

# Statins May Offer Protection During Flu Outbreaks

BY PATRICE WENDLING  
Chicago Bureau

NICE, FRANCE — A provocative study has identified an association between the use of statins and favorable outcomes during influenza epidemics.

In the retrospective cohort analysis, statin therapy was associated with substantial reductions in mainly respiratory diseases, but also in death from all causes, Dr. Theo Verheij said at the 16th European Congress of Clinical Microbiology and Infectious Diseases.

As for the mechanism, it is theorized that statins could have anti-inflammatory properties or an effect on immune status, he said. Three small studies have shown that statins have an anti-inflammatory effect in patients with bacteremia. In addition, a recent study identified an association between statin use and reduced sepsis in patients hospitalized for acute coronary syndrome, ischemic stroke, or revascularization (*Lancet* 2006;367:372-3).

Dr. Verheij and his colleagues assessed

patients aged 50 years or older from the primary care network of the University Medical Center in Utrecht, the Netherlands. The patients were followed up during eight epidemic and nonepidemic influenza seasons from 1998 to 2003, said Dr. Verheij, a professor of general practice with the university.

The primary end point was a composite of community-acquired pneumonia, prednisone-treated acute respiratory disease, MI, stroke, and death from all causes. The analyses were adjusted for age, gender, insurance, medications, medical conditions including diabetes mellitus and psychiatric disorders, and influenza vaccination.

A total of 22,638 patients provided 130,558 person-periods (each influenza season was considered a period). Statin therapy (simvastatin, pravastatin, fluvastatin, atorvastatin, and rosuvastatin) was used in 6,982 (5.3%) person-periods and influenza vaccinations in 36,556 (28%). The primary end point occurred in 3.2% of person-pe-

riods, and most events (72%) were respiratory, he reported.

During influenza epidemics, statin therapy was associated with a 33% reduction in the primary end point (relative risk 0.67), a 26% reduction in respiratory dis-

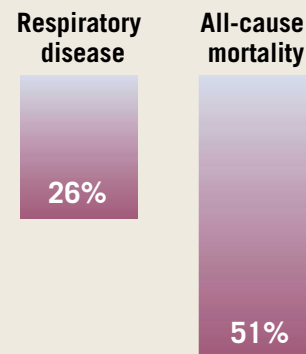
ease (RR 0.74), and a 51% reduction in all-cause mortality (RR 0.49); these results were significantly different from outcomes in patients who were not using statins. The risk of pneumonia was reduced by 28% (RR 0.62) and the risk of acute respiratory disease was reduced by 21% (RR 0.79).

The findings were consistent across subgroups defined by age, cardiovascular disease, or exposure to influenza vaccination. In nonepidemic influenza seasons, there was no significant reduction in risk, except for all-cause death.

A dose-response relationship convinced the investigators that statin therapy provided a protective effect, Dr. Verheij said. Statin therapy was associated with a 33% reduction of any event among patients taking less than two daily defined doses and a 44% reduction among those taking two or more daily defined doses (RR 0.67 and 0.56, respectively, compared with patients who did not use statins).

The findings should be used to direct future studies into potential implications, particularly during pandemics, he said. ■

## Respiratory Disease Risk Reduced During Flu Epidemics in Statin Users



Note: Based on a study of 22,638 patients.  
Source: Dr. Verheij

ELSEVIER GLOBAL MEDICAL NEWS

## Refrigerator-Stable FluMist Found Comparable to Frozen

BY JANE SALODOF  
MacNEIL  
Southwest Bureau

SAN FRANCISCO — An experimental refrigerator-stable formulation of the live attenuated influenza vaccine marketed as FluMist was comparable to the approved frozen formulation in a phase III trial presented in a poster at the annual meeting of the Pediatric

The new formulation has two advantages over the approved FluMist, according to Dr. Block, who is in private practice in Bardstown, Ky. It is administered in a smaller volume, and physicians can store it in a refrigerator.

The immunogenicity trial was conducted at 26 U.S. sites from July 2004 to May 2005. Investigators randomized 981 subjects, of whom 942 could be evaluated for safety and 878 for immunogenicity. The latter analysis included 332 children aged 5-8 years and 546 subjects aged 9-49 years.

