Management of Influenza – An Update for 2009

Influenza vaccination is currently recommended for the elderly and those with underlying conditions (Table 1). Infants younger than 6 months of age, who have the highest hospitalization rates are not eligible; however, they can be protected by immunization of their mothers during pregnancy (1). These categories emcompass at least 85% of the total U.S. population, or about 250 million persons. Persons at increased risk for complications from influenza virus infection may benefit most by having the healthy persons around them vaccinated (2).

The Influenza Vaccine

The formula for the influenza vaccine is updated every year on the basis of worldwide surveillance by the collaborating centers of the World Health Organization (WHO). Those variants of the three prevalent viruses in the human population that are most likely to cause outbreaks in the upcoming season are incorporated into the vaccine (Table 2). Table 1 lists the six influenza vaccines that are licensed to be distributed in the United States for the 2008-2009 season.

Efficacy of the Vaccine

The efficacy of influenza vaccines in school children and adults in the workforce ranges from 70 to 90% in years in which a good match is attained between the vaccine antigen and the epidemic virus. (In a year in which there is a bad match between the vaccine antigen and the epidemic virus, the efficacy of the vaccine can range from 0 to 50%). Both the trivalent inactivated vaccine and the live attenuated influenza vaccine are well tolerated. The most common side effects are tenderness at the site of the injection with the trivalent inactivated vaccine and transient sore throat or nasal stuffiness with the live attenuated influenza vaccine. The efficacy of the live attenuated influenza vaccine is superior to that of the trivalent inactivated vaccine for children. The live attenuated influenza vaccine provides 30 to 50% better protection than the trivalent inactivated vaccine. Live attenuated influenza vaccine has the advantage of administration by nasal spray, initiating a benign limited infection, this stimulates mucosal and humoral immunity, and often results in better cross-protection against new variant viruses than does the trivalent inactivated vaccine.

Management

Obtaining cultures in sentinel clinics is important to provide a sample of viruses that can be characterized for both antigenic properties and sensitivity to antiviral drugs. (Influenza A viruses are more resistant to antiviral agents).

New rapid point-of-care molecular can assist physicians in decisions regarding the use of antiviral therapy. The sensitivity of these new tests varies according to the type of test and the properties of the circulating viruses, and typically ranges from 60 to 80%; the specificity of these tests is about 90%. It should be noted that confirmation of the diagnosis of influenza by means of a rapid test is not essential for antiviral treatment in the midst of an influenza outbreak. Under those circumstances, the clinical diagnosis that is based on symptoms of fever and cough at presentation is as accurate as most point-of-care rapid detection tests for persons older than 5 years of age (3).

Indications for Antiviral Therapy

Therapy: Antiviral treatment is most effective when it is initiated within 48 hours after the onset of illness. Anyone who may have a serious outcome should be treated (ACIP 2008). Although the effectiveness of antiviral therapy is greater the earlier the treatment is initiated, treatment is indicated for infected hospitalized patients even if the duration of illness is more than 48 hours since treatment may not only benefit the patients but may also reduce the risk of nosocomial spread of infection.

The adamantanes, amantadine and rimantadine, are currently not recommended for use in the United Sates because almost all influenza A (H3N2) viruses are resistant to them, and they are not effective against influenza B viruses (4, 5). When influenza A (H1N1) viruses predominate, however, these drugs may still be useful if they are used in combination with a neuraminidase inhibitor (Oseltamavir, Zanamivir). Unfortunately, an increasing proportion of influenza A (H1N1) viruses are resistant to oseltamivir, the oral neuraminidase inhibitor, but not to zanamivir. Oseltamavir should be used alone only if local surveillance data indicates that the circulating viruses are Influenza A (H3N2) or Influenza B (4). Zanamivir is a neuraminidase inhibitor that is administered by active inhalation, a method that may not be practical for debilitated patients or for children younger than 7 years of age, and is contraindicated for those with reactive airway disease (Table 3). (Influenza B viruses have decreasing sensitivity to both of these neuraminidase inhibitors in Japan, where oseltamivir is used extensively).

