AIDS BRIEFS

WHY ANTIRETROVIRALS CANNOT ERADICATE HIV

A new study, published in the November edition of the *Journal of Clinical Investigation*, helps to understand why those who have been on antiretrovirals for many years, maintaining an undetectable viral load, cannot eradicate HIV.

American and Canadian researchers studied 11 HIV-positive people who had been successfully receiving antiretroviral therapy for up to 9 years. They showed that all 11 patients had CD4 cells infected with HIV that was still able to reproduce. Most of these patients also had high levels of the DNA that HIV produces inserted into cells after the virus had infected both active and resting CD4 cells. Most of the persistent HIV was found in active rather than in resting CD4 cells.

Researchers then further examined the activated and resting CD4 cells. They found HIV proviral DNA in both cell types, but significantly more in activated CD4 cells than in resting cells. The team also found that activated CD4 cells could produce detectable HIV virions. Tests of the genetic structure of HIV isolated from both resting and activated CD4 cells showed that there is bi-directional HIV infection between resting and activated CD4 cell compartments.

This study, contrary to what many people think, shows that it is the activated CD4 cell compartment that holds most of the persisting HIV infection in people with undetectable viral loads as a result of extended antiretroviral therapy. This, according to the authors, is 'compelling' evidence for this compartment being a major contributor to the continual reseeding of HIV reservoirs. Latent CD4 cells infected with HIV could be reactivated as a consequence of normal responses to infections, the authors suggest. The implications of these findings for treatment include providing treatment with a reagent to dampen cellular activation and the spread of HIV to other cells. Patients taking effective HIV therapy could also use additional antiretrovirals as entry inhibitors, so further suppressing HIV replication.

Chun T-W, *et al. J Clin Invest* 2005; **115:** 3250-3255.

INCIDENCE OF TB IS HIGH AFTER STARTING ANTIRETROVIRALS

The well-known Médecins Sans Frontières (MSF) antiretroviral treatment programmes in poor countries are highlighting a high incidence of tuberculosis (TB) in people soon after they start antiretrovirals. Current treatment guidelines recommend that, wherever possible, the first 2 months of TB treatment should be given without giving antiretroviral treatment as well. This is to avoid interaction between nevirapine and rifampicin and to reduce the risk of an immune reconstitution syndrome. The latter is relatively common in those with a past history of TB.

However, according to the authors of this study, of more concern is the possibility that antiretroviral treatment may be started without a diagnosis of TB, often more difficult in those who are HIV-positive, as it is often smear-negative or extrapulmonary.

MSF surveyed 3 151 patients receiving antiretroviral treatment in Kenya, Malawi, Cameroon, Cambodia and Thailand. They showed an incidence of between 4.8 and 17.6 cases of pulmonary TB per 100 person years of follow-up. Most cases occurred during the first 3 months of treatment.

Although patients in Thailand and Cambodia have more advanced HIV disease (over two-thirds had CD4 cell counts of < 50 and half had WHO stage 4 disease, compared with one-third in African countries), the incidence of TB was no greater in these patients.

MSF points to the lack of an available rapid test for TB before starting an HIV-positive person on antiretrovirals. The MSF doctors think that most of the early TB cases among those taking antiretroviral treatment are not diagnosed, either because diagnostic tests do not pick up the TB, or because symptoms are not clear. They recommend that programmes dependent on nevirapine for HIV treatment and rifampicin for TB treatment need access to more expensive, alternative drugs to manage this problem, particularly as the numbers treated, grow. Patients have to interrupt antiretroviral treatment in order to treat TB successfully and there are no clinical trial data that would allow confident prescription of rifampicin and nevirapine together.

Bonnet M, *et al. Int J Tuberculosis Lung Dis* 2005; **9:** S59.

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