

HATiP

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Southern African HIV Clinicians' Society: new treatment guidelines

ART recommended for all with CD4 counts below 350, say South African doctors

Antiretroviral therapy should be recommended to all people with HIV who have CD4 cell counts below 350 cells/mm³ regardless of whether they have symptoms of HIV disease or not, according to new guidelines from the Southern African HIV Clinicians' Society published in the Summer 2008 edition of the Society's journal.

Current South African Department of Health guidelines recommend that treatment should start when the CD4 count falls below 200 cells/mm³, or when a person has WHO stage 4 symptoms, regardless of CD4 cell count.

The South African physicians' recommendation on when to start treatment comes soon after similar recommendations in [Europe](#), the [United States](#) and the [United Kingdom](#), all endorsed by leading HIV specialists.

Although the guidelines will have no immediate effect on HIV treatment in the public sector, where Department of Health guidelines issued in 2003 prevail, the South African HIV Clinicians' Society guidelines will be influential in the private sector, and will be used to lobby for changes to public sector guidelines.

New first-line drugs recommended

In first line treatment, efavirenz or nevirapine should be used alongside AZT/3TC, abacavir/3TC or tenofovir/FTC.

The new guidelines do not recommend the use of stavudine (d4T) due to the high rates of toxicity seen with the drug. Stavudine may cause peripheral neuropathy, fat loss (lipoatrophy) and lactic acidosis. The latter is a life-threatening side-effect, and has been seen most frequently in women with high body mass.

"Public sector programmes are urged to consider dropping stavudine from first-line ART, or at least to make alternative NRTIs available in the case of toxicity," the guidelines state. The World Health Organization [recommended in 2006](#) that stavudine should be dropped from first-line regimens wherever possible.

The South African guidelines note that AZT is associated with lipoatrophy, but continue to recommend it as an option for first-line treatment.

For second line therapy, the Southern African HIV Clinicians' Society recommends the use of AZT/ddl or tenofovir/FTC, coupled with a protease inhibitor - either lopinavir or atazanavir or saquinavir boosted with low-dose ritonavir.

AZT/ddl is recommended for use after tenofovir or abacavir-based first-line treatment, while tenofovir/FTC is recommended for use after AZT or d4T-based first-line treatment (although AZT/ddl may also be used after d4T-based first-line treatment).

In patients with resistance to protease inhibitors, NNRTIs and nucleoside analogues, the guidelines recommend that in the absence of integrase inhibitors or newer protease inhibitors such as darunavir, currently unavailable in southern Africa, lopinavir/ritonavir should be used since it is likely to have the greatest activity against PI-resistant viruses. FTC or 3TC may also

prove useful, since maintenance of the M184V mutation associated with these drugs impairs viral replication and is associated with lower viral load. There is no point in using efavirenz or nevirapine because they do not impair viral fitness.

Pregnant women

All pregnant women should receive three-drug antiretroviral therapy, regardless of CD4 cell count, the South African clinicians recommend. Their view directly contradicts the [guidelines issued by South Africa's Department of Health in February 2008](#), which also diverged from World Health Organization guidance by recommending seven days of AZT treatment for infants only, after single dose nevirapine for mother and child at the time of delivery.

The Department of Health guidelines on prevention of mother to child transmission guidelines were condemned at the time by Southern African HIV Clinicians' Society president Dr Francois Venter, who said that South Africa was a middle income country behaving like an economic basket case.

The Southern African HIV Clinicians' Society recommends that pregnant women should start treatment within two weeks of the first clinic visit if they have been adequately prepared regarding adherence and HIV status disclosure. However, treatment should not start in the first trimester of pregnancy unless a woman is seriously ill due to HIV, due to any possible harmful effects on the developing foetus.

In women with a CD4 cell count below 250 cells/mm³, treatment during pregnancy should be based on nevirapine, but in women with CD4 counts above this level, a boosted protease inhibitor should be used due to [the increased risk of hepatitis associated with nevirapine rash](#).

After delivery, antiretroviral therapy should continue throughout the breastfeeding period. Women with CD4 counts below 350 should continue treatment indefinitely, while women with CD4 counts above 350 should stop when breastfeeding is discontinued.

