# updAIDS in SA Family Practice

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## *upd*AIDS in SAFP

In response to the changing landscape of HIV/AIDS, particularly in resource-limited settings, to support the improvement of antiretroviral therapy (ART), revisions and harmonisation of the clinical staging and case definitions for surveillance are required. For this reason, the World Health Organisation (WHO) in collaboration with the Centers for Disease Control and Prevention (CDC), held two expert consultative meetings, in June 2004 in Saas Fe, Switzerland and in December 2004 in Nairobi, Kenya to review and revise the 1994 WHO clinical staging system and AIDS case definitions. HIV/AIDS surveillance has been used for the monitoring of temporal, geographical and risk-group trends and for estimating the burden of HIV/AIDS-related disease. Surveillance definitions were introduced in 1982, and many different definitions have been used for national and international reporting.[1] The clinical case definitions recommended by the WHO in 1985 and revised in 1994 are designed for use in resource-limited settings. They require confirmation of HIV infection by means of serological testing. These surveillance definitions were introduced before the widespread use of ART, which can restore many patients with severe disease to health, and reverse disease progression. Surveillance now needs to capture those patients in need of ART. The revisions made were based upon the best available evidence or, where evidence was inconclusive or unavailable, on the balance of expert opinion.

The article in the present edition of *upd***AIDS** in SAFP describes the new WHO clinical staging system and case definitions for adolescents and adults as agreed during the second meeting, held in Nairobi.[2] The revisions are also designed to reflect that, with the use of ART, HIV is a manageable chronic disease. ART changes the prognosis and can reverse the inevitable progression through the clinical stages. The revisions were designed to strengthen clinical staging and the AIDS case definitions for both adults and children, and to simplify and standardise definitions for use by a cross-section of health providers, programme managers and surveillance officers. They were also intended to harmonise paediatric and adult clinical staging and AIDS case definitions so as to improve patient management, patient monitoring and surveillance efforts. The staging and case definition of AIDS for infants and children will be discussed in the next issue of *upd***AIDS** in SAFP. The revisions provide greater consistency between the adult and paediatric staging and harmonise clinical case definitions and surveillance definitions. In addition, the new approach provides immunological staging based upon the degree of immunocompromise and prognosis, which facilitates follow-up care.

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2. http://www.who/hiv/2005.02


## Views on news: TB, HIV and poverty

Massive population growth and the dual epidemic of HIV and TB are the key challenges for the international community over the next 50 years. Demographer John Cleland of the London School of Hygiene and Tropical Medicine, that the world's population crossed the 6,5 billion mark in July, with the 9 billion mark expected to be cracked around 2050. Africa's steadily increasing fertility rates will triple population figures on the continent by 2050. Life expectancy in southern Africa, which has the highest HIV infection rate in the world, has fallen from 62 in the 1990s to 48 years now. This figure is expected to drop to 43 in the next decade before a slow recovery starts. Cleland said some 3 million people died of HIV/AIDS-related illnesses last year, while 5 million people became infected, taking the global tally to 40 million. According to UN figures, South Africa's HIV population stands at 5,3 million, followed closely by India with 5,1 million.

In sub-Saharan Africa, the HIV epidemic is accompanied by a rapidly increasing incidence of tuberculosis (TB). The World Health Organisation's (WHO) regional committee for Africa has declared TB a major emergency in Africa. The annual number of new TB cases in 18 African countries has quadrupled since 1990 and is continuing to rise across the continent, killing more than 500 000 people every year. In South Africa alone, 1000 people die from TB every day. The declaration, made in August, calls on African member states to:

- Develop and implement, with immediate effect, emergency strategies to control the worsening of the epidemic,
- Rapidly improve TB case detection, and
- Improve the quantity and quality of staff involved in TB control.

In Africa, the vicious cycle of poverty and population increase, coupled with the inter-relationship between poverty and the HIV / TB dual epidemic, threatens the existence of many individuals and affects communities deeply. A rigorous effort needs to be made by politicians, economists, social scientists and health professionals to address this devastating disaster.

