Hot News

New DHHS Guidelines Recommend Antiretroviral Therapy to All HIV-Infected Persons

The U.S. Department of Health and Human Services (DHHS) released on March 27, 2012 an updated version of its guidelines on the use of antiretroviral agents. The DHHS panel now recommends that antiretroviral therapy should be offered to everyone diagnosed with HIV. Other highlights include new sections on aging with HIV and drug costs, as well as updates on treatment as prevention, and recommendations for using new antivirals against hepatitis C in HIV/HCV-coinfected individuals.

There is growing attention on the interplay between HIV and aging. Key considerations when caring for older HIV-infected patients are the following: (i) antiretroviral therapy should be given in all patients > 50 years of age, regardless of CD4 counts, because the risk of non-AIDS-related complications is increased and blunted CD4 recovery is common in older HIV-infected patients; (ii) adverse events of the medication occur more frequently in older than younger HIV-infected individuals. Therefore, the bone, kidney, metabolic, cardiovascular, and liver function of older HIV-infected adults should be monitored closely; (iii) the risk of drug interactions between antiretrovirals and other medications commonly used in older HIV-infected patients is increased and should be assessed regularly, especially when starting or switching antiretroviral therapy and/or concomitant medications; (iv) HIV doctors and primary care providers should work together to optimize the medical care of older HIV-infected patients with complex comorbidities; and (v) counseling to prevent secondary transmission of HIV remains an important aspect of care of older HIV-infected patients.

People with HIV appear to be aging faster. Whether HIV disease or its treatment might lead to an accelerated aging process is unclear. Conditions associated with aging, such as heart disease, neurocognitive decline, and bone weakening, develop somewhat earlier among people living with HIV, including those on effective antiretroviral therapy. On the other hand, aging complicates antiretroviral treatment itself.

The other new section is an appendix on drug costs, which simply lists the average wholesale price of approved antiretroviral drugs and fixed-dose combination pills. In the section on treatment initiation, the major change is a recommendation for treatment of all people with HIV, primarily based on increasing evidence showing the harmful impact of ongoing HIV replication on AIDS and non-AIDS disease progression. In addition, this recommendation reflects emerging data showing the benefit of effective antiretroviral therapy in preventing secondary transmission of HIV. Patients starting treatment should be willing and able to commit to treatment and should understand the benefits and risks of therapy and the importance of adherence. Patients may choose to postpone therapy, and providers, on a case-by-case basis, may elect to defer therapy on the basis of clinical and/or psychosocial factors.

The final major update regards prevention of secondary HIV transmission. Citing the HTPN 052 study, the guidelines state that effective antiretroviral therapy greatly reduces the risk of secondary HIV transmission. This protection is mitigated by the challenges of optimal antiretroviral adherence, along with some evidence that risk-taking behavior may increase when people believe they are on suppressive therapy.

Pablo Labarga
Department of Infectious Diseases
Hospital Carlos III
Madrid, Spain

Coinfection with Hepatitis B Virus Negatively Impacts HIV Disease Progression

Chronic hepatitis B virus (HBV) infection currently affects 5-10% of individuals with HIV infection in developed countries, despite HBV vaccination being widely available and effective for preventing HBV infection. It is well established that HIV alters the natural history of chronic hepatitis B, producing higher serum HBV DNA concentrations, lower liver enzymes, and faster progression to liver cirrhosis, particularly in those with low CD4 cell counts. However, controversial results have been reported regarding the impact of HBV infection on HIV disease progression. Lack of agreement among studies might be due to the heterogeneity in study populations and/or differences in the endpoints checked and lack of consideration of all virologic and host variables.

A recent report by Chun, et al. (J Infect Dis. 2012;205:185-93) has evaluated the impact of HBV infection on HIV outcomes in a well characterized cohort of HIV seroconverters from the US Military HIV Natural History Study (NHS). Of 5,261 participants enrolled in the NHS, the study was limited to 2,352 individuals with HIV seroconversion estimated within three years and whose HBV status was determined within two years of HIV seroconversion. All patients were classified as HBV negative (73.6%), resolved HBV (20.2%), isolated HBcAb (3.5%), or chronic HBV (2.7%). The authors found that HBV

infection had a negative impact on HIV outcomes. The multivariate risk of AIDS-defining illness or death was significantly higher in patients with chronic HBV compared to those HBV negative. These findings remained consistent across multivariable models used for the analysis, adjusting for demographics, baseline and time-updated CD4 cell counts, and the use of antiretroviral therapy. Moreover, sensitivity analyses accounting for possible confounders, such as year of HIV diagnosis and the relative availability of HAART, did not change the conclusions.

