Malnutrition and Variability in CD4+ Cell Counts in African Populations

To the Editor—Williams et al. [1] investigated a mathematical model to predict the distribution of CD4+ cell counts among HIV-positive adults by use of the distribution among HIV-negative adults in African populations. The study was mainly based on data collected in South Africa and Zambia. The authors noted that CD4+ cell counts vary widely within and among populations. The CD4+ cell count distributions among HIV-negative people had a higher mean in South Africa than in Zambia, but the mean rate of decrease in CD4+ cell count among HIV-positive people was higher in South Africa, and mean survival was shorter in South Africa than in Zambia at a given CD4+ cell count. The authors did not provide an explanation for these observations, which are important for the prediction of mortality at a given CD4+ cell count. Predictions of disease progression and mortality inform the decision-making process about the commencement of antiretroviral treatment in an individual HIV-infected patient.

The authors’ findings could be explained by the impact of nutritional status on CD4+ cell counts. In malnutrition, the thymus gland undergoes severe atrophy due to apoptosis-induced thymocyte depletion, particularly affecting the immature CD4+ cells, as well as a decrease in cell proliferation [2]. This process has been linked to decreased leptin and increased glucocorticoid levels in malnutrition [3]. CD4+ cell counts were found to be lower in children with nonedematous malnutrition than in those with edematous malnutrition [4]. The population in Zambia at the time the studies the authors referred to were conducted had a significantly higher proportion of malnourished people than did the population in South Africa, where the economic conditions started to improve with increased rates of obesity [5, 6]. This may explain the lower mean CD4+ cell count among HIV-negative people in the Zambian study. It is unlikely that the lower mean CD4+ cell count in Zambia was due to an increased burden of other infectious diseases, because increased cytokine levels due to ongoing infections would (for example via tumor necrosis factor and NF-κB–mediated long terminal repeat–driven increased HIV transcription) have led to accelerated disease progression and increased mortality due to HIV infection. Malnutrition rather than increased infectious-disease burden is, therefore, also the most likely explanation for the finding of a study in Ethiopia in which, at lower CD4+ cell counts, life expectancy in HIV-positive patients was similar to that in The Netherlands [6]. Low CD4+ cell counts due to malnutrition are associated with a more functional immune system than are low CD4+ cell counts due to HIV-induced T cell apoptosis, and many immune functions are well preserved in people with malnutrition [7]. Future mathematical models predicting disease progression and mortality in HIV-positive populations need to relate CD4+ cell counts to body mass index.

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References

Reply to Eisenhut

To the Editor—Eisenhut [1] discusses the role of malnutrition as a determinant of CD4+ cell counts, especially in Africa. It is known that genetic, immunological, physiological, and behavioral factors are associated with CD4+ cell counts within and among populations, and we referred to some of these factors in our article [2]. However, our intention was not to explain the reasons for this variation but, rather, to investigate the more limited question of the relationship between the distributions of CD4+ cell counts among HIV-positive and HIV-negative people from the same population. The surprising conclusion was that, in populations in which the initial mean CD4+ cell count is low,