New Flu Vaccines Hold Promise, Challenges

BY ROXANNA GUILFORD-BLAKE

EXPERT ANALYSIS FROM THE INTERNATIONAL CONFERENCE ON EMERGING INFECTIOUS DISEASES

ATLANTA — New influenza vaccine development is evolving rapidly, with approximately 75 different technologies currently in various stages, said Rick Bright, Ph.D., scientific director for the influenza vaccine project at Program for Appropriate Technology in Health, a global nonprofit health group.

And new vaccines are desperately needed: Current seasonal vaccines are only 30%-50% effective in older adults, and candidate vaccines for pandemics "are poorly immunogenic in clinical studies," Dr. Bright said at the meeting.

Current influenza vaccines may be safe and immunogenic, but they are highly vulnerable to antigenic drift and shift, which compromise efficacy and require reformulation and repeated immunization.

In addition, vaccine development is costly, complicated, and time consuming. As the recent 2009 H1N1 influenza outbreak demonstrates, the conventional production process is poorly equipped to respond to a pandemic, Dr. Bright said.

He discussed three promising types of influenza vaccines: live attenuated influenza viruses (LAIV), recombinant viruslike particles (VLP), and plant-based production of vaccines. Each holds promise, but all involve significant challenges.

LAIV: Innovative Yet Decades Old

LAIVs have been used to combat seasonal influenza for decades in some parts of the world, including the United States and Russia, but Dr. Bright nevertheless characterized them as innovative. They have yet to be widely accepted or distributed, despite a strong safety record and low cost. In fact, he said, LAIV is the lowest-cost influenza vaccine available today. It's easy to produce and purify; it has a broad immune response, including some mucosal and cellular immunity; and it is efficacious in naive populations, Dr. Bright said.

The conventional influenza vaccine production process is poorly equipped to respond to a pandemic.

DR. BRIGHT

There are challenges, however. LAIV "doesn't follow the known, established correlates of immunity," which can lead to regulatory and licensing hurdles.

Moreover, LAIVs are less effective in nonnaive adults, and there are current limitations on their use in children and some high-risk groups. But, he added, some of those limitations are based on "unfounded fears of the risk of reassortment."

VLP: Dealing With Vectors

VLP vaccines, with many varieties in early-stage development, show promise of being both low cost and high yield, with a rapid (12-week) production cycle, he said. Dr. Bright explained that although VLPs contain multiple influenza proteins to resemble virions, they contain no genetic material, and therefore they do not replicate or cause infection.

Safety is an issue because all VLPs "rely on some sort of vector." The challenge is to remove—or demonstrate the safety of—the residual vectors, he said, noting that such concerns could lead to regulatory challenges.

Plant-Based Vaccines: Speedy Development

Plant-based vaccines have been advancing steadily since 2000, he reported. Such vaccines can be produced very rapidly, at about 8 weeks from sequencing to release. New approaches to plant-based expression create high yields with low production costs. Moreover, he said, the approach is "suitable for mixing and matching constantly emerging strains."

Safety appears to be less of a concern than it is for VLPs, according to Dr. Bright, because plant-based vaccines are free of animal cells, microbial pathogens, and animal viruses. But "there are many things we don't know about the safety of plant-based proteins," he cautioned.

Researchers are exploring the issue of low immunogenicity with plant-based vaccines, he said. Like the VLPs, plant-based vaccines will likely benefit from an adjuvant. ■

Disclosures: *Dr. Bright disclosed receiving stock as part of a management position in 2006 from Novavax Inc.*

Many Parents Are Open to Public Health Settings for H1N1 Flu Shots

BY ROXANNA GUILFORD-BLAKE

FROM THE NATIONAL IMMUNIZATION CONFERENCE

ATLANTA — Parents prefer to have their children receive the 2009 H1N1 flu vaccine in the primary care setting, but many are open to schools and other venues, according to an August 2009 national survey.

