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On Drugs and Therapeutics

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Influenza Vaccine 2005-2006

Annual immunization against influenza A and B is the most effective method of preventing infection and has been shown to reduce associated complications. A future issue of *The Medical Letter* will review drug prophylaxis and treatment of influenza.

VACCINE FORMULATIONS — Two types of influenza vaccine are available in the US: inactivated intramuscular vaccine and a live-attenuated intranasal vaccine (*FluMist*). A new brand of inactivated influenza vaccine (*Fluarix*), available in Europe for many years, was recently approved by the FDA for use in adults.¹

Thimerosal (a mercury-containing preservative) is present in some formulations of inactivated influenza vaccine. Multi-dose vials of inactivated vaccine contain about 25 mcg of mercury per 0.5-mL dose, while single-dose formulations contain <1.25 mcg per dose. Although there has been public concern about risks to children from thimerosal in vaccines, there is no evidence that it has had any adverse effects, except possibly some local hypersensitivity reactions.²

VACCINE COMPOSITION — The vaccine for the current season includes a new influenza A H3N2 strain, A/California/7/2004, which is used in the live vaccine. A/NewYork/55/2004, which is antigenically equivalent to A/California/7/2004, is used in the inactivated vaccines. The influenza A (H1N1) and influenza B strains are the same as last season: A/New Caledonia/20/99 and B/Jiangsu/10/2003, which is antigenically equivalent to B/Shanghai/361/2002.³

RECOMMENDATIONS — Based on the duration of protective antibodies and the timing of influenza circulation, the optimal time for vaccination is during October or November. In recent years, the inactivated vaccine supply in October has not been sufficient to vaccinate everyone. This year the CDC recommends that inactivated vaccine be targeted initially to those at high risk of complications from influenza, such as pregnant women in any trimester, persons ≥ 65 years old, children 6-23 months of age and patients 2-64 years old with chronic medical conditions. Household contacts and caregivers of children <6 months old and healthcare workers should also be vaccinated first.¹ After targeting of high-risk groups, inactivated vaccine should be offered to everyone, particularly persons ≥ 50 years old, until the end of the influenza season in April.⁴

FluMist,⁵ the live-attenuated vaccine, can be offered at any time to eligible individuals. It is approved for use in

INFLUENZA VACCINES

VACCINE	FORMULATION	MERCURY CONTENT	AGE INDICATION	COST ¹
Inactivated (split virus)				
<i>Fluarix</i> (GlaxoSmithKline)	0.5 mL syringe ²	<1.25 mcg	≥ 18 years	\$11.00
<i>Fluvirin</i> (Chiron)	5 mL multidose vial	24.5 mcg/0.5 mL dose	≥ 4 years	11.00 ³
	0.5 mL syringe ²	<1 mcg	≥ 4 years	13.65
<i>Fluzone</i> (Sanofi-Pasteur)	5 mL multidose vial	25 mcg/0.5 mL dose	≥ 6 months	10.70 ³
	0.25 mL syringe ²	none	6-35 months	13.00
	0.5 mL syringe ²	none	≥ 3 years	14.00
Live (attenuated virus)				
<i>FluMist</i> (MedImmune)	sprayer ⁴	none	5-49 years ⁵	20.70 ⁶

1. Price according to the manufacturer. Price includes a \$0.75 excise tax.

2. Syringes are sold in boxes of 10.

3. Cost of a 0.5-mL dose.

4. Each syringe-like sprayer contains a single 0.5-mL dose (0.25 mL in each nostril); sold in boxes of 10.

5. Approved for intranasal use in healthy, non-pregnant persons 5-49 years old.

6. Price for a non-returnable sprayer. Price for a returnable sprayer is \$25.25.

healthy, non-pregnant persons between ages 5 and 49. It should not be used in patients who are immunosuppressed and is not recommended for those with chronic cardiovascular, pulmonary, renal or metabolic disease.

