Influenza Vaccine: A Long Way from Hong Kong

The first hint that another round of "Asian flu" might be in the offing came in mid-July when an unidentified strain of influenza was reported in Hong Kong. At this point, international health authorities began to take the steps that in the United States should lead to distribution late this month of the first limited supplies of vaccine effective against the new strain.

The process of identifying a flu strain, producing a vaccine, and distributing it follows a well-defined pattern. This time the process began on 17 July, when W. K. Chang of the Hong Kong medical health department sent specimens to the World Health Organization's (WHO) international flu headquarters in London, which is the center of the world influenza warning system. One of WHO's main tasks is to be on the lookout for new types of flu, to characterize a flu strain rapidly when it appears, and to distribute specimens of the strain to any of WHO's 78 national flu centers interested in developing a vaccine.

On 29 July, Chang sent additional specimens of the new flu strain to the U.S. National Communicable Disease Center (NCDC) in Atlanta, Georgia. Besides serving as WHO's Western Hemispheric center, NCDC's responsibility is to monitor and maintain surveillance on all flu outbreaks in the United States. NCDC, in turn, notified the Department of Health, Education, and Welfare's Division of Biologics Standards (DBS) in Washington. DBS's responsibility is to establish U.S. standards for the production of a suitable vaccine, and to prepare a seed virus, which can be supplied to manufacturers if and when the Public Health Service recommends that a vaccine be manufactured.

On 17 August, about a month after the flu initially was reported in Hong Kong, NCDC in Atlanta and World Health in London definitely identified the Hong Kong flu as an A-2 strain (closely akin to the 1957 Asian flu strain). Both organizations also announced that the strain is a major A-2 "drift," requiring a special serum.

On 4 September, the Public Health Service's Advisory Committee on Immunization Practices met with representatives of the World Health Organization to discuss further outbreaks of the Hong Kong flu in Japan, Australia, and Singapore, and to assess the possibilities of an epidemic in the United States. On the basis of the committee's suggestions, U.S. Surgeon General William Stewart recommended, on 6 September, that licensed U.S. manufacturers produce an influenza vaccine.

In early September, DBS received a seed virus from Japan, which had developed the serum more quickly than the U.S. had. The DBS shipped isolates of the inactive serum on 9 September to five manufacturers licensed to make the vaccine in the United States.

The virus is adapted to fertilized chicken eggs, later harvested from the eggs, concentrated, purified, killed with formaldehyde, and then adjusted to specified vaccine potency standards. Under optimum conditions the entire adaptation process may take 2 to 3 months.

There are many variables in the production process and it is often difficult for manufacturers to predict what quantities of the vaccine will be available. Often the vaccine growth rate and subsequent yield vary greatly from batch to batch. Manufacturers also may have mixed feelings about producing vaccines, which do not earn large profits. If the vaccine is not ready in time for an epidemic, there is an unused surplus, resulting in a loss. Production costs are high, and manufacturers often face additional problems, such as difficulties in obtaining a sufficient quantity of fertilized eggs.

DBS works closely with the manufacturers during the actual production process; it checks manufacturers' harvests for impurities, and later inspects their batches to insure acceptable standards of safety, purity, and potency.

While DBS regulates the production of flu vaccine, it does not control distribution of the vaccine, which is sold on the open market. Public Health Service officials say that even government health services have no special access to the vaccine. Individual physicians and Public Health Service directors are responsible for insuring that high-risk groups—the aged and the chronically ill—receive the vaccine first. While the government can only recommend distribution to certain groups, PHS has indicated that the U.S. Army has a contract arrangement with the manufacturers to obtain enough vaccine to meet military needs. Although these regular orders for flu vaccine are generally filled months in advance, it is not clear how the military's demands will affect supplies of the new Hong Kong flu vaccine, and Department of Defense officials are not eager to talk about it.

Last week, Stewart said that the first U.S. supplies of vaccine to combat the Hong Kong flu would be available in late November, but warned that the supplies will be extremely limited and should be used exclusively for persons in the high-risk categories. "We should be able to achieve enough immunization of high-risk groups to prevent many serious illnesses and possibly death," Stewart said, but gave no figures on the actual amounts that will be available for these groups in late November, or available in the near future for the rest of the population.

The NCDC reports that vaccines are usually about 60 percent effective. Influenza is a generally mild epidemic illness, but can lead to serious complications. NCDC says the first and worst epidemic of Asian flu in the United States occurred in 1957, when flu-associated deaths numbered more than 62,000. Subsequent outbreaks have been less severe: NCDC reports that the two other recent high-mortality years were 1960, with 43,500 flu-associated deaths, and 1963, with 46,300 such deaths. No figures are available on last year's epidemic. (The 1918 influenza epidemic killed 445,000 persons in the United States.)

Most flu-associated deaths occur among the aged and the chronically ill. Bruce Dull, assistant director of NCDC, told *Science* that he does not foresee any serious shortages of the Hong Kong flu vaccine for these high-risk priority groups if PHS recommendations for use of the vaccine are carefully followed by physicians and public health officials.

Hong Kong flu is expected to increase in the U.S. in late December or early January.—MARTI MUELLER