Delivery of Antiretroviral Therapy in Sub-Saharan Africa

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(See the article by Lawn et al. on pages 770–6)

By the end of 2005, it was estimated that, globally, 40.3 million adults and children (range, 36.7–45.3 million) were living with HIV infection, 25.8 million of whom were in sub-Saharan Africa [1]. On World AIDS Day (1 December 2003), the World Health Organization/Joint United Nations Programme on HIV/AIDS (WHO/UNAIDS) initiative “3 by 5” was launched [2]. Its ambitious objective was to deliver antiretroviral therapy (ART) to 3 million people in low- and middle-income countries—from a baseline of ~400,000—by the end of 2005. However, the effort fell short of its target. Treatment coverage in certain middle-income countries exceeded 80%, but in the poorer countries of Latin America, the Caribbean, Eastern Europe, and most of Asia, there is a long way to go. Similarly, by the end of 2005, only ~810,000 people in sub-Saharan Africa were receiving ART; 17% of those in need of therapy (i.e., those with WHO stage 4 disease or with CD4 cell counts <200 cells/μL). Global expenditure on AIDS has increased from $4.7 billion (in US dollars) in 2003 to $8.3 billion in 2005, much of which has come from the US President’s Emergency Plan For AIDS Relief; from the Global Fund to Fight AIDS, TB and Malaria; and from the World Bank. A further goal of universal access to ART by 2010 has been set by G8 leaders and has been endorsed by United Nations member states.

There are 2 simple, pertinent questions that need to be addressed: how do we best deliver ART using the most of scarce resources? At the same time, how do we prevent new infections? Close to 1 million people may have started receiving ART in sub-Saharan Africa, but it has been estimated that there were 3.2 million (range, 2.8–3.9 million) new infections in 2005. Although the questions might be simple, the answers are not. Evaluation of programs and more operational and fundamental research are needed to find the best models that can integrate HIV prevention and ART delivery. Candidate models will span the spectrum of care facilities, from regional and district hospitals, to the various levels of health centers, and finally to the community and to the home. As usual, there will be no “one size fits all” solution.

In this issue of the journal, Lawn et al. [3] add another small but important piece to the ART delivery question. The authors studied mortality in a treatment-naive cohort that received ART over 3 years in a community health center in Cape Town, South Africa. A number of studies, including their own, have demonstrated that the majority of deaths that occur in the first year or so of treatment take place in the first few months after initiation of ART. This simply reflects the advanced state of immunodeficiency of most patients when therapy is started. However, Lawn and colleagues have now examined the “queue”—that is, the period between identifying a patient as needing treatment and enrolling him or her in the treatment program and actually initiating drug therapy. They observed mortality rates of 33.3, 19.1, and 2.9 deaths/100 person-years in the pretreatment interval, the first 4 months of ART (early treatment), and after 4 months (late deaths), respectively. Pretreatment and early treatment deaths accounted for 87% of mortality. Late mortality was low, and patient retention within the cohort was very good.

The median duration of the pretreatment period was 34 days (interquartile range, 28–50 days); thus, the time spent in this period by some patients was substantial. As with mortality in the early treatment phase, there was a strong association with advanced immunosuppression. The authors highlight the need to better understand the reasons for pretreatment mortality and why patients enter similar ART programs with such advanced disease. They list the possible reasons as barriers to voluntary counselling and testing, impaired access to health care, lack of routine blood CD4 cell count analysis, health system delays in referral to ART clinics, waiting times before starting treatment, and the criteria for initiation of therapy. They argue that a pretreatment
period is important for “careful evaluation, investigation, and treatment of opportunistic infections, and thorough preparation of patients for ART” (page 774). Although physicians in this study were able to “fast-track” patients with more severe immunodeficiency, the authors believe that this pretreatment preparation period is important in terms of later adherence and good virological and immunological responses. Nevertheless, there is a balance of risk and benefit in this waiting period that must be attained. Realistically, the biggest impact on the reduction of mortality in the queue will come when treatment in sub-Saharan Africa can be initiated earlier in the natural progression of HIV infection. However, because ART is currently provided to only \( \sim 17\% \) of those with advanced disease in the region and because of the general lack of cheap, routine CD4 cell count analysis, the goal of reduction of mortality in the queue is something of a distant one. Meanwhile, other factors that Lawn et al. [3] have listed as probably contributing to pretreatment mortality must be further evaluated.

The challenges set by ART roll-out targets in sub-Saharan Africa are enormous. The focus on HIV prevention must not be lost, but should be integrated with ART delivery; both should not jeopardize other vital health programs, such as tuberculosis and malaria treatment programs, child health care and immunization efforts, and antenatal services. As far as is possible, HIV prevention and ART delivery should be integrated with these programs in a comprehensive primary health care model. Health systems are already overstretched, and human resources are limited. If coverage is to expand appropriately and equitably we need to define the best models of delivery to prevent the compromise of quality of care to an unacceptable degree. To what extent can the role of health care professionals and non-professionals be extended? Good adherence to treatment and the maintenance of an expanded, long-term free drug supply are essential to prevent the emergence of resistance. Affordable second-line regimens are urgently required. Pediatric care and treatment must be prioritized. How can we best strengthen partnerships between funders, academia, policy makers, and implementers? This list of challenges is not meant to be comprehensive; it is very long, and time is not on our side.

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References