EFFICACY — Antibodies reach protective levels about 2 weeks after injection of inactivated influenza vaccine and generally persist for 6 months or longer. In some elderly patients, serum antibody levels fall below protective levels in 4 months or less. The efficacy of inactivated vaccine in preventing influenza is generally about 80% (less in the elderly), but can vary each year depending on the match between the vaccine and circulating strains.⁶

In clinical trials comparing live to inactivated vaccine, the live vaccine appeared to be similarly effective in adults, and possibly more effective in children.⁷ In addition, the live vaccine has been shown to provide protection against new variants of influenza A (H1N1) and B for at least 2 years.⁸

ADVERSE EFFECTS — Except for soreness at the injection site, adverse reactions to inactivated influenza vaccine are uncommon. Fever, myalgia, and malaise can occur. Whether inactivated influenza vaccine can cause Guillain-Barré syndrome is controversial.⁹

The live-virus vaccine is generally well tolerated, but it can cause mild runny nose, nasal congestion and sore throat, and has been reported to increase the incidence of asthma exacerbations. Transmission of vaccine-strain virus occurred once in an unpublished study of young children attending day care, but has not been reported in practice. Healthcare workers, family members and other close contacts of severely immunosuppressed patients (e.g., hematopoietic stem cell transplant recipients) who have received the live-virus vaccine should avoid contact with the immunosuppressed person for 7 days after vaccination because of the theoretical risk of transmission of the vaccine-strain virus.

Both the live and inactivated vaccines are made from virus grown in eggs; hypersensitivity reactions, presumably to egg protein, can occur.

DOSAGE — A single 0.5 mL IM dose of inactivated influenza vaccine is recommended for adults and children ≥ 3 years old; 0.25 mL is recommended for children 6-35 months old. Children younger than 9 years of age who are being vaccinated for the first time should receive 2 doses at least 4 weeks apart, with the second dose given before December if possible. If a child younger than 9 years old received a single dose

of either inactivated or live vaccine last season, only one dose is needed this season.

FluMist is given as a single 0.5 mL dose (0.25 mL in each nostril); previously unimmunized children 5-8 years old should receive 2 doses at least 6 weeks apart.

REDUCED DOSE — Intradermal administration of a reduced dose of influenza vaccine has been investigated as a means to both improve immunogenicity and “stretch” the available supply.¹⁰ In a randomized study of 119 patients, intradermal immunization with a vaccine containing 6 mcg of each antigen was compared to standard vaccination (15 mcg of each antigen) and found to have similar immunogenicity in patients 18-60 years old, but lower immunogenicity in patients older than 60.¹¹ A similar study of intradermal administration in 100 healthy adults 18-40 years old used just 3 mcg of each antigen (one-fifth the standard dose) and also found immunogenicity to be similar to that of standard vaccination.¹² A 7.75-mcg dose of each antigen given intramuscularly to healthy adults 18-49 years old has also been shown to be immunogenic.¹³ The clinical efficacy of these approaches is unknown.

AVIAN INFLUENZA — Most human cases of avian influenza have occurred in patients who had close contact with infected poultry.¹⁴⁻¹⁶ There is no commercial influenza vaccine available for pathogenic strains of avian influenza (H5N1, H7N2, H9N2, H7N3, H7N7). Since standard commercially available influenza vaccines include N1 and N2, it is biologically plausible that they might offer some protection against avian flu strains with these neuraminidases.

As part of its pandemic-preparedness plan, the US Department of Health and Human Services is supporting clinical trials of investigational lots of vaccine against H5N1 influenza.¹⁷ The US State Department is providing the neuraminidase inhibitor oseltamivir (*Tamiflu*), which has been effective *in vitro* against H5N1 influenza, to its embassies in Southeast Asia for use by US government employees and their families.

The CDC recommends that travelers to countries in Asia with documented avian flu outbreaks eat only well-cooked poultry products and avoid live poultry markets, farms and contact with surfaces that appear to be contaminated with poultry feces. Travelers should wash their hands frequently with soap and water or use an alcohol-based hand rub.

CONCLUSION — Available inactivated influenza vaccine should be targeted initially to persons at increased

risk of complications from infection with influenza virus, healthcare workers and close contacts of children <6 months old. The live-virus vaccine (*FluMist*), which is at least as effective as the killed vaccine, is recommended for use in healthy, non-pregnant persons 5-49 years old. Everyone without a contraindication should be vaccinated against influenza. □

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