

Conference Insights:

a Continuing Education Series

In This Issue:

Influenza Updates

**47th Annual Meeting of the
Infectious Diseases Society of America
October 29–November 1, 2009
Philadelphia, PA**

Dear Reader:

This year's influenza season has already become one of the most dynamic in recent memory, and promises to present continuing challenges for patients and the US healthcare system. The unexpected emergence in most states of the 2009 H1N1 viral strain and early influenza activity attributed to this strain have created a rapidly changing landscape for care providers and patients alike. As this issue of *Conference Insights* goes to press, we have yet to see how the potential cocirculation of both 2009 H1N1 and seasonal influenza viral strains, and the likelihood of a third wave in early 2010, will impact the full 2009-2010 flu season.

Presentations on influenza commanded high interest at this year's annual meeting of the Infectious Diseases Society of America (October 29–November 1, 2009), and this issue of *Conference Insights* offers an overview of key points for healthcare providers based on select information presented by national and international experts in this area. This issue presents a "snapshot in time" of current thought around the detection and management of influenza, and the importance of vaccination strategies. Where appropriate, we have included additional information resources from the Centers for Disease Control and Prevention and state department of health websites, which we encourage you to visit frequently to continue your self-education beyond this activity. We hope that this information and associated resources will be helpful as you discuss influenza with your patients and colleagues.

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Disclosure of Conflicts of Interest

All faculty members participating in continuing medical education programs sponsored by MedEDirect are expected to disclose any real or perceived conflict of interest related to the content of the activity.

Dr Septimus reports that he serves on a paid speaker's bureau as a planner, presenter, or reviewer for Sage Pharmaceuticals Inc, Merck & Co. Inc, and Cubist Pharmaceuticals Inc.

Barbara Jones, Bill Jacobs, and Gudrun Hibberd have nothing to disclose.

Needs Statement

The novel influenza A strain is a recently identified pathogen that has been declared a pandemic pathogen by the World Health Organization (WHO) (Centers for Disease Control and Prevention. <http://www.cdc.gov/h1n1flu/update.htm>. Accessed November 30, 2009). In preparation for the 2009-2010 influenza season, public health agencies and healthcare facilities are evaluating policies and procedures to address the uncertain epidemiology and virulence of this strain against the background of seasonal influenza preparedness (Fiore AE et al. *MMWR Morb Mortal Wkly Rep.* 2009;58(RR-8):1-52). Vaccine trials started in early August and their results will help guide final development of the vaccination campaign, which should begin later in the year (Collin N et al. *Vaccine.* 2009;27:5184-5186; Butler D. *Nature.* 2009;460:562; Centers for Disease Control and Prevention. <http://cdc.gov/h1n1flu>. Updated November 25, 2009. Accessed November 30, 2009). In light of these fast-paced changes, healthcare providers are being challenged to rapidly integrate and disseminate current information on the prevention, detection, and management of influenza to their peers and patients. This activity will provide a concise review of key presentations from the 2009 Infectious Diseases Society of America annual meeting in order to empower healthcare providers with the most current information for the 2009-2010 influenza season.

Accreditation Statements

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Accreditation Statement: MedEDirect is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

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This activity has been assigned ACPE Universal Activity Number 0498-0000-09-001-H01-P and will award 1.0 contact hour (0.1 CEUs).

Learning Objectives

This is a knowledge and application type of activity whereby the learner will:

- Review the epidemiology and unique virulence factors associated with the 2009 A/H1N1 influenza virus
- Discuss emerging vaccine and antiviral treatment options
- Describe the public health implications of novel influenza strains and their pandemic potential

Target Audience

This educational program is intended for physicians, pharmacists, and other healthcare professionals involved with the prevention, detection, and management of viral and respiratory infections.

Estimated Time of Completion

This activity should take approximately 1.0 hour to complete.

