How Can Earlier Entry of Patients into Antiretroviral Programs in Low-Income Countries Be Promoted?

Sir—We read with interest the editorial by Colebunders et al. [1] concerning the ongoing challenges of providing antiretroviral treatment (ART) access for persons infected with HIV in Africa. At an antiretroviral service in Kampala, Uganda, a key issue highlighted by the authors was that the mean CD4 cell count at initiation of ART was just 63 cells/μL; the majority of patients presented to the service with advanced symptomatic disease. Late presentation is costly in terms of morbidity, mortality, and use of secondary health care resources and also limits the potential for restoration of immune function [2, 3]. In a community-based ART program in Gugulethu, South Africa, we have initiated treatment for >1000 patients over a period of 3 years, and yet the median CD4 cell count at enrollment has remained at <100 cells/μL. Early optimism that this measurement would increase once the backlog of patients with very advanced disease had received ART has not materialized here or in Kampala.

A key challenge is how to identify and initiate ART among patients with less advanced disease. This is most readily done among patients interfacing with the health care system. An obvious target population is those with tuberculosis (TB), the most common opportunistic infection in low-income countries. Indeed, 55% of patients entering our program have a history of TB. Because TB occurs across the full range of HIV-associated immunodeficiency [4], a significant proportion of HIV-infected patients with TB might be expected to have early disease. We analyzed the CD4 cell counts of patients enrolling into our ART program who either were currently receiving or had recently completed treatment for TB. These data revealed that the majority had very advanced disease (median CD4 cell count, 65 cells/μL); the CD4 cell count distribution also suggests that few additional patients would have had CD4 cell counts of >200 cells/μL (figure 1A). This finding confirms observations that the relative risk and burden of TB rise steeply with advanced immunodeficiency [6, 7]. Thus, although TB clinics in this community provide a key opportunity to identify

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**Figure 1.** CD4 cell counts in blood samples from HIV-infected patients enrolled in a community-based antiretroviral treatment (ART) program who were currently receiving antituberculosis treatment or had completed antituberculosis treatment within the 6 months prior to enrollment in the ART program (A) or who were women identified within the antenatal service (B). For each group of patients, their frequency distribution stratified by baseline CD4 cell count is given. All patients were enrolled in the ART program under the World Health Organization guidelines (2002) [5], and so CD4 cell counts are <200 cells/μL. TB, tuberculosis.
HIV-infected individuals, in general they do not provide access to patients with early disease.

In contrast, however, HIV-infected pregnant mothers identified in antenatal clinics and referred to our ART program had a median CD4 cell count (127 cells/μL) twice that of patients with TB and exceeding that of the overall treatment cohort (figure 1B). The CD4 cell count distribution also suggests that it is likely that a substantial proportion of antenatal patients also had CD4 cell counts of >200 cells/μL. Because the antenatal HIV serore prevalence rate is ~30% in this community [8], antenatal clinics represent a key opportunity for identifying many patients with less-advanced immunodeficiency. Treatment of these patients is likely not only to result in better outcomes but also to prevent vertical transmission of HIV. Thus, provision of facilities for HIV testing and CD4 cell count measurement at antenatal clinics warrants prioritization as access to ART is increased in low-income countries. Furthermore, although costly, provision of CD4 cell count measurements at other voluntary counseling and testing facilities would also help identify other asymptomatic individuals with less-advanced disease who are eligible for ART.

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References

Reply to Lawn and Wood

Sir—We agree with Lawn and Wood [1] that patients should be enrolled earlier into antiretroviral treatment (ART) programs. This will benefit HIV-infected individuals and speed up the antiretroviral “rollout” process. Starting ART before patients develop opportunistic infections prevents unnecessary deaths, reduces drug interactions between the antiretrovirals and other drugs, and probably decreases the incidence of immune reactivation inflammatory syndrome. The cost of these complications with their attendant hospitalization is substantial, and these resources are better used for ART.

To start ART earlier, CD4+ lymphocyte counts must be available on a larger, decentralized scale. This will require cheaper and simpler methods for testing CD4+ lymphocyte counts. Ideally, measurement of CD4+ lymphocyte counts should be offered at voluntary counseling and testing sites, antenatal clinics, and tuberculosis (TB) treatment centers. The fact that, in the South African experience, HIV-seropositive patients with TB had a mean CD4+ lymphocyte count of 65 cells/μL suggests that these patients were referred for ART when both illnesses were far advanced. Diagnostic and treatment delays for TB must be effectively addressed.

Either the CD4+ lymphocyte count testing should be done at the site where the HIV testing was done or samples should be referred to a reference laboratory with systems that guarantee rapid and reliable return of results. On the basis of CD4+ lymphocyte count results, asymptomatic or paucisymptomatic patients could be referred for early ART. The rollout of CD4+ lymphocyte count testing will not only reduce transportation costs for patients but also enable ART centers to work more efficiently because they will be able to start ART in patients less likely to develop complications and they will not be overwhelmed by patients who do not require treatment.

Earlier initiation of ART in low-income countries must be promoted. This will require additional fiscal and human resources, but, in the long run, the overall cost to society will be substantially less, with reduced health care costs for management of opportunistic infections, including TB, and with more healthy, productive individuals and societies.

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