Correspondence

Who Will Bridge the HIV Treatment-Prevention Gap?

To the Editor—On World AIDS Day 2007, the Journal published a supplement called “The Realities of Antiretroviral Therapy Rollout—Challenges to Successful Programmatic Implementation.” Surprisingly, none of the 14 articles in the supplement discusses in any meaningful way the importance of linking antiretroviral therapy (ART) services with the prevention of HIV infection. It is not that prevention was excluded from the mandate of the conference leading to the supplement—it seems simply to have been forgotten. After years of struggle for a comprehensive approach to the goal of “universal access to HIV treatment, care, prevention, and support” [1], it appears that the global discussion on linking and integrating the prevention of HIV infection with treatment and care has not fully reached clinicians and infectious diseases specialists.

We would have liked to see 3 things in the supplement.

1. There must be an acknowledgement that we cannot treat our way out of the epidemic. Despite current prevention efforts, 2.5 million new HIV infections occur annually [2]. Barring death from unrelated events, all infected individuals will eventually need treatment and care. If current scale-up rates continue, the goal of universal access by 2010 will fall far short, reaching 4.6 million individuals in 2010, only two-thirds of those who need antiretroviral drugs today, and at a cost of $15.4 billion [3]. We do not have these resources, and health-care systems are already stretched.

2. There must be a discussion of the role of and opportunities for prevention of HIV transmission in ART roll-out. Four meta-analyses have shown that individuals who know they are infected with HIV alter their behavior in a positive manner [4], particularly those in partnerships. In a prospective cohort study in rural Uganda, unsafe sex was sharply reduced by 70% in HIV-positive individuals 6 months after initiating ART [5]. In sub-Saharan Africa, serological discordance among couples is high [6]. Studies from serologically discordant couples show that counseling together with the provision of condoms is effective in preventing HIV transmission [7, 8], and counseling of the couple is particularly effective [9].

3. There must be an endorsement of the importance of HIV testing and counseling as a gateway to ART, care, and prevention of HIV infection. In sub-Saharan Africa, a median of only 12% of men and 10% of women have been tested and know their HIV infection status [10]. To enhance the number of persons who know their serological status, and thus may benefit from therapy but also may contribute to decreased HIV transmission, the World Health Organization has recently called for provider-initiated HIV testing and counseling in health facilities [10]. Although the supplement focused on individuals with known HIV seropositivity in care, a discussion of how to increase these numbers and simultaneously enhance the prevention of HIV infection would have been appropriate.

Linking treatment with prevention remains an overriding and critical public health challenge for the health sector, particularly in view of the sustainability of ART roll-out in resource-poor countries. Without a reduction in the incidence of HIV infection, ART and care will eventually fail. Strengthening programs to prevent HIV infection therefore serves the best interests of ART services. Yet surprisingly, the supplement is silent about this issue.

The prevention of HIV infection, like treatment, is for life—in both meanings of the words. The supplement was based on a scientific meeting in South Africa in October 2006, jointly organized by Harvard University and the South African Medical Research Council. This meeting missed an outstanding opportunity to discuss the fact that neither treatment nor prevention alone will stem the flow of this devastating epidemic in sub-Saharan Africa. Treatment, care and prevention must be brought to scale jointly—and they have a large potential for reinforcing each other.

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References


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Influenza Pandemics, Immune Cross-Reactivity, and Pandemic Control Strategies

To the Editor — In the 15 January 2008 issue of the Journal, Andreasen et al. show that in the 1918–1919 A/H1N1 influenza pandemic in Copenhagen, the lethal fall wave was preceded by a summer wave that was caused by a precursor pandemic virus that was transmitted efficiently but was not extremely virulent [1]. Interestingly, when preceded by this mild summer wave, the fall wave was less lethal, suggesting that the low transmissibility of the fall wave may be explained by partial cross-protection from subsequent summer exposure to a related influenza virus.

We have recently shown that a proportion of healthy subjects display cross-reacting humoral and cellular immune responses between human (H3N2/ H1N1) and avian HPAI (H5N1) influenza strains [2]. In particular, a low incidence of CD4 T cells specific for H5N1 was detected in several persons at baseline, and seasonal vaccine administration enhanced the incidence of reactive CD4 T cells. We also observed that seasonal vaccination was able to raise the level of neutralizing antibodies against influenza (H5N1) in a large number of subjects (table 1). These findings highlight the possibility of boosting cross-type cellular and humoral immunity against the highly pathogenic avian influenza A virus subtype H5N1 by using seasonal influenza vaccination.

A similar cross-reactive immunity was previously shown in animal models, which resulted in protection against H5N1 viral challenge. In particular, Lu et al. [3] studied influenza vaccines based on H5 hemagglutinin from a nonpathogenic avian influenza virus for the ability to induce cross-reactive immunity and/or cross-protection against a highly pathogenic H5N1 strain. These vaccines provided cross-protection from systemic infection, severe disease, and death after lethal challenges with H5N1 virus. Substantial levels of serum anti-H5 IgG were detected in mice that received vaccine. Moreover, Ichinohe et al. [4] evaluated the ability of currently licensed seasonal influenza vaccine to confer cross-protection against highly pathogenic H5N1 influenza virus in mice. Vaccinated mice manifested cross-reactivity of mucosal IgA and serum IgG with H5N1 virus, as well as both reduced H5N1 virus titers in nasal-wash samples, and an increased survival rate after challenge with H5N1 virus. Finally, Sandbulte et al. [5], by using DNA vaccination against the neuraminidase of a human H1N1 strain, showed an elicited serum IgG response to human N1 and robust protection against challenge with the homologous virus. Interestingly, vaccinated mice were partially protected from lethal challenge with the H5N1 virus; serum samples transferred from vaccinated mice to vaccination-naive animals conferred similar protection against mortality due to H5N1.

Moreover, mathematical models have shown that for diseases with antigenic drift, cross-reactive response not only may protect the population through classical herd immunity, but may reduce the chance of new variants being produced by limiting the number of affected subjects. Subsequent epidemics may therefore be milder as a result of this positive feedback [6]. The retrospective epidemiological data on 1918–1919 A/H1N1 influenza dual wave [1], as well as our data on vaccinated healthy persons [2], strongly suggest that cross-reactive immunity may also be protective in humans.

Overall, these data support the hypothesis that the cross-protective immunity induced by previous infections,