

## TREATMENT INTENSIFICATION DOES NOT REDUCE RESIDUAL HIV-1 VIREMIA IN PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY

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In HIV-1-infected individuals taking highly active antiretroviral therapy (HAART), viremia is reduced below 50 copies of HIV-1 RNA/ml plasma. Using sensitive assays for viremia, low-level viremia is detectable over prolonged periods in most infected individuals. Previously we noted relatively slow decay of HIV-1 viremia during suppressive therapy (Palmer et al., 2008), and modeling studies predict the stability of the residual reservoir is the result of long lived cells and not active replication (Sedaghat et al., 2008). The nature of HIV replication during suppressive therapy remains uncertain, however, and there is continued controversy over whether the residual viremia results from ongoing cycles of viral replication. To address this question, we conducted two prospective studies to assess the effect of antiretroviral treatment intensification on residual viremia in 15 HIV-1-infected individuals on suppressive HAART. Using an ultrasensitive HIV-1 RNA assay with a limit of detection of 1 copy/ml, we found that levels of viremia were not reduced by treatment intensification with three different antiretroviral agents (efavirenz, lopinavir/ritonavir, or atazanavir/ritonavir). The lack of decay was not associated with the presence of drug-resistant virus or suboptimal drug concentrations. Our results suggest that residual viremia is not the product of ongoing, complete cycles of viral replication but rather of virus output from stable reservoirs of infection. New strategies will be necessary to eradicate HIV infection.