Women who are diagnosed with HIV around the time of labour, who are not receiving antiretroviral therapy, should receive single dose nevirapine at the onset of labour, and AZT/3TC for one week after delivery to minimise the risk of NNRTI resistance [caused by the very long half-life of nevirapine](#).

ART and TB

TB can occur at a wide range of CD4 counts and is not an automatic indication for starting treatment unless it is extrapulmonary or disseminated. In order to reduce the risk of toxicity and [immune reconstitution syndrome](#), the guidelines recommend:

- In those with CD4 counts below 200, ART should be started 2-8 weeks after starting TB treatment, when it is clear that TB treatment is tolerated and symptoms are improving.
- In those with CD4 counts between 200 and 350, ART should be delayed until after the 2-month intensive phase of TB treatment has been completed.
- CD4 above 350: defer ART.

Monitoring

When patients are preparing to start ART, they should undergo the following baseline tests:

- CD4 count
- Liver function: ALT may be sufficient.

- Full blood count
- Hepatitis B surface antigen.
- Serum creatinine to calculate creatinine clearance and urinalysis for proteinuria.

Whilst on treatment, the following monitoring should be carried out for all patients:

- With AZT: monitor full blood counts during first six months of treatment for anaemia.
- Hepatotoxicity: monitor ALT in patients receiving nevirapine at weeks 2, 4, 16 and then every three months. Any elevations with symptoms of hepatitis should be regarded as an indication to stop, and monitoring should take place weekly in people with ALT levels between 2.5 and 5 times the upper limit of normal. If ALT levels rise above five times the upper limit of normal, stop the drug presumed to be causing liver enzyme elevation; if above ten times the upper limit of normal, stop all antiretrovirals.
- Screen for active hepatitis B infection in all patients, and watch for hepatitis flares in patients with underlying hepatitis B or C due to immune reconstitution after starting treatment. Use tenofovir and 3TC or FTC in patients with hepatitis B, and continue this backbone if there is a need to switch to second-line therapy, since these are the only hepatitis B drugs available.
- Creatinine: if creatinine clearance is less than 50ml/min, tenofovir should be avoided and dosages of ddI, 3TC and d4T should be reduced; if below 10ml/min dosages should be further reduced. [See US HIV Medicine Association guidelines for further details.](#)

Preparing for treatment

Patient readiness for therapy is as important as the medical indications for commencing therapy.

- Patient must demonstrate insight.
- Patient must be informed that lifelong therapy is essential.
- Patient must be aware of importance of adherence.
- Patient must have been adequately informed about side-effects.
- Patient must have established the ability to attend reliably and have attended at least two or three visits before commencing therapy.

Patients should be provided with information on the following:

- ART as lifelong therapy.
- the importance of adherence
- side-effects of ART, and what to do if side-effects occur.

Active depression or substance abuse should be dealt with. Formulate a personal treatment plan, including drug storage and strategies for missed doses, with your patient. Disclosure of HIV status should be strongly encouraged as this has been shown to be an important determinant of adherence. Patients should be encouraged to join a support group or identify a treatment 'buddy'. Adequate counselling about safer sex practices must be provided to prevent transmitting to others or reinfection with a different strain.

Reference

Adult Guidelines Committee. *Antiretroviral therapy in adults*, January 2008. Journal of the Southern African HIV Clinicians Society, p18-31, 2008.

Clinical staging of HIV disease - featured news report

Oral candidiasis is a reliable marker of low CD4 counts and HIV disease progression in Zimbabwean women

Oral candidiasis (OC), or oral thrush, diagnosed by nurses was a simple and reliable marker of HIV disease progression in Zimbabwean women, according to the findings of a prospective study published in the April 15th edition of the *Journal of Acquired Immune Deficiency Syndromes*.

An estimated 24.7 million people live with HIV/AIDS in sub-Saharan Africa where co-infection with tuberculosis (TB) is common. There are concerted national and international efforts to make antiretroviral drug treatment (ART) widely available. Daily cotrimoxazole (CTX) prophylaxis is recommended for all HIV/AIDS patients to ward off opportunistic infections.

