Federal Preparedness for Flu Pandemic Spelled Out

Draft of federal plan calls for stockpiling vaccines and developing antiviral drugs and prophylaxis.

BY DAVID STERNBERG
Contributing Writer

BALTIMORE — Acknowledging that "flu has a huge news factor," Bruce Gellin, M.D., spelled out the federal influenza pandemic preparedness plan at a biodefense research meeting sponsored by the American Society for Microbiology.

The Department of Health and Human Services' draft Pandemic Influenza Response and Preparedness Plan, developed in August 2004, includes influenza control, stockpiling vaccines, developing antiviral drugs and prophylaxis, providing quality medical care, and maintaining community services, said Dr. Gellin, director of the National Vaccine Program Office, a division of HHS. The World Health Organization originally developed pandemic preparedness guidelines in 1999 for other organizations to follow.

"There are a lot of unknowns," said Dr. Gellin. "When will a pandemic occur? How bad will it be? And will there be major social and economic fallout? We need to continue to identify unmet questions."

Improving vaccine preparedness is a major focus of the HHS plan. To that end, Dr. Gellin said the United States must enhance annual influenza vaccine use, ensure a year-round egg supply, increase and diversify U.S. manufacturing capacity, and improve the ability to rapidly develop reference strains.

As for antiviral drugs, the U.S. government currently stockpiles 2 million doses of Tamiflu (oseltamivir) and 4 million doses of Flumadine (rimantadine). He acknowledged the need for a greater stockpile of these drugs, as well as a push for other therapies besides antivirals.

Even in the case of a mild pandemic, Dr. Gellin emphasized the heightened need for inpatient medical services and effective triaging of patients, noting that there would be about a 25% increase in demand for inpatient and ICU beds, and ventilators.

A few key issues remain unresolved, according to Dr. Gellin, including determining priority groups for early vaccine and antiviral use in the event of a pandemic; purchase and distribution of public- and private-sector vaccinations; and legal issues, including indemnification, liability protection, and compensation.

Two other significant issues addressed in the pandemic plan are development of new vaccines and therapeutics.

Richard J. Webby, Ph.D., of St. Jude Children's Hospital in Memphis, pointed out the many considerations for creating a vaccine in response to an emerging influenza pandemic.

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DR. GELLIN

"There is no way of accurately predicting what strain it might be; there is enormous diversity of viruses in animal reservoirs, and some viruses are highly pathogenic," he said.

But a procedure called reverse genetics has been significant in Dr. Webby's work at St. Jude's in accelerating the development of vaccines. Reverse genetics begins with a cloned segment of DNA and introduces programmed mutations back into the genome to investigate gene and protein function.

"Reverse genetics is likely to play a key role in future inactivated and attenuated vaccine strategies," said Dr. Webby.

As for antivirals, the existing therapeutics are M2 ion channel inhibitors and neuraminidase inhibitors (NAIs), said Simon P. Tucker, Ph.D., of Biota Holdings Ltd., in Melbourne, Australia.

The M2s are Symmetrel (amantadine) and Flumadine, both of which are dosed at 100 mg twice a day. The NAIs are Relenza (zanamivir) and Tamiflu. Relenza is dosed at 10 mg twice daily and Tamiflu at 75 mg twice daily, said Dr. Tucker.

There are some basic differences between the two drug classes, Dr. Tucker said. M2s are used only for influenza A and have a high clinical resistance; NAIs are effective against both influenza A and B and have a low clinical resistance.

For these reasons, NAIs, particularly Tamiflu, are prescribed more often than M2s, he said. Most prescriptions are written by family physicians; most of the patients are aged 20-59 years, he said.

Dr. Tucker noted that another drug class is under development—long-acting neuraminidase inhibitors (LANIs)—and has exhibited some early success.

One LANI monomer (R-118958) has been shown to be more potent and more effective than Relenza, said Dr. Tucker. He noted a few of the advantages to LANIs: one-time-only therapy, once-weekly prophylaxis, and an optimal use for interpandemic cases.

