Controlling HIV/AIDS

The Obstacles and Opportunities Ahead

At the 19th International AIDS Conference, held in Washington, DC, in July 2012 (AIDS 2012), there were sobering reminders that controlling the human immunodeficiency virus (HIV) and caring for infected individuals are much easier said than done. There was also considerable optimism about eventually ending the global HIV/AIDS pandemic.[1]

Even without a vaccine, the primary reasons for optimism are the effectiveness of antiretroviral therapy in treating and preventing HIV infection and the increased availability of resources for programs in low- and middle-income nations. Deaths from AIDS-related causes peaked in the United States in 1995, and globally in 2005. At present, there are more people living with HIV than ever before, but many fewer new infections each year than earlier in the epidemic. Of the estimated 34.2 million people living with HIV worldwide in 2011, about 8 million had access to antiretroviral therapy, 20% more than in 2010.

The primary reasons for pessimism are the practical difficulties of providing effective and timely treatment to all who need it, even in countries with ample health care resources. For example, a far higher percentage of people with HIV infection in the United States should be diagnosed, treated, engaged in care, and have a suppressed viral load than is currently the case.[2,3]

At AIDS 2012, as the conference was known, the Centers for Disease Control and Prevention released an analysis showing that 82% of the estimated 1.1 million people in the United States living with HIV infection know that they are infected; 33% are prescribed antiretroviral therapy; and only 25% are virally suppressed, as defined by a recent HIV viral load test indicating 200 copies/mL or lower.[4] Of the groups examined, African Americans and people aged between 25 and 34 years were the least likely to receive ongoing care and to have their virus suppressed.

Many presentations made clear that targeted community-based approaches are essential to prevent new infections and to keep some infected individuals engaged in regular care. The ongoing HIV Prevention Trials Network (HPTN) 065 study[5] has received attention for evaluating modest financial incentives (in the form of gift cards) to encourage people who test positive to seek care and to take effective treatment. Funded by the National Institute for Allergy and Infectious Diseases, the trial is being conducted in the Bronx, New York, and Washington, DC, areas with high rates of HIV/AIDS, particularly among African Americans and Latinos. At the test sites that offer financial incentives, an infected subject could receive up to about $400 in gift cards over a year for completing various requirements, including achieving and maintaining viral suppression. If the incentives work, debate about their role in routine HIV care is likely. It is remarkable to pay some people to take their HIV medications at the same time that other infected individuals cannot afford their medications.

When highly active antiretroviral therapy became available in the mid-1990s, it rapidly changed the course of the AIDS epidemic, reducing the risk of HIV transmission and allowing infected individuals to live longer and healthier. There was concern, however, that if antiretroviral therapy were to be started too soon, it would have little clinical benefit and that the toxic effects of the medications and the development of resistant HIV viruses would outweigh the potential advantages of suppressing the virus. It has taken nearly 2 decades for antiretroviral therapy to be increasingly recommended for all people with HIV infection, regardless of their CD4 cell count, their age, how long they have been infected, or other illnesses they may have. Better and more convenient drug regimens have been introduced. Data have accumulated about the relation between ongoing viral replication and the progression of AIDS and other diseases, even before the immune system weakens, as assessed by a decreasing CD4 cell count. The additional benefit of preventing HIV transmission to an uninfected partner has been established.[6]

In March 2012, the Department of Health and Human Services panel on antiretroviral guidelines for all adults with HIV infection and adolescents recommended antiretroviral therapy "for all HIV-infected individuals."[7] In July 2012, an International Antiviral Society–USA panel made a similar recommendation for adults.[8] Despite their broad recommendations, both panels cautioned that the strength and quality of the evidence for treatment is highest for people with lower CD4 cell counts, for pregnant women, and for people with certain conditions such as an opportunistic infection, HIV-associated nephropathy, or coinfection with hepatitis B virus. The World Health Organization is also revising its guidelines, expected to be released in 2013, and will incorporate emerging information about the benefits of early treatment.

The best evidence of benefit from antiretroviral therapy is for people with CD4 cell counts below 350/μL. By comparison, a normal CD4 cell count can range from 500/μL to 1000/μL. Many HIV-infected individuals with normal CD4 cell counts may not even know that they are infected. If they know, they may feel completely well and

have understandable questions about taking potent antiretroviral agents with potential toxic effects every day, for an indefinite period of time. They may also be concerned about the costs of the medications as well as potential stigma and discrimination. Moreover, it would be challenging, although not impossible, for governments, public health officials, and the major international providers of HIV funding to offer treatment to all people with HIV infection and to provide them with high-quality and ongoing care. Based on the number of people living with HIV in 2011 and already receiving treatment, about 26 million more people throughout the world would need access to antiretroviral therapy. In the United States, hundreds of thousands more people would need to be diagnosed, treated, and engaged in HIV care; such individuals often lack insurance or coverage for antiretroviral medications.[3,4]

To strengthen the case for treating all HIV-infected individuals, additional evidence of the benefits for people with CD4 cell counts above 350/μL is needed. For those with cell counts between 350/μL and 550/μL, such evidence is developing. The HPTN 052 study established that early antiretroviral therapy prevents the sexual transmission of HIV to an uninfected partner.[6] The trial also found that in HIV-1–infected subjects with CD4 counts between 350/μL and 550/μL, those receiving early therapy had fewer clinical events (driven mainly by a decreased incidence of extrapulmonary tuberculosis) than subjects whose therapy was delayed until their CD4 count declined below 250/μL or an AIDS-related illness developed.[6] At AIDS 2012, the HPTN 052 study team reported additional follow-up data, confirming that early antiretroviral therapy can reduce the incidence of tuberculosis and other AIDS-related diseases.[9]

So far, randomized trials have provided little information about the best approach to treating people with HIV infection and CD4 counts above 500/μL. The ongoing Strategic Timing of Antiretroviral Treatment (START) study is comparing immediate antiretroviral therapy and therapy deferred until the CD4 cell count declines to below 350/μL or AIDS develops.[10] Eligible people are 18 years or older, infected with HIV but have never had antiretroviral therapy for HIV, and have CD4 cell counts above 500/μL. Scheduled to be completed in 2015, the START trial has enrolled about two-thirds of a projected 4000 subjects.

Ending the global HIV/AIDS epidemic remains an aspiration for the future. Despite the abundant obstacles, the news from AIDS 2012 is that controlling the epidemic is feasible now.

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