Tamiflu Prophylaxis Expands Down to Age 1

BY TIMOTHY F. KIRN
Sacramento Bureau

The Food and Drug Administration has expanded the approval of oseltamivir to include prophylaxis in children as young as 1 year who have had close contact with someone infected with influenza A or B.

Oseltamivir (Tamiflu) has until now only been approved for the treatment of children older than 1 year who were themselves infected.

The FDA reported that the data used for this expanded indication came from a study of the spread of influenza in households, which enrolled 1,100 subjects, of whom 222 were children 1-12 years old.

That study found that 17% of family contacts in the placebo group became ill with confirmed flu, compared with only 3% of those treated with oseltamivir within 48 hours after exposure. That benefit mirrored the one seen in adults. Prophylactic treatment in the study was a single dosing of the drug (30-60 mg, depending on patient weight) taken every day for 10 days.

Side effects seen in the prevention study were similar to side effects seen in treatment studies, with vomiting the most common.

Dr. Kathryn M. Edwards, an influenza-vaccine and infectious-disease expert, said she was pleased by the FDA action and thought this new indication was important—not just in the event that the avian flu hits the United States, but for seasonal flu as well.

"I think this drug can be very helpful," Dr. Edwards, a professor of pediatrics at Vanderbilt, University, Nashville, Tenn., said in an interview. "Influenza is a serious illness. When my [patients] have the flu, and I confirm it, I treat them."

This new approval does not obviate the need for yearly flu vaccination, the FDA noted. It is still recommended that pediatric patients get vaccinated.

In November, the FDA's Pediatric Advisory Committee reviewed safety data on oseltamivir and concluded there were no new safety concerns regarding the drug and no cause for concern about any neuropsychiatric events.

Possible neuropsychiatric events had been reported to the Roche Pharmaceuticals Inc. safety database. Through June 2005, a total of 67 neuropsychiatric events had been reported in 59 patients, with 19 cases of convulsion/encephalitis/encephalopathy, 15 cases of depressed consciousness, and 13 cases of hallucination/delirium, according to information provided by Roche to the FDA. However, in 51 of the patients, there was an alternative explanation for the event, and in 6 cases there was incomplete information, leaving only two cases—both described as cases of "abnormal behavior"—that could not be ruled out as possibly vaccine-associated.

The vast majority of these cases were reported from Japan, where the drug is used much more frequently than anywhere else in the world, and only one of the 59 cases occurred in the United States. To date, more than 13 million doses of oseltamivir have been administered to children less than 16 years of age, and, in the United States, oseltamivir is the most prescribed antiviral medication, according to Roche.

Roche has been asked by the FDA to update the labeling of oseltamivir to warn of the rare possibility of skin rash and other hypersensitivity reactions (anaphylaxis).

In other recent oseltamivir news, Vietnamese officials have reported that in four of eight avian flu cases treated with oseltamivir, the drug was not effective. In two of those cases, the patients had or developed resistant disease. One of those cases was in a 13-year-old girl, who was definitely known to have been treated early with adequate doses (N. Engl. J. Med. 2005;353:2667-72). In the other two cases, the drug probably was started too late, reported Dr. Menno de Jong of the Hospital for Tropical Diseases, Ho Chi Minh City.

Dr. Anne Moscona, professor of pediatrics and microbiology and immunology at Weill Medical College of Cornell University, New York, said in an accompanying editorial that this confirmation of resistant avian flu highlighted the need to discourage the general population from stockpiling the medication, since nonphysicians would be more likely to misuse the drug, which would favor the development of more resistance (N. Engl. J. Med. 2005;353:2633-6).

Misuse of oseltamivir in children would be particularly worrisome, since children are usually a main source of the spread of influenza in a community, have higher viral loads, and excrete virus for a longer period of time. ■

Today's Rapid Strep Tests May Obviate Backup Cultures

BY DIANA MAHONEY
New England Bureau

CAMBRIDGE, MASS. — Backup throat cultures following negative rapid group A strep detection tests may no longer be necessary in some practices, Michael Pichichero, M.D., said at a conference on pediatric infectious diseases.

To determine whether the standard procedure can be discontinued, clinicians can undertake a simple investigation to assess the sensitivity of commercial rapid immunochemical antigen test kits as they are used in their practices, Dr. Pichichero suggested at the conference, sponsored by Boston University, PEDIATRIC NEWS, and FAMILY PRACTICE NEWS.

"In the early 1990s, published studies evaluating the accuracy of rapid strep tests, compared with throat culture, suggested the rapid tests had really good specificity, but the sensitivity in the clinical setting of office-based practices wasn't there," said Dr. Pichichero of the University of Rochester (N.Y.) Medical Center.

Because of the sensitivity limitations, the American Academy of Pediatrics recommended in its 2000 Red Book—and continues to recommend—that all negative rapid diagnostic tests for group A strep pharyngitis be backed up by throat culture.

Because of the very high specificity of the rapid tests, a positive test result does not require throat culture confirmation, noted Dr. Pichichero, who is also in private practice in Rochester.

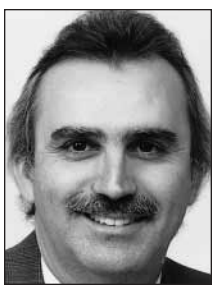
Since the early 1990s, the rapid strep tests have matured and new products have emerged, "and at some point it seemed to us that the sensitivity was getting better too," Dr. Pichichero said.

To test this hypothesis, Dr. Pichichero and his colleagues conducted a retrospective analysis reviewing 11,427 of the rapid group A strep tests performed in their practice between January 1996 and June 1999.

Of the 11,427 tests, 8,385 were negative and 3,042 were positive. Patients testing positive began antibiotic treatment immediately. Nearly all of the patients testing negative—8,234 of 8,385, or 98%—received backup cultures.

"Only 2% of the patients with negative rapid tests cultured positive on follow-up. You can't expect much better sensitivity than that, even with throat culture," Dr. Pichichero said.

The findings cannot necessarily be generalized across practices, however.



'First you have to know who you are culturing. We only culture patients who we think have strep.'

DR. PICHICHERO

"There are some important considerations. First, you have to know who you're culturing. We only culture patients who we think have strep. If you culture patients with upper respiratory infections, for example, you're going to have more issues," Dr. Pichichero said. "The other important thing is, you have got to use a good test, and a good test is probably not one that costs less than a dollar. You're going to have to spend about $1.50-$2.00—well worth the expense if the return is good sensitivity and a reduction in the costs associated with cultures."

One way to gauge the performance of rapid strep tests is "to look at your own practice," he suggested. "Take a look at the last hundred negative rapid tests performed in your office. If the follow-up cultures for 90 or more of them are negative, that should tell you that, for the patients you're testing and the way you're using the tests, you can probably stop the follow-up cultures." ■

Imported Congenital Rubella Syndrome Case Seen in N.H.

Consider congenital rubella syndrome in infants with compatible signs, particularly immigrants from countries without rubella control programs, the Centers for Disease Control and Prevention advised.

In 2004, a 10-week-old infant born to a mother who had emigrated from Côte d'Ivoire was brought to a New Hampshire emergency department with fever, vomiting, irritability, and poor feeding. While hospitalized, the infant—who had been born with a cataract in her left eye—was diagnosed with microcephaly, patent ductus arteriosus, bilateral hearing impairment, hepatosplenomegaly, and failure to thrive (MMWR 2005;54:1160-1).

Congenital rubella syndrome was suspected and confirmed by positive rubella IgM and positive urine and nasopharyngeal cultures. The genetic sequence was found to be that of a wild-type rubella virus similar to one found in Uganda in 2001, the CDC said.

Soon after conception, the mother had come into contact with refugees from one of four transit centers in Cote d'Ivoire where there had been a rubella outbreak during February-April 2004. She had reported no history of symptoms of acute rubella infection such as rash, fever, lymphadenopathy, or arthralgia. However, subclinical infections are estimated to occur in up to 50% of rubella cases.

—Miriam E. Tucker