The push is on to develop a swine flu vaccine

By Jo Seltzer, Special to the Beacon
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When you get immunized for the H1N1 swine flu virus this fall, researchers from Saint Louis University will be "deciders" of how the vaccine is administered.

For almost two decades the Center for Vaccine Development at SLU has been one of only eight Vaccine and Treatment Evaluation Units funded by the National Institutes of Health for clinical trials on new vaccines.

This year, in addition to testing the normal seasonal flu vaccine, they will be participating in an intense, accelerated clinical research effort aimed at containing the present pandemic. Cases of H1N1 infection may peak as early as October, so the dosage schedule must be standardized well before then.

Robert Belshe, MD
Photo courtesy of Saint Louis University

"Companies know how to make influenza vaccines," stated Dr. Robert Belshe, Director of the School of Medicine's division of Infectious Diseases and the Center for Vaccine Development. "The problem is knowing how much viral antigen protein to put into the shots."

And, he added, this virus is so novel that children and adults under 50 will not have much protection against it. Children routinely get two doses of flu vaccine the first year they are immunized. For this flu, it is slightly possible that adults also may need two doses. Most virologists, including Belshe, think that think one dose for adults will be sufficient due to immunologic priming from previous H1 infections.

How many shots?

Sharon Frey, MD.
Photo courtesy of Saint Louis University

Nonetheless, the vaccines against this H1N1 will provide little cross protection again the normal seasonal influenzas, and vice versa. So the population will need at least two different flu shots this year.

Dr. Sharon Frey, professor of infectious diseases at SLU and faculty member at the vaccine center, will head an investigation to see if both kinds of flu shots can be given at once. 400 healthy

adult volunteers between 18 and 64, and 400 adults 65 or older will test variations of schedules for efficacy and safety. If no safety concerns arise, the same studies will begin on healthy children.

At the same time, researchers at other Treatment Evaluation Units will be testing two different strengths of the vaccine in one or two doses. Again, if no safety concerns arise, the same studies will begin on healthy children.

The pandemic flu of 1918 was caused by an H1N1 virus. According to Dr. Robert Belshe, that virus entered into pigs, and continued to circulate and mutate there. The "remnants of 1918" have acquired the ability to re-enter into humans and are causing the present pandemic. However, the symptoms of this flu are the same as the seasonal flu.

It is important to test the vaccine on children, as they are most likely to get the disease. This novel flu thrives in warm humid weather, unlike the seasonal influenzas. The usual seasonal influenzas survive in cool dry air. Therefore, once school starts and children with their less-than-perfect hygienic habits are kept indoors in warm and crowded classrooms, the number of swine flu cases will probably take off. And the children will pass the disease right on to their parents.

Testing will begin very soon. 18 million doses (at 15 micrograms/vial) are ready now; 60-80 million will be ready for the bottling process by August 15. 193 million doses in total are contracted for.

Volunteer's blood will first be drawn for antibody titer 21 days after the first injection. The push will be on to get the data sets completed as soon as possible.

How it works

Vaccines are made from a coat protein of killed influenza virus, explained Dr. Belshe. The coat has two different protein components:

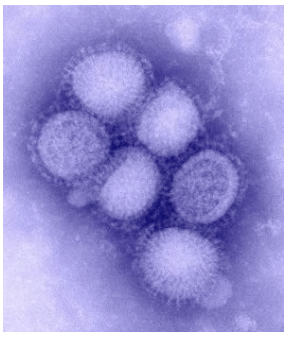
- Hemagglutinin, so called because it can cause red blood cells to clump together, is 70 percent of the coat. It is the "H" in H1N1. The virus uses hemagglutinin to attach to mucous cells in the respiratory tract. These mucous cells have a receptor protein, sialic acid, all over their surface that binds the hemagglutinin. Once bound, the virus can get into the cell and replicate itself many, many times

The very first symptoms of flu infection are cough and fever. Cold-like symptoms come later. The virus first binds to the sialic acid receptors on the mucous membranes of the trachea, causing the tell-tale cough.

- Neuraminidase, an enzyme, is the other coat protein. Neuraminidase releases the newly made viruses as they bud off the host cell. It is the "N" in H1N1. The anti-flu drugs Tamiflu and Relenza keep neuraminidase from working.

Antibodies are made to hemagglutinin, and work as well as antibodies to whole killed viruses without causing side effects such as fever. Effective antibodies block the portion of the hemagglutinin that binds to sialic acid. The diagram shows how blocking antibodies work in the lab assay that measures antibody titer in the blood.

But the viral coat proteins are constantly evolving. In fact, says Dr. Belshe, "We'll never get rid of the flu. Its ecological niche is its ability to survive by mutating."



H1N1 Virus
Photo provided by the Centers for Disease Control

Epidemiologists are hoping that the novel swine flu virus H1N1 will not mutate into a more virulent form. The disease as seen in the present pandemic is no more severe than a seasonal flu. And Tamiflu can reduce its severity if given early. It is classified as a pandemic because it has spread world-wide, and has a very large population that is susceptible to it.

The pandemic will die when nearly everyone has acquired immunity either through vaccination or infection. Not everyone infected becomes sick. The virus will continue to mutate, and will probably be one target of the next year's seasonal flu vaccine.

"It won't be like 1918," predicts Dr. Belshe, "because we know how to take care of flu."