An earlier start for HIV therapy

Three recent studies[1,2,3] bolster the argument for initiating antiretroviral therapy for HIV infection earlier than previously thought. Such arguments have been brewing for a while now, say three experts.

> "Permitting a chronic virus associated with immune destruction such as HIV to replicate unchecked when there was an alternative never made much sense.—Diane Havlir"

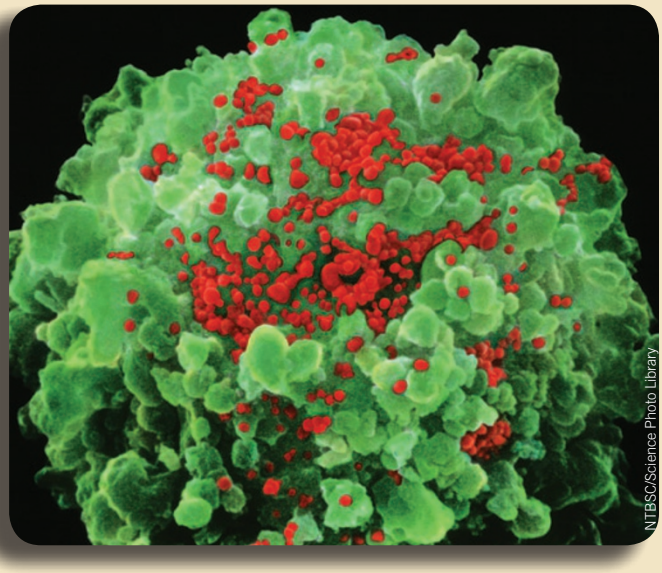
Diane Havlir:

The dispute over when to start antiretroviral therapy in resourced countries has changed. For years, drug toxicity dominated the debate and weighed heavily on the side of delayed therapy. Earlier antiretroviral therapy is now favored because it provides protection against not only traditional HIV-related infections and malignancies but also liver, heart and renal disease and, potentially, premature immunologic senescence and cognitive decline.

This new landscape has arisen owing to the convergence of data from large epidemiological cohorts and immunological studies and the availability of less toxic antiretroviral agents. Permitting a chronic virus associated with immune destruction such as HIV to replicate unchecked when there was an alternative never made much sense. With more solid evidence to support early therapy, we have much to gain by early HIV identification and engagement in care.

We also have much to gain by unpacking and understanding the pathogenesis, determinants, genetics and optimization of immune restoration. These insights will propel even more individualized approaches to therapy, enabling clinicians and patients to fine-tune the balance between drug toxicity and concerns for long-term health.

Chief, HIV/AIDS Division at San Francisco General Hospital, and Professor of Medicine, University of California, San Francisco, USA.



T lymphocyte (green) infected with HIV (red).

Timothy Schacker:

These studies add to the growing body of evidence that clinical outcomes are markedly improved in HIV infection with early administration of antiretroviral therapy. Two of them are observational studies of more than 62,000 people showing reduced mortality, and the other documents a partial restoration of humoral immune function. These results are representative of several recent studies with similar results, including pathogenesis-based studies that show cumulative damage to immune structures and function from prolonged viral replication. Collectively, these data suggest that if the goal is to protect (or restore) immune function and improve clinical outcome, treatment should be started early in the course of disease.

Professor of Medicine, University of Minnesota, Minneapolis, Minnesota, USA.

Mark A Wainberg:

These three studies reach remarkably similar conclusions about when to initiate antiretroviral therapy, despite very different approaches.

Two of the studies[1,2] each analyzed a large number of clinical trials and concluded that patient long-term survival was best assured if therapy was started when $CD4^+$ cell counts were relatively high, that is, >350 cells per ml in one study and >500 cells per ml in the other. The third study[3] convincingly offers a mechanistic basis for these observations by demonstrating that HIV-1–infected infants who began therapy during the first year of life maintained more robust B cell immunological function and responded better to standard vaccinations than children for whom treatment was deferred.

These results are also consistent with recent data on elevated cancer risks in HIV-infected persons, a finding that is widely attributed to HIV-mediated damage to immune-based tumor surveillance mechanisms.

Director, McGill AIDS Centre, Montreal, Quebec, Canada.

1. When to Start Consortium *et al.* Timing of initiation of antiretroviral therapy in AIDS-free HIV-1–infected patients: a collaborative analysis of 18 HIV cohort studies. *Lancet* **373**, 1352–1363 (2009).
2. Kitahata, M.M. *et al.* Effect of early versus deferred antiretroviral therapy for HIV on survival. *N. Engl. J. Med.* **360**, 1815–1826 (2009).
3. Pensieroso, S. *et al.* Timing of HAART defines the integrity of memory B cells and the longevity of humoral responses in HIV-1 in vertically-infected children. *Proc. Natl. Acad. Sci. USA* **106**, 7939–7944 (2009).