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AIDS: "Hit Hard, Hit Early" Taking Hits (Part 2)

By Pat French

Part 1 of this series described the uncertainties facing both people infected with human immunodeficiency virus (HIV) and their physicians as they try to make decisions about antiviral treatment—when to begin treatment, how to measure its effects, and when to change treatment, among others.

Unfortunately, and unlike guidelines for treatment of other disorders, there are no results from large, long-term, randomized trials from which to draw objective conclusions about the clinical outcomes of treating (or not treating) HIV infection.

One DCRI researcher continues the effort to address some of these questions. Dr. John Hamilton, an infectious disease specialist here at Duke, has submitted proposals to the National Institute of Allergy and Infectious Disease (NIAID) to study clinical outcomes in patients on therapy who are randomized to different treatment strategies — one arm of the study would focus on intensive treatment, in which viral load is maintained at a very low level, and the other arm would tolerate modest levels of virus.

"The improved outcomes seen over the last several years in HIV-infected people have occurred despite noncompliance with complicated antiviral regimens, and despite our inability to eradicate the virus from the body," notes Hamilton. "This disconnect between treatment and outcomes deserves further study."

Hamilton, with his colleagues in the Veterans Administration (VA) Research Center on AIDS and HIV infection (RCAHI) and Kaiser Permanente healthcare system, submitted a proposal in 1999 to address the question of when to switch treatments, but the proposal was not funded by the NIH.

When a later NIH Workshop concluded that "when to switch" was one of the two most important research questions for which answers were needed, the same group resubmitted another proposal, entitled Strategy of When to Institute Therapeutic CHanges (SWITCH).

Their study would examine long-term survival among people with maximal suppression of HIV (<1000 copies of HIV-RNA/mL) versus those with modest viral replication (1000 to 20,000 RNA copies/mL). Patients will be able to change their treatment if they are found to have >1000 and >20,000 copies/mL, respectively, in the two treatment arms during the study. The study also will monitor patients' CD4+ counts.

This study has several important features that set it apart from previous work:

- it examines the relationship between a surrogate marker and a "hard" clinical endpoint
- it has a large enough sample size (~4200 people) to be able to detect differences in outcomes reliably

- it follows patients to a minimum of 5 years, longer than most previous studies

As Hamilton notes, "More than half of the 49 recommendations in the guidelines are based upon 'expert opinion' instead of clinical data. It seems prudent to critically and objectively examine the actual clinical benefits and liabilities of progressively more intensive antiretroviral therapy."

The group expects a recommendation from a Peer Review Group in the next month and a decision from the NIH Council for funding by early summer.

Once again, the guidelines (and Hamilton) urge HIV-positive people already taking the cocktail to check with their doctors before stopping or changing medicines.

For the most recent guidelines, click [here](#). For the previous version of the guidelines, click [here](#).