Method of Participation

There are no fees for participating in and receiving credit for this activity. The participant should read the objectives and meeting report, answer the multiple-choice post-test, complete the answer sheet with registration and evaluation, and return via:

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Support Statement

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SUMMARY HIGHLIGHTS

Summary Highlights From the CDC's Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season

- Most healthy people who develop an illness consistent with uncomplicated influenza, or people who appear to be recovering from influenza, do not need antiviral medications for treatment or prophylaxis. However, those who present with suspected influenza and more severe symptoms, such as evidence of lower respiratory tract infection or clinical deterioration, should receive prompt empiric antiviral therapy, regardless of previous health or age
- Treatment with oseltamivir or zanamivir is recommended for all people with suspected or confirmed influenza requiring hospitalization
- Early empiric treatment with oseltamivir or zanamivir should be considered for people with suspected or confirmed influenza who are at higher risk for complications, including:
 - Children younger than 2 years
 - Persons aged 65 years or older
 - Pregnant women and women up to 2 weeks postpartum (including following pregnancy loss)
 - People of any age with certain chronic medical or immunosuppressive conditions
 - People younger than 19 years who are receiving long-term aspirin therapy
- Children aged 2 years to 4 years are more likely to require hospitalization or urgent medical evaluation for influenza compared with older children and adults, although the risk is much lower than for children younger than 2 years
- Treatment, when indicated, should be initiated as early as possible because the benefits are greatest when started within the first 2 days of illness. In severe cases, therapy can be started after 48 hours
- Treatment should not be delayed for laboratory confirmation of influenza because a negative rapid test for influenza does not rule out influenza
- Currently circulating 2009 H1N1 viruses are susceptible to oseltamivir and zanamivir, but resistant to amantadine and rimantadine; however, antiviral treatment regimens might change according to new antiviral resistance or viral surveillance information

Note: The full text of the recommendations is available at the website of the Centers for Disease Control and Prevention (CDC) at <http://www.cdc.gov/h1n1flu/recommendations.htm>.

The 1918 Influenza Pandemic Virus as a Model for 2009 Pandemic H1N1

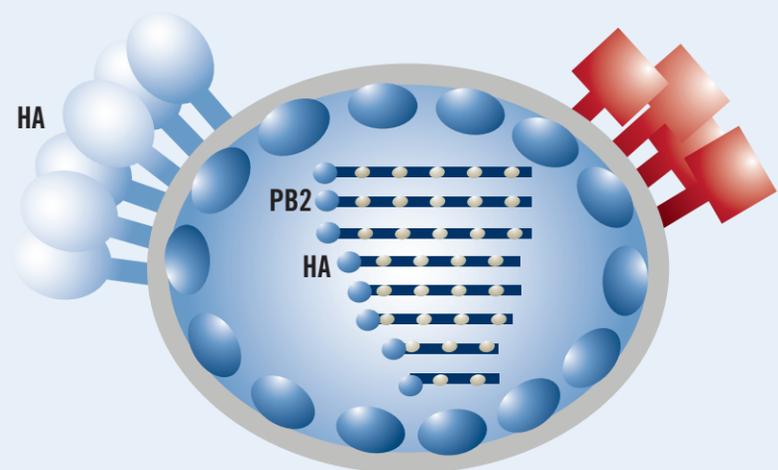
Transmissibility, Susceptibility, and Patterns of Resistance of the 2009 Pandemic H1N1 Influenza Virus

In 2005, scientists at the Centers for Disease Control and Prevention (CDC) succeeded in reconstructing the influenza virus that was responsible for the 1918 flu pandemic (Tumpey TM et al. *Science*. 2005;310:77-80). The 1918 "Spanish flu" pandemic claimed the lives of 20 million to 50 million people worldwide, including 675,000 victims in the United States. A striking feature of the outbreak was an unusually high rate of death among otherwise healthy people aged 15 to 34 years.

In April 2009, a novel influenza virus—H1N1 subtype of swine origin—was first detected. Within 9 weeks, the World Health Organization (WHO) reported cases of H1N1 influenza in all of its tracked regions. On June 11, the WHO declared that an influenza pandemic was under way. As of late October, the WHO has reported more than 7820 deaths due to swine flu. Young people, especially the very young, are at greatest health risk from the 2009 pandemic H1N1 influenza virus. Healthy older people, especially the very old, may be somewhat protected.

At the 47th Annual Meeting of the Infectious Diseases Society of America (IDSA), held in Philadelphia from October 29 to November 1, 2009, researchers presented results from studies that shed light on the virulence and transmission of the flu virus, as well as its patterns of susceptibility and immunity, treatments, and resistance to some antiviral medications.

Figure 1. Resurrection of the 1918 Influenza: What Did We Learn?



Our findings suggests that "human" adaption of the HA and PB2 proteins of H1N1 avian influenza viruses are required to generate viruses readily transmissible through the air.