# Clinical staging of HIV / AIDS in adults and adolescents

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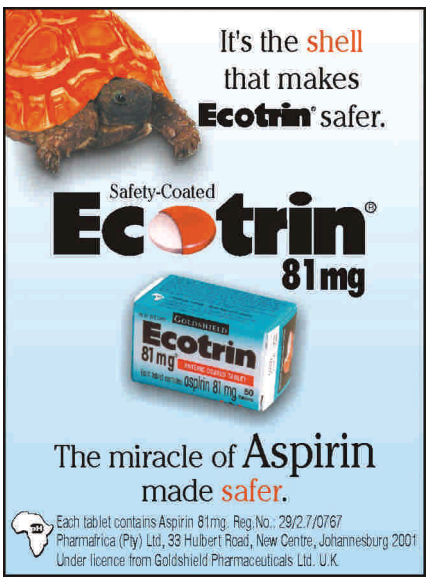
Infection with the human immunodeficiency virus (HIV) leads to an insidious and progressive loss of immune function that eventually results in the opportunistic infections and malignancies that are used to define the presence of the Acquired Immunodeficiency Syndrome or AIDS. The time from transmission to the development of AIDS varies considerably between individuals, but typically averages approximately 10 to 12 years in the absence of treatment directed against HIV. The natural history of HIV infection can be described in terms of disease stages, each of which relates to particular levels of immune system functionality, viral replication and clinical symptoms. Transmission of HIV is the first stage of infection, and the stage without which none of the subsequent stages can occur. HIV may be transmitted via a variety of mechanisms, including sexual intercourse, injection drug use, transfusion of blood products, mother-to-child transmission, organ transplantation and occupational exposure.

After establishing the diagnosis of HIV infection, the results have to be discussed with the patient or, in the case of babies or children, with the infected child's parents or guardian. The further management of the patient has to be planned and needs to be discussed with the infected individual or the parents. The diagnosis of HIV has far-reaching consequences for the patient's family, partner and friends The patient not only needs to receive as much relevant information as possible about the condition, but also a supportive environment in which a doctor-patient partnership can grow. The counselling process is ongoing, there are no quick answers and the physician must assist his/her client in developing coping skills [1,2].

The most important step in the planning of further management is the clinical staging of the HIV-infected patient. Clinical staging needs to be performed at determination of HIV infection, and on entry to clinical care to help guide antiretroviral therapy (ART) and care-related decisions. Assessment of clinical stage at each clinical visit also provides useful information on current clinical status, and can guide clinical decision-making.

Clinical classification systems were initially developed for epidemio-logical surveillance and not designed for the care of patients. The first surveil-lance




definitions were introduced in 1982, and many different definitions have been used for national and international reporting[3]. The clinical disease classification system of the Centers for Disease Control and Prevention (CDC) in the USA is based on immunological parameters ($CD_4$ counts), clinical parameters and virological para-meters and requires laboratory confirmation of many clinical events. This is designed for surveillance, but is also frequently used for clinical management purposes. The clinical case definitions recommended by the WHO in 1985, and revised in 1994, are designed for use in resource-limited settings. They require confirmation of HIV infection by means of serological testing.

The surveillance definitions were introduced before the widespread use of ART. Surveillance now needs to capture those patients in need of ART. To address the new context and to harmonise the classification systems for adults and for children, The WHO developed and published the ***Interim who clinical staging of hiv/aids and hiv/aids case definitions for surveillance*** for the African Region[4]. These were designed to:

1. Be used for assessment at base-line or entry into HIV care to guide decisions on when to start co-trimoxazole prophylaxis, start ART and other HIV-related interventions.
2. Provide simple guidance to assist clinical care providers on when to start, substitute, switch or stop ART in HIV-infected adults and adolescents, or to trigger referral as outlined in the WHO ART guidelines for a public health approach.[5]
3. Be used to assess current clinical status of individuals in HIV care, either with or without ART.
4. Encourage clinical care providers to offer diagnostic testing for HIV in adults and adolescents exhibiting the clinical events suggestive of HIV disease.
5. Prompt urgent offer of HIV diagnostic testing for stage 3 or stage 4 events either on site, or by referral for testing to a site where immediate assessment by HIV care providers able to initiate ART can be performed.
6. Be used to guide clinicians in assessing the response to ART, particularly where viral load and/or $CD_4$ counts or percentages are not widely or easily available.

