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Coping with the influenza vaccine shortage

■ ABSTRACT

Faced with a shortage of the inactivated intramuscular influenza vaccine this year, the Centers for Disease Control and Prevention (CDC) has revised its guidelines for immunization and use of antiviral agents. The most rational solution at this time is to direct the supply of scarce vaccine to patients at highest risk of influenza-related complications.

■ KEY POINTS

This year, the CDC is recommending vaccinating people 65 years and older (rather than age 50 and older) and is advising healthy people between the ages of 2 years and 64 years to forgo immunization. The live-attenuated, intranasal influenza vaccine is another option.

Four antiviral agents are available for treating influenza. Three of these agents are also approved for preventing influenza, but they should be used mainly in the setting of an outbreak or in those who cannot be immunized but are at high risk of complications from influenza.

General measures to avoid transmission of respiratory viruses, particularly hand-washing and covering coughs and sneezes, are very effective and should be emphasized this flu season.

Giving smaller doses of the inactivated vaccine either intramuscularly or intradermally appears promising but is not currently recommended

IN OCTOBER 2004, the nation was informed that almost half its supply of influenza vaccine will not be released, owing to contamination problems affecting one of its two suppliers. The sudden shortage has resulted in panic among patients and health care providers alike.

A bit of good news is that the flu season that ended in September in the Southern Hemisphere was associated with mild-to-moderate disease activity.¹ The A (H3N2)/Fujian/411/02-like strain predominated, a strain similar to the A (H3N2) component of the 2004–2005 influenza vaccine. During October 3–16, 2004, only sporadic influenza activity was reported in the United States.¹

The bad news is that we will have to ration supplies, reserving what we have for people at highest risk. Measures to this end are in place. Cooperation from the public and health care providers will be imperative to implement these measures.

■ HOW AND WHY THE SHORTAGE OCCURRED

In 1994, there were five manufacturers of influenza vaccine in the United States. Since then, several companies decided to stop making it, owing to difficult production procedures, strict government regulations, unpredictable consumer demand, a relatively low profit margin compared with other pharmaceutical products, and lack of liability protection from expensive lawsuits.

At the same time, since Medicare began reimbursing for influenza vaccination in 1991, demand for vaccine has been rising, reaching 83 million doses in the 2003–2004 season. However, since the severity of any particular

influenza season is difficult to predict, vaccine manufacturers expect to discard about 10% of their product each year.

Influenza vaccine differs from other vaccines in that it has to be manufactured anew every year to match the expected circulating influenza strains. The current production process, which relies on growing the virus in eggs, starts in late February of each year when the World Health Organization decides on the three vaccine components (two type A viruses and one type B). This process must follow a tight schedule, since starting early may omit important emerging strains, and delaying too long would not give enough time for the tedious procedures to be completed in time before the flu season.

Even though there has been an increase in investment in influenza-related activities under President Bush from \$39 million to \$283 million, much more is needed to shift vaccine development from the cumbersome egg-based production process to new cell culture technologies.

The only two companies that currently make the flu shot for the United States, Aventis and Chiron, were poised to supply 100 million doses for the 2004–2005 flu season. News of a limited problem with a small amount of the Chiron product first appeared in September 2004. However, on October 5, 2004, Chiron announced that none of its 48 million doses would be released, due to bacterial contamination. The nation's supply was cut in half overnight, leaving public health administrators, physicians, and the general public in a quandary.

■ WHO SHOULD GET A FLU SHOT THIS YEAR?

On October 25, 2004, the Centers for Disease Control and Prevention (CDC)² revised its recommendations for influenza vaccination for the 2004–2005 flu season to include:

- Children age 6 months to 23 months. This was actually added to the recommendations for the first time in April 2004.³
- Adults 65 years of age and older. This had been the age recommendation up until the year 2000, when all adults 50 years of age and older were included.

- Adults and children with chronic medical conditions, including heart disease, lung disease, kidney disease, metabolic disease, hemoglobinopathies, or immunosuppression caused by diseases such as human immunodeficiency virus infection or by medications, such as in bone marrow and organ transplant recipients.
- All women who will be pregnant this flu season, regardless of which trimester of pregnancy they will be in.
- Residents of nursing homes and chronic care facilities, regardless of age.
- Children and adolescents 6 months to 18 years of age who are receiving aspirin daily and thus are at increased risk of developing Reye syndrome if they contract influenza.
- Health care workers who are in direct patient contact.
- Household contacts and out-of-home caregivers for children under 6 months old. The original 2004 recommendations published in April included people who take care of children under 23 months old. If someone belonging to one of the above groups attempts to get vaccinated and his or her health care provider cannot provide the vaccine, he or she should be advised to contact the local health department, or to search for public clinics that may have the flu shot by accessing www.findaflushot.com/lungusa. [However, when CCJM staff checked this web site in mid-November, many zip codes did not show any flu shot clinics being conducted.]

Whom not to vaccinate

It is more important in the setting of shortage to remember whom *not* to give the flu shot to:

- Children younger than 6 months
- Healthy people 2 to 64 years old
- People with known anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine.

Mild upper respiratory tract infections, particularly in the absence of fever, should not preclude vaccination.

■ WHAT ELSE CAN BE DONE?

In addition to the above revised recommendations, the following measures should aid in resolving the shortage problem.