Identification of Proteins That Enable Transmission of Avian Influenza Virus

Influenza pandemics result from the emergence of a novel influenza A virus subtype that can spread efficiently from person to person due to the absence of preexisting immunity to the novel hemagglutinin (HA). Until recently, it was not known which genes conferred efficient transmission of epidemic and pandemic influenza in humans. Terence M. Tumpey, PhD, who led the original work at the CDC to characterize the structure of the 1918 pandemic

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Mortality in 1918

The mortality rates associated with the 1918 influenza pandemic have been a topic of interest to investigators, with evidence ranging from the suggestion that the virus may have disrupted innate immune responses (Billharz R et al. *J Virol.* 2009;83:10557-10570) to the recent suggestion that high-dose aspirin therapy (up to 8-31 g/day) used after the turn of the century may have compromised pulmonary integrity following viral infection (Starlo KM. *Clin Infect Dis.* 2009;49:1405-1410).

flu virus, has recently identified the molecular properties that can enable effective airborne transmission of the viruses in a ferret model. (The ferret is thought to be an ideal model for human flu, with similar symptoms [sneezing, nasal discharge] and similar distribution of sialic acid receptors.) Dr Tumpey and colleagues found that transmissibility of the 1918 pandemic influenza virus depended on the adaptation of only 2 proteins: HA and PB2 (Figure 1). Influenza viruses were also shown to be able to replicate efficiently at the temperature of the mammalian airway (Van Hoeven N et al. *PNAS.* 2009;106:3366-3371).

An intriguing additional finding was that a small change in the virus could prevent airborne transmission between ferrets in adjacent wired cages. “One of our initial striking findings was that, with the 1918 virus, we were able to abolish transmission [of the virus among ferrets] with just 2 amino acid changes,” Dr Tumpey said.

Dr Tumpey’s group has also gathered pathogenesis and transmission data about differences between the pandemic H1N1 and seasonal influenza strain. “With H1N1,” Dr Tumpey said, “there is significant weight loss, ranging from 9% to 17%. With seasonal [flu], there may be a transient dip in weight anywhere from 3% to 5%.” In comparison with seasonal strains, H1N1 is associated with high viral titers

in lung tissue. And, in a feature not typical of the seasonal strain of influenza, the researchers found infectious virus in the intestinal tracts of ill ferrets.

Adaptive Immunity and Cross-Reactive Antibody Responses to the 2009 Pandemic H1N1 Influenza Virus

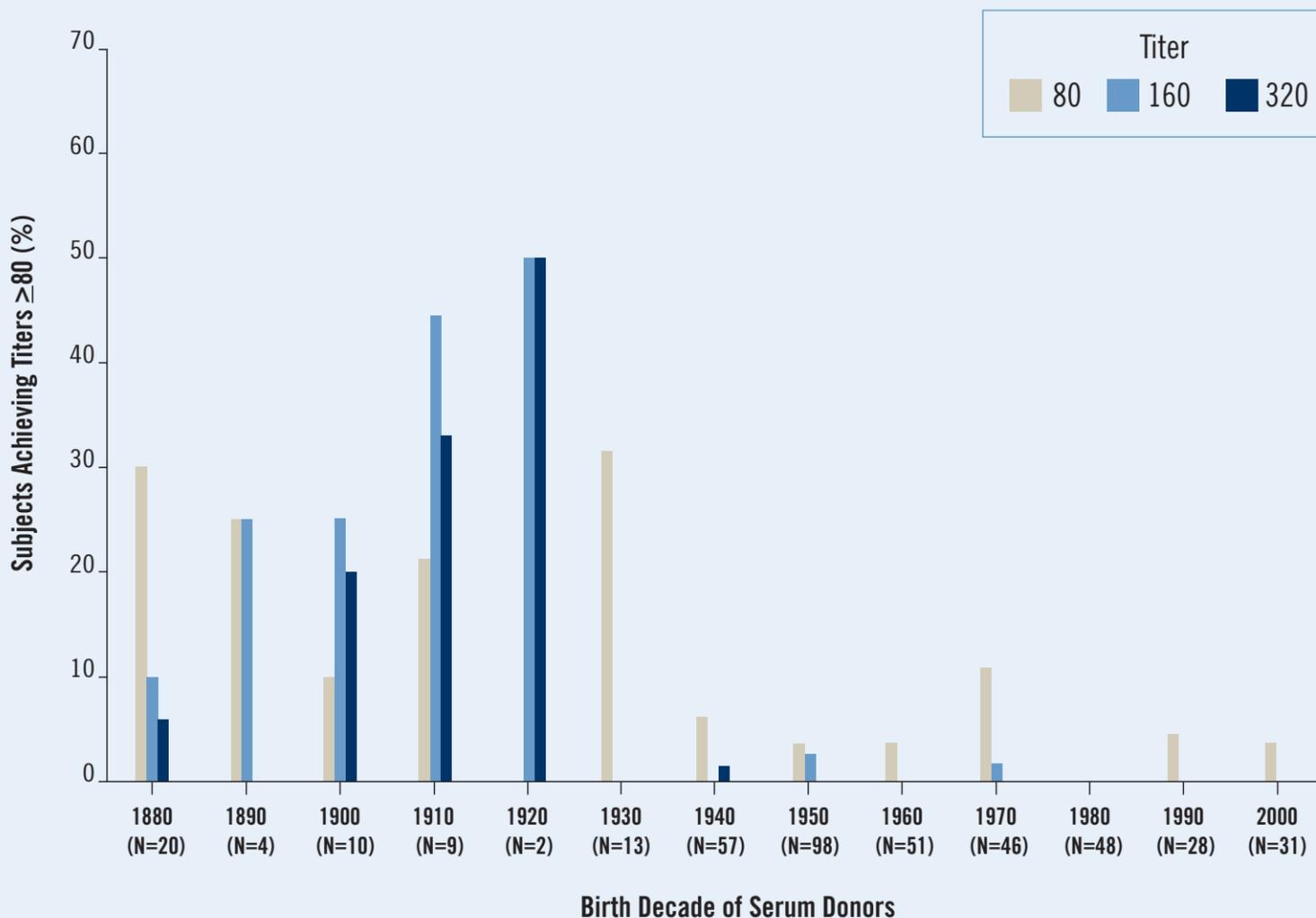
Elderly immunity is embedded in the antigen

