral manifestations of HIV disease.

Cause	Disease
Fungal	Candidiasis
Viral	Herpes simplex ulceration Herpes zoster ulceration Hairy leukoplakia
Bacterial	Gingivitis
Malignancy	Kaposi's sarcoma
Other	Aphthous ulcers

Lymphadenopathy

Intense immune activity early in the HIV infection leads to lymph node hyperplasia and lymphadenopathy. As the disease progresses, the lymph node architecture is destroyed causing lymphadenopathy to disappear in later stages of disease. In some patients the lymphadenopathy reappears on initiation of antiretrovirals, since prior to AIDS, the immune system has a degree of self-regeneration.

Persistent Generalized Lymphadenopathy (PGL)

This condition has a specific clinical definition that is as follows:

- Following seroconversion
- Usually bilateral
- Lymphadenopathy in ≥ 2 sites for ≥ 3 months

Patients are often concerned about the lymphadenopathy. Providing an explanation would often put the patient's mind at rest. The question however arises, when does a clinician need to investigate lymph gland further?

"Suspicious" lymph glands

Lymph glands should be investigated further if:

- unilateral
- matted
- red and tender
- draining

Differential diagnosis of lymphadenopathy

- TB
- Lymphoma
- Kaposi's sarcoma
- Metastatic carcinoma
- fungal infection

A wide needle aspirate air-dried for AFB, fixed and sent for cytology will yield the diagnosis in 60-80% of patients. Excision biopsy would be the next step if aspiration does not provide a diagnosis.

Treatment is then given depending on the diagnosis.

5. FURTHER READING

- Kilby JM, Saag MS. Natural history of HIV disease. In: Merigan TC, Bartlett JG, Bolognesi D (Eds). *Textbook of AIDS Medicine* (2nd Edition). Williams & Wilkens: Baltimore, 1999: 49-50.

Addendum. Table of the World Health Organization Clinical Staging System of HIV for adults and adolescents.

<p>WHO Stage 1 Acute retroviral infection Asymptomatic infection Persistent generalised lymphadenopathy <i>Performance scale 1: asymptomatic with normal activity</i></p> <p>WHO Stage 2 Weight loss < 10% of body weight Minor mucocutaneous manifestations Herpes zoster shingles Recurrent upper airways infections <i>Performance scale 2: symptomatic with normal activity</i></p> <p>WHO Stage 3 Weight loss > 10% of body weight Unexplained chronic diarrhoea > 1 month Unexplained prolonged fever (intermittent or constant) > 1 month Oral candidiasis Vulvovaginal candidiasis Oral hairy leukoplakia Pulmonary tuberculosis Severe bacterial infections <i>Performance scale 3: in bed <50% of normal daytime during past month</i></p> <p>WHO Stage 4, AIDS-defining conditions</p> <p>Cancers Lymphoma Kaposi's sarcoma (KS) Invasive cervical cancer</p> <p>Bacteria Extrapulmonary tuberculosis Atypical mycobacteriosis Pneumocystis jiroveci pneumonia (PCP) Recurrent pneumonia Salmonella septicaemia Toxoplasmosis</p> <p>Fungal infections Candidiasis of the oesophagus, trachea, bronchi or lungs Cryptosporidiosis Intestinal isosporiasis or microsporidiosis Cryptococcus meningitis Other systemic mycosis</p> <p>Viral infections Cytomegalovirus (CMV) Herpes simplex virus ulceration > 1 month HIV encephalopathy</p> <p>Other Progressive multifocal leuko-encephalopathy HIV wasting syndrome <i>Performance scale 4: In bed > 50% of daytime during the past month</i></p>
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