Educating Public a Key Challenge

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advised that initial vaccination efforts focus on immunizing as many people as possible in five target groups: emergency medical personnel, pregnant women, children and adults aged 6 months to 24 years, caregivers and cohabitants of children younger than 6 months, and adults aged 25-64 years who are immunocompromised or who have chronic health conditions that may increase their flu risk.

Physicians are likely to have their hands full educating groups targeted for the novel influenza A (H1N1) immunization. Current seasonal influenza coverage among the five key groups is estimated at only 20%-50%, according to Dr. Anthony J. Fiore of the Center's for Disease Control and Prevention's Influenza Division.

The immunization recommendations were made by the Advisory Committee on Immunization Practices of the CDC at a special 1-day meeting. The primary targets for novel influenza A (H1N1) (nH1N1) immunization effort total about 159 million individuals in the United States.

If vaccine demand exceeds availability, subgroups of the larger group, totaling 42 million people, should receive priority. The first subgroups—pregnant women and household and caregiver contacts for infants younger than 6 months of age—remain unchanged as a priority. The next subgroups include health care and emergency personnel in direct contact with patients; children aged 6 months through 4 years of age; and children with chronic medical conditions.

When vaccine availability is sufficient at the local level to routinely vaccinate initial target populations, a decision should be made in cooperation with state and local health authorities to vaccinate healthy adults aged 25-64 years first, then individuals aged 65 years and older. The last recommendation, in contrast to seasonal influenza vaccination recommendations, reflects the fact that older individuals thus far have been at lower risk for the novel influenza A H1N1 virus.

Dr. Doug Campos-Outcalt, the liaison to ACIP from the American Academy of Family Physicians, said that AAFP will likely support the prioritization scheme but may not issue a formal endorsement. Rather, the academy will probably provide a link on its website directing members to the CDC recommendations and "will be encouraging members to communicate and cooperate with state and local health departments, and to the extent they can, provide vaccines at their clinical sites," Dr. Campos-Outcalt, associate head of family and community medicine at the University of Arizona, Phoenix, said in an interview. According to Dr. Fiore, new recommendations were needed because the federal government's 2007 pandemic vaccine priority guidance had been developed for the scenario of a severe pandemic with the potential for social disruption of critical infrastructure. The ACIP's Influenza Working Group concluded that current epidemiologic and immunologic evidence, combined with updated information on vaccine supply and availability timelines, indicated a need to revise recommendations that had been made during prepandemic planning.

In drafting the document that ACIP voted on, the working group assumed the following: that the severity of illness and groups at higher risk for infection or complications will be similar to what has already been observed; that the safety profile and antigen content of novel H1N1 vaccines will be similar to that of seasonal vaccine; and that adequate supplies of licensed unadjuvanted vaccine can be produced for all by approximately February 2010 but that enough vaccines for all will not be available before the next pandemic wave, expected this fall.

The working group made the assumption that pandemic vaccine and seasonal vaccine availability will overlap and both will be recommended for many population groups, that two doses will be needed for protection, and that one dose will provide minimal or no protection. Also, that initial demand for vaccination would be approximately the same as for seasonal vaccine but could increase quickly as community transmission increases, that vaccine distribution will be timely, and, finally, that "recommendation implementation will pose many challenges," the working group's document said.

Dr. Campos-Outcalt, who is also assistant dean of outreach and multicultural affairs at the university, agrees. "I think prioritization will be a short lived process. The problem will more likely be convincing the public to be vaccinated, not deciding on who should receive it first." ■

Diagnostic Wrinkles Anticipated in Novel Influenza A (H1N1) Pandemic

BY BRUCE JANCIN

VAIL, COLO. — Recent anecdotal reports suggest that the diagnosis of novel influenza A (H1N1) should not be ruled out by a negative upper respiratory tract specimen in a patient with pneumonia.

There have been two patients at Albany (N.Y.) Medical Center and one in Denver who were hospitalized with severe lower respiratory tract infections whose nasopharyngeal swabs were negative for influenza A by rapid tests—but who had endotracheal aspirates positive for the novel H1N1 virus by culture and polymerase chain reaction.

