Is pre-pandemic mass vaccination a viable prevention strategy for novel Influenza A subtype H5N1 in humans?

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Summary of Findings:

- Public Health experts are concerned that the next human influenza pandemic will be caused by the novel Influenza A virus H5N1, since that subtype has been persistently circulating globally in poultry.
- Vaccination is the most effective strategy for preventing influenza infection in humans and reducing the severity of disease caused by influenza viruses.
- Pre-pandemic mass vaccination in humans for the H5N1 virus is not currently used as a control strategy since the virus is constantly changing and public health officials cannot accurately predict the pandemic strain.
- The effectiveness of influenza vaccines depend in part on the degree of similarity between the virus strain in the vaccine and the virus in circulation that is causing disease.
- Virus mutations yield families of closely related new strain variants, known as clades. The pre-pandemic influenza vaccine concept aims to raise human immune protection through cross-clade immunity from vaccine developed from the current avian influenza A H5N1 clade 1 virus, which will provide some protection against potentially new types of H5N1 viruses.
- A pre-pandemic vaccine is more cost effective than waiting to develop a new vaccination from a novel viral strain in the event of a pandemic if the pandemic strain is antigenically similar to the vaccine strain, however, the vaccine may be completely ineffective if major differences exist in the novel pandemic strain.

Background

Seasonal influenza vaccines, i.e., flu shots, are reformulated annually to target the currently circulating influenza viruses. As flu spreads around the world, new strains emerge due to antigenic drift; these are mutations in the virus which changes the influenza virus strain and provides an advantage over the original virus. Annual immunization is recommended for optimal protection against the constantly changing seasonal flu virus.

Occasionally, entirely new subtypes of the influenza virus emerge; this is called antigenic shift, and these big changes can cause outbreaks that are pandemic. There have been three major worldwide pandemics in the past century that have caused global devastation: the H1N1 Spanish Influenza of 1918, the H2N2 Asian Influenza of 1957, and the H3N2 Hong Kong Influenza of 1968. There is concern that the next influenza pandemic will be caused by a novel Influenza A virus. Influenza A (H5N1) occurs mostly in poultry, and although most avian influenza viruses do not cause disease in humans, some are considered zoonotic, meaning they can transfer from animals to humans.

Occurrences of human-to-human spread of H5N1 in recent years are causing concern about its pandemic potential. From 2003 through January 20, 2016, there have been 846 confirmed human cases of Influenza A, subtype H5N1, reported to the World Health Organization (WHO) from 16 countries, in which 449 people have died. Although these episodes are infrequent and lack sustained human-to-human transmission, the mortality rate is high. Further
genetic reassortment of the virus could make human-to-human spread easier and could cause a global influenza pandemic.

**Hazards of Influenza A H5N1**

- It is difficult to predict the morbidity and mortality potential associated with a pandemic strain of Influenza A (H5N1), however the 1918 pandemic caused over 50 million deaths worldwide\(^3\). Approximately one-third of the U.S. population was infected, and average life expectancy was reduced by over 13 years\(^4\).
- The World Health Organization (WHO) and international experts believe that the world is now closer to another influenza pandemic than at any time since 1968, when the last of the previous century's three pandemics began\(^5\).
- Utilizing current models of disease transmission incorporating historical data, it has been projected that the next influenza pandemic could potentially result in the deaths of up to 2 million people in the United States alone\(^6\).

**Pandemic preparedness**

- Vaccines have been developed for use in humans for the two known variants of H5N1, though they are not currently available commercially. The intent is a government stockpile for public health authorities to distribute in the event of a pandemic. The United States government has already stockpiled enough vaccine to protect more than 3 million people\(^6\).
- If the pandemic is caused by a new strain, development of a vaccine would take several months at least. Even after vaccine production begins, there would not be enough doses of new vaccine available quickly enough to protect everyone initially exposed.
- Effective allocation of existing influenza vaccine could play a crucial role in preventing influenza and minimizing its effects on health and society when a pandemic arrives.

**Pre-pandemic vaccine effectiveness**

- Since H5N1 avian influenza viruses have the ability to mutate, yielding families of closely related new variants, scientists believe that a pre-pandemic vaccine developed from an H5N1 clade 1 virus will provide at least partial protection against new virus strains\(^7\).
- The pre-pandemic vaccines being developed have been shown to be both safe and capable of stimulating development of immune protection against some H5N1 viruses. A two-dose regimen is required to produce sufficient antibodies to reduce the risk of infection by 45% in those who receive the vaccine\(^8\).
- Influenza vaccination is less effective in children and the elderly in preventing illness, but may reduce severity of disease and incidence of complications.

**Benefits and goals of global pre-pandemic immunization**

- The World Bank has estimated that an influenza pandemic would cost the world economy $800 billion during the first year\(^9\). A pre-pandemic vaccine with at least 30% efficacy is more cost effective than waiting to develop a new vaccine from a novel viral strain in the event of a pandemic\(^10\).
- Pre-immunizing could help reduce health consequences during a pandemic. Populations to be considered for pre-pandemic H5N1 immunization include families in poultry farming populations, patients that are at high risk of developing flu-related complications, and healthcare workers. Pre-immunization of the general population may also be considered. The goal of the pandemic influenza vaccinations is to immunize all persons who choose to be vaccinated\(^11\).

**Concerns against mass pre-pandemic immunization**

- Between three and ten billion dollars are needed for funding a global influenza pandemic action plan and vaccine development\(^5\). Collaboration and collective investments from national governments, private sectors, non-governmental organizations, and foundations will be necessary to fund this effort.
- WHO expert groups point out that the pandemic virus may be quite different than what people are immunized against and therefore the vaccine may not be protective. Any decision about whether to use
avian flu vaccines as a hedge against pandemic influenza must be done so with full knowledge of this fundamental uncertainty. 

- If the vaccine results in little effectiveness, people will have been put unnecessarily at risk of adverse reaction to the vaccine, and it will have been an unnecessary expenditure of resources.

References