Even into the 10th decade of life, 1918 pandemic influenza survivors retain highly functional, virus-neutralizing antibodies to this especially virulent strain of flu. After exposure to the virus, circulating B memory cells lay in wait, even for decades, for another H1N1 virus to return. Because the 2009 pandemic H1N1 influenza virus bears enough similarity to the 1918 pandemic strain, a population that is typically at higher risk from seasonal flu—the elderly—displays an unusual level of protection from this pandemic strain.

Adaptive immunity may be at work. James E. Crowe Jr, MD, from Vanderbilt University Medical Center in Nashville, Tennessee, analyzed the CDC’s 1918 virus sequencing information and recombinant 1918 HA protein antigen from 30 subjects born before 1915 (Yu X et al. *Nature.* 2008;455:532-536). Each displayed seroreactivity with the 1918 virus. Seven of 8 donor samples secreted antibodies that bound 1918 HA. When B cells were isolated from the elderly subjects, 5 monoclonal antibodies were generated that displayed neutralizing activity against the virus. According to Dr Crowe, “These antibodies cross-reacted with the genetically similar HA of a 1930 swine H1N1 influenza strain, but not with more contemporary human influenza viruses.” In about the mid-1940s, he said, the 1918 virus stopped passing through the human population and was replaced by other viruses.

In studies with mice, antibodies to the 1918 HA protein seemed to confer protection from the lethal consequences of infection with the virus. “We took these antibodies and put them in mice, then infected them with a fatal dose, waited 1 day and treated with antibodies. They survived 100%; the antibodies were therapeutic,” Dr Crowe said. These results provide the first direct evidence in humans of immunity at the molecular level to the 1918 virus.

Figure 2. Neutralizing Antibody Titers Against the 2009 H1N1 Virus



Adapted from Hancock et al. *N Engl J Med.* September 10, 2009 [epub].

Age-Related Cross-Reactive Antibody Response to the 2009 Pandemic H1N1 Influenza Virus Reflects History of Seasonal Influenza Strains

When a group of investigators from the CDC sought to determine whether vaccination with the seasonal nonadjuvanted or adjuvanted influenza vaccines would confer cross-reactive antibody response to 2009 H1N1, they found that it did not. However, the results from an assay using stored serum samples from persons who donated blood or were vaccinated with recent seasonal or 1976 swine influenza vaccines generated an interesting picture of susceptibility to pandemic H1N1 flu by age group (Hancock K et al. *N Engl J Med*. September 10, 2009 [epub]). Persons younger than 30 years displayed little evidence of cross-reactive antibodies to the 2009 H1N1 virus; only 4% of individuals who were born after 1970 had cross-reactive antibody titers of 40 or more against the 2009 H1N1 virus. However, 34% of individuals born before 1950 had titers of 80 or more. Subjects who were born before 1930, who had probably been exposed to a 1918-like H1N1 virus in their lifetimes, had the highest titers against the 2009 pandemic H1N1 influenza virus (Figure 2).

