Viral Load Testing in Resource-Limited Settings

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(See the article by Calmy et al. on pages 128–34 and the brief report by Bagchi et al. on pages 135–8)

A man who leapt off the roof of a 10-story building was asked by a person in a fifth-floor window how he was doing as he flew past. "Fine so far," he replied.

The impact of antiretroviral therapy on HIV-associated morbidity and mortality where it has been available has been one of the most dramatic examples of the benefits that accrue from investment in the academic and industrial biomedical research enterprise [1, 2]. The speed and success of this effort has been the result of a hypothesis-driven research effort that has closely linked clinical investigation with emerging information about the pathogenesis of the disease, using advancements on either front to drive the other. The result has been that we probably know more about the relationships among the virus, the host, and the natural history of this infection than is the case in any other disease in medicine. Because of what we know about these relationships, there is much less room for speculation about the prognostic implications of certain therapeutic decisions in this disease than in many others.

Although some in the health policy community have argued that making antiretroviral therapy available in resource-limited settings would not be feasible or would not be a good public policy investment, data emerged very quickly after pilot programs were initiated that refuted this data-free speculation [3]. When treated with potent combinations of antiretroviral drugs in settings where appropriate adherence support can be provided, viral suppression rates very similar to those observed in high-resource settings can be achieved [3]. Initial efforts to deliver antiretroviral drugs in resource-limited settings were not unlike those observed in the West in the late 1980s. The results have been remarkable in settings as diverse as Haiti, Zimbabwe, and India [4–6]. Economic models have very clearly pointed to the cost-effectiveness of investment in contemporary antiretroviral therapy in resource-limited settings [7].

Now that the benefits of antiretroviral therapy have been as clearly demonstrated in resource-limited settings as in high-resource settings, we are moving from what will be viewed, in retrospect, as short-term demonstration projects to a sustained effort. Because need will exceed resources (as continues to be the case in many parts of the United States) for some time to come, investments must be made strategically, to maximize the benefits for the most people over the longest term. Initial investment priorities were primarily directed at training medical personnel and at purchasing antiretroviral drugs. A rapidly expanding provider pool composed of talented and committed individuals has struggled to implement antiretroviral therapy for as many people as possible with the resources brought to bear. Laboratory infrastructure has been slower to develop. Because it was not initially available in many places in which antiretroviral therapy was implemented, it was hoped that clinical characteristics or simpler laboratory studies (such as determination of total lymphocyte counts) could be substituted for CD4 cell testing to guide therapy. Using a large body of prospective data from the University of Alabama, in this issue of *Clinical Infectious Diseases,* Bagchi et al. [8] have demonstrated that neither clinical findings nor CD4 cell counts are adequate predictors of viral suppression. Furthermore, a recently published economic model based on a clinical trial in the Cote d'Ivoire has shown that the development of CD4 cell testing to guide therapy is a sound public health policy [9]. Efforts to make CD4 cell testing more widely available are now underway, as is a large research effort to simplify and lower the cost of this technology [10].

The health policy and treatment community have been much slower to embrace the use of plasma HIV-1 RNA monitoring to guide antiretroviral therapy in resource-limited settings [11]. This has been driven by a combination of cost and the lack of availability of this technology in many parts of the resource-limited world. As Calmy and her colleagues per-

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suasively argue in this issue of the journal, this reticence is extremely short sighted [12]. We are still living with the legacy of our period of incomplete viral suppression in this country from the pre-HAART era. The price of this legacy is borne by individual patients who now must use more complicated, toxic and costly regimens. Private and government payers bear the cost of increased HIV- and therapy-related morbidity, more-costly treatment regimens, and a much greater need for resistance testing. The period of incomplete suppression has seeded the population with substantial amounts of drug-resistant virus that is now being transmitted with such a frequency that recently issued US treatment guidelines now recommend viral resistance testing before even the first treatment regimen is administered [13, 14]. Dealing with these issues in high-resource settings is difficult; doing so in resource-limited settings will be even more difficult.

Although the short-term reductions in morbidity and mortality associated with the introduction of antiretroviral therapy in resource-limited settings have been gratifying, it is imperative to look to the future as we acknowledge that the need for antiretroviral therapy is not going to disappear any time soon. Prevention programs have slowed the spread of the virus, but there is no indication that these programs can stop the epidemic. There is little reason for optimism about the prospects for the development of an effective HIV vaccine in the near future. With these realities in mind, it is imperative that we not ignore the lessons of our experience with antiretroviral therapy in high-resource settings as treatment moves forward in resource-limited settings. Viral load testing is the only currently available means to avoid the consequences of detecting the early failure of antiretroviral therapy for both the individual and the population at large. Things have improved immensely for those living with HIV infection in resource-limited settings who have been fortunate to be on the first wave of therapy. Nonetheless, we must avoid invoking the "fifth-floor syndrome" by failing to act to prevent what we know will happen if viral load testing is not expanded in concert with the access to antiretroviral drugs.

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