Some limitations of the study must be highlighted. First, the causes of AIDS-defining illness and deaths were not defined; therefore it is not possible to determine the contribution of liver-related deaths to the outcome. Second, the severity of HBV infections measuring HBV DNA levels or liver fibrosis stage were not reported. These are important determinants of the likelihood of HBV disease progression. Finally, the authors also found an increased risk of AIDS or death, which is not well explained being in the HAART era.

Previously, Dore, et al. (AIDS. 2010;24:857-65) highlighted that HIV/HBV coinfected patients enrolled in the SMART study experienced HBV rebound following HAART discontinuation (including anti-HBV active drugs) and this was significantly associated with a faster CD4 decline, confirming the harmful contribution of uncontrolled HBV infection on HIV disease progression.

The higher risk of AIDS or deaths in HIV patients with chronic HBV infection compared with HIV-monoinfected individuals supports even more the imperative need to prevent the burden of HIV/HBV coinfection, promoting routine HBV screening in all HIV-infected individuals, and providing HBV vaccination to susceptible individuals and optimal HIV/HBV treatment to carriers.

Eva Poveda
Department of Infectious Diseases
Hospital Carlos III
Madrid, Spain

Vectored Immunoprophylaxis - An Innovative Approach to Prevent HIV Infection

Despite the numerous efforts made to develop an effective vaccine, immunization against HIV infection remains an elusive goal. Vaccine trials performed to date have shown either no efficacy or even a trend towards a higher infection in the vaccinated population (Cohen, et al. Science. 2007;318(5853):1048-9). The only exception was reported by the so-called "Thai Trial", which showed a protective effect in 31% of individuals receiving the combined vaccine RV144 (Rerks-Ngarm, et al. New Engl J Med. 2009;361(23): 2209-20). This rate of protective effect, although significant and encouraging for the HIV vaccination field, is far from desirable to provide a global effective protection.

Recent research on molecular biology has yielded useful tools for developing new strategies towards HIV immunization and/or eradication. A significant step has been the recent identification of new broadly neutralizing antibodies, which largely expands the previous limited list. The Protocol G was an international initiative that included seven countries in Africa, along with Australia, Thailand, the UK, and the USA. Using a new technology for the identification of clonal antibodies with high power and breadth to inhibit HIV replication, 17 new antibodies were discovered (Walker, et al. Nature. 2011;477(7365):416-7). Some of these antibodies are 100-times more potent in inhibiting major circulating HIV subtypes than the earlier ones. Given its high activity, this major discovery has given impetus again to research in the vaccination field, focused on the development of antigens that enable the immune system to produce any of these broadly neutralizing antibodies.

A new strategy towards HIV immunoprophylaxis has been recently suggested by Balazs, et al. (Nature. 2012;481(7379):81-4), which consists of bypassing the immune system learning process using gene therapy. Basically, gene information encoding broadly neutralizing antibodies is introduced into somatic cells, which then will produce these antibodies indefinitely. This approach has already yielded positive results in a mice model injected with distinct recombinant vectors. The authors found that the introduction of b12 antibody information into muscle tissue from mice cells produced sufficient antibodies to prevent HIV infection, even against an intravenous dose 100-times higher than that required to infect control animals. With more recent neutralizing antibodies, such as VRC01, the results were even more impressive, requiring much lower antibody concentrations to prevent HIV infection. Although these encouraging results need to be confirmed in other animal models and human trials, the results provide a critical proof-of-concept. If finally proven effective, this strategy might be used to prevent infection from pathogens for which neutralizing antibodies can be found.

The impact of HIV infection on social health and economics worldwide is overwhelming. In the absence of an effective vaccine or curative treatment, innovative strategies for the eradication of the virus or new forms of immunization have to be developed. Gene therapy stands as a very promising approach. Moreover, lessons learned in the HIV field might later be translated to other pathogens.

Eduardo Seclén
Department of Infectious Diseases
Hospital Carlos III
Madrid, Spain