Latin America in an immunocompetent patient with a limb infection that was cured without amputation.

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Measurement of Human Immunodeficiency Virus (HIV) Type 1 RNA Load Distinguishes Progressive Infection from Nonprogressive HIV-1 Infection in Men and Women

The HIV-1 load in plasma or serum has been found to correlate with disease progression in men as well as response to antiviral therapy and transmission of HIV-1 from mother to child [1–7]. Because the worldwide incidence of HIV-1 infection among women, including those in the United States, has increased dramatically in recent years, studies of viral load need to include women as well as men to determine if the relationship between HIV-1 load and disease progression applies to both genders. To investigate distinctive patterns of HIV-1 disease progression and their relationship to viral load in both women and men, we used reverse transcription quantitative competitive PCR (RT QC-PCR) to measure serum or plasma HIV-1 RNA levels in four groups of well-characterized HIV-1 infected patients. We retrospectively studied 45 patients, including 22 women and 23 men. These HIV-1-infected adults were stratified, on the basis of patterns of clinical HIV-1 disease progression, into the following four categories:

Category 1, long-term nonprogressive disease ($n = 7$). These patients had been infected at least 8 years and had $CD4^+$ cell counts of $>450/mm^3$ at the most recent measurement. None of these patients had received antiretroviral treatment.

Category 2, clinically stable nonprogressive disease ($n = 12$). These patients had $CD4^+$ cell counts of $200–450/mm^3$. Eleven of these patients had received antiretroviral treatment.

Category 3, progressive HIV-1-related disease ($n = 9$). The disease was considered progressive if the patient developed any of the following problems during the 1- to 2-year observation period after the blood was collected: an AIDS-defining opportunistic infection, wasting, or any other HIV-related clinical condition; p24 antigenemia; or a loss of >100 $CD4^+$ cells/mm^3. None of these patients had histories of opportunistic infections at the time the blood specimen was obtained. Eight patients had received antiretroviral treatment.

Category 4, a history of AIDS-defining opportunistic infections at the time the blood was collected ($n = 17$). Eleven of these patients were taking antiretroviral drugs.

Each of the patients in categories 1–3 were followed up clinically for at least 1–2 years after the specimen was obtained. Six women in category 4 (patients 40–45) were included in a substudy of the Womens Interagency HIV Study (WIHS) in the Bronx, New York, and they provided plasma. All other patients were patients at Long Island Jewish Medical Center (New Hyde Park, NY), and they provided serum. HIV-1 RNA was extracted from frozen serum or plasma and quantitated by means of RT QC-PCR with use of a modification of the technique of Piatak et al. [1, 6]. Correlations between $CD4^+$ cell count, HIV-1 RNA level, and disease category were studied by using the nonparametric Spearman correlation coefficient and its P value.

We first analyzed how the HIV-1 RNA load related to the category of disease. When the four categories were analyzed statistically as a whole, we found that the mean HIV-1 RNA load increased with increasing category of disease progression (Spearman correlation = 0.73; $P = .0001$; figure 1). This correlation also pertained when the populations of men and women in each group were analyzed separately (Spearman correlation = 0.74; $P = .0001$ for men; Spearman correlation = 0.73; $P = .0001$ for women).

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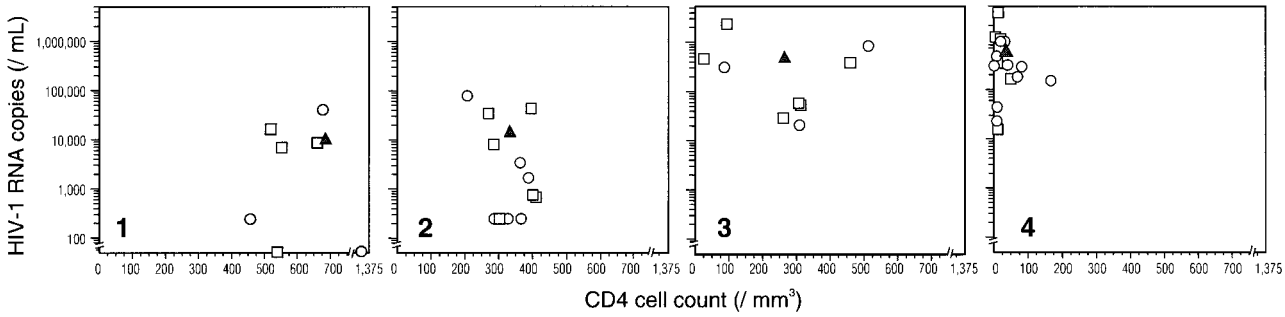

Figure 1. HIV-1 RNA levels and $CD4^+$ cell counts for patients in each category of disease progression (see categories 1–4 in text); ○ = individual women, □ = individual men, ▲ = mean values for men and women combined.

The most striking differences in viral loads were observed when the two groups of patients with progressive disease (categories 3 and 4) were compared with the groups who had nonprogressive disease (categories 1 and 2) (figure 1). HIV-1 RNA loads of <50,000 copies/mL were strongly correlated with nonprogressive disease, and HIV-1 RNA loads of >50,000 copies/mL were correlated with progressive disease. These relationships were statistically significant for men ($P < .0001$), women ($P < .01$), and the combined group of all patients ($P < .0001$, Fisher's exact test). There was a small fraction of patients in categories 3 and 4 who had low viral loads. Antiviral treatment may have contributed to the low RNA levels in some of these patients.

We found that the mean HIV-1 RNA load increased with decreasing $CD4^+$ cell counts in both men and women (Spearman correlation = −0.64; $P = .001$ for men; Spearman correlation = −0.60; $P = .003$ for women; Spearman correlation = −0.62; $P = .0001$ for men and women combined). However, the HIV-1 RNA load in most cases was an earlier predictor of disease progression than was the $CD4^+$ cell count.

There were no statistically significant differences between the genders in either viral load or $CD4^+$ cell count in any of the categories of disease progression (Wilcoxon rank sum test).

In this study, we found a strong correlation of viral load with disease progression for both men and women; this correlation was statistically significant for both men and women. These data are consistent with the concept that there may be HIV-1 RNA thresholds that play a role in determining clinical outcomes [6, 7]. Measurement of HIV-1 RNA appears to be clinically useful in predicting disease progression and monitoring the effectiveness of antiviral therapy in women as well as in men.

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