

# Push is on for better flu shot

## It could take decade to create universal vaccine

By Deborah Kotz

GLOBE STAFF

With a flu season that arrived earlier and more harshly than usual, government health officials have been loudly sounding the call for everyone to be immunized, while more quietly encouraging efforts to develop a better vaccine that would protect against many more strains of the virus.

The vaccines in use today are only about 60 percent effective, last for only a single flu season, and take months to produce — which left Americans initially unprotected in 2009 when the swine flu pandemic arose without much warning.

Incremental progress has been made: Next year, two firms will for the first time produce a quadrivalent vaccine, which contains four strains rather than the three in current vaccines. And the Food and Drug Administration last week approved the first gene-based flu vaccine, which uses DNA technologies to produce mass quantities of the virus in insect cells instead of chicken eggs.

While that will enable faster manufacturing and make more vaccine available to those with egg allergies, it may not increase the effectiveness.

"From the standard of protection, there's nothing new here," said Michael Osterholm, an epidemiologist at the University of Minnesota's Center for Infectious Disease Research and Policy. In an analysis of flu immunizations published last October, he and his colleagues

called for more funding for a universal flu vaccine that would protect against hundreds of flu strains and potentially last for a decade or more.

Most important, it would work better than current vaccines for the most vulnerable populations, such as the elderly and patients with weakened immune systems, who have a greater risk of dying from the flu compared with young healthy people.

Developing such a vaccine and testing it will require millions in research funding that's currently lacking. "The problem we've found is that no one is investing a sufficient amount of money to get past the initial work," Osterholm said. "It might take up to a billion dollars to get a single universal vaccine onto the market."

The National Institute of Allergy and Infectious Diseases allocated \$260 million last year for influenza research. "We selectively prioritize influenza research to a point where even when our budget is flat, we make sure to increase it," said Dr. Anthony Fauci, the institute's director. "We've had this sense of urgency since the threat of bird flu."

But Fauci estimated that Americans won't have access to a universal flu vaccine for quite some time. "Ten years would be a conservative estimate," he said, "but if we're lucky, we can have one in five."

One of the biggest hurdles rests in the flu virus's transformational skills. The virus's DNA mutates constantly, leading to new strains. Flu vaccines are designed to get the body to produce an immune response only to specific strains, and that immune response usually lasts

less than a year or two.

In 2009, researchers at the Dana-Farber Cancer Institute and elsewhere determined a major reason flu viruses continuously outwitted the body's immune defenses. The virus has a lollipop-shaped protein, called hemagglutinin, that serves as a key to enter healthy cells and create more flu viruses. The head of the lollipop evolves rapidly and differs from strain to strain.

While traditional vaccines target and destroy the head of the lollipop, a universal vaccine could be designed to work against multiple strains if it aimed for the lollipop's stem, which tends not to change.

Such a vaccine would also have the potential to be more potent — though it would undoubtedly be more expensive than the yearly flu shot.

"This finding was the eureka moment," said Dr. Wayne Marasco, an immunologist at Dana-Farber who coauthored the paper on the research and is developing a broader-acting vaccine. "We realized if we could destroy this stalk machinery, we could completely disable the flu virus."

Researchers have recently begun testing some universal vaccines in small human trials to see whether any are safe enough to test for effectiveness.

"This is an optimistic period in the field of universal flu vaccines," said Dr. Gary Nabel, chief scientific officer at the Cambridge office of Sanofi, which makes flu vaccines. That company has been testing several vaccine components.

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