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# Take these steps to improve your flu season preparedness

The 6 strategies outlined here can help you reduce the risk of illness and limit its severity if contracted.

## PRACTICE RECOMMENDATIONS

- › Recommend influenza vaccination for all patients at least 6 months old unless a specific contraindication exists. **(A)**
- › Recommend pneumococcal vaccination to appropriate patients to reduce the risk for a common complication of influenza. **(A)**
- › Encourage hygiene-based measures to limit infection, including frequent handwashing or use of a hand sanitizer. **(B)**
- › Prescribe oseltamivir to hospitalized influenza patients to limit the duration and severity of infection. **(B)**

### Strength of recommendation (SOR)

- (A)** Good-quality patient-oriented evidence
- (B)** Inconsistent or limited-quality patient-oriented evidence
- (C)** Consensus, usual practice, opinion, disease-oriented evidence, case series

Last year's influenza season was severe enough that hospitals around the United States set up special evaluation areas beyond their emergency departments, at times spilling over to tents or other temporary structures in what otherwise would be parking lots. The scale and potential severity of the annual epidemic can be difficult to convey to our patients, who sometimes say "just the flu" to refer to an illness responsible for more than 170 pediatric deaths in the United States this past year.<sup>1</sup> The Centers for Disease Control and Prevention (CDC) recently updated its 5-year estimates of influenza-related deaths in the United States; influenza mortality ranges from about 12,000 deaths in a mild season (such as 2011-2012) to 56,000 in a more severe season (eg, 2012-2013).<sup>2</sup>

Although influenza cannot be completely prevented, the following strategies can help reduce the risk for the illness and limit its severity if contracted.

## Prevention

### Strategy 1: Vaccinate against influenza

While the efficacy of vaccines varies from year to year, vaccination remains the core of influenza prevention efforts. In this decade, vaccine effectiveness has ranged from 19% to 60%.<sup>3</sup> However, models suggest that even when the vaccine is only 20% effective, vaccinating 140 million people (the average number of doses delivered annually in the United States over the past 5 seasons) prevents 21 million infections, 130,000 hospitalizations, and more than 61,000 deaths.<sup>4</sup> In a case-control study, Flannery et al found that vaccination was 65% effective in preventing laboratory-confirmed influenza-associated death in children over 4 seasons (July 2010 through June 2014).<sup>5</sup>

Deciding who should be vaccinated is simpler than in prior years: Rather than targeting people who are at higher risk (those ages 65 and older, or those with comorbidities), the current CDC recommendation is to vaccinate nearly everyone ages 6 months or older, with limited exceptions.<sup>6,7</sup> (See TABLE 1<sup>8</sup>).

TABLE 1

Contraindications and precautions for the use of influenza vaccines<sup>8</sup>

	Contraindications	Precautions
All influenza vaccines	History of severe allergic reaction to any component of the vaccine	Moderate-to-severe acute illness (may postpone vaccine)
		History of Guillaine-Barré syndrome within 6 wks of prior influenza vaccine
Live attenuated vaccine (FluMist)	Children ages 2-4 yrs with asthma or wheezing in the past 12 mos	Asthma in people 5 yrs of age or older
	Concurrent aspirin or salicylate-containing therapy in children and adolescents	Other underlying medical conditions that might predispose to complications after influenza infection
	Immunocompromised people and their close contacts and caregivers	
	Pregnancy	
	Use of influenza antivirals within previous 48 hrs	

**Formulations.** Many types of influenza vaccine are approved for use in the United States; these differ in the number of strains included (3 or 4), the amount of antigen present for each strain, the presence of an adjuvant, the growth medium used for the virus, and the route of administration (see TABLE 2<sup>9</sup>). The relative merits of each type are a matter of some debate. There is ongoing research into the comparative efficacy of vaccines comprised of egg- vs cell-based cultures, as well as studies comparing high-dose or adjuvant vaccines to standard-dose inactivated vaccines.