Biota Holdings Ltd. was involved in the development of Relenza and is currently developing LANIs under a contract from the National Institutes of Health. ■

Changes in Primary Care Needed to Boost Immunization Rates in High-Risk Adults

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Using ancillary staff to obtain patient immunization and medication histories before the patient sees the physician could go a long way toward improving immunization rates among high-risk adults, Linda Hill, M.D., said at the National Immunization Conference sponsored by the Centers for Disease Control and Prevention.

Despite long-standing recommendations for annual influenza vaccine and one-time pneumococcal vaccination for adults aged 18-49 with chronic lung, cardiovascular, metabolic, and immunosuppressive conditions, overall coverage levels are only 20% for influenza vaccine and 8% for Pneumovax. Rates are just slightly better for diabetic patients, at 27% and 15%.

The Healthy People 2010 goal is 60% for both vaccines, said Dr. Hill of the department of preventive and family medicine at the University of California, San Diego.

In an effort to determine what types of preventive health issues are addressed during a typical office visit, Dr. Hill and her associates audiotaped 37 visits of patients ages 20-50 years with chronic conditions. Patients were seen at three community health centers and one private practice from September 2003 to January 2005.

The average visit lasted about 13 minutes. About 5 minutes were spent taking the patient's history, half a minute on providing generic health information, another 1-2 minutes on evaluations such as explaining test results, and about a half minute on the physical exam. Only fractions of minutes each were spent offering health recommendations, such as "you should get more exercise"; discussing preventive services other than immunizations, such as mammograms; and discussing and/or planning immunizations.

Of the 24 visits in which immunizations were discussed, the discussion took a little over a minute. But when immunizations were discussed and the patient actually got a shot, less than half a minute was spent on the discussion. And during those 24 visits, no other preventive health issues were discussed, noted Dr. Hill, who is also associate director of the Center for Behavioral Epidemiology and Community Health at San Diego State University.

Previous data have shown that, more than any patient characteristic, physician advice is the greatest predictor of receipt of immunizations.

Of interest, on average more than half of the visit (8 of the 13 minutes) was spent discussing the history, mostly the patient's medications. Although this isn't surprising, the actual discussion tended to be more about trying to figure out what the patient was taking and in what dose than about assessing the appropriateness of the dose or explaining to the patient what it was for.

Previous data have shown that, more than any patient characteristic, physician advice is the greatest predictor of receipt of immunizations. Moreover, physician immunization advice is more likely to occur when the physician to staff ratio is at least 1:4 and when the time spent with the physician is at least half of the visit time.

It would make sense to have ancillary staff members obtain and document immunization and medication histories prior to seeing the physician, thereby leaving the physician more time for more complex decisions and for talking with the patient about important preventive health measures such as immunization, Dr. Hill said. ■

HHS Funds Speedy Vaccine Development

The U.S. Department of Health and Human Services recently awarded $97 million to Sanofi Pasteur to speed development of a manufacturing technique that could cut the time it takes to get an influenza vaccine to market. But the technique, which involves growing flu strains in cell culture, initially will be used only to create a vaccine against a pandemic strain.

Traditionally, vaccine production takes at least 9 months, from the time strains are selected for inclusion to when the shot is ready for distribution. The new technique might cut a few weeks off that process, with most of the savings coming in the beginning.

Under the current manufacturing scenario, influenza strains must be adapted so they can be grown in chicken eggs. Delays come when the strains either cannot be grown in eggs or are difficult to grow. With the new technique, the strain would not need adaptation because it would be grown in a human cell line. The line—of retinal cells—was developed by a Sanofi partner, Crucell, a Dutch biotechnology company.

Even though many experts think the cell culture will be more reliable than eggs for growing influenza vaccine strains, there is no guarantee. And even if the manufacturing technique is successful, it will still have to be approved by the Food and Drug Administration.

Sanofi Pasteur said it anticipates beginning human trials late next year. The HHS contract provides funds only for phase I and II studies, but the company said it anticipates continuing through phase III and on to market.

As part of the HHS contract, the company is also required to complete a feasibility study for supplying up to 300 million doses a year. Currently, the company has no plans for building a manufacturing facility that could accommodate that production, according to a spokesman.

—Alicia Ault