

Pandemic Fears? Try Growing Flu Vaccine Fast In Insect Cells (Not Eggs)

Science Daily — An experimental flu vaccine made in insect cells -- not in eggs, where flu vaccines currently available in the United States are grown -- is safe and as effective as conventional vaccines in protecting people against the flu, according to results published in the April 11 issue of the *Journal of the American Medical Association*.

Removing eggs from the flu vaccine manufacturing process is one option for health officials seeking to protect the population from seasonal flu as well as a potential bird-flu pandemic. Using eggs to grow vaccine takes time; a flu vaccine that relies on a different technology is capable of being produced in large amounts much more quickly, a key advantage if a bird flu pandemic were to occur.

"Eggs can be very cumbersome to work with," said John Treanor, M.D., the flu expert at the University of Rochester Medical Center who led the study of 460 people reported in *JAMA*.

"When you need hundreds of millions of fertilized eggs, you're dealing with a whole host of agricultural issues, as well as scientific concerns regarding the flu virus itself. Flu viruses can be temperamental, and it's not always an easy matter to get the virus to grow as you want in eggs."

The use of cell culture systems to grow vaccines -- using viruses as tiny factories to churn out mass amounts of vaccines -- is a growing business. A similar technology using human cell lines is used to produce the hepatitis B vaccine, while one form of a vaccine against human papilloma virus is made using the same insect cell line used in the *JAMA* study.

In the study conducted by Treanor, together with colleagues at Cincinnati Children's Hospital and the University of Virginia, scientists tested a vaccine called FluBIOk that is made by Protein Sciences Corp. of Meriden, Ct. FluBIOk relies on a virus known as baculovirus, which normally infects insects, to churn out the key components of the flu virus in a cell line drawn from caterpillars.

In the study funded by the company of 460 healthy people ages 18 to 49, one-third of the participants received a smaller dose of the vaccine (75 micrograms), one-third received a larger dose (135 micrograms), and one-third received a placebo shot that didn't include vaccine. Each of the "real" shots included vaccine designed to protect against the three strains of flu that had been predicted to be the greatest threat during the 2004-2005 winter, when the study was conducted.

As the scientists expected, both the smaller dose and the larger dose caused an immune reaction generally considered effective for fighting off the flu, with the larger dose creating a stronger immune response. The side effects of the vaccine were the same as those usually reported from a typical flu shot -- mainly mild arm pain.

Then, in the months that followed, there were seven cases of flu in the group that had not received the vaccine, compared to two cases in the group that received the smaller dose, and no cases in the group that received the larger dose. Together, the two vaccines reduced flu infection rate by 86 percent.

"Even though the study was small, the results are very promising," said Treanor, who is professor of Medicine and of Microbiology and Immunology and director of the Vaccine and Treatment Evaluation Unit at the University of Rochester. "While we certainly hoped and expected the vaccine to be protective, you don't know that until you actually test it. We've shown that the vaccine does work in the real world."

Freedom from the egg brings implications important to a world facing the threat of pandemic bird flu.

For decades the nation's efforts to prevent flu have centered on growing flu virus in hundreds of millions of fertilized eggs, with each egg containing less than a teaspoonful of material that will ultimately become part of a vaccine. It's typically a six-month process to produce enough flu vaccine to protect the public.

Taking eggs out of the process would likely slice one or two months off the production process, Treanor said. In case of a bird-flu pandemic, that would allow manufacturers to ramp up vaccine production more quickly than if they had to wait for the production of millions of eggs. Not relying on chicken eggs might also be advisable in case a bird flu pandemic hits chicken flocks hard. The insect-cell technology also simplifies the manufacturing process in another way: A live flu virus is needed when growing vaccine in eggs, a danger when working with a potent bird-flu strain.

The technology would also help make it possible to boost the dose that patients receive, by increasing the nation's capacity to churn out vaccine. That's especially crucial in the fight against bird flu, as Treanor and other scientists have shown that an experimental vaccine appears to be effectively only at high doses.

The experimental vaccine differs from approved vaccines in another way as well. The experimental vaccine focuses on a portion of the flu virus known as the hemagglutinin, which the virus uses to attach to blood cells. Unlike conventional vaccines, FluBIOk does not also include neuraminidase, an enzyme that allows a flu virus to replicate and spread. While the hemagglutinin is the focus of most vaccines, scientists have been curious to measure how a vaccine without neuraminidase performs.

Other Rochester authors on the paper include Christine Hay, M.D., assistant professor of Medicine; Hua Liang, Ph.D., associate professor of Biostatistics; and Jeanne Holden-Wiltse, M.P.H., research associate in Biostatistics and Computational Biology. Also participating were nurse practitioner Carrie Nolan and nurses Diane O'Brien, Pat Smith, and Mary Lou Werthman. Other authors include physicians Gilbert M. Schiff, Rebecca Brady, and Anthony Meyer from Cincinnati Children's Hospital; Frederick Hayden, M.D., of the University of Virginia; Adam Gilbert, Ph.D., of Ockham Development Corp.; and Manon Cox, Ph.D., of Protein Sciences Corp.

Note: This story has been adapted from a news release issued by University of Rochester Medical Center.