

New Flu Vaccines Offer Promise, Challenges

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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 told attendees.

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 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, including safety, immunogenicity, scalability, and regulatory issues.

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, he said.

Current seasonal influenza vaccines are only 30%-50% effective in older adults.

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.”

Over the last few years, LAIV technology has expanded into development of both seasonal and pandemic vaccines.

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, Dr. Bright 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 said.

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

Dengue Fever Re-Emerges in Florida After 75-Year Hiatus

FROM THE INTERNATIONAL CONFERENCE ON
EMERGING INFECTIOUS DISEASES

ATLANTA — An estimated 5% of the Key West, Fla., population—more than 1,000 people—showed evidence of recent exposure to dengue virus in 2009, according to the Centers for Disease Control and Prevention and the Florida Department of Health.

Dengue is the most common mosquito-transmitted virus and causes 25,000 deaths each year, according to the CDC. From 1946 to 1980, no cases of dengue acquired in the continental United States were reported, and there has not been an outbreak in Florida since 1934.

These cases represent the re-emergence of dengue fever in Florida (and elsewhere in the United States) after 75 years, Dr. Harold Margolis, chief of the dengue branch at CDC said at the 2010 International Conference on Emerging Infectious Diseases.

After three locally acquired cases of dengue fever were initially reported in 2009, scientists from the CDC and the Florida Department of Health conducted a study to estimate the potential exposure of the Key West population to dengue virus.

Since 1980, a few locally acquired U.S. cas-

es have been confirmed along the Texas-Mexico border, which coincided with large outbreaks in neighboring Mexican cities. In recent years, there has been an increase in epidemic dengue in the tropics and subtropics, including in Puerto Rico, the CDC reported.

In September 2009, two dengue infections in Key West residents without recent travel were confirmed. By the end of 2009, 27 cases had been identified.



Aedes aegypti mosquitoes spread dengue virus to more than 1,000 people in Key West, Fla.

COURTESY CDC/JAMES GATHANY

In a poster presented at the meeting, a total of 240 blood samples were collected from randomly selected households in Key West and tested for the presence of virus or evidence of a previous dengue infection. Among the samples, 4.95% had dengue active in their systems or had dengue antibodies. The strain was similar to strains from Mexico, according to study investigator Glen Gallagher of the CDC’s dengue branch in Puerto Rico.

The take-away for physicians is that dengue fever can be a potential diagnosis even in patients without a history of travel, he said in an interview.

The CDC and the FDH continue to monitor cases in and around Key West.

Mr. Gallagher reported that he had no conflicts.

Waterborne Illnesses Cost U.S. \$539 Million Per Year

FROM THE INTERNATIONAL
CONFERENCE ON EMERGING
INFECTIOUS DISEASES

ATLANTA — Hospitalizations for three common waterborne diseases cost the U.S. health care system as much as \$539 million annually, according to investigators from the Centers for Disease Control and Prevention.

Modest investments in preventing the three most common waterborne diseases in the United States—Legionnaires’ disease, cryptosporidiosis, and giardiasis—would cut the disease rates and lead to significant health care cost savings, concluded study coauthor Michael Beach, Ph.D., associate director for healthy water at the CDC. He presented his study findings at the conference.

Such interventions include public education campaigns, appropriate maintenance of building water systems, and regular inspection of pools and other recreational water facilities.

Dr. Beach and his colleagues used data from the 2004-2007 MarketScan databases, a large insurance claims-based data repository for commercial, Medicare, and Medicaid claims, to estimate the hospitalization costs for the three diseases.

For each case, they calculated the cost paid by the insurer, the out-of-



COURTESY JANICE HANEY/CDC

Legionella pneumophila infections cost \$34,000 per hospitalization.

pocket cost to the patient, and the total amount paid.

The average length of stay was 4 days for patients with giardiasis, 6 days for those with cryptosporidiosis, and 10 days for those with Legionnaires’ disease.

In-patient hospitalization costs per case averaged more than \$34,000 for Legionnaires’ disease, approximately \$9,000 for giardiasis, and more than \$21,000 for cryptosporidiosis, the authors reported.

Estimated annual costs for hospitalization for the three diseases were \$154-\$539 million, including \$44-\$147 million in payments from Medicare and Medicaid. For the individual diseases, those costs were: giardiasis, \$16-\$63 million; cryptosporidiosis, \$37-\$145 million; and Legionnaires’ disease, \$101-\$321 million.

The researchers reported having no conflicts of interest.