Practical Approaches to Influenza

For Primary Care Professionals

CALIFORNIA ACADEMY OF FAMILY PHYSICIANS

Sponsored by The California Academy of Family Physicians

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This activity is designed for family physicians, and other primary care physicians and professionals. It is developed to assist in the prevention and treatment of seasonal influenza.

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This activity is supported by an educational grant from Roche.

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Seasonal influenza epidemics typically occur during the winter and are a major public health burden. Influenza is one of the most common illnesses among patients of primary care physicians, with as many as 1 in 5 adults infected. Each year in the United States, influenza causes 36,000 preventable deaths and 226,000 hospitalizations. Although influenza occurs in all age groups, rates of infection are highest among children, who then act as a reservoir for infection to the family. Rates of serious illness are highest among adults aged ≥65 years, children aged <2 years, and persons of any age who have a medical condition that increases their risk for complications.

LEARNING OUTCOMES:

At the conclusion of this activity, participants should be able to:

1. Identify key populations at high risk, and triage those populations for vaccination and other preventive measures
2. Develop a vaccination program, and effectively vaccinate patients for influenza
3. Differentiate flu symptoms from similar presentations, and appropriately counsel patients on treatment options
4. Investigate office systems changes with the potential to improve or enhance vaccination and treatment program, including patient registries
5. Incorporate new vaccinations and pharmacologic agents for the treatment of influenza

Recommendation	Evidence Grade	Website
The Canadian Task Force on Preventive Health Care recommends influenza vaccination in healthy adults (A recommendation) & children (A recommendation).	A=there is good evidence to recommend the clinical preventive action.	www.guideline.gov/summary/summary.aspx?doc_id=6525&nbr=004091&string=influenza
The Canadian Task Force on Preventive Care found good evidence to support neuraminidase inhibitor prophylaxis in the household setting if it can be initiated within 36-48 hours of symptom onset in the index case (A recommendation).		
The American Academy of Pediatrics Committee on Infectious Diseases recommends that healthcare professionals should be diligent with their efforts, through tracking & reminder systems, to ensure that children traditionally at high risk of severe disease & complications from influenza infection receive annual influenza immunization. High-risk children & adolescents who should receive priority for influenza immunization are those with the following (evidence grade II-3): • Asthma or other chronic pulmonary diseases, such as cystic fibrosis • Hemodynamically significant cardiac disease • HIV infection • Sickle cell anemia & other hemoglobinopathies • Diseases requiring long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki disease • Chronic renal dysfunction • Chronic metabolic disease, such as diabetes mellitus Other individuals who should receive priority for influenza immunization include women who will be in their second or third trimester of pregnancy during influenza seasons & persons who are in close contact with high-risk children (evidence grade II-3), including all healthcare professionals in contact with pediatric patients in hospital & outpatient settings & household contacts & out-of-home caregivers of high-risk individuals of any age.	II-3=evidence obtained from multiple time series with or without the intervention, or dramatic results in uncontrolled experiments.	www.guideline.gov/summary/summary.aspx?ss=15&doc_id=4860&nbr=3501
The American Academy of Pediatrics Committee on Infectious Diseases recommends influenza immunization of household contacts & out-of-home caregivers of children younger than 24 months (evidence grade III). Immunization of close contacts of children younger than 6 months may be particularly important, because these infants will not be immunized.	III=opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	
The Healthcare Infection Control Practices Advisory Committee (HICPAC) & the Advisory Committee on Immunization Practices (ACIP) recommend offering influenza vaccine annually to all eligible healthcare personnel to protect staff, patients, & family members & to decrease absenteeism. Use of either available vaccine (inactivated & live, attenuated influenza vaccine [LAIV]) is recommended for eligible persons. During periods when inactivated vaccine is in short supply, use of LAIV is especially encouraged when feasible for eligible healthcare personnel (category IA).	IA=strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.	www.guideline.gov/summary/summary.aspx?doc_id=8697&nbr=004844&string=influenza
The Healthcare Infection Control Practices Advisory Committee (HICPAC) & the Advisory Committee on Immunization Practices (ACIP) recommend providing influenza vaccination to healthcare professionals at the work site & at no cost as one component of employee health programs. Use strategies that have been demonstrated to increase influenza vaccine acceptance, including vaccination clinics, mobile carts, vaccination access during all work shifts, & modeling & support by institutional leaders (category IB). Obtain a signed declination from healthcare personnel who decline influenza vaccination for reasons other than medical contraindications (category II).	IB=strongly recommended for implementation & supported by certain experimental, clinical, or epidemiologic studies & a strong theoretic rationale; II=suggested for implementation & supported by suggestive clinical or epidemiologic studies, or a theoretical rationale.	
The American Academy of Family Physicians recommends immunizing all persons aged 50 years & older for influenza.	Recommend=although evidence exists which demonstrates net benefit, either the benefit is only moderate in magnitude or the evidence supporting a substantial benefit is only fair. The intervention is perceived to be cost effective & acceptable to most patients.	www.guideline.gov/summary/summary.aspx?doc_id=8185&nbr=004570&string=influenza
Patient reminder & recall systems in primary care settings are effective in improving immunization rates within developed countries. All types of reminder were effective (postcards, letters, telephone, or autodialer calls), with telephone being most effective, but most costly.	Systematic review of randomized controlled trials, controlled before & after studies, & interrupted time series studies written in English found increase in immunization rates due to reminders in the range of 1-20 percentage points.	www.cochrane.org/reviews/en/ab003941.html

