

His test for hepatitis C antibody was negative, but an enzyme immunoassay for HIV type 1 (HIV-1) was repeatedly reactive, and the result on a Western blot assay that was performed as part of the clinical protocol to confirm a reactive enzyme immunoassay was indeterminate, with a single band that was positive for glycoprotein 160 (GP160). An HIV nucleic acid amplification test was ordered to rule out cross-reactivity caused by the influenza vaccination; the patient's viral load was undetectable by this method. In accordance with accepted screening algorithms,<sup>1</sup> we thus considered the patient to be HIV-negative with a high level of confidence. At one month, his viral load remained undetectable (<50 copies per milliliter), and the results on Western blotting had reverted to non-reactive.

A case-control study<sup>2</sup> of 101 blood donors who had been vaccinated against influenza and 191 matched controls showed that recent inoculation with any brand of influenza vaccine was significantly associated with a false positive screening assay for HIV antibodies. Guidelines of both Johns Hopkins and the New York State Department of Health list influenza vaccination as a known cause of indeterminate results on Western blotting for HIV antibodies.<sup>3</sup> Furthermore, digital reconstructions of both molecules demonstrate a striking homology between the transmembrane domains of HIV-1 envelope proteins and the influenza envelope protein hemagglutinin, although whether this homology accounts for the false positive assay reactions is unclear.<sup>4</sup>

The HIV GP160 protein exists only in the intracellular domain, where it is cleaved into GP41 and GP120 oligomers. Since GP160 itself is not present in mature HIV virions,<sup>5</sup> GP160 proteins

and antibodies against these proteins should be absent not only from the Western blot assays but also in most cases from the serum of HIV-infected patients.

Given the escalating international awareness of various influenza strains, it is very important to remind patients and clinicians that influenza vaccination may cause cross-reactivity with HIV antibody assays. The time course for such cross-reactivity remains uncertain. Moreover, if the screening algorithm for acute HIV infection had called for the use of a nucleic acid amplification test instead of the Western blot assay to confirm the enzyme immunoassay, the index patient would not have received an indeterminate result.

Christian P. Erickson, M.D.

USHealthworks  
Los Angeles, CA 90245  
christianerickson@alumni.duke.edu

Todd McNiff, M.D., M.S.P.H.

Mount Sinai Medical Center  
Miami Beach, FL 33140

Jeffrey D. Klausner, M.D., M.P.H.

San Francisco Department of Public Health  
San Francisco, CA 94103

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## Oseltamivir Resistance in Influenza A (H5N1) Infection

**TO THE EDITOR:** De Jong et al. (Dec. 22 issue)<sup>1</sup> report resistance to oseltamivir in two of three recent deaths from influenza A (H5N1) virus infection and recommend investigation into new antiviral drugs for use either alone or in combination with oseltamivir. Zanamivir is another licensed neuraminidase inhibitor. Studies with nebulized and intravenous preparations suggest that zanamivir has good safety and efficacy, even in patients with underlying respiratory disease.<sup>2-4</sup> The H274Y mutation that confers resistance to oseltamivir in patients with H5N1 infection does

not confer cross-resistance to zanamivir, a phenomenon attributable to differences in binding properties.<sup>5</sup> A treatment regimen combining these two neuraminidase inhibitors would be expected to reduce the opportunity for the selection of resistant mutants, in a manner akin to the use of dual nucleoside analogues in antiretroviral therapy.

Ravindra K. Gupta, M.P.H., M.R.C.P.

Jonathan S. Nguyen-Van-Tam, M.B.E., D.M.

Health Protection Agency  
London NW9 5HT, United Kingdom

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**THE AUTHORS REPLY:** Zanamivir is an attractive antiviral drug for combined treatment of influenza A (H5N1) because of nonoverlapping resistance patterns in this drug and oseltamivir. However, the licensed preparation of zanamivir may be less appealing since it is administered by inhalation, which provides drugs predominantly to the upper respiratory tract. Since human infection with current strains of influenza H5N1 can be associated with disseminated infection and replication in the lower respiratory tract and

extrapulmonary sites,<sup>1-3</sup> combined treatment with nebulized zanamivir and oral oseltamivir would be likely to result in monotherapy in the lower respiratory tract and nonrespiratory sites. Although it would be important to evaluate the effects of combined treatment with zanamivir in influenza H5N1, the route of administration will need to be carefully considered.

Menno D. de Jong, M.D., Ph.D.

Oxford University Clinical Research Unit  
Ho Chi Minh City, Vietnam  
mddejong@hcm.vnn.vn

Tran Tinh Hien, M.D., Ph.D.

Hospital for Tropical Diseases  
Ho Chi Minh City, Vietnam

Jeremy Farrar, D.Phil., F.R.C.P.

Oxford University Clinical Research Unit  
Ho Chi Minh City, Vietnam

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## Infliximab for Ulcerative Colitis

**TO THE EDITOR:** As Rutgeerts et al. mention in their article about infliximab for ulcerative colitis (Dec. 8 issue),<sup>1</sup> nocturnal fecal incontinence in patients who have an ileoanal pouch is, indeed, an “inconvenience” that is reminiscent of their presurgery symptoms of colitis (but without the debilitating disease). However, Hahnloser et al. do not state the overall prevalence as 24 percent.<sup>2</sup> Their data actually show that the proportion of patients with more than two episodes of nocturnal staining per week was 5 percent. The proportion increased to 24 percent only after 15 years, by which time the population had aged to a mean of 50 years and included patients up to 77 years of age. This increase mainly reflected postpartum and senescent decline in sphincter strength<sup>3-5</sup> in a population that was 50 percent female and included patients 10 to 30 years older than those in the trial of Rutgeerts et al.

There is little to recommend changes in practice on the basis of this trial, considering that half the data are short term. Only one third of the pa-

tients achieved remission, approximately 10 to 24 percent had a serious adverse event, and long-term safety is not known. The cumulative risks and financial burden would be considerable for these young patients.

Conor J. Shields, M.D.

Desmond C. Winter, M.D.

University College Dublin  
Dublin 00004, Ireland  
dwinter@eircom.net

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