

## Long road ahead in developing effective avian flu vaccination strategy, Stanford expert says

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The near inevitability that influenza will explode into a pandemic in the coming few years has kept researchers searching for a way to prevent the worst effects of infection. The ultimate prize is a highly effective vaccine that could be produced and deployed rapidly.

But developing a vaccine against one of the most talked about types of influenza - the H5, or avian flu - is proving to be more vexing than first thought.

"Making a vaccine for H5 is more difficult than anticipated, even beyond the necessity of making it on the fly," said Harry Greenberg, MD, the Joseph D. Grant Professor at the Stanford University School of Medicine. "At every level there are difficulties."

Greenberg, who is an expert on flu vaccines but is not involved in the effort to develop an avian flu vaccine, will discuss vaccination strategies at the American Association for the Advancement of Science's annual meeting in San Francisco during a session titled, "The present and future for influenza vaccines."

H5, in the language of influenza researchers, refers to one of the proteins found on the surface of the virus molecule. Avian flu has infected wild birds in several countries and when the virus has mutated and jumped from birds to humans, it has killed more than half of those infected with

it.

The first hurdle to developing an H5 vaccine lies in the current method of producing influenza vaccines in chicken eggs. A virus that kills birds will also kill bird eggs. So the vaccine would either have to be made from a virus that is similar to - but not the same as - the deadly virus, or without the egg. "These hurdles are quite surmountable," said Greenberg.

What is proving more difficult is that the H5 molecule is not a powerhouse at stimulating an immune reaction. Probably two shots will be required to fully immunize someone against H5. Unless a chemical known as an adjuvant that boosts the vaccine's effectiveness is used, "we will need a ton of vaccine, which means there will be less to go around," said Greenberg.

Thus far, there are very few FDA-approved adjuvants, so any new ones must go through the years-long drug approval process. "We have a long way to go to find the ideal adjuvant," he said.

Greenberg was involved with the development of the live vaccine against the more common strains of influenza that is currently in use; a live vaccine strategy is also being pursued for H5. "There is clear data from studies in children under the age of 2, who lack any prior exposure to influenza, that the live vaccine is much better at producing immunity," he said. "However, I wouldn't bet on it being the same in adults, but I can hope."

Another strategy for preparing for pandemic flu is "priming," in which the population is vaccinated prior to any outbreak in that hopes that if there is a pandemic a few years later, those who had the priming dose could be immunized with smaller and fewer doses of vaccine. Greenberg said that while priming is a good idea, more work is needed to prove its effectiveness as a strategy. He added that it will be hard to convince

people to get immunized against something that hasn't made an appearance yet. "But if it were me, I'd be happy to get an H5 priming dose," he said.

Source: Stanford University Medical Center

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