COMMENTARY

Strategy for Distribution of Influenza Vaccine to High-Risk Groups and Children

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Despite evidence that vaccinating schoolchildren against influenza is effective in limiting community-level transmission, the United States has had a long-standing government strategy of recommending that vaccine be concentrated primarily in high-risk groups and distributed to those people who keep the health system and social infrastructure operating. Because of this year’s influenza vaccine shortage, a plan was enacted to distribute the limited vaccine stock to these groups first. This vaccination strategy, based on direct protection of those most at risk, has not been very effective in reducing influenza morbidity and mortality. Although it is too late to make changes this year, the current influenza vaccine crisis affords the opportunity to examine an alternative for future years. The alternative plan, supported by mathematical models and influenza field studies, would be to concentrate vaccine in schoolchildren, the population group most responsible for transmission, while also covering the reachable high-risk groups, who would also receive considerable indirect protection. In conjunction with a plan to ensure an adequate vaccine supply, this alternative influenza vaccination strategy would help control interpandemic influenza and be instrumental in preparing for pandemic influenza. The effectiveness of the alternative plan could be assessed through nationwide community studies.

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THE CURRENT INFLUENZA VACCINE CRISIS

Evidence and analysis have shown that vaccination of schoolchildren has been the key to reducing influenza transmission during recent years in the United States (1–8). However, our influenza policy in the face of the current vaccine shortage has been to vaccinate high-risk and other groups rather than schoolchildren (9, 10). On October 5, 2004, the Chiron Corporation (Emeryville, California) informed the national Centers for Disease Control and Prevention that none of the 50 million doses of trivalent inactivated influenza vaccine that it had produced for the United States would be available for the 2004–2005 influenza season (9). Literally overnight, the planned vaccine supply for the country was cut almost in half. The 57 million doses of vaccine available from the two other companies were not enough to cover the roughly 85 million people at high risk of influenza-related death and morbidity in the United States.

In response, the Centers for Disease Control and Prevention recommended a program whereby the health system offered vaccine to only those on the list given in figure 1, which totals about 100 million people (11). This strategy has caused considerable confusion about who should receive the vaccine. The recommendation differs little from the recommended distribution of influenza vaccine over the last
several decades, with the one exception being those not in the designated groups to refrain from being vaccinated. Except for the swine influenza vaccination campaign of 1976, the recommendation has been to give influenza vaccine to certain groups of high-risk people, those who have direct contact with high-risk people, and those who keep the health system and social infrastructure operating (10).

However, coverage of the targeted groups is not very good. For a typical interpandemic influenza season, the resulting vaccine coverage has been about 5 percent of children, 23 percent of adults less than 65 years of age, and 68 percent of adults 65 years of age or older (7). During the last five influenza seasons starting in 1999, about 80 million doses of influenza vaccine have been delivered in the United States per season, resulting in about 30 percent of the US population being vaccinated. This vaccine distribution has had little effect on influenza transmission and a relatively small effect on overall influenza morbidity and mortality. Influenza vaccination of the elderly has been shown to have a moderate, but important effect on mortality in that age group (12, 13). Each year, influenza is responsible for at least an average of 36,000 excess pneumonia and influenza deaths in the United States, mostly in the elderly (14). Although it is too late to change vaccination strategies this year, the current crisis of very limited quantities of vaccine gives us a chance to revisit what the best vaccination strategy should be for future years.

AN ALTERNATIVE STRATEGY

An alternative vaccination strategy to the one described above would be to cover the high-risk population at the current levels while concentrating the remainder of the vaccine in schoolchildren 5–18 years of age. Such a distribution would give the reachable high-risk population some direct protection while greatly curtailing the spread of influenza in the general population by concentrating vaccine in the group most responsible for community-wide transmission. Since influenza A (H3N2) was introduced in the United States in 1968–1969, schoolchildren have consistently had the highest illness attack rates of all age groups. This attack rate pattern has generally been true for years in which influenza A (H3N2), A (H1N1), or B has circulated widely (15–18). High rates of transmission to and among children are due to more exposure potential and less prior immunity in these children compared with adults. Even when controlling for prior immunity, the household secondary attack rate for children was estimated to be twice that for adults (19).

