Universal Access to Antiretroviral Therapy: When, Not If

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(See the article by Spacek et al. on pages 252–9)

The global HIV/AIDS pandemic poses the greatest global health challenge in recent history. Effective, large-scale treatment of the several million infected individuals has appeared to present an almost insurmountable task.

An ambitious global approach to this challenge was developed by the World Health Organization (WHO) “3 by 5” program in 2003, with the goal of providing treatment to 3 million affected individuals in low- and middle-income countries by the end of 2005 [1]. Although the immediate goal of the “3 by 5” program has not been achieved, >500,000 Africans are now receiving antiretroviral therapy (ART). This initial WHO initiative has been of tremendous value in shifting the international emphasis from “if” to “when” universal access to antiretroviral treatment can be achieved. An additional thoughtful analysis of the essential elements of an effective approach to worldwide scale-up of ART was presented by the Institute of Medicine in early 2005 [2].

With this background, the article by Spacek et al. [3] in this issue of Clinical Infectious Diseases provides welcome new data that highlight both the unique opportunities and the enormous challenges still posed by the imminent rapid scaling up of ART in sub-Saharan Africa. The clinical responses achieved 9 months after initiating HAART for a cohort of severely immunocompromised Ugandan individuals are most gratifying. Two-thirds of these patients achieved suppression of plasma HIV-1 to levels below detectable limits in an ambulatory setting without the support of a clinical trial infrastructure. These results compare well with those generally achieved in economically advanced industrialized nations [3]. Especially striking were the clinical outcomes. A total of 93% of patients were unable to hold a job when HAART was initiated, yet 85% reported feeling “good” to “excellent” following at least 12 weeks of treatment, and 96% reported better performance at home or work. None of the patients felt weaker while receiving HAART. These short-term clinical results in economically disadvantaged individuals with non-B clade HIV infection are comparable with the outcomes observed in larger cohorts of less severely immunocompromised individuals in industrialized nations [4, 5].

Results of resistance testing for the one-third of patients who did not achieve sustained suppression of viral replication point to an enormous challenge posed by large-scale rollout of HAART in sub-Saharan Africa. Virologic failure and development of resistant strains in these individuals was strongly associated with interruption of treatment for >4 days. Inability to purchase antiretroviral drugs was the major reason for treatment interruption, occurring twice as often as toxicity and/or illness. This further highlights the necessity of eliminating financial as well as structural barriers to continued access to antiretroviral drugs for all individuals receiving ART.

In the data available for 36 individuals with detectable viral loads, 75% of patients had virus with genotypes conferring resistance to nonnucleoside reverse-transcriptase inhibitors, most commonly due to the K103N mutation. This resistance poses major problems. Nonnucleoside reverse-transcriptase inhibitors have been and will continue to be widely used in ART rollout programs throughout the developing world because of a number of attractive characteristics, including ease of
administration (once or twice daily), relative lack of immediate and long-term toxicity, stability in storage at high ambient temperatures, and very low cost in relation to protease inhibitors. Because of these advantages, nonnucleoside reverse-transcriptase inhibitors will remain the first-line therapeutic choice in resource-restricted nations for the foreseeable future.

As PEPFAR, GFATM, and other international donors increasingly make HAART available throughout resource-restricted regions, a major challenge will be to minimize interruption of therapy. Adherence to HAART will be critical. The article by Spacek et al. [3] and earlier reports from India [6] and Africa [7] suggest that patient adherence may prove to be a lesser problem in resource-restricted countries than in the industrialized world. Such information, however, has been obtained from relatively small cohorts of patients for whom a great deal of time and effort has been committed to pretreatment education. It will be a major challenge to replicate this experience during rapid scale-up of HAART [8]. An equally great challenge will be to develop effective ART supply chains that can ensure an uninterrupted supply of antiviral drugs to persons receiving HAART, especially in more-remote rural regions. Once effective supply chains have been established, assurance of long-term sustainability will demand continued close coordination between each affected nation and the international donor community.

Yet to be effectively addressed is the availability of second-line therapy, based on ritonavir-boosted protease inhibitors, which will be in increasing demand as a substantial subset of individuals develop nonnucleoside reverse-transcriptase inhibitor resistance mutations. This issue will demand continued and increasing collaboration between pharmaceutical manufacturers, the international donor community, and the governments of resource-restricted nations.

The encouraging results presented by Spacek et al. [3] add further support to the developing international consensus that HAART can effectively be delivered in sub-Saharan Africa if adequate attention is directed toward structural and behavioral barriers. The expressed commitments of PEPFAR and GFATM leadership to harmonize initiatives with integrated national AIDS prevention, care, and treatment programs provide a realistic basis to believe that effective HIV/AIDS care and treatment will be available throughout sub-Saharan Africa before the end of the current decade.

Acknowledgments

Potential conflicts of interest. C.C.J.C.: no conflicts.

References