New or recurrent stage 4 events may suggest failure of response to treatment; whereas new or recurrent stage 2 or stage 3 events may suggest an inadequate response to treatment, potentially because of poor adherence. However, further evidence is required in order to determine the

**Table 1:** Revised WHO Clinical Staging of HIV for Adults and Adolescents

| |
|---|
| **Primary HIV infection**<br>Asymptomatic<br>Acute retroviral syndrome |
| **Clinical Stage 1**<br>Asymptomatic<br>Persistent generalised lymphadenopathy (PGL) |
| **Clinical Stage 2**<br>Moderate unexplained weight loss (< 10% of presumed or measured body weight)<br>Recurrent respiratory tract infections (sinusitis, bronchitis, pharyngitis, otitis media)<br>Herpes zoster<br>Angular cheilitis<br>Recurrent oral ulcerations<br>Papular pruritic eruptions<br>Seborrhoeic dermatitis<br>Fungal nail infections of fingers |
| **Clinical Stage 3**<br>Severe weight loss (> 10% of presumed or measured body weight)<br>Unexplained chronic diarrhoea for > 1 month<br>Unexplained persistent fever (intermittent or constant for >1month)<br>Oral candidiasis<br>Oral hairy leukoplakia<br>Pulmonary tuberculosis (TB) diagnosed in last 2 years<br>Severe presumed bacterial infections (e.g. pneumonia, arthritis, meningitis, bacteraemia)<br>Acute necrotising ulcerative stomatitis, gingivitis or periodontitis<br>Anaemia (< 8 g/dl), and/or neutropenia (< 500/mm$^3$) and/or thrombocytopenia (< 50 000/mm$^3$) for > 1 month |
| **Clinical Stage 4**<br>HIV wasting syndrome<br>Pneumocystis pneumonia<br>Recurrent severe or radiological bacterial pneumonia<br>Chronic herpes simplex infection (orolabial, genital or anorectal > 1 month's duration)<br>Extrapulmonary TB<br>Kaposi's sarcoma<br>Central nervous system toxoplasmosis<br>HIV encephalopathy<br>Extrapulmonary cryptococcosis including meningitis<br>Disseminated non-tuberculous mycobacteria infection<br>Progressive multifocal leukoencephalopathy (PML)<br>Candida of oesophagus, trachea, bronchi or lungs<br>Cryptosporidiosis<br>Isosporiasis<br>Visceral herpes simplex infection<br>Cytomegalovirus infection of any organ other than liver, spleen or lymph nodes<br>Any disseminated mycosis (e.g. histoplasmosis, coccidiomycosis, penicilliosis)<br>Recurrent non-typhoidal salmonella septicaemia<br>Lymphoma (cerebral or B cell non-Hodgkins)<br>Invasive cervical carcinoma<br>Visceral leishmaniasis |

**Table 2:** $CD_4$ levels in relation to the severity of immunosuppression

| | |
|---|---|
| No significant immunosuppression | > 500/mm$^3$ |
| Mild immunosuppression | 350 - 499/mm$^3$ |
| Advanced immunosuppression | 200 - 349/mm$^3$ |
| Severe immunosuppression | < 200/mm$^3$ |

The $CD_4$ cell count is the strongest determinant of the clinical complications of HIV infection[6,7] as presented in Table 3.

significance of staging events once ART has commenced. Clinical events in the first three months after ART has begun may be caused by immune reconstitution inflammatory syndrome (IRIS) rather than a poor response to ART. The present concerns focus on the staging of the disease in adolescents and adults, whereas the next issue will be to look at the staging and case definition of HIV/AIDS in infants and children younger than 15 years. The new staging classification for adults and adolescents is presented in Table 1. The cut-off age of 15 years is applied, as this is the usual cut off for WHO surveillance definitions.