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EPIDEMIOLOGY

SEASONAL INFLUENZA

Seasonal influenza epidemics typically occur during the winter and are a major public health burden. Influenza is one of the most common illnesses among patients of primary care physicians (PCPs), with as many as one in 5 adults infected.[1] Each year in the United States, influenza causes 36,000 preventable deaths and 226,000 hospitalizations.[2] Although influenza occurs in all age groups, rates of infection are highest among children, who then act as a reservoir for infection to the family. Rates of serious illness are highest among adults aged ≥65 years, children aged <2 years, and persons of any age who have a medical condition that increases their risk for complications.[2]

The very young (<2 years) and very elderly (≥65 years) are at the highest risk for hospitalization.[2] Among children aged <5 years, hospitalization rates range from 100/100,000 children for those without high-risk conditions to 500/100,000 children for those with an underlying condition that puts them at an increased risk (eg, preterm baby with chronic lung disease).[2] Influenza-related deaths of adults aged ≥65 years account for ≥90% of deaths attributed to influenza.[2] The mortality rate is 0.4 to 0.6/100,000 among persons aged 0 to 49 years, 7.5/100,000 among those aged 50 to 64 years, and 98.3/100,000 among persons aged ≥65 years.[2]

INFLUENZA VIRUS

In the last 30 years, 3 kinds of readily transmissible influenza virus, which are responsible for seasonal influenza, have circulated globally among humans: 2 type A viruses (H3N2 and H1N1) and a type B virus.[2] More recently, the influenza A virus subtype H1N2 emerged, probably after genetic reassortment between H1N1 and H3N2 viruses (antigenic shift).[2] Both influenza A and B viruses are further separated into groups based on antigenic characteristics.[2] New influenza virus variants occur from frequent antigenic change (antigenic drift) by point mutations that arise during viral replication; influenza B viruses undergo antigenic drift less rapidly than influenza A viruses.[2] Frequent development of antigenic variants through antigenic drift is the virologic basis for seasonal epidemics and the reason for incorporating new strains in each year's influenza vaccine, which is why annual vaccination is necessary.[2] Antibody against one influenza type or subtype confers limited or no protection against another type or subtype, and antibody to one antigenic variant of influenza virus might not completely protect against a new variant of the same type or subtype.[2]

PANDEMIC INFLUENZA

Pandemic influenza occurs rarely (3 times in the 20th century, last in 1968), but is usually associated with more severe illness and greater risk of death than seasonal influenza. The original reservoir of influenza A viruses is water fowl, among which circulate a large number of subtypes. The type A H5N1 avian influenza virus currently circulating in Asia and some other regions is a potential pandemic threat, but has been transmitted from birds to humans on a limited basis and does not readily transmit from person to person.[3] The emergence of a readily transmissible form of H5N1 among humans would pose a threat to global public health. This could occur through genetic reassortment (antigenic shift) within an avian or animal host involving simultaneous infection with 2 different strains of influenza A virus (eg, H3N2 and H5N1). Alternatively, a series of mutations in the H5N1 avian virus (antigenic drift) could also create a new subtype that can be transmitted between people. Because most people will not have immunity to a new subtype and it will take time to produce a vaccine against this virus, pandemic influenza would probably result; however, it is impossible to say whether or when this virus will cause a pandemic.[3]