Antigenic Shift and Drift

Two mechanisms control variations in the influenza virus that influence its potential to cause illness and death from year to year: antigenic shift and antigenic drift. Major changes in the surface glycoproteins of an influenza virus—called antigenic shift—lead to worldwide influenza pandemics. Since 1889, major antigenic shifts have occurred 7 times. H2N2 viruses circulated in 1889, followed by H3N8 in 1900, H1N1 in 1918, H2N2 in 1957, H3N2 in 1968, and H1N1 in 1977. (A smaller variation, antigenic drift, is responsible for point mutations.) There have been 3 recorded influenza pandemics prior to the 2009 pandemic: the well-known 1918 “Spanish flu” and pandemics in 1957 and 1968 (Smith GJ et al. *Proc Natl Acad Sci U S A*. 2009;106:11709-11712). The current H1N1 virus is a “triple reassortment” of swine, human, and avian viral sources, whereas the 1977 virus is the progenitor of the current strain of seasonal flu.

Emergence of the Novel Swine-Origin Influenza A (H1N1) Virus in Humans: a Timeline and Risk to Children

In April 2009, public health professionals first identified a novel swine-origin influenza A (H1N1) virus (S-OIV) in specimens from 2 epidemiologically unlinked patients in the United States. (The same strain was identified approximately contemporaneously in Mexico, Canada, and elsewhere.) Real-time reverse-transcriptase polymerase chain reaction testing was performed at the CDC. Between April 15 and May 5, 2009, 642 confirmed cases of S-OIV were identified from 41 states. Sixty percent of patients were aged 18 years or younger. Nine percent of 399 patients for whom hospitalization information was available required hospitalization. Hospitalization data for 22 patients indicated that more than half (12) of patients displayed features that placed them at increased risk for serious influenza, including pneumonia, admission to the intensive care unit, and respiratory failure. Two patients died (Dawood FS et al. *N Engl J Med*. 2009;360:2605-2615).

A profile of elevated risk for young people emerged from later hospital records. Children younger than 2 years had rates of hospitalization that were 2.3 times higher than rates for children 2 to 4 years old from April through September, according to the CDC’s Emerging Infections Program laboratory-confirmed influenza hospitalization surveillance system. Children aged 2 to 4 years had slightly higher rates of hospitalization than children aged 5 to 17 years. And hospitalization rates among children younger than 2 years were 4.5 times greater than rates for adults (hospitalization rates by age group are updated regularly at www.cdc.gov/flu/weekly).

Treating Influenza in an Era of Antiviral Resistance For persons at high risk: treat early and empirically

As the 2009 flu season matures, a split picture of its lethality is emerging. On the one hand, most patients who have contracted the 2009 H1N1 influenza virus infection have had a self-limited respiratory illness similar to typical seasonal influenza, according to the CDC, which provides daily situation updates on its website (www.cdc.gov). On the other hand, thousands of deaths have occurred globally from pandemic H1N1. Major public health efforts are under way to limit its transmission and associated morbidity and mortality, including early, empiric use of antiviral medication and strategies to contain antiviral resistance.

The CDC generally has recommended priority use of antiviral medications for people who are hospitalized with influenza and those at increased risk for influenza-related complications. On October 16, 2009, the agency took a more aggressive stance, recommending early empiric treatment with neuraminidase inhibitors oseltamivir or zanamivir for people with suspected or confirmed influenza who are at higher risk for complications. On October 23, 2009, the FDA authorized the use of IV peramivir for certain hospitalized adult and pediatric patients with H1N1 virus infection under the emergency use authorization, allowing physicians access on a compassionate care basis without institutional review board approval (<http://www.cdc.gov/h1n1flu/eua/peramivir.htm>). The latest to come from the CDC is a suggestion that clinicians start treatment with antiviral medications ahead of a confirmatory diagnosis in at-risk patients. Alicia Fry, MD, MPH, speaking about complications and resistance patterns of influenza, explained: “We are urging clinicians not to rely on the rapid test to confirm influenza infection, and not to wait to get a confirmatory assay, but instead to begin treatment.”

