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INFLUENZA ANTIVIRAL AGENTS: NEW RECOMMENDATIONS

Immunization remains the most effective way to prevent influenza, and flu vaccine is now recommended annually for everyone ≥6 months of age.[1] However, antiviral medications also have their place, and CDC has recently updated its recommendations for their use.[2] This issue of the *CD Summary* reviews the highlights of these recommendations.

NEW EFFICACY DATA

More than a decade ago, randomized controlled trials (RCTs) showed that, if given within the first two days of illness, neuraminidase inhibitors could shorten the duration of influenza by about a day.[3–5] Recently, observational studies, although not the gold standard RCT, have been piling up data suggesting that oseltamivir can prevent death from influenza. A prospective cohort study of patients hospitalized with influenza in Toronto found that 103 of 327 adults admitted with influenza were given oseltamivir; after controlling for other factors like age, morbidity, and nursing home residence, those who got the drug were only 21% as likely to have died by day 15 as those who didn't.[6] Similarly, multivariate analysis in a prospective cohort of adults hospitalized with influenza in Hong Kong found that patients who received oseltamivir were only 27% as likely to die in hospital as those who didn't get the drug; outcomes were better with earlier treatment, but better late than never: mortality was significantly reduced with treatment begun up to 96 hours after illness onset.[7]

WHOM TO TREAT

Prompt antiviral treatment — before test results are available — is recommended for any patient with suspected influenza who is hospitalized, has severe or progressive disease, or who is at high risk for complications (Box). Begin treatment as soon as possible. Don't withhold treatment based on a negative rapid test for influenza, because these tests are insensitive: they miss about half the cases.[8]

Use clinical judgment when deciding whether to treat low-risk outpatients; antivirals may shorten the illness if they can be started within 48 hours of onset, but if started later, they are unlikely to be of benefit.

Indications for treatment of influenza with antiviral agents

Confirmed or suspected influenza in patients who
- are hospitalized
- have severe, complicated, or progressive illness, or
- are at higher risk for influenza complications

Persons at higher risk for influenza complications
- children <2 years of age
- adults ≥65 years of age or older
- residents of nursing homes and other chronic-care facilities
- persons that have any of the following conditions or disorders:
  - chronic pulmonary disease, including asthma
  - cardiovascular disease, except for hypertension alone
  - renal disease
  - hepatic disease
  - hematological disease
  - metabolic disorders, such as diabetes
  - neurologic and neurodevelopment conditions
- persons with immunosuppression
- women who are pregnant or postpartum (within 2 weeks after delivery)
- persons less than 19 years of age receiving long-term aspirin therapy
- American Indians or Alaska Natives
- morbidly obese persons

VIRAL SUSCEPTIBILITY

Both neuraminidase inhibitors are effective against currently circulating strains of both influenza A and B. CDC has tested 1,055 strains this season; only one has been resistant to oseltamivir, and none of 805 tested have been resistant to zanamivir.[9]

As for amantadine and rimantadine: forget 'em. Influenza B never was susceptible, and among the influenza A strains that have circulated in recent years, essentially all have been resistant.

CHEMOPROPHYLAXIS

Chemoprophylaxis should not be a substitute for immunization when vaccine is available. In deciding whether to administer prophylaxis following an exposure, consider the patient's exposure history and risk of influenza complications. For most patients, watchful waiting and prompt treatment at the first sign of symptoms is a prudent alternative to chemoprophylaxis.

In some cases, such as during outbreaks among nursing home residents or other high-risk groups, chemoprophylaxis may be the way to go; many randomized clinical trials have demonstrated its efficacy,[10] though how long to continue the prophylactic meds may be problematic. If you have an outbreak on your hands, consult your friendly neighborhood public health department.

DOSE

The Table (*verso*) details dosages for both treatment and chemoprophylaxis of influenza using neuraminidase inhibitors.

FOR MORE INFORMATION

Consult FluBites early and often: www.oregon.gov/DHS/ph/acd/flu/surveil.shtml

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Recommended dosages for influenza antiviral medications

Age (Years)	Zanamavir		Oseltamivir	
	Treatment	Chemoprophylaxis	Treatment	Chemoprophylaxis
1–4	Not Applicable		**Twice**-daily dose, varies by weight*	**Once**-daily dose, varies by weight*
5–6	Not Applicable	10 mg (2 inhalations) **once** daily		
7–9	10 mg (2 inhalations) **twice** daily			
10–12				
≥13			75 mg **twice** daily	75 mg **once** daily

*The dose for treatment and chemoprophylaxis is the same; but give once daily for prophylaxis and twice daily for treatment, as follows:

≥1 year old and ≤15 kg: 30 mg
15.1–23 kg: 45 mg twice daily
23.1–40 kg: 60 mg twice daily
>40 kg: use adult dose

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TRAVEL ADVISORY: VACCINATE!

Immunizations have eliminated or dramatically decreased the incidence of many diseases in the US. A recent event highlighted the importance of timely vaccination to protect both individuals and the community from illness when traveling outside of the United States with children.

A Clark County, Washington, infant returning from a trip to India developed a rash on the day of his return flight to the United States. Being less than 12 months of age, the infant had not yet been immunized with measles-mumps-rubella vaccine (MMR), which is typically given at 12–15 months of age. When ill, the infant was seen in clinic and then again at the outpatient laboratory before being diagnosed with measles. The Clark County Health Department had to issue a press release to notify patients who had been exposed in either of the two medical settings, while the Multnomah County Health Department notified passengers and airline crew of their possible exposure. Staff in both health departments helped exposed patients to assess their immunization status and advised whether vaccination or immune globulin was warranted.

This episode was preventable. Children who will be traveling abroad are advised to get certain shots (e.g., MMR) ahead of the routine schedule; because of his upcoming travel, this infant could have been given MMR as early as 6 months of age.

Parents traveling abroad with young children should be advised to check with their health care provider at least one month before departure. An early immunization can protect the individual child, nip a costly outbreak in the bud, and maybe even save a life. For more information on modifying the immunization schedule for young children and infants before international travel, visit: *wwwnc.cdc.gov/travel/yellowbook/2010/chapter-7/vaccine-recommendations-for-infants-and-children.aspx*..