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EDITORIAL

New pre-pandemic avian flu vaccine progress

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Human infections with highly pathogenic avian influenza A (H5N1) viruses present a serious and highly complex public health challenge. In May 1997, the first human case of H5N1 virus infection was identified and by the end of the same year a total of 18 cases had been confirmed. In 2003 and 2004, H5N1 viruses re-emerged and spread rapidly among poultry in several Asian countries with associated human infections. Since February 2003, millions of birds have been infected and more than 360 human cases recorded, with more than 230 deaths in 12 countries in Africa, Asia and Europe. Currently, H5N1 is an avian pathogen that has had a devastating agricultural and economic impact on the communities it has affected. Although it causes infections relatively rarely in people, when they occur, such infections have been frequently fatal. However, H5N1 viruses continue to evolve and could develop into a much greater public health threat if they acquire the ability to cause sustained and widespread human-to-human transmission. Such a transformation could result in the next influenza pandemic. Addressing H5N1 as an agricultural, zoonotic and potential pandemic threat has proved to be complex and problematic for public health and animal health agencies and authorities (1).

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Recently, the World Health Organization (WHO) and vaccine manufacturers said that about 100 million courses of pandemic influenza vaccine based on the H5N1 avian influenza strain could be produced immediately with standard technology. Experts now anticipate that global production capacity will rise to 4.5 billion pandemic immunization courses per year in 2010 (2).

The European Union has approved its first pre-pandemic vaccine, targeted against H5N1 influenza. The vaccine, manufactured by GlaxoSmithKline (GSK) and marketed under the name Prepandrix, uses a proprietary oil-and-water adjuvant to substantially reduce the amount of antigen needed to generate an immune response. The announcement coincided with the IDSA-sponsored Seasonal and Pandemic Influenza 2008 conference this May.

The GSK vaccine uses antigen derived from the same strain of virus, A/Vietnam/1194/04, as a vaccine developed earlier by Sanofi Pasteur and included in the U.S. stockpile. However, the GSK vaccine generated immune responses predictive of protection using just 3.8 µg of antigen, compared to 90 µg in the unadjuvanted Sanofi Pasteur vaccine currently in the U.S. stockpile. Seasonal influenza vaccines generally include 15µg of antigen per virus strain (3).

The H5N1 vaccine strain is a clade 1 virus, but clade 2 has become dominant throughout Southeast

Asia. However, the vaccines show some degree of cross-reactivity with other strains (1,4).

In this regard, the question is, "Do we want to stockpile vaccines in warehouses, or in people's arms?" In other words, in the absence of a pandemic, how widely should these vaccines be used?

If an H5N1 pandemic strikes, it would take months to produce a vaccine based on the pandemic strain. Those who received pre-pandemic vaccine ahead of time might have some immunity. The pre-pandemic vaccine might even serve as a priming vaccine, with the pandemic-strain vaccine acting as a booster.

However, the 1976 swine flu outbreak provides some cautionary lessons on mass vaccination in response to an uncertain threat. One lesson: "Expect the unexpected," he said. Milder-than-expected influenza, a manufacturing mix-up, and, finally, Guillain-Barre syndrome scuttled the swine flu mass vaccination campaign. If H5N1 pre-pandemic vaccination is undertaken, surveillance would be essential to detect unusual events. Effective communications about benefits and risks also would be crucial.

Of course, there is no guarantee for the next influenza pandemic to be caused by H5N1, but considerable progress has been made as a result of H5N1 that can be applied to any influenza pandemic, as well as to seasonal influenza. Research development authorities, listed $1.3 billion in contracts awarded to companies to expand domestic vaccine manufacturing. The agency also is supporting research combining antigens and adjuvants from different manufacturers in order to minimize the amount of antigen needed, a novel approach called "mix-n-match"(3).

We should encourage development of biomedical tools against biological, chemical, nuclear, and radiological threats to national security. In addition to influenza vaccine development, we should develop antivirals and rapid diagnostics for influenza and other infectious diseases.

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