None of the younger children had been vaccinated before. They received two doses of FluMist, 46-60 days apart. Participants 9 years of age and older received one dose. The dose used with the new formulation was 0.2 mL (0.1 mL in each nostril) vs. 0.5 mL (0.25 mL in each nostril) with the approved formulation.

FluMist manufacturer MedImmune Inc. of Gaithersburg, Md., sponsored the study. MedImmune is seeking approval of the new formulation for use in healthy children aged 6-59 months as well as in healthy children and adults aged 5-49 years, for whom the original formulation was approved in 2003. ■



**The two intranasal FluMist formulations had equivalent immunogenicity against three influenza strains.**

DR. BLOCK

Academic Societies.

Dr. Stan L. Block reported that the two intranasal FluMist formulations had equivalent immunogenicity against three influenza strains (two type A and one type B). Seroreponse rates and reactivity events were comparable in the randomized, double-blind study.

Diarrhea, upper abdominal pain, and nausea were the most frequently reported adverse events. All occurred in less than 5% of patients, regardless of formulation. No serious side effects were attributed to either version of the live attenuated influenza vaccine.

## Possible GI Route for Avian Influenza In Humans: Interpret Data Cautiously

BY KATE JOHNSON  
Montreal Bureau

Evidence for a gastrointestinal route for human avian influenza infection should be interpreted cautiously, according to Dr. William Schaffner, chair of the department of preventive medicine at Vanderbilt University in Nashville, Tenn.

As the H5N1 virus continues its global march amid fears that it may mutate to become more easily transmissible, a study published last year suggesting a gastrointestinal portal is getting renewed attention.

Last year, Dr. Menno D. de Jong, head of the virology department at the Oxford University Clinical Research Unit in Ho Chi Minh City, Vietnam, published a case report of a child who died of avian influenza after an atypical gastrointestinal presentation, fecal evidence of the H5N1 virus, and no respiratory symptoms at presentation (*N. Engl. J. Med.* 2005;352:686-91).

This case and several other published reports suggest that the gastrointestinal tract may also be vulnerable to the infection, Dr. de Jong was reported as saying.

"The presence of viable virus in the feces of our patient has important implications for transmission, infection control, and public health," Dr. de Jong and his colleagues wrote. This "highlights a potential route of human-to-human transmission, especially in

combination with crowded living conditions and diarrhea."

To date, experts consider human-to-human transmission of avian influenza very rare, but they agree that if the H5N1 virus becomes easily transmissible among humans, it likely would trigger a global pandemic. Recent studies have suggested that the preferential attachment of the virus to cells in the lower rather than the upper



**This limited gastrointestinal evidence of the H5N1 virus should not cause alarm, but 'we should keep an eye on it.'**

DR. SCHAFFNER

human respiratory tract may explain why it is not easily spread by coughing and sneezing (*Science* 2006;312:399). But the possibility of gastrointestinal infection suggests the potential for much easier fecal-oral transmission.

Dr. Schaffner, who is also professor of medicine in the division of infectious diseases at Vanderbilt, says a couple of isolated reports of gastrointestinal evidence of the H5N1 virus should not cause alarm. "There is nothing we know about the general epidemiology of influenza that would suggest this is a form of transmission that is in any way noteworthy, although we should keep an eye on it," he said in an interview.

A similar gastrointestinal presentation, with diarrhea as the initial symptom and with no respiratory illness, has been described elsewhere (*Emerg. Infect. Dis.* 2004;10:1321-4), Dr. de Jong said in an interview, and other researchers have also documented intestinal replication of the H5N1 virus in humans (*Emerg. Infect. Dis.* 2005;11:1036-41).

In addition, there are reports of human infection in which patients' only exposure to the virus was through the consumption of duck blood or undercooked poultry, Dr. de Jong said (*N. Engl. J. Med.* 2005;353:1374-85).

"The spectrum of influenza H5N1 is wider than previously thought," he wrote. "Clinical surveillance of influenza H5N1 should focus not only on respiratory illness, but also on clusters of unexplained deaths or severe illnesses of any kind."

Dr. Schaffner said that even if gastrointestinal infection is shown to be more common than previously thought, preventive measures are already being taken.

"We already have one public health response that works well for both respiratory and intestinal infections," he said. "Hand washing is one of the most effective ways to interrupt intestinal transmission of known viruses and bacteria that are spread in stool." ■