Clinical decision-making to initiate CTX prophylaxis and ART depends on a combination of laboratory assays and key clinical findings. Laboratory tests - viral load and CD4 counts - are costly, require expensive equipment, a critical mass of highly trained technicians, and are largely available only in research settings. Before access to ART became widely available, only a few rich patients were able to afford ART and the required clinical monitoring involving high-tech assays. However, as more and more patients gain access to ART, there is an urgent need for low-tech, simple, inexpensive tests which can be easily carried out by relatively untrained staff in poor rural and urban clinic settings. Such low-tech assays could be used to identify patients who need to start CTX prophylaxis and ART, and HIV-infected TB patients who require prophylaxis.

There is a clear inverse correlation between the prevalence of oral candidiasis, a common HIV-related oral disease, on one hand, and CD4 counts and ART use on the other. OC is therefore an important clinical finding from a diagnostic point of view and could complement low-tech assays such as manual total lymphocyte counts and haemoglobin counts in supporting clinical decision-making in resource-poor settings.

There is a paucity of studies on the usefulness of oral candidiasis as an accurate marker of HIV disease stage in clinic settings with no high-tech facilities. Previous studies of oral candidiasis in HIV/AIDS patients in Africa have relied on the diagnosis provided by dentists. Since most resource-poor settings do not have dentists, it is imperative that non-dental health care workers play a proactive role in the diagnosis of oral candidiasis.

Oral thrush is a fairly distinctive condition, usually presenting as white patches in the mouth, tongue or gums. The lesions may be painful and cause discomfort when eating.

A team of US and Zimbabwean researchers investigated the prevalence of oral candidiasis in relation to HIV sero-status and CD4 counts in Zimbabwean women, as well as the validity of diagnosis by trained nurses compared with that by an oral surgeon.

The study sites were family planning clinics in Harare, Zimbabwe. The study participants were women of reproductive age who were participating in two on-going HIV studies between November 2001

and November 2005; HIV testing and CD4 counts were carried out as part of the studies.

HIV-infected and HIV non-infected women received free dental care. OC was diagnosed by three nurses trained in the clinical diagnosis of HIV-related oral mucosal lesions and independently by an oral surgeon who was blinded to the patients' HIV sero-status. All patients with oral mucosal lesions and OC received appropriate treatment.

A total of 461 (320 HIV-infected, 141 uninfected) women were seen by nurses and an oral surgeon within a two-week period. The median age of HIV-infected women was slightly higher than those of non-infected women (30 versus 27). One-third of the HIV-infected women had a CD4 count less than 200 cells/mm³.

Oral thrush was more common among HIV-infected women than in uninfected women. It was the most common lesion diagnosed in nearly one quarter of HIV-infected women, whereas hairy leukoplakia and Kaposi's sarcoma were found in less than 3%. The prevalence of OC diagnosed by nurses or the surgeon was a function of the CD4 count, being significantly higher among women with a CD4 count less than 200 cells/mm³ than in women with a CD4 count from 200 to 499 cells/mm³ or a CD4 count higher than 499 cells/mm³.

When diagnosis by the oral surgeon was used as a gold standard against which the nurses' diagnosis was compared, there was a reasonably good agreement between the diagnoses by nurses and

the surgeon. The study showed that a nurse correctly identified at least seven out of ten OC cases and nine out of ten non-OC cases correctly.

In conclusion, the study results suggest that appropriately trained nurses can stage HIV disease in resource-poor settings through OC diagnosis, and that continuing education for nurses to correctly identify HIV-related clinical conditions such as OC can improve clinical decision-making for the care of HIV/AIDS patients in resource-poor settings.

Reference

Chidzonga MM et al. *Oral candidiasis as a marker of HIV disease progression among Zimbabwean women*. J Acquir Immune Defic Syndr 47:579–584, 2008.

Oral candidiasis image courtesy of <http://www.aids-images.ch/>, a free online library of AIDS-related images that can be downloaded as PowerPoint slides, collated by Prof. Bernard Hirschel of Geneva University Hospital, Switzerland. Photo credit: Prof. J. Samson, Geneva.

about HATiP

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The newsletter is edited by Theo Smart (Cape Town) and Keith Alcorn, NAM's Senior Editor (London).

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