Previously, the CDC has recommended preferential use (or avoidance) of some vaccine types, based on their efficacy. For the 2018-2019 flu season, however, the CDC has rescinded its recommendation against vaccine containing live attenuated virus (LAIV; FluMist brand) and expresses no preference for any vaccine formulation for patients of appropriate age and health status.<sup>10</sup> The American Academy of Pediatrics (AAP), however, is recommends that LAIV be used only if patients and their families decline injectable vaccines.<sup>11</sup>

**Timing.** Influenza vaccines are now distributed as early as July to some locations, raising concerns about waning immunity from early vaccination (July/August) if the influenza season does not peak until

February or March.<sup>8,12,13</sup> Currently, the CDC recommends balancing the possible benefit of delayed vaccination against the risks of missed opportunities to vaccinate, a possible early season, and logistical problems related to vaccinating the same number of people in a smaller time interval. Offering vaccination by the end of October, if possible, is recommended in order for immunity to develop by mid-November.<sup>8</sup> Note: Children ages 6 months to 8 years will need to receive their initial vaccination in 2 half-doses administered at least 28 days apart; completing their vaccination by the end of October would require starting the process weeks earlier.

**Strategy 2: Make use of chemoprophylaxis**

Preventive use of antiviral medication (chemoprophylaxis) may be a useful adjunct or alternative to vaccination in certain circumstances: if the patient is at high risk for complications, has been exposed to someone with influenza, has contraindications to vaccination, or received the vaccine within the past 2 weeks. The CDC also suggests that chemoprophylaxis be considered for those with immune deficiencies or who are otherwise immunosuppressed after exposure.<sup>14</sup> Antivirals can also be used to control outbreaks in long-term care facilities; in these cases, the recommended regimen is daily administration for at least


INSTANT POLL

What percentage of your patients decline the flu vaccine each year?

<25%

25%

50%

>50%

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**TABLE 2**

**Influenza vaccine options for the upcoming season<sup>9</sup>**

Type of vaccine	Brands available	Approved age range
Live attenuated virus	FluMist Quadrivalent	2-49 yrs
Inactivated virus, egg-derived	Afluria	≥5 yrs*
	Fluvirin	≥4 yrs
	Afluria Quadrivalent	≥5 yrs
	Fluarix Quadrivalent	≥6 mos
	FluLaval Quadrivalent	≥6 mos
	Fluzone Quadrivalent	≥6 mos*
Inactivated virus, cell culture	Flucelvax Quadrivalent	≥4 yrs
Recombinant	Flublok	≥18 yrs
	Flublok Quadrivalent	≥18 yrs
Adjuvanted inactivated virus	Fluad	≥65 yrs
High-dose inactivated virus	Fluzone High-Dose	≥65 yrs
Intradermal inactivated virus	Fluzone Intradermal Quadrivalent	18-64 yrs

\*Different packaging forms have different recommended ages; widest age ranges are shown.

2 weeks, continuing until at least 7 days after the identification of the last case.<sup>14</sup> Oseltamivir (Tamiflu) and zanamivir (Relenza) are the recommended prophylactic agents; a related intravenous medication, peramivir (Rapivab), is recommended for treatment only (see TABLE 3<sup>14</sup>).

**Strategy 3: Prevent comorbidities and opportunistic infections**

Morbidity associated with influenza often comes from secondary infection. Pneumonia is among the most common complications, so influenza season is a good time to ensure that patients are appropriately vaccinated against pneumococcus, as well. Pneumococcal conjugate vaccine (Prevnar or PCV13) is recommended for children younger than 2 years of age, to be administered in a series of 4 doses: at 2, 4, 6, and 12-15 months. Vaccination with PCV13 is also recommended for those ages 65 or older, to be followed at least one year later with pneumococcal polysaccharide vaccine (Pneumovax or PPSV23).<sup>15</sup> Additional doses of PCV13, PPSV23, or both may be indicated, depending on health status.