This year, healthy people 2–64 years old are asked to forgo vaccination

**TABLE 1****Antiviral influenza medications**

MEDICATION	INFLUENZA TYPES	ROUTE	PREVENTIVE DOSE (ADULTS)	THERAPEUTIC DOSE (ADULTS)	SIDE EFFECTS
Amantadine (Symmetrel)	A	Oral	100 mg twice a day	100 mg twice a day	Gastrointestinal upset Central nervous system symptoms
Rimantadine (Flumadine)	A	Oral	100 mg twice a day	100 mg twice a day	Gastrointestinal upset
Oseltamivir (Tamiflu)	A and B	Oral	75 mg daily	75 mg daily	Gastrointestinal upset
Zanamivir (Relenza)	A and B	Oral Inhalation	Pending	10 mg twice a day	Bronchospasm

Promoting good health habits

Good health habits that prevent the spread of influenza include hand-washing, covering coughs and sneezes, avoiding touching one's nose, eyes, or mouth, particularly during upper respiratory infections, staying away from people with upper respiratory infections, and staying home from work or school if one suspects he or she has influenza.

General healthy habits, including getting adequate rest, drinking plenty of fluids, eating a healthy diet, and exercising regularly, should also aid in maintaining the immune system to fight off infection.

Looking for more vaccine

Aventis recently announced a plan to redistribute 22.4 million doses of its remaining supply and to manufacture 2.6 million additional doses by January 2005.

Officials from the US Food and Drug Administration (FDA) are looking to other countries to get additional doses of flu vaccine this season. There are approximately 18 influenza vaccine manufacturers worldwide.

The government is cracking down on fraudulent merchants and those profiteering from the vaccine shortage, and warns of vaccine scams on the Internet.

Giving nasal vaccine

Healthy people ages 5 to 49 years old can receive the intranasal, live-attenuated influenza vaccine, even if they care for babies under 6 months of age or if they are in close contact with immunosuppressed individuals who are not deemed to be severely immunosuppressed,

such as hematopoietic stem cell transplant recipients. Similarly, health care providers can receive the live-attenuated vaccine if they are not in contact with severely immunosuppressed patients.³ (Although the CDC does not specify what types of transplant recipients are severely immunosuppressed, I believe all bone marrow and solid organ transplant recipients should be considered so, at least for 6–12 months after transplantation.)

This year, only 1.1 million doses of this vaccine were made, but the manufacturer has recently announced that 2 million additional doses will be available by the end of December.

When to use antiviral medications

Influenza antiviral medications should be judiciously used for both prevention and treatment of influenza.⁴ The CDC encourages the use of either amantadine or rimantadine for prophylaxis and use of oseltamivir or zanamivir for treatment (TABLE 1).

People who are at high risk for serious complications of influenza benefit the most from antiviral medications. Patients should be treated if they present within 2 days of the onset of illness and either have life-threatening influenza or are at high risk for serious complications of influenza. Symptoms that should prompt the use of an antiviral agent are the sudden onset of fever, headache, and dry cough during the epidemic period.

In addition, antiviral prophylaxis should be given to residents of nursing homes and hospitals in which there is an institutional outbreak, regardless of their vaccination status. In this situation the health care providers

Antiviral prophylaxis should be given in hospitals and nursing homes during an outbreak



should also receive chemoprophylaxis for 2 weeks following vaccination.

Any person who is at high risk for influenza-related complications should receive chemoprophylaxis for 7 days if he or she is exposed to a person with known influenza.

The government has purchased and stockpiled enough antiviral medications to treat 7 million people. Assuming the current production capabilities, the FDA estimates that enough supply for treating 40 million people will be available through this flu season. If the local supply of antiviral medications is adequate, antiviral chemoprophylaxis may also be considered during seasonal outbreaks (typically 6–8 weeks) for people at high risk of serious influenza-related complications if they cannot get vaccinated or are not expected to mount a protective immune response to vaccination due to immunosuppressive conditions or medications.

Antiviral agents should not be used for prophylaxis in people in the community who are not at high risk for influenza-related complications.

Will there be enough vaccine?

The new estimates for the 2004–2005 flu season suggest that approximately 98 million Americans should be given priority for influenza vaccination.⁵ The expected supply from Aventis and MedImmune should be sufficient for those at highest risk of influenza-related complications, who are the people most likely to be vaccinated in any year, according to prior estimates.⁶

Can vaccine doses be split?

One potential approach to the vaccine shortage is to split each dose into two doses, thus doubling the number of potential vaccinees.⁷ In addition, two recent studies^{8,9} showed that intradermal injection of a reduced dose (20% in one study, 40% in the other) was as immunogenic as the intramuscular route, but was associated with a significantly higher incidence of side effects. However, these approaches have only been studied in healthy adults, not those at risk for influenza-related complications. In addition, although low doses have shown adequate immunogenicity, the clinical efficacy of such approaches has not been evaluated. The CDC thus does not recommend them, even in the setting of vaccine shortage.

How to avoid wasting vaccine

Every attempt should be made to avoid wasting any dose of the vaccine. Prefilling large number of syringes for vaccination clinics increases the risk for administration errors, as well as for inappropriate storage conditions, which may result in reduced vaccine potency or bacterial overgrowth in vaccines that do not contain a preservative. Reserving vaccine for second doses for children being vaccinated for the first time should be avoided. Proper communication between hospital-based and outpatient vaccination programs should be in place to avoid unintended revaccination.¹⁰

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