The use of combination therapy which includes ribavirin may be considered. Ribavirin, delivered in aerosol form is licensed for use against respiratory syncytial virus infection and it has been effective in clinical trials involving young adults with influenza A or B infection (Table 3). So, the use of ribavirin in combination with appropriate adamantanes or neuraminidase inhibitors has been proposed in immunocompromised patients with influenza.

Prophylaxis: Short-term prophylaxis is indicated for house-hold contacts of infected persons, especially if they are at high risk for complications. Persons who are vaccinated with the trivalent inactivated vaccine after influenza viruses have started circulating in the community should receive antiviral prophylaxis for 14 days, the time necessary for a serum antibody response to develop. Prophylaxis is not necessary for those who receive live attenuated influenza vaccine; this vaccine confers almost immediate protection. Health care workers who have been exposed to the virus should receive prophylaxis if they have not been immunized.

References

1. Advisory Committee on Immunization Practices (ACIP) 2008. Prevention and Control of Influenza. Morbid Mortality Weekly report 2008;57 (RR-7):1-60.

2. Kwong JC, Stukel TA, Lim J, et al. The effect of universal influenza immunization on mortality and health. PLoS Med 2008;5:e211.

3. Ohmit SE, Monto AS. Symptomatic predictors of influenza virus positivity in children during the influenza season. Clin Infect Dis 2006;43:564-568.

4. Center for Disease Control. Recommendation for the use of Influenza antiviral medications in the setting of Oseltamivir resistance among circulating Influenza A (H1N1) viruses. 2008-2009 Influenza season.

5. Glezen WP. Prevention and Treatment of Seasonal Influenza. N Eng J Med 2008;359:2579-2588.

Tables

Table 1:

ACIP Recommendations for Influenza Vaccination (1)

Persons greater than age 50
Children age 6 months – 18 years

Persons with any one of the following

Underlying medical conditions
Pregnant
Healthcare workers
Household contacts of high risk patients

Table 2: Influenza Vaccines Available in the United States, 2008-2009.*

Vaccine	Trade Name	Manufacturer	Approved Age	Mercury Content *µg per 0.5 ml*	Route
LA/IV	FluMist	Medimmune	2-49 yr (healthy persons)	0	intranasal
TIV	Fluzone	Sanofi Pasteur	≥ 6 mo	25 (multidose vial); 0 (single-dose prefilled syringe)	intramuscular
TIV	Fluvirin	Novartis Vaccines	≥ 4 yr	25.4 (multidose vial); 0 (single-dose prefilled syringe)	intramuscular
TIV	Fluarix	GlaxoSmithKline	≥ 18 yr	<1.0 (single-dose prefilled syringe)	intramuscular
TIV	FluLaval	GlaxoSmithKline	≥ 18 yr	25 (multidose vial)	intramuscular
TIV	Afluria	CSL Biotherapies	≥ 18 yr	25 (multidose vial); 0 (single-dose prefilled syringe)	intramuscular

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Table 3: Antiviral Agents for Treatment of and Prophylaxis against Influenza

Drug	Formulation	Adult Dose		Common Side Effects
		Treatment	Prophylaxis	
Oseltamivir (Tamiflu, Roche)	75-mg capsule	1 capsule twice a day for 5 days	1 capsule/day	Nausea, vomiting
Zanamivir (Relenza, GlaxoSmithKline)	5 mg per inhalation (Diskhaler)	2 inhalations twice a day for 5 days	2 inhalations/day	Bronchospasm
Amantadine (Symmetrel, Endo Pharmaceuticals)	100-mg tablet	1 tablet twice a day for 3-5 days	1 table/day	CNS effects: seizures, insomnia
Rimantadine (Flumadine, Forst Laboratories)	100-mg tablet	1 tablet twice a day for 5 days	1 tablet/day	_
Ribavirin (Virazole, Valeant Pharmaceuticals)	60 mg/ml in reservoir	Aerosol for 2 hr every 8 hr for 5 days or as indicated	Not applicable	_

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