**Strategy 4: Encourage good hygiene**

The availability of immunizations and anti-

virals does not replace good hygiene. Frequent handwashing reduces the transmission of respiratory viruses, including influenza.<sup>16</sup> Few studies have evaluated the use of alcohol-based hand sanitizers, but available evidence suggests they are effective in lowering viral transmission.<sup>16</sup>

Barriers, such as masks, gloves, and gowns, are helpful for health care workers.<sup>16</sup> Surgical masks are often considered more comfortable to wear than N95 respirators. It may therefore be welcome news that when a 2009 randomized study assessed their use by hospital-based nurses, masks were non-inferior in protecting these health care workers against influenza.<sup>17</sup>

■ **Presenteeism**, the practice of going to work while sick, should be discouraged. People at risk for influenza may wish to avoid crowds during flu season; those with symptoms should be encouraged to stay home and limit contact with others.

**Treatment**

**Strategy 1: Make prompt use of antivirals**

Despite available preventive measures, tens of millions of people in the United States develop influenza every year. Use of antiviral medication, begun early in the course of ill-

TABLE 3

Influenza antivirals for prophylaxis and treatment<sup>14\*</sup>

	Osetamivir (Tamiflu) oral	Zanamivir (Relenza) inhaled	Peramivir (Rapivab) intravenous
<b>Prevention</b>	<b>7-day course</b>	<b>7-day course</b>	<b>Not indicated for prevention</b>
	<3 mo Only if critical need 3-12 mo 3 mg/kg/dose, once daily ≤15 kg 30 mg/d 15-23 kg 45 mg/d 23-40 kg 60 mg/d >40 kg 75 mg/d Adults 75 mg/d	Ages ≥5 yrs Two 5-mg inhalations once daily	
<b>Treatment</b>	<b>5-day course</b>	<b>5-day course</b>	<b>Single dose</b>
	<1 yr 3 mg/kg/dose, twice daily ≤15 kg 30 mg BID 15-23 kg 45 mg BID 23-40 kg 60 mg BID >40 kg 75 mg BID Adults 75 mg BID	Ages ≥7 yrs Two 5-mg inhalations twice daily	Ages 2-12 yrs 12 mg/kg dose, 600 mg max, infused over at least 15 min  Ages ≥13 yrs 600 mg dose, infused over at least 15 min
<b>Cautions</b>	AEs: Nausea, vomiting, headache. Reports of serious skin reactions	Not recommended for hospitalized patients. Caution in asthma, COPD, other respiratory disease. AEs: bronchospasm, sinusitis, dizziness, ENT infections, allergic facial/oropharyngeal edema, skin rash	Not recommended for hospitalized patients. AE: diarrhea

AE, adverse effect; CDC, Centers for Disease Control & Prevention; COPD, chronic obstructive pulmonary disease; ENT, ear, nose, and throat; FDA, Food & Drug Administration.

\*All of these medications have had post-marketing reports of transient neuropsychiatric events, including self-injury and delirium. Dosing changes for oseltamivir and peramivir use in patients with renal impairment are not shown. Use of oseltamivir to treat influenza in infants younger than 14 days of age, or for prophylaxis in infants 3 months to 12 months, are not FDA-approved indications; however, these uses are recommended by the CDC.

ness, can reduce the duration of symptoms and may reduce the risk for complications.

■ **The neuraminidase inhibitor (NI) group** of antivirals—oseltamivir, zanamivir, and peramivir—is effective against influenza types A and B and current resistance rates are low.

■ **The adamantane family** of antivirals, amantadine and rimantadine, treat type A only. Since the circulating influenza strains in the past several seasons have demonstrated resistance >99%, these medications are not currently recommended.<sup>14</sup>

■ **NIs reduce the duration** of influenza symptoms by 10% to 20%, shortening the illness by 6 to 24 hours.<sup>18,19</sup> In otherwise healthy

patients, this benefit must be balanced against the increased risk for nausea and vomiting (oseltamivir), bronchospasm and sinusitis (zanamivir), and diarrhea (peramivir). In adults, NIs reduce the risk for lower respiratory tract complications and hospitalization. A 2015 meta-analysis by Dobson et al found a relative risk for hospitalization among those prescribed oseltamivir vs placebo of 37%.<sup>18</sup>

In the past, antivirals were used only in high-risk patients, such as children younger than 2 years, adults older than 65 years, and those with chronic health conditions.<sup>14</sup> Now, antivirals are recommended for those who are at higher risk for complications (see TABLE 4),

➤  
Offering  
vaccination  
by the end  
of October,  
if possible, is  
recommended  
in order for  
immunity to  
develop by  
mid-November.