Intensified efforts to stem rates of serious or fatal illness by early intervention with antivirals are accompanied by an unfolding story of antiviral resistance, which Dr Fry explained. The 2009 H1N1 influenza viruses are susceptible to the neuraminidase inhibitor antiviral medications oseltamivir and zanamivir, but are resistant to the adamantane antiviral medications amantadine and rimantadine. This susceptibility pattern is not new; it is the same as that observed among seasonal influenza A (H3N2) and B viruses in recent years. “The first headline story on antiviral resistance came with the H3N2 subtype,” said Dr Fry. “We saw for the first time in 2002-2003 an increase in resistance in Hong Kong, and in 2005, even in the US. Now almost all H3N2 viruses that are circulating in Asia and the US and most other countries are resistant to the adamantanes.” Almost all of the H3N2 viruses that CDC scientists have tested are susceptible to oseltamivir and zanamivir.

Resistance to adamantanes has been observed with the seasonal H1N1 virus. Similar to the situation with H3N2 viruses, China and Hong Kong have led the way. Almost all of the seasonal H1N1 viruses in China and Hong Kong are now resistant to the adamantanes. A lower proportion of H1N1 virus infections are resistant to adamantanes in the United States. Fortunately, oseltamivir resistance appears to be rare at this time, according to CDC reports. But it is not nonexistent. Oseltamivir-resistant 2009 H1N1 viruses have been identified, typically among people who develop illness while receiving the agent for chemoprophylaxis, or in immunocompromised patients with influenza who are receiving treatment. Cases numbering in the high teens have been reported in the United States. All but one has been associated with the acquisition of resistance while treatment or chemoprophylaxis with oseltamivir was under way.

Recently, a clear case of transmission of resistant virus from one person to another has received attention in the press and raised concern in public health circles. In the midst of a 2009 outbreak of H1N1 at a summer camp in North Carolina that struck 65 youths, about 600 healthy campers and staff received chemoprophylaxis with oseltamivir. Two previously healthy girls experienced clinical influenza symptoms after starting the chemoprophylaxis. CDC analysis established that the mutations in both girls were identical, thus confirming a transmission of resistant virus from one girl to the other.

In line with intensified public health efforts to control the spread of resistant influenza viruses, CDC scientists have recently developed a high-throughput pyrosequencing test that can rapidly detect one known molecular marker of resistance to adamantanes and neuraminidase inhibitors in influenza A (H5N1) viruses. The test, which was described by Larisa V. Gubavara in a separate presentation, is allowing for rapid processing of a very high number of specimens. It will enable better tracking of natural and acquired drug resistance (Deyde VM et al. *Antimicrob Agents Chemother*. 2009;53:1039-1047).

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What's New in Seasonal Influenza Vaccine Strategies?

Public health initiatives aim for improved vaccine coverage and more effective vaccines

Even before the 2009 pandemic H1N1 influenza virus burst upon the worldwide stage, public health professionals were grappling with challenges to the effective management of seasonal influenza, which is responsible for 36,000 deaths annually in the United States and as many as 1.5 million deaths worldwide. Seasonal flu is associated with high complication rates among vulnerable populations, such as the elderly, and low rates of vaccination, even among at-risk persons.

US vaccine strategy aims to address these issues with expanded vaccine recommendations and new vaccine development programs that include a high-dose option, according to Kathleen M. Neuzil, MD, MPH, from Seattle, Washington, a recognized expert in the field and a member of the CDC Advisory Committee on Immunization Practices (ACIP). Dr Neuzil chairs the Influenza Vaccine Working Group.

Since 2000, the ACIP has steadily expanded the population groups for whom annual vaccination is recommended. Now, approximately 83% of the US population is specifically advised to receive annual influenza vaccination. “Were it not for the pandemic,” Dr Neuzil said, “the big news would be that this is the first year with the full universal pediatric recommendation, beginning at the age of 6 months” (Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2009;58(RR-08):1-52).

The American public has not taken vaccination for influenza as seriously as it does immunization for other illnesses. Flu immunization rates are low for small children and youngsters at high risk, for pregnant women, and among healthcare workers. And recent history has shown a growing complacency. “Historically, in the

The 2009 Vaccine Access Dilemma

A recent mathematical model confirms that early vaccination can save lives and reduce overall costs (Khazeni N et al. *Ann Intern Med*. October 5, 2009 [e-pub ahead of print]), but recent delays in vaccine availability (Kresse H, Rovini H. *Nature Rev Drug Discov*. 2009;8:841-842) continue to blunt early implementation schemes, and local guideline modification of vaccination strategies by state departments of health (<http://www.flu.gov>) will likely come into play as the influenza season moves into 2010.