The findings have implications for vaccine delivery in general and, in particular, for future mass immunization efforts, said Sarah Clark of the division of general pediatrics at the University of Michigan, Ann Arbor.

VITALS

Major Finding: 32% of parents preferred only primary care providers, 14% would accept any of the settings, 11% would accept any setting except retail locations, and 10% would accept only PCPs or schools.

Data Source: A survey of 1,678 parents asked if they would consider getting their child's 2009 H1N1 influenza shot in one of four settings: health departments, schools, local retail locations, or primary care providers.

Disclosures: None was reported.

The survey of parents—the C.S. Mott Children's Hospital National Poll on Children's Health—may be the first assessment of public acceptance of various settings for H1N1 flu vaccination for children.

The survey included the following question: "In which of these settings would you consider getting your child(ren) vaccinated against H1N1 influenza?" The 1,678 respondents chose from the following options: health departments, schools, local retail locations, and primary care providers. All respondents were asked the question, including the 29% who indicated they definitely or probably would not vaccinate their child against H1N1 flu.

The most preferred setting was the primary care provider's office, with 82% responding "yes," 11% "not sure," and 7% "no." School vaccination clinics were the second most preferred venue: 43% said "yes"; 23%, "not sure"; and 34%, "no."

Health department clinics came in third (34% "yes," 21% "not sure," 45% "no"), and retail settings were last (24% "yes," 27% "not sure," 49% "no").

When responses were aggregated across the settings, they revealed that 32% preferred only primary care providers, 14% would accept any of the settings, 11% would accept any setting except retail locations, and 10% would accept only the primary care setting or schools.

Ms. Clark emphasized that the survey identified only intentions, which can change. Moreover, it did not capture other settings, such as emergency departments.

Models for vaccinating in alternative settings exist in several states, Ms. Clark said at the conference sponsored by the Centers for Disease Control and Prevention. For example, Rhode Island and Hawaii developed a system for H1N1 flu vaccination whereby school-aged children were vaccinated at school, and pediatricians were asked not to vaccinate them in the office setting. (They did vaccinate children not yet in school.)

"The definition of the school versus pediatrician role worked well in both states, and this model is a nice example of how public health and medicine can work together to provide broad access to vaccines for all children, without sacrificing clinical capacity," she said. ■

HIV-Exposed Babies Okay at Age 15 Months

BY BRUCE JANCIN

FROM THE EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

VIENNA — Uninfected children born to HIV-positive mothers showed a reassuring absence of impaired immune function at 15 months, both quantitatively and qualitatively, in a case-control study.

This finding, if confirmed, would have major implications for health care resource allocation in light of the growing number of uninfected children with HIV-positive mothers worldwide, Dr. Lilian Kolte noted at the meeting.

She reported on 20 HIV-exposed but uninfected 15-month-old children of HIV-positive mothers and 10 age- and sex-matched controls, all of whom had comprehensive immunologic evaluation.

The study was undertaken because uninfected children born to HIV-infected mothers typically have low CD4 counts, reduced thymic output, and other immunologic abnormalities at birth. This raises a key question: Do the deficits persist beyond infancy?

The answer provided by this study is "no." The immune deficits present at birth in these children are not long term, according to Dr. Kolte of Copenhagen University Hospital.

Thymic output as determined by polymerase chain reaction measurement of CD4+ cells containing T-cell receptor excision circles did not differ at age 15 months between the HIV-exposed and control children. Neither did total and naive CD4 and CD8 counts. Levels of *Haemophilus influenzae* type B protective antibodies in response to vaccination were comparable in the two groups.

Moreover, levels of the cytokines interleukin-1B, -2, -4, -6, -8, and -10; transforming growth factor–beta; and interferon-gamma were similar in the two groups of children as well. Thymic size as estimated by ultrasound was about one-third less in the HIV-exposed group. However, the two groups of children were similar in terms of birth weight as well as height and weight at age 15 months. ■

Disclosures: *Dr. Kolte reported no conflicts of interest.*