

Flu Expert Calls for More Research Into Statin Use

BY JONATHAN GARDNER
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PARIS — Public health authorities should develop a research agenda on the use of statins as treatment and prophylaxis in the event of an influenza pandemic, a top researcher said at an international conference on avian influenza in humans.

Data suggest statins could be useful in combating side effects such as pneumonia, sepsis, bacteremia, and pulmonary disease, said Dr. David Fedson, coordinator of the Macroepidemiology of Influenza Vaccination Study Group and a former professor of medicine at the University of Virginia, Charlottesville. They could be an alterna-

tive treatment in the first wave of a pandemic, when vaccines may not be available.

Statin can interfere with inflammation and with virus transport, assembly, and budding, while aiding endothelial and epithelial cell function and immune response, Dr. Fedson said. These qualities could make statins an effective treatment option in the event that avian influenza H5N1 mutates into a form that can infect humans more easily.

Should such a mutation take place, vaccine manufacturers first will need to match their vaccine to the virus and then ramp up production, which will mean that the first regions to be affected could be defenseless against the pandemic.

"In the event of an H5N1 pandemic, the global demand will easily be on the order of 3-4 billion doses, and probably much more," Dr. Fedson said. "Yet today, if the world's vaccine companies were asked to produce [vaccine], in 6 months they could produce enough ... to vaccinate fewer than 100 million people. Vaccination will not be a realistic possibility for 85% of the world's population that do not live in countries with vaccine companies, and it will be difficult even for those who do."

By comparison, generic statins are inexpensive—\$1.75 for 5 days' worth of dosage in the United States—and they can be produced worldwide, Dr. Fedson said.

Among the evidence in favor of statins'

protective qualities, Dr. Fedson said, are studies showing a reduction of up to 92% in bacteremia-attributable mortality in patients who take statins; a reduction of up to 25% in sepsis mortality in those who have previously taken statins; and a 53% reduction in 30-day pneumonia mortality in those who have taken statins.

However, international health officials need to embark on a statin research agenda to explore unanswered questions, Dr. Fedson said. Researchers need to perform clinical and epidemiologic studies examining hospitalization and mortality. They also must compare the effects of previous statin use with continuing statin use and compare treatment with prophylaxis. ■

No Change in Flu Guidance for Partially Immunized Children Under 9 Years of Age

BY MIRIAM E. TUCKER
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ATLANTA — Children less than 9 years of age who received just one dose of influenza vaccine the first time they were immunized against influenza still don't require a second dose the following season ... at least for now.

That was the vote from the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention at its summer meeting.

Current recommendations from ACIP and the American Academy of Pediatrics call for previously unvaccinated children aged 6 months to 9 years to receive two doses of inactivated influenza vaccine, administered at least 1 month apart. For the live attenuated influenza vaccine (FluMist), children aged 5-8 years who had not previously received either type of influenza vaccine should receive two doses, separated by 6-10 weeks. If a child received only one dose in the previous year, only one dose is required (MMWR 2006;55[early release]:1-41).

However, published and unpublished data suggesting that children may not be adequately protected without receiving two doses in one season—particularly in the response to influenza B strains—have prompted both the ACIP and the AAP to consider recommending that partially immunized children receive a second dose the following season. But after much discussion, ACIP members ultimately decided to wait until more of the data are published.

The AAP's Committee on Infectious Disease (COID) had been leaning toward recommending a second dose prior to the ACIP meeting. But, given ACIP's decision, the COID also may de-

cide to wait, COID chair Dr. Keith R. Powell, vice president and Noah Miller Chair of Pediatrics at Children's Hospital Medical Center of Akron (Ohio), and professor and chair of pediatrics at Northeastern Ohio Universities, Rootstown, said in an interview.

Dr. Kathleen M. Neuzil, a vaccine researcher from the University of Washington, Seattle, summarized the recent data, which include very limited information on immunogenicity in children

under the age of 2 years. Children aged 2-6 years with no detectable hemagglutination inhibition assay antibody levels have lower responses than do children with detectable levels, suggesting that "preexisting immunity or infection matters." Moreover, historical data suggest antibody responses to influenza B vaccine or infection can be substantially lower, compared

with responses following influenza A vaccine or infection, she said.

