

HATiP

HIV & AIDS Treatment in Practice

Issue 28 | 20 May 2004



In this issue:

Symptoms versus laboratory monitoring as criteria for starting treatment; *page 2*

- Key Points
- The Study
- The WHO staging system for HIV disease
- How should people's need for treatment be determined?
- Use of other laboratory markers
- Total lymphocyte count
- What are the practical implications of these findings?
- References

Symptoms versus laboratory monitoring as criteria for starting treatment

Key Points

- Research from South Africa published this week has important implications for countries and treatment programmes trying to decide how to choose which patients should receive antiretroviral therapy first.
- The findings support WHO recommendations that symptoms should be used as the primary way to decide when patients are ready for treatment.
- The study also shows that where resources are especially limited, treating only those with AIDS-defining illnesses results in a much higher number of deaths averted than if the same number of patients were selected for treatment using other, more generous criteria. The findings reinforce the choice of many programmes in their early stages to ration treatment to the sickest patients.
- Although laboratory monitoring is important in monitoring the long-term success of therapy it is not essential that it be in place when ARVS are introduced. The use of CD4 cell counting would not have improved the ability of doctors to select patients who needed treatment.
- Teaching health care workers to recognise potential symptoms of HIV disease and encourage HIV testing is likely to be a better investment in the early stages of treatment scale-up than extensive construction of laboratories capable of carrying out CD4 counts.

The Study

Giving antiretroviral therapy to all patients with symptomatic HIV disease is likely to result in fewer deaths among HIV-positive people in resource-limited settings than using the WHO staging system with CD4 cell counting for identifying patients who need treatment, according to a report in the May 21st edition of AIDS.

However, treating only people with AIDS-defining illnesses might be the best way of prioritising scarce resources, the researchers found.

In 2003 the World Health Organisation recommended that, where CD4 cell counting is available, all patients with stage IV HIV disease and all patients with CD4 cell counts below 350 cells/mm³ with stage III HIV disease should receive antiretroviral treatment. They also recommended that patients in stages I and II should receive treatment if they have CD4 counts below 200 cells/mm³.

Subsequent recommendations for scaling up treatment agreed in November 2003 switched the emphasis to treating all patients with stage III or IV symptomatic HIV disease, regardless of CD4 cell count. According to these recommendations, which were drawn up to assist rapid scale up of treatment, CD4 cell counting is desirable largely as a baseline for assessing the future benefit of treatment.

In more developed health care systems a CD4 cell count is used to decide when to start treatment, and it is usually recommended to begin treatment when the CD4 cell count lies between 350 and 200 cells/mm³

The WHO staging system for HIV disease

Where CD4 cell counting is not available the World Health Organisation's staging system has been proposed as a mechanism for deciding which patients require treatment.

WHO stage IV HIV disease corresponds to a diagnosis of AIDS.

For further information on illnesses diagnostic of AIDS, consult a WHO guide to the staging system by [clicking here](#).

Patients with WHO stage III disease have substantial immune system damage, are at high risk of disease progression and might be expected to present with some or all of the following symptoms:

- Oral thrush
- Vaginal thrush
- Chronic diarrhoea that has lasted at least one month
- Serious bacterial infections of the lungs, infections of wounds that will not go away without antibiotic treatment
- Persistent cough, fever, weight loss and other symptoms indicative of tuberculosis
- White furry patches on the side of the tongue (oral hairy leucoplakia)
- A feverish state for much of the time in the past month
- Weight loss of at least 10% of the body weight

At this stage, people with HIV infection are likely to be spending much more time in bed than usual, but will be able to go about their normal lives for at least half the days in the previous month.

Stage I HIV infection corresponds to asymptomatic HIV infection, and stage II HIV infection corresponds to the presence of minor symptoms such as skin infections like pruritic rashes, frequent ear, nose and throat infections and moderate weight loss.

How should people's need for treatment be determined?

Researchers from the University of Cape Town reported on the clinical outcomes of patients enrolled into the Cape Town AIDS Cohort between 1995 and 2001. Patients who obtained antiretrovirals through clinical trials or private means (n=292) were compared with those who did not (n=981).

The researchers had information on CD4 cell counts for both groups of patients, and obtained information on deaths from clinic records or the municipal registry of deaths.

HAART-treated patients were followed for an average of 17.4 months, non-treated patients for an average of 14.4 months.

The researchers used the data to compare the effects of five different thresholds for starting treatment on the likelihood of death. They compared the risk of death in HAART-treated patients and five different groups of untreated patients:

- All stage IV patients and stage III patients with CD4 counts below 350, and stage I and II patients with CD4 cell counts below 200
- All stage IV patients and all other patients with CD4 counts below 200
- Patients with WHO stage III and IV symptoms
- Patients with AIDS-defining illnesses
- Patients with CD4 cell counts below 200 cells/mm³

They found that by treating only those with AIDS-defining illnesses they would have averted the largest number of deaths per 100 person years of treatment (74%), even though this threshold

would have resulted in the smallest numbers on treatment (only 12.9% of all untreated patients would be eligible for treatment). The analysis does not discuss the number of days of hospitalisation that might be averted by different strategies however, but this would be an important consideration in many health care systems.

