H1N1 Meets HIV

February 18, 2010 By Tim Horn

People with HIV are generally no more likely to experience severe complications of H1N1 influenza virus than people not infected with HIV, according to studies reported on Wednesday, February 17, at the 17th Conference on Retroviruses and Opportunistic Infections (CROI). However, studies presented here also paint a conflicting picture regarding the ability of H1N1 vaccines to spark sufficient immune responses against the virus in people with HIV hoping to avoid the novel influenza virus still circulating the globe.

Though H1N1 continues to spread in regions throughout the world, it has not resulted in the high number of serious complications, hospitalizations and deaths many public health experts initially feared. In fact, according to a February 12 report from the U.S. Centers for Disease Control and Prevention (CDC), the proportion of deaths attributed to pneumonia and influenza continues to decrease and is now lower than expected for this time of year.

Questions remain, however, regarding the effects of H1N1 in people living with HIV. HIV-positive people are still considered to be at high risk for H1N1-related complications, according to the CDC, yet little data have been available to either confirm or refute this rightfully cautious assumption. What's more, little information has been reported regarding the effectiveness of H1N1 vaccination in people living with HIV.

Answers to these questions surfaced at CROI in the form of several poster presentations—many of which were submitted as "late-breakers."

Risk of Complications and Death

Three studies reported at CROI suggest the clinical presentation of H1N1 in people living with HIV is not distinct from that reported in HIV-negative individuals, although the risk of serious disease and death appears higher than average in HIV-positive individuals with advanced HIV disease.

According to Ariel Campos-Loza, MD, and his colleagues at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ) in Mexico City, H1N1 virus infection was infrequent in HIV-positive patients followed in the clinic during the initial epidemic wave (April through June 2009). What's more, HIV-infected patients represented only a small fraction of all H1N1 cases seen at INCMNSZ.

Campos-Loza said that the rates of hospitalization, mechanical ventilation and survival were

similar between HIV-positive and HIV-negative patients who had H1N1. Among 11 HIV-positive patients with H1N1, only three were hospitalized and one died—all of whom had AIDS. In contrast, mild influenza occurred in patients with CD4 counts above 300. “Late stage of HIV disease and poor HIV control may influence the severity and outcome of H1N1 in HIV-infected individuals,” he said.

A second study, reported by Esteban Martinez, MD, and his colleagues of the Hospital Clinico Provincial de Barcelona, concluded that HIV infection did not make H1N1 influenza more severe, nor did H1N1 have a major effect on HIV infection.

Except for higher rates of gastrointestinal symptoms among people living with HIV—37 percent versus 18 percent—clinical features of H1N1 were similar between HIV-positive and HIV-negative patients cared for at the hospital between April and December 2009. In fact, pneumonia and respiratory failure were less common among HIV-positive people than those who were HIV negative. People living with HIV with confirmed H1N1 were also less likely to be admitted to the hospital and recovered more rapidly than HIV-negative individuals with H1N1.

Of note, HIV-positive individuals were much more likely to be prescribed Tamiflu (oseltamivir), likely because of increased vigilance among health care providers caring for people living with HIV believed to be at a higher risk for H1N1-related complications.

H1N1 infection did not appear to have an effect on HIV disease progression. CD4 cell counts and viral loads documented at the time of H1N1 diagnosis were unchanged four to six weeks later.

Data presented by Gustavo Reyes-Teran, MD, and his colleagues at the Instituto Nacional de Enfermedades Respiratorias (INER) in Mexico City painted a slightly more grim picture, likely because many of the HIV-positive people at INER were receiving care for underlying respiratory diseases, including Pneumocystis pneumonia and tuberculosis. Of 27 HIV-positive, H1N1-positive patients seen during the initial months of the Mexico City epidemic, 14 required hospitalization and six died. “Opportunistic infections mask symptoms and [X-ray] signs of influenza, resulting in delayed [H1N1] treatment,” Reyes-Teran said.

He also noted that some HIV-positive patients had H1N1 virus detectable in their lungs after standard five-day courses of Tamiflu. This, he feared, may increase the risk of developing H1N1 drug resistance, which can potentially be spread to others.

H1N1 Vaccine Immune Responses

The H1N1 vaccine is recommended for all HIV-positive people. Yet little is known about its effectiveness—notably its ability to induce a sufficient antibody response to H1N1—in people with HIV, who are generally less likely to experience robust immune responses to vaccines compared with HIV-negative individuals. Three studies at CROI presented conflicting data on this topic.

Kate Sullivan, MD, of the University of Pennsylvania School of Medicine and her colleagues

evaluated the immune response to an inactive H1N1 vaccine in 120 HIV-positive individuals. All but one patient were receiving antiretroviral (ARV) therapy.

Thirty of the patients enrolled had H1N1 antibody levels consistent with protection against infection, likely because of previous exposure to the virus. Among the 89 participants without evidence of previous exposure to H1N1, only 61 percent developed antibody levels capable of defending against H1N1 three weeks after receiving the vaccine. In comparison, about 95 percent of those between 18 and 60 years old, and 79.2 percent of those older than 60, in the general population achieve a sufficient antibody response to H1N1 within three weeks post-vaccination.

Sullivan's group noted that non-responders had lower CD4 counts and had undetectable viral loads for a shorter period of time than responders. Among those who didn't have a sufficient immune response, the average CD4 count at the time of vaccination was 394 cells, compared with 501 cells among vaccine responders. And the duration of undetectable viral loads was 19 months among non-responders, compared with 31 months among vaccine responders.

Sullivan said that one way to potentially increase efficacy is to use vaccines containing adjuvants—compounds that help prime the immune system to better respond to antigens in vaccines. None of the H1N1 vaccines available in the United States use adjuvants, because of limited data regarding safety and efficacy.

Unfortunately, a poster presentation by Markus Bickel, MD, and his colleagues at Goethe University Hospital in Frankfurt indicated that an adjuvanated H1N1 vaccine may not make a great deal of difference.

According to Bickel, only 69 percent of the HIV-positive people who received an adjuvanated vaccine in his clinic developed sufficient antibody responses to H1N1 within three weeks. Those who did respond tended to be younger (45 versus 49 years old) and have a higher CD4 count (532 versus 475 cells).

Interestingly, a French study conducted by Odile Launay, MD, of the Hôpitaux de Paris and her colleagues found higher rates of antibody responses to H1N1, using both non-adjuvanated and adjuvanated vaccines. About 95 percent of HIV-positive patients receiving the adjuvanated vaccine had sufficient antibody responses after three weeks, compared with 77 percent of patients receiving the non-adjuvanated vaccine.

Bickel and Launay both question whether a second dose of an adjuvanated or non-adjuvanated H1N1 vaccine might further increase the antibody response rates in people living with HIV. Unfortunately, no one has conducted studies to explore this possibility.