TABLE 4

## Patients at higher risk for complications from influenza<sup>14</sup>

The CDC recommends antiviral treatment for suspected or confirmed influenza in people "at higher risk for complications." High-risk groups include:	
<b>Age</b>	<ul style="list-style-type: none"> <li>• Children &lt;2 yrs</li> <li>• Adults ages ≥65 yrs</li> <li>• People &lt;19 yrs who are receiving long-term aspirin therapy</li> </ul>
<b>Race/ethnicity</b>	<ul style="list-style-type: none"> <li>• American Indians/Alaska natives</li> </ul>
<b>Setting</b>	<ul style="list-style-type: none"> <li>• Residents of nursing homes and other chronic care facilities</li> </ul>
<b>General health status</b>	<ul style="list-style-type: none"> <li>• People with immunosuppression, such as that caused by medications or by HIV infection</li> <li>• Women who are pregnant or postpartum (within 2 wks of delivery)</li> <li>• People who are extremely obese (ie, body mass index is ≥40)</li> </ul>
<b>Comorbid conditions</b>	<ul style="list-style-type: none"> <li>• Chronic pulmonary disorders (eg, asthma)</li> <li>• Cardiovascular disease (except hypertension alone)</li> <li>• Renal disorders</li> <li>• Hepatic disorders</li> <li>• Hematologic disorders (eg, sickle cell disease)</li> <li>• Metabolic disorders (eg, diabetes)</li> <li>• Neurologic and neurodevelopmental conditions (eg, disorders of the brain, spinal cord, peripheral nerve, and muscle [such as cerebral palsy], epilepsy [seizure disorders], stroke, intellectual disability, moderate-to-severe developmental delay, muscular dystrophy, or spinal cord injury)</li> </ul>

CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus.

those with "severe, complicated, or progressive illness," and hospitalized patients.<sup>14</sup>

Antiviral treatment may have some value for hospitalized patients when started even 5 days after symptom onset. Treatment may be extended beyond the usual recommendations (5 days for oseltamivir or zanamivir) in immunosuppressed patients or the critically ill. Additionally, recent guidelines include consideration of antiviral treatment in outpatients who are at normal risk if treatment can be started within 48 hours of symptom onset.<sup>14</sup>

The CDC currently recommends use of oseltamivir rather than other antivirals for most hospitalized patients, based on the availability of data on its use in this setting.<sup>14</sup> Intravenous peramivir is recommended for patients who cannot tolerate or absorb oral medication; inhaled zanamivir or IV peramivir are preferred for patients with end-stage renal disease who are not undergoing dialysis (see TABLE 3).<sup>14</sup>

### Strategy 2: Exercise caution when it comes to supportive care

There are other medications that may offer symptom relief or prevent complications, especially when antivirals are contraindicated or unavailable.

■ **Corticosteroids** are recommended as part of the treatment of community-acquired pneumonia,<sup>20</sup> but their role in influenza is controversial. A 2016 Cochrane review<sup>21</sup> found no randomized controlled trials on the topic. Although the balance of available data from observational studies indicated that use of corticosteroids was associated with increased mortality, the authors also noted that all the studies included in their meta-analysis were of "very low quality." They concluded that "the use of steroids in influenza remains a clinical judgement call."

■ **Statins** may be associated with improved outcomes in influenza and pneumonia. Studies thus far have given contradictory

results,<sup>22,23</sup> and a planned Cochrane review of the question has been withdrawn.<sup>24</sup>

■ **Over-the-counter medications**, such as aspirin, acetaminophen, and ibuprofen are often used to manage the fever and myalgia associated with influenza. Patients should be cautioned against using the same ingredient in multiple different branded medications. Acetaminophen, for example, is not limited to Tylenol-branded products. To avoid Reye's syndrome, children and teens with febrile illness, such as influenza, should not use aspirin. **JFP**

#### CORRESPONDENCE

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