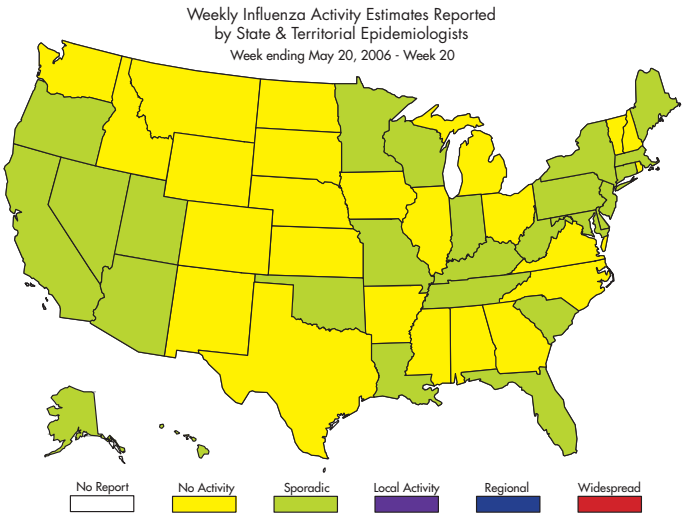
The extensive media coverage around the avian influenza may cause anxiety among some patients. PCPs should validate patients' anxiety, but put into perspective the low chance of infection and stress that surveillance in the United States is ready to detect any avian influenza viruses that begin to circulate. Patients' anxiety can be redirected toward preventing seasonal influenza by encouraging annual vaccination. There are also many reasons beyond an influenza pandemic for emergency preparedness measures that anticipate disruption of essential services; advise patients to always be prepared for a 2-week period with food, water, cash, batteries, and essential household items.

IDENTIFYING INFLUENZA ILLNESS

Appropriate treatment of patients with influenza and measures to prevent the infection of close contacts depend on timely diagnosis. Uncomplicated influenza is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (eg, fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis).[2] However, respiratory illnesses caused by influenza viruses are difficult to distinguish from illnesses caused by other respiratory pathogens (eg, rhinoviruses, adenoviruses, parainfluenza, coronavirus) on the basis of signs and symptoms alone.[2,4] In addition, the elderly frequently have atypical signs and symptoms (eg, only low-grade fever, lassitude, confusion, and nasal obstruction), so diagnosing influenza in this population can be even more difficult.[5]

When faced with a patient with influenza-like illness, a physician must be able to estimate the probability of influenza as opposed to other infections, which guides the need for further diagnostic testing and treatment.[4] The sensitivity and predictive value of clinical definitions vary depending on the circulation level of other respiratory pathogens and influenza, with greater predictive value during the influenza season.[2] When influenza circulates within the community, patients with an influenza-like illness who have both cough and fever (≥37.8°C) within 48 hours of symptom onset are likely to have influenza (80% positive predictive value),[6] but outside the influenza season the predictive value falls. The frequency of infections attributable to the various viral agents that cause influenza-like illness varies geographically and from week to week throughout the influenza season.[4] Weekly epidemiologic reports from the CDC (www.cdc.gov/flu/weekly/ and

Figure 1. Example of weekly activity estimates reported by the CDC



www.cdc.gov/mmwr/) provide physicians with laboratory surveillance data for the predominant circulating types, subtypes, and strains of influenza viruses, influenza-like illness frequency, and regional variability of outbreaks (Figure 1). Similar reports are available from state health departments, which may also separately report pediatric and adult data. PCPs should use this data to ascertain if influenza is circulating in their communities and which populations are most likely to be affected. Based on this information, and depending on the patient's vaccination status and presence of comorbid conditions, some physicians might choose to treat empirically with antiviral drugs while others might choose testing.[4]

Diagnostic tests available for influenza include viral culture, serology, rapid antigen testing, polymerase chain reaction, and immunofluorescence assays.[2] The rapid diagnostic tests for influenza viruses that are approved for use in outpatient settings differ in the types of influenza they detect and whether they can distinguish between influenza types.[2]

Who to Test: The decision to use rapid diagnostic testing at the point of care can vary throughout the influenza season, depending on the patient's age, the presence of comorbid conditions, the setting, the prevalence of disease in the community, and whether or not a definitive diagnosis would impact the patient's treatment.[4] In some situations, diagnostic testing can aid clinical judgment and help guide treatment decisions, but all patients with influenza-like illness do not warrant testing, particularly when not considering treatment.

At the beginning of the season it may be appropriate to use rapid point-of-care testing for the first few patients who present to the office with influenza-like illness to establish that influenza is circulating in your population, but testing is not particularly helpful for an adult patient with influenza-like illness at the height of influenza season. However, the diagnosis of influenza in the pediatric population requires definitive diagnostic tests to distinguish it from respiratory syncytial virus (RSV) infection, particularly in children aged less than 2 years or high-risk children who did not receive palivizumab. A nasal swab applied to a glass plate and stained with monoclonal antibodies can rapidly distinguish RSV from influenza A or B infection to guide treatment decisions.

VACCINATION

Annual influenza vaccination is the primary method to prevent seasonal influenza and its complications. The trivalent inactivated influenza vaccines and the live attenuated influenza vaccine (LAIV) are available for use in the United States.[2] Vaccine virus strains are updated annually based on global surveillance for circulating influenza viruses.[2] Viruses for both vaccines are initially grown in eggs. The inactivated vaccine virus is made noninfectious by a similar process used during the second World War, but is now more potent and purified, and therefore no longer reactogenic. Inactivated influenza vaccine cannot produce signs or symptoms of influenza infection and is not associated with significant side effects. LAIV contains live attenuated virus and therefore has the potential to produce mild upper respiratory signs or symptoms. LAIV is administered intranasally, whereas inactivated influenza vaccine is administered by intramuscular injection. Inactivated influenza vaccine is approved for persons aged ≥6 months, including those with chronic medical conditions.[2] LAIV is approved for use among healthy persons aged 5 to 49 years (including healthcare workers) who are not in contact with immunocompromised hosts, and is an alternative for people who are afraid of needles.

The effectiveness of the inactivated influenza vaccine depends on the age and immunocompetence of the recipient, the degree of similarity between the viruses in the vaccine and those in circulation, and the outcome being measured (eg, prevention of culture-positive influenza virus illness, prevention of influenza-associated hospitalizations or deaths, seroconversion to vaccine serotypes, or prevention of seroconversion to circulating influenza virus subtypes).[2] The vaccine is generally 70% to 90% effective in preventing seasonal influenza among healthy adults aged <65 years, and also decreases work absenteeism and use of healthcare resources in this population.[2] Older persons (aged ≥65 years) can have lower postvaccination antibody titers and may remain susceptible to influenza infection; however, vaccination among adults aged ≥65 years helps prevent secondary complications from influenza and reduces their risk for influenza-related hospitalization and death.[2] Among older persons not living in nursing homes, the vaccine has an efficacy of 58% against influenza respiratory illness and is 30% to 70% effective in preventing hospitalization. Among older persons who reside in nursing homes, the effectiveness in preventing influenza illness ranges from 30% to 42%, but the

vaccine can be 50% to 60% effective in preventing influenza-related hospitalization or pneumonia and 80% effective in preventing influenza-related death.[2,7,8]

The LAIV elicits a local mucosal immune response in the nasal passages in addition to a systemic immune response. It is more than 90% effective against culture-confirmed influenza, reduces episodes of otitis media—a frequent complication of influenza in young children—by 30%, and decreases antibiotic use.[9] The current LAIV formulation requires frozen storage, so breaking the cold chain could decrease the antigenicity of the vaccine.

Improved vaccines with a higher level of protection are needed. Technologies such as cell-based cultures that allow rapid and mass production of vaccines are long-term solutions, particularly if facing a new virus strain. However, even though the existing vaccines are not completely effective in preventing influenza infection, they do prevent complications and death, but are underutilized.

RECOMMENDATIONS FOR VACCINATION

Changes in the Centers for Disease Control and Prevention (CDC) recommendations for who to vaccinate generally increase the target population each year. For the 2006-2007 influenza season, persons for whom annual influenza vaccination is recommended by the Advisory Committee on Immunization Practices (ACIP) are shown in Box 1.[2]

The recommendation for influenza vaccination in children was extended from 6-23 months to 6-59 months because children are the reservoir of infection for adults in the home environment, including the high-risk elderly population and an increasing number of immunocompromised persons. A study demonstrated that use of the 7-valent pneumococcal conjugate vaccine in children substantially reduced the incidence of invasive pneumococcal disease among older adults caused by those 7 conjugate vaccine serotypes.[10] In contrast, disease caused by the 16 other serotypes in the 23-valent pneumococcal vaccine used in adults did not decline over time.[10]

Vaccination is recommended for persons aged 50-64 years because this group has an increased prevalence (34%) of persons with high-risk conditions, but who have low rates of vaccination.[2] Persons aged 50-64 years without high-risk conditions also benefit from vaccination in the form of decreased rates of influenza illness, decreased work absenteeism, and decreased need for medical visits and antibiotics.[2] In addition, 50 years is an age when many other preventive services begin.

Recommendations have also been extended beyond protecting the person who receives the vaccine to people who are in households or frequent contact with patients who are at risk of complications; for example, healthcare workers, most of whom are not at risk for complications but can serve as a reservoir of infection for their patients; and those in contact with children under 6 months of age or elderly adults.

WHEN TO VACCINATE

The optimal time for vaccination in most populations is usually during October-November. It is thought to be unlikely that seasonal influenza vaccine will be in short supply again, as has occurred in the past, but if supplies of vaccine are not adequate, ACIP recommends that physicians focus their vaccination

BOX 1: PERSONS FOR WHOM INFLUENZA VACCINATION IS RECOMMENDED BY THE ACIP

- Children aged 6-59 months
- Women who will be pregnant during the influenza season
- Persons aged ≥50 years
- Children and adolescents (aged 6 months to 18 years) who receive long-term aspirin therapy and might therefore be at risk for Reye syndrome after influenza infection
- Adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma (hypertension not considered a high-risk condition)
- Adults or children who required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or imuno-deficiency (including that caused by medications or HIV)
- Adults or children who have any condition (eg, cognitive dysfunction, spinal cord injury, seizure disorder, or other neuromuscular disorder) that can compromise respiratory function or the handling of respiratory secretions, or that can increase the risk for aspiration
- Residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions
- Persons who live with or care for persons at high risk for influenza-related complications, including healthy household contacts and caregivers of children aged 0-59 months
- Healthcare workers

efforts in October primarily on persons aged ≥50 years, persons aged <50 years at increased risk for influenza-related complications (including children aged 6-59 months), household contacts of persons at high risk, and healthcare workers.[2] In addition, the CDC will issue guidelines tiering who should receive vaccine first in a shortage situation based on the circulating influenza virus strain that season; for example, most influenza in nursing homes is caused by influenza A H3N2. Efforts to vaccinate other persons who wish to decrease their risk for infection should not begin until November, unless such persons request vaccination in October if vaccine supplies are sufficient. Influenza vaccine should be offered throughout the influenza season (through March), even after influenza activity has been documented in the community.[2]

Given sufficient supply of vaccine, the United States is moving toward universal vaccination because it can be difficult to identify everyone who is in close contact with high-risk persons. Immunizing the entire population will invoke herd immunity and drastically slow the spread of an epidemic influenza strain.

VACCINATION COVERAGE

Despite recommendations for influenza vaccination, rates of vaccination are low amongst many groups; Figure 2 shows coverage levels among adult target population groups, none of which exceed 65%, and as low as 13% to 15% among pregnant women and household contacts (aged 18-49 years) of high-risk persons.[2] Although annual vaccination is recommended for healthcare workers and has been shown to reduce work absenteeism and cause fewer deaths among nursing home patients, the coverage level is only 42%.[2] Vaccination levels are also low among children at increased risk for complications;[2] for example, studies have documented influenza vaccination rates of 5% to 25% in children with asthma.[11-14] This may occur because families and individuals may have beliefs and barriers to influenza vaccination, which PCPs should take the time to identify and address.