## IMMUNOLOGICAL STAGING OF HIV INFECTION IN ADULTS AND ADOLESCENTS

Clinical staging can be used effectively without access to $CD_4$ or other laboratory testing. However, $CD_4$ testing is useful for determining the degree of immunocompromise and, where $CD_4$ facilities are available, they should be used to support and reinforce clinical decisionmaking. Data on $CD_4$ levels are not a prerequisite for starting ART and should only be used in conjunction with consideration of the clinical stage. In addition to the new clinical staging system, the WHO proposes immunological staging based on $CD_4$ counts, as presented in Table 2. Immunological staging of disease reverses with successful ART.

The $CD_4$ cell count is the strongest determinant of the clinical complications of HIV infection[6,7], as presented in Table 3. The median life expectancy of people with AIDS in South Africa without antiretroviral therapy is 18 months[7]. However, some patients survive for many years even without antiretroviral therapy. In recent years, morbidity and mortality rates among people with AIDS have decreased dramatically with the advent of highly active antiretroviral therapy (HAART) and advances in the treatment and prevention of opportunistic infections.

**Table 3:** Correlation of the onset of HIV-related complications with $CD_4$ count

| $CD_4$ count (cells/mm$^3$) | Infectious | Non-infectious † |
|---|---|---|
| > 500 | Vaginal candidiasis | Persistent generalised lymphadenopathy (PGL)<br>Guillain-Barré syndrome<br>Bell's palsy<br>Aseptic meningitis<br>Parotidomegaly |
| 200 – 500 | Pulmonary tuberculosis<br>Pneumonia (bacterial)<br>Herpes zoster<br>Oral candidiasis<br>Oral hairy leukoplakia<br>Oesophageal candidiasis | Cervical intraepithelial neoplasia<br>Cervical cancer<br>Mononeuritis multiplex<br>Idiopathic thrombocytopenic purpura (ITP)<br>Hodgkin's lymphoma<br>Lymphocytic interstitial pneumonitis<br>Kaposi's sarcoma |
| 50 – 200 | Extrapulmonary tuberculosis<br>*Pneumocystis carinii* pneumonia<br>Cryptococcal meningitis<br>Toxoplasmosis<br>Cryptosporidiosis (chronic)<br>Microsporidiosis<br>Histoplasmosis (disseminated)<br>Chronic herpes simplex ulcers<br>Septicaemia (non-typhoid salmonella) | Wasting<br>Anaemia<br>Peripheral neuropathy<br>HIV-associated dementia<br>Non-Hodgkins lymphoma<br>Cardiomyopathy<br>Vacuolar myelopathy |
| < 50 | Cytomegalovirus (disseminated)<br>*Mycobacterium avium* complex (disseminated) | |

† Some complications listed as 'non-infectious' may be associated with microbes

**Table 4:** Criteria for initiating ART in adults and adolescents

| Clinical stage | Treatment |
|---|---|
| Stage 4 | Treat with ART |
| Stage 3 | Consider treatment: $CD_4$ count, if available, can guide the urgency with which ART should be started |
| Stages 1 or 2 | Treat with ART only if $CD_4$ <200/mm$^3$ |

$CD_4$ counts can be used to monitor responses to treatment, although they are not essential. Absolute CD4 values also fluctuate with intercurrent illness and with physiological and test variability, so the trend over two or three repeated measurements is usually more informative than individual values. Note that, during the course of acute HIV infection, the $CD_4$ count may reach very low levels and then recover.

There is strong evidence for the clinical benefit of ART in adults with advanced HIV/AIDS as determined clinically or immunologically. The precise clinical and or immunological criteria for initiating ART are usually outlined in national treatment guidelines. Existing WHO recommendations are provided on the WHO website[5] and summarised in Table 4.

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