Study shows that HIV antiretroviral treatment should start earlier

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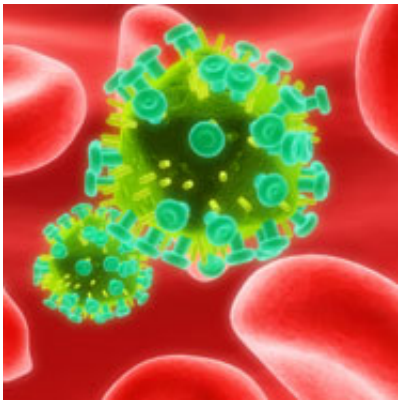

A 3D rendered image of the HIV virus

(PhysOrg.com) -- A new analysis of more than 45,000 people with HIV in Europe and North America suggests that the minimum CD4-cell count threshold for initiation of combination antiretroviral therapy (cART) should be 350 cells per µL of blood. This is at the upper limit of levels for starting cART currently recommended in many countries.

The findings are published in an article in an upcoming edition of *The* Lancet, written by Jonathan Sterne, Professor of Medical Statistics and Epidemiology, University of Bristol, and colleagues from the When To Start Consortium of observational cohort studies of people with HIV.

The CD4-cell count at which cART should be started is a central,

unresolved issue in the care of HIV-1 infected patients.

In the absence of randomised controlled trials, the authors analysed data from 18 prospective studies from Europe and North America, of which 15 provided eligible patients who had not previously been treated with antiretroviral drugs. Patients were included if they had started cART (while AIDS-free, with a CD4-cell count less than 550 cells per μLm and with no history of injecting-drug use) on or after January 1, 1998. Data from patients followed up in seven cohorts in the era before the introduction of cART were used to estimate the relationship between when treatment started and AIDS related events or death.

Data was obtained for 21,247 patients who were followed up during the era before the introduction of cART and 24,444 patients who were followed up from the start of treatment. Deferring combination therapy until a CD4-cell count of 251-350 cells per μL was associated with a 28 per cent higher rate of AIDS and death than starting therapy in the range 351-450 cells per μL. The adverse effect of deferring treatment increased with decreasing CD4-cell count threshold. Deferred initiation of combination therapy in the above ranges was also associated with higher mortality rates (13 per cent), though the effect on mortality was less than the effect on the combined endpoint of AIDS and death.

The authors said: “When patients and their physicians consider starting antiretroviral treatment, they must balance its beneficial effects on rates of progression to AIDS and death with several other issues. Eradication of HIV from an individual is not currently possible; therefore, treatment is expected to be lifelong. Antiretroviral drugs can be inconvenient to take, and have side effects that include nausea, diarrhoea and headache. Combination antiretroviral therapy is associated with serious toxic effects including redistribution of body fat, hepatitis, renal failure and mitochondrial toxicity, and an increased risk of cardiovascular disease. However, these toxic effects are to an extent avoidable through choice of

drug regimen.

“Our findings should help to guide physicians and patients in deciding when to start antiretroviral treatment. The evolution of guidelines has been compared to the swings of a pendulum, from initial enthusiasm for early treatment, through to caution because of concern about toxic effects and the risk of resistance and loss of treatment options, to more recent calls for earlier treatment. The International AIDS Society USA panel recommended in August, 2008, that antiretroviral therapy is started in individuals with CD4-cell counts less than 350 cells per μL, and that this decision should be individualised when the CD4-cell count is greater than 350 cells per μL."

Recent US and European guidelines make similar recommendations. They added: “Unfortunately, many patients are not diagnosed with HIV until their CD4 count has fallen well below 350 cells per μL, sometimes even below 200 cells per μL. It is important that people at possible risk of having HIV get tested regularly so that if found to be infected they can receive the necessary care and treatment.

"Because we found evidence that deferring treatment until the patient’s CD4-cell count is less than 350 cells per μL was associated with increased progression rates, and in view of diminished concerns about toxic effects and resistance, our results suggest that 350 cells per μL should be the minimum threshold at which antiretroviral therapy should be started.”

In an accompanying comment, Dr Robin Wood, The Desmond Tutu HIV Centre, University of Cape Town, South Africa, and Dr Stephen D Lawn, The Desmond Tutu HIV Centre, University of Cape Town, South Africa and London School of Hygiene and Tropical Medicine, UK, said: “The question of when to start ART might have more than one right answer. WHO guidelines for resource-limited settings currently

recommend initiation of ART before blood CD4 counts fall below 200 cells per μL with an upper threshold of 350 cells per μL. To inform these recommendations, randomised controlled trials should include patients living in resource-limited settings."

More information: www.thelancet.com/

Provided by University of Bristol (news : web)