Mathematical models

Detailed mathematical models of influenza epidemics show that for those strains that transmit well among children, distribution of influenza vaccine to about 70 percent of these children greatly reduces transmission in the entire community to below epidemic levels (4–7). Optimization methods applied to these models illustrate that when vaccine quantities are limited, concentrating vaccine in schoolchildren is optimal for reducing overall influenza morbidity or mortality (4, 8). If the 70 percent threshold in children can be reached, then high-risk people are protected even if they are not vaccinated. Since there are about 60 million schoolchildren in the United States, about 42 million doses of vaccine would be needed to get below the epidemic threshold. Thus, even this year, we would have had enough vaccine to reduce transmission in the entire country by concentrating vaccine in schoolchildren. According to the models, we would save more lives and prevent more illness by using this strategy as opposed to the current one of limiting vaccine to portions of the population groups given in figure 1. Even if the 70 percent threshold in schoolchildren could not be reached, the models show that coverage of as low as 50 percent would still result in a considerable reduction in transmission for the entire population (5–7). Although the mathematical models suggest concentrating limited quantities of vaccine in schoolchildren, in practice it would be important additionally to vaccinate as many high-risk people as possible.

Epidemiologic field studies and observations

Evidence from community trials suggests that mass vaccination of children can be effective in reducing influenza transmission in the entire community. Monto et al. (1) vacci-
nated 85 percent of the school-age children in Tecumseh, Michigan, against influenza A (H3N2) just before the epidemic in 1968, resulting in a 67 percent decrease in the epidemic influenza-like illness attack rate in Tecumseh compared with neighboring Adrian. In an ongoing community vaccine study in central Texas with trivalent, cold-adapted influenza vaccine, age-specific medically attended acute respiratory illness in the intervention communities of Temple and Belton, Texas, is compared with that in the communities of Waco, and Bryan and College Station, Texas. For the influenza seasons 1997–2001, vaccination of approximately 20–25 percent of children in the intervention communities resulted in an 8–18 percent indirect reduction of medically attended acute respiratory illness events in adults older than 35 years of age (2). This result is consistent with predictions from the above-described mathematical models. For the 2004–2005 influenza season, investigators in the Texas study are vaccinating a large proportion of schoolchildren in the Temple-Belton area, thus obtaining a good estimate of the community-level effect of mass vaccination of schoolchildren.

The Japanese national strategy from 1962 to 1987 was to vaccinate schoolchildren to control epidemic influenza. Approximately 80 percent of Japanese schoolchildren received an inactivated influenza vaccine annually. A reassessment of the Japanese experience demonstrated that influenza vaccination of schoolchildren prevented an estimated 37,000–49,000 excess deaths per year among elderly adults (3).

A POSSIBLE FUTURE STRATEGY

The best strategy for minimizing the number of influenza-related deaths and morbidity for interpandemic influenza would be to concentrate vaccine in the high-risk and high-transmitting population groups simultaneously. For the most recent influenza years, the goal would be to vaccinate approximately 70 percent of the schoolchildren and as many other people in the categories given in figure 1 as possible.

This strategy would probably reduce community transmission to very low levels. Even if only 50 percent of the schoolchildren could be vaccinated, community-wide transmission would be reduced considerably (5–7). Given that many high-risk people are never vaccinated, we calculate that our recommended vaccination strategy would require about 120 million doses of vaccine per season. To guarantee adequate quantities and optimal distribution, the US government should guarantee that at least 120 million doses of vaccine will be bought and distributed each year. This goal would help stabilize production. In addition, mass vaccination of schoolchildren would probably have to involve active school system participation, as occurs with other vaccines. In addition, schoolchildren could be vaccinated with the live attenuated vaccine, trivalent, cold-adapted influenza vaccine, which is easy to administer and well tolerated by this age group (2). Weycker et al. (7) showed that mass vaccination of schoolchildren could be highly cost-effective. Such a strategy would mean that we would not only be effective in dealing with interpandemic influenza but, when a pandemic strain arises, would also have the vaccine manufacturing and distribution system in place for using limited quantities of vaccine as they became available (20).

If a strategy of vaccinating schoolchildren is adopted, it will be important to evaluate the success of the program. One option would be to implement the strategy in some states but not others. The incidence of influenza in the different age groups could be monitored and compared between states with and without the strategy of vaccinating schoolchildren. In essence, the entire country could participate in one large community trial. The results would demonstrate whether the strategy was successful.

For decades, many influenza researchers have thought that vaccinating schoolchildren would be an important method to reduce transmission of influenza, thus reducing morbidity and mortality through the indirect effects. Why has a corresponding strategy never been recommended in the United States?

We do not know the answer but offer a plausible explanation. Only in the past decade or so have US public health officials begun taking potential indirect effects of vaccina-

tion more seriously in making recommendations for vaccination schedules and for licensure. Previously, only direct protective effects of vaccination were considered important. Schoolchildren are not considered a high-risk group for influenza and thus were left out of the recommendations. The current vaccine shortage provides an opportunity to revisit the option of vaccinating schoolchildren in addition to people at high risk of serious morbidity and mortality. It is a strategy whose time has come.

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REFERENCES

6. Halloran ME, Longini IM, Cowart DM, et al. Community inter-