In a published study from Dr. Neuzil's group, giving 6- to 23-month-old children one dose of influenza vaccine in the spring and another the following autumn was not inferior to giving both doses during flu season. But that study was conducted in the 2002-2003 and 2003-2004 seasons, when the three antigens in the vaccine didn't change (Pediatrics 2005;115:1039-47).

Several yet-unpublished studies conducted during the 2004-2005 season—when two of the antigens differed from the previous season's vaccine—have yielded different results.

In two of those studies, also done in 6- to 23-month-olds who received the first dose in either the spring or the fall, response to the second dose differed by antigen. In 2003-2004, one of the strains was A/Panama/2007/99 (H3N2). In 2004-2005, the H3N2 strain

had "drifted" to A/Wyoming/03/2003. Although the children who had been "primed" with the 2003-2004 vaccine had a less robust response to the H3N2 component than did those who received two doses of the identical vaccine, about 70% still had protective antibody levels in one of the studies, while priming had no impact on the H3N2 response in the other study.

In contrast, response to the B strain, which was completely different between the two seasons (B/HongKong/1434/2002 in 2003-2004 vs. B/Jiangsu/10/2003 in 2004-2005), was dramatically lower among those who received just one compared with two identical vaccine doses, in both studies.

A prospective, open-label study comparing one dose with two doses in the fall in vaccine-naïve 5- to 8-year-olds yielded similar results: Two doses in the same season were better than one, and preexisting antibody was the strongest predictor of antibody response after one dose. In this study, one-third of the children did not achieve "protective" responses to the B antigen, even after two doses. However, other data suggest that results may differ greatly depending upon how the antibody response to B is measured, Dr. Neuzil remarked.

In a fourth unpublished study of children aged 6-21 months, giving two vaccine doses in the same year was 82% effective in preventing influenza-like illness, compared with 62% with two vaccines given in different years.

ACIP member Dr. Ban Mishu Allos summed up the committee's view prior to its vote: "We have a lot of data that haven't been published yet. We need to look at them further. ... Given all that, I'm not in favor of changing."

Dr. Michael Decker of Fluzone manufacturer Sanofi Pasteur said ideally the recommendation should change every year: One dose would be needed if the vaccine strains are similar to those of the previous year, two doses if they aren't, though such a proposal "is probably unfeasible." ■

New Prioritization of Children Aged 2-5 in Flu Vaccine Shortage

ATLANTA — The prioritization plan for use of inactivated influenza vaccine in the event of a supply shortage or delay has been updated to reflect the recently designated high-risk status of children aged 24-59 months.

The vote, of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention at its summer meeting, must be approved by CDC and published before it becomes official. If approved, the new prioritization scheme will look like this:

Tier 1

- 1A • Persons aged 65 years and older with comorbid conditions
 - Residents of long-term care facilities
- 1B • Persons aged 2-64 years with comorbid conditions
 - Persons aged 65 years and older without comorbid conditions
 - Children aged 6-23 months
 - Pregnant women
- 1C • Children aged 24-59 months
 - Health care personnel
 - Household contacts and out-of-home caregivers of children aged less than 6 months

Tier 2

- Household contacts of children and adults at increased risk for influenza-related complications
- Healthy persons aged 50-64 years

Tier 3

- Persons aged 5-49 years without high-risk conditions

In most vaccine shortfall situations, all three groups in tier 1 can be considered top priority, followed by tiers 2 and 3. It would be necessary to further prioritize risk groups 1A, 1B, and 1C separately only on rare occasions when the supply is extremely limited, Nicole M. Smith, Ph.D., said at the meeting. More information about the use of influenza vaccine and antiviral agents is available at www.cdc.gov/mmwr/preview/mmwrhtml/rr55e628a1.htm.

—Miriam E. Tucker