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chloroquine–chloroguanide (a drug combination used successfully by travelers for several decades but now abandoned because of poor protective efficacy) are similar. On the basis of adverse-event profiles, mefloquine clearly is associated with a statistically significant higher risk of neuropsychiatric symptoms than other antimalarial drugs, as I explained in my review. For most travelers who are considered good candidates for mefloquine prophylaxis, including pregnant women and young children, the regimen carries distinct advantages in terms of cost, convenience, proven efficacy, and demonstrated safety. The suggestion that the safety and adverse-event profiles of mefloquine hinge on very early and limited clinical trials in special populations may mislead readers; mefloquine has been widely used by the traveling public for more than a decade. The responsibility for the decision to recommend mefloquine as first-line or as alternative prophylaxis rests with the national authorities weighing factors of safety, efficacy, cost, and other determinants of effectiveness in the context of the populations they serve.

J. Kevin Baird, Ph.D.
U.S. Naval Medical Research Unit No. 2, Jakarta, Indonesia
American Embassy
FPO AP 96520 USA
baird@namru2.org

Respiratory Syncytial Virus Infection in Elderly Adults

TO THE EDITOR: Falsey et al. (April 28 issue), in their report on respiratory syncytial virus (RSV) infection in elderly and high-risk adults,1 claim that “the symptoms and signs of RSV infection and those of influenza were not substantially different” and also that the demographic and clinical characteristics of the patients with influenza and of those with RSV infection were similar. If the clinical manifestations of the two diseases were the same, and if the populations that were affected could not be distinguished, how do the authors explain the striking differences between the patients with influenza and those with RSV infection in the rate of office visits (42 percent vs. 17 percent, respectively) and use of antibiotics (33 percent vs. 9 percent)?

Most clinicians make treatment decisions on the basis of a combination of science, experience, and intuition. I suspect that there was some difference that was either not captured or not quantified that influenced both patients’ decisions to see a physician and physicians’ decisions to prescribe an antibiotic.

Kenneth J. Gorelick, M.D.
1 Maplewood Dr.
Newtown Square, PA 19073
pulmon@comcast.net


TO THE EDITOR: Falsey and colleagues probably underestimate the burden of influenza-related mortality among elderly patients. Influenza-related hospitalization often results from secondary bacterial infection that occurs after the virus is cleared, hampering confirmation of the presence of the virus by viral isolation, polymerase-chain-reaction analysis, or serologic studies on admission. Studies of excess mortality,1,2 which sidestep the difficulties of case ascertainment, set the current mortality burden associated with influenza in the elderly at three times that of RSV infection.

This point pales, however, beside the fascinating data presented by Falsey et al. on the benefits of influenza vaccine. Vaccine coverage among elderly hospitalized patients with confirmed influenza was 68 percent, as compared with 75 percent among those with RSV infection, indicating that the efficacy of vaccination in preventing influenza-related hospitalizations was only 29 percent (95 percent confidence interval, 2 to 48 percent). A single clinical trial of influenza vaccination in the elderly showed that the efficacy of the vaccine against mild influenza was 57 percent.3 Cohort studies without laboratory confirmation show an astonishing benefit in terms of mortality from all causes in the elderly, but such studies are prone to self-selection bias and overestimation.2,4 We think the study by Falsey et al. may come closest to the truth for severe
outcomes because it analyzed influenza-specific hospitalizations, and the presence of elderly controls who were hospitalized with RSV infection eliminated self-selection bias. We agree wholeheartedly with Falsey et al. that better vaccine formulations for the elderly are needed.

Lone Simonsen, Ph.D.
National Institute of Allergy and Infectious Diseases
Bethesda, MD 20892

Cecile Viboud, Ph.D.
Fogarty International Center
Bethesda, MD 20892


THE AUTHORS REPLY: Gorelick suggests that the clinical characteristics of influenza and RSV infection were probably different since significantly greater numbers of otherwise healthy elderly patients with influenza visited a physician and were prescribed antibiotics. We and other investigators have noted that the presence of fever and gastrointestinal symptoms are more common with influenza, whereas rhinorrhea and wheezing are more common with RSV infection.1-4 However, the degree of overlap limits the usefulness of signs and symptoms for clinical diagnosis in individual patients. Furthermore, these clinical differences become increasingly blurred in high-risk groups. Clearly, healthy, elderly patients infected with influenza virus felt worse than those with RSV infection, as evidenced by the acute functional effect we observed. However, the only significant difference was the presence of dyspnea (25 percent among those with influenza vs. 5 percent among those with RSV infection, P=0.05). We understand the need for busy practitioners to make treatment decisions on the basis of clinical grounds, but we maintain that everything that looks like “the flu” in the winter is not. Rapid, sensitive, and specific viral diagnostic tests might help augment intuition.

We agree with Simonsen and Viboud that influenza-related mortality may have been underestimated in our study. Although serologic studies may identify influenza in some patients hospitalized with secondary bacterial infections, those with rapidly rising antibody titers would certainly be missed. In addition, influenza epidemics have been associated with peaks in cardiovascular and cerebrovascular events, and influenza-related hospitalizations due to these diagnoses would not have been captured in our study.5 However, the same may also hold true for RSV infection, especially with regard to secondary bacterial infections. Our data indicate that 10 percent of patients with RSV infection and 7 percent of patients with influenza A had mixed viral–bacterial infections at the time of hospitalization.

With regard to the efficacy of influenza vaccine, we caution readers that our study was not designed to evaluate vaccine efficacy. We agree that the patients with RSV infection constitute an excellent control group; however, the vaccination status of each patient was ascertained by interview but not confirmed. In addition, during two of the four years of study, the availability of influenza vaccine was delayed, and we did not attempt to evaluate the timing of vaccination with regard to the onset of influenza. Nonetheless, we wholeheartedly agree that our data confirm the need for better influenza-vaccine formulations.

Ann R. Falsey, M.D.
Edward E. Walsh, M.D.
University of Rochester School of Medicine
Rochester, NY 14618

Ann.Falsey@viahealth.org