6- to 23-month-old group, there has been a high rate of vaccination. Now, we are seeing stagnant coverage in this group, at about 40%. Compared with other childhood vaccines in this age group, the rate of vaccination may reach 50% for one dose, but not above 30% to 35% for full vaccination,” Dr Neuzil said. Pregnant women are clearly recognized as having excess morbidity from seasonal flu. Yet the vast majority of them do not receive a flu vaccination. This year, vaccination rates for pregnant women, no doubt due to pandemic H1N1, are at “an historical high” at 20%. Maternal immunization is crucial, not only for the mother, but also for the infant, for whom no influenza vaccines are licensed until the age of 6 months.

Even in people older than 65 years, a group that has historically had the highest rates of coverage, tracking data have shown a plateau in coverage. The same has been seen with younger persons with high-risk conditions.

Healthcare workers constitute another group that, paradoxically, has not achieved the coverage that policymakers would like to see. To help ensure that a population in a position to spread flu to vulnerable ill patients does not do so, the IDSA has recently issued a statement strengthening its policy of mandatory vaccination for healthcare workers. “This is challenging,” said Dr Neuzil, “and there is a lot of debate among our colleagues. But experts believed that the step was necessary. Many individual institutions are expected to implement their own policies of mandated vaccination.”

New Vaccine Initiatives

High-dose flu vaccine offers more protection for elderly persons

Better influenza control might come from more precise tailoring of vaccines to different age and risk groups. Two recently published studies—one in elderly subjects, and one in healthy, younger adults—suggest that a customized approach may well improve outcomes across a spectrum of population groups.

Elderly people, despite reasonably high immunization rates, have traditionally suffered an excess of mortality from seasonal flu. Elderly immune systems are not as active as those of younger adults, it is reasoned, and the standard flu vaccine dose might not provide adequate protection. When in one large study the dose was increased to 4 times the standard dose, people aged 65 years and older produced up to twice as many antibodies as the group randomized to the standard dose, with acceptable safety results.

The large phase 3 trial, which was published in July (Falsey AR et al. *J Infect Dis*. 2009;200:172-180), enrolled more than 3800 volunteers aged 65 years and older, and estimated the absolute and relative efficacies of 2 dosing strategies. Subjects were randomized to either high-dose trivalent, inactivated influenza vaccine (60 µg of hemagglutinin) or the standard licensed dose of 15 µg of hemagglutinin. Seroconversion rates 28 days postvaccination were higher in the high-dose group receiving vaccine against type A strains (H1N1 or H3N2) and were similar for the type B strain compared with the standard-dose vaccine. Seroprotection was higher in the high-dose group compared with the standard-dose group for all 3 strains. Local reactions were higher for the high-dose group, but were mild to moderate. This high-dose option is hoped to be approved and available for the 2010-2011 flu season.

Inactivated flu vaccine more efficacious in healthy younger adults, aged 18-49 years

“For several years, we have seen data showing that the relative efficacy of the live vaccine was better than the attenuated vaccine in the younger age group,” Dr Neuzil said. These findings were overturned by results from a recently published randomized, placebo-controlled trial first started in 2004 and updated each subsequent year. According to the data, for the 2007-2008 flu season the inactivated vaccine was overall 50% more efficacious in preventing laboratory-confirmed, symptomatic, influenza A (predominantly H3N2) than was the live attenuated virus in healthy adults aged 18 to 49 years (Monto AS et al. *N Engl J Med*. 2009;361:1260-1267). These data confirm and strengthen 2004 data showing the same outcome. In contrast, vaccination studies in children aged 6 months to 59 months demonstrated that attenuated vaccines are more effective than inactivated vaccines (Belshe RB et al. *N Engl J Med*. 2007;356:685-696).

In other new influenza vaccine initiatives, the CDC is collaborating with private-sector partners to test a new skin patch delivery system. And in a separate academic partnership, the agency is testing strategies that do not rely on the growth of viruses in eggs. This could boost both the speed of production and the supply of vaccine, a significant issue this year with the 2009 pandemic H1N1. ■



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