Treating those with symptomatic HIV disease in WHO stages III and IV would have averted just as many deaths as treating everyone according to the 2003 WHO treatment guidelines (40 vs 30 per 100 person years of treatment) but substantially fewer people would have required antiretroviral therapy (44.5% vs 56.7%). Using a CD4 cell count threshold of 200 cells/mm³ resulted in the lowest level of deaths averted (29.6 per 100 person years of treatment), but almost 50% of patients would have received treatment.

However the authors also note that if treatment is confined to those who are symptomatic, 41% of asymptomatic patients with CD4 cell counts below 200 cells/mm³ would not have been eligible for treatment.

The question this study cannot answer is: does the inability to measure CD4 cell counts and detect patients with CD4 cell counts below 200 cells/mm³ make a substantial difference to patients' eventual response to HAART and risk of death if they are already receiving cotrimoxazole prophylaxis? In the Cape Town cohort patients not on HAART who received cotrimoxazole were significantly less likely to die during follow-up.

A study of all patients receiving antiretroviral therapy in the Canadian province of British Columbia has shown that whilst the risk of death after commencing HAART increases significantly once the CD4 cell count falls below 200 cells/mm³, HAART's ability to prevent death is sharply reduced only when the CD4 cell count falls below 50 cells/mm³.

The authors suggest that treatment programmes need to look carefully at WHO's 3 x 5 treatment model when planning how to use scarce resources.

Use of other laboratory markers

"Implementation of the 2003 revised WHO guidelines in sub-Saharan Africa could result in a significantly larger number of eligible individuals but with lower impact on mortality than an alternative strategy based on clinical parameters."

Similar findings are reported in the same issue of AIDS by French and Malawian researchers who report on the value of WHO clinical staging, body mass index, haemoglobin and total lymphocyte count as markers for beginning HAART among patients at a hospital in Chiradzulu, Malawi.

206 patients diagnosed HIV-positive by the clinic were included in the analysis. The use of WHO clinical staging proved to be the most sensitive measure of immune deficiency, the researchers found. This method identified 81% of patients with CD4 counts below 200 cells/mm³ amongst stage IV patients and 71% of patients with CD4 counts below 200 among stage III patients.

In contrast use of total lymphocyte counts to determine whether patients with WHO stage III disease needed treatment was 'poorly sensitive', although it might help to identify patients at WHO stage I or II who had CD4 cell counts below 200 cells/mm³.

Body mass index and haemoglobinaemia provided little extra information to influence decisions on when to treat, the researchers report.

"In rural settings, the scarcity of resources and the massive need for treatment require markers as simple as possible to initiate HAART. WHO clinical stages 3 or 4 thus appear to be a valuable universal marker."

Total lymphocyte count

Measuring the total lymphocyte count has also been proposed as an alternative to CD4 cell counting. It requires only basic laboratory equipment.

© Copyright NAM — All rights reserved. Please photocopy and pass on.

NAM publishes a wide range of publications on treatment for HIV. For details contact:

NAM, 77a Tradescant Road, London, SW8 1XJ, UK

tel +44 20 3242 0820 fax +44 20 3242 0839 email info@nam.org.uk web www.aidsmap.com

The value of measuring the total lymphocyte count is discussed in more detail in an [accompanying article](#), which reviews conflicting evidence from recent studies on the usefulness of this measure.

What are the practical implications of these findings?

Taken together, the findings of these studies suggest that when scaling up antiretroviral therapy, the introduction of CD4 counting is less of a priority than basic training for health care workers. Greater attention should be paid to ensuring that:

- all health care workers can identify the symptoms of stage III or IV HIV disease
- all health care workers can counsel patients that HIV testing may be appropriate if they have any of the symptoms.

An HIV test should be considered if a patient has any of the opportunistic infections related to HIV infection (including tuberculosis) or has one or more of the following conditions:

- unexplained weight loss or loss of appetite
- prolonged period of fever; especially at night
- chronic watery diarrhoea of unknown cause;
- swollen lymph nodes (generalised lymphadenopathy);
- persistent skin disorders including skin rashes, itching, herpes simplex ulcers, herpes zoster (shingles), seborrhoeic dermatitis, warts; anal itching or discomfort.
- neurological problems including dementia in patients less than 50 years old, or sudden onsets of unexplained psychosis, peripheral neuropathy, and Bell's palsy;
- persistent cough, breathing problems or pneumonia;
- persistent vaginal thrush
- oral thrush or pain when swallowing that might indicate thrush in the throat/gullet
- severe or recurrent bacterial infections including wound infections (septicaemia), chronic sinusitis.

Recognition of symptoms, staging of HIV disease and monitoring requirements in resource-limited settings are discussed in more detail in NAM's training toolkit <http://www.aidsmap.com/publications/toolkit/> Treating HIV & AIDS specifically the module entitled Clinical monitoring and laboratory tests. (If you have not already done so, you will need to register in order to view this resource online).

References

Badri M, Bekker LG, Orrell C et al. Initiating highly active antiretroviral therapy in sub-Saharan Africa: an assessment of the revised World Health Organization scaling-up guidelines. *AIDS* 18: 1159-1168, 2004.

Tassie JM, Marquardt T, Damisoni H et al. Indirect markers to initiate highly active antiretroviral therapy in a rural African setting. *AIDS* 18: 1226 - 27, 2004.

about HATiP

A regular electronic newsletter for health care workers and community-based organisations on HIV treatment in resource-limited settings.

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

For further information please visit the HATIP section of aidsmap.com