Hot News

Highly Efficient Transmission of Prions by Transfusions

Bovine spongiform encephalopathy, commonly known as "mad cow disease", is a fatal neurodegenerative disease in cattle, with a long period of incubation that causes a spongy degeneration in the brain and spinal cord. The disease may be transmitted to human beings by eating food contaminated with the brain, spinal cord, or digestive tract of infected carcasses. In 1996, a new variant of the Creutzfeldt-Jakob disease (vCJD or nvCJD) that causes an incurable and fatal degenerative neurological disorder was identified in humans. Prions are the infectious agents for the transmissible spongiform encephalopathies (TSE) and vCJD disease.

The UK and France are the two nations most affected to date by vCJD. The presence of the vCJD agent in lymphoid tissues of patients incubating the disease has raised the possibility of blood-borne transmission. Indeed, several cases of vCJD have been identified in patients transfused with blood products from asymptomatic donors in England. In the absence of a large-scale screening test, it is difficult to establish the prevalence of infection in blood donors and transfused patients. Moreover, the lack of validated screening tests requires the use of risk-reduction procedures to maximize the protection against vCJD transmission by transfusions. Current measures to prevent vCJD transmission by blood products mainly rely on the assumption that the level of infectivity is low and directly correlated with the infectious titer in blood and blood products.

Andréoletti, et al. (PLoS Pathog. 2012;8:e1002782), using a TSE sheep infection model, have recently demonstrated that the intravenous administration of a few hundred microliters of blood (~200 µl), as measured by inoculation into brain, is sufficient to transmit the disease to transfusion recipients with 100% efficacy. These authors also noticed that this high efficiency of disease transmission is crucially dependent on the viability of the transfused white blood cells rather than on their infectious titer. These findings provide new insights into the pathogenesis of TSE diseases and highlight that the main current assumptions about vCJD blood transmission should be revised. As with HTLV-1, plasma exhibits a low transmissibility of prions. However, cellular blood products may be highly infectious. Thus, it seems crucial that universal leucoreduction procedures are applied to all blood transfusion products.

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

Antiretroviral Therapy for Prevention: Let´s See the Forest for the Trees

The most recent estimates indicate that by the end of 2010 there were 34 million people living with HIV infection, 70% of them in sub-Saharan Africa. In parallel, 1.1 million HIV-infected patients develop tuberculosis (TB) every year, which is the main cause of death in 24% of HIV individuals in Africa. Last June, the World Health Organization (WHO) issued an update on "Antiretroviral Treatment as Prevention of HIV and TB" (Available at http://www.who.int/hiv/pub/mtct/programmatic_update_tasp/en/index.html).

Based on the results of the randomized trial HPTN 052 and other observational studies (Anglemyer A, Rutherford GW, Baggaley RC, Egger M, Siegfried N. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. Cochrane Database Syst Rev. 2011;10:CD009153), which have proven that introduction of antiretroviral therapy (ART) in developing countries may reduce HIV and TB morbidity, mortality, and spread, the WHO has announced a review of the 2010 ART guidelines. Interestingly, in a preliminary circulating draft, the CD4 count threshold for beginning therapy is still 350 cells/µl.

Plasma HIV RNA concentration is the key risk factor for HIV transmission (Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med. 2000; 342:921-9). However, the HPTN 052 trial has shown that HIV seroconversion among serodiscordant couples was reduced by 96% when the infected partner was under ART and had preserved CD4 counts, as compared with < 350 cells/µl. The benefit of ART in vertical HIV transmission is well known, and the WHO 2010 guidelines recommend therapy in pregnant women with CD4 counts < 350 cells/µl. In women with better immune status, only perinatal prophylaxis is recommended. On the other hand, a recent WHO meta-analysis has found that ART reduces the risk of TB disease by 65%, independent of CD4 counts. Moreover, modeling studies in African countries estimate that ART initiation two or five years after HIV seroconversion may reduce the TB incidence by 63 or 48%, respectively (Meyer-Rath G, Over M. HIV Treatment as Prevention: Modelling the Cost of Antiretroviral Treatment-tate of the Art and Future Directions. PLoS Med. 2012:9(7);e1001247. doi:10.1371/journal.pmed.1001247).

With all this information, the WHO supports in 2012 that ART should be indicated for life and regardless of CD4 counts in subjects living with serodiscordant

couples and in all pregnant women. Other HIV groups that may also benefit from early ART are homosexual men, sex workers, and intravenous drug users. Patients at high risk for TB should also receive ART. Scaling-up ART requires a significant economic effort, although there are already data supporting the cost-efficiency of this strategy. With respect to possible HIV risk compensation in patients receiving ART, the WHO considers that ART availability in developing countries is already promoting earlier HIV diagnosis.

In summary, in the battle to contain the spread HIV infection, the WHO wants to incorporate ART as a key element of its strategy. It is assumed that the benefit for the infected patient may extend to protection of the community. There is no doubt that with caring for trees, the forest will be safer.

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