Negative results from the upper tract do not rule out H1N1 in patients with lower tract infections.

DR. WEINBERG

"That's something to watch for. It would be consistent with findings in animal models showing the virus replicates very well in the lower respiratory tract," said Dr. Adriana Weinberg, who reported on the cases at a conference on pediatric infectious diseases sponsored by the Children's Hospital, Denver.

"As the pandemic evolves, perhaps we may see more cases with florid infection in the lower respiratory tract and not so much virus in the upper respiratory tract," said Dr. Weinberg, professor of medicine, pediatrics, and pathology and medical director of the clinical virology laboratory at the University of Colorado Hospital, Aurora.

At present, the preferred specimens for making the diagnosis of novel H1N1 are the same as for seasonal influenza: nasal washings in children and nasopharyngeal aspirates or swabs in adults. That being said, negative results on those upper respiratory tract specimens do not necessarily rule out novel H1N1 in patients with lower respiratory tract infections.

"In these patients, you may want to proceed with obtaining an induced sputum, an endotracheal aspirate, or a bronchoalveolar lavage specimen to rule out the pandemic strain," according to Dr. Weinberg.

Most diagnostic tests for seasonal influenza A or A plus B will also pick up the pandemic strain. A caveat is that the rapid tests, which in general are not terribly sensitive for the diagnosis of seasonal influenza viruses, appear to be even less sensitive for novel H1N1.

"A positive rapid test indicates you may be dealing with the pandemic strain, but a negative test does not rule out pandemic influenza. However, culture and PCR [polymerase chain reaction] are extremely sensitive for this strain," she continued.

The Centers for Disease Control and Prevention has acted quickly in preparing tools for the diagnosis of novel H1N1. Regular PCR and culture cannot differentiate between seasonal influenza A and the novel H1N1 strain. But just 2 weeks after the first U.S. case of novel H1N1 disease was diagnosed in April, the CDC began sending out to U.S. sentinel laboratories PCR kits that are highly specific for the virus. Less than 2 months later, those kits were onsite at 233 U.S. laboratories, including all state health department laboratories, and at 386 international laboratories.

Physicians can expect to see lots more patients with a prominent gastrointestinal presentation.

More than 90% of those patients presented with fever and cough, and two-thirds had a sore throat—all typical of seasonal influenza—but in addition, 25% presented with diarrhea and 25% had vomiting. ■

Oseltamivir-Resistant H1N1 Identified in U.S.

BY MIRIAM E. TUCKER

Oseltamivir-resistant novel influenza A (H1N1) virus infection has been identified in the United States for the first time, in two severely immunosuppressed patients in Seattle.

The two cases—a teenaged male and a woman in her 40s—are both leukemia patients who have undergone hematopoietic stem cell transplants. Both were initially infected with oseltamivir-susceptible viruses which later developed resistance during antiviral treatment, the Centers for Disease Control and Prevention reported.

The two patients were treated at different hospitals and were not linked epidemiologically. There was no evidence of transmission of the oseltamivir-resistant virus to health care providers or contacts of either patient, the CDC said.

In both patients, the viruses were found to be susceptible to zanamivir by neuraminidase inhibition assay. Sequence analysis showed that the oseltamivir resistance was not the result of gene reassortment with seasonal influenza A (H1N1) virus.

The CDC recommends that immunosuppressed patients receive annual influenza vaccination, even though in some the immune response can be decreased. Clinicians caring for immunosuppressed patients who are infected with novel H1N1 should be aware of the potential of antiviral drug resistance during therapy and prolonged viral shedding, the CDC said.

The public health risk of virus transmission from these two cases appears to be low. Washington state, in collaboration with CDC, is conducting enhanced surveillance for oseltamivir resistance among novel H1N1 virus strains isolated from patients in hospitals and in the community.

Oseltamivir or zanamivir are recommended for treatment of all hospitalized patients with suspected or confirmed novel H1N1 and for outpatients at increased risk for influenza-related complications.

Zanamivir should be considered the treatment of choice in immunosuppressed patients with oseltamivir-resistant novel H1N1 infection, except for those with underlying airway disease. ■

Guidance on treatment and prevention is available at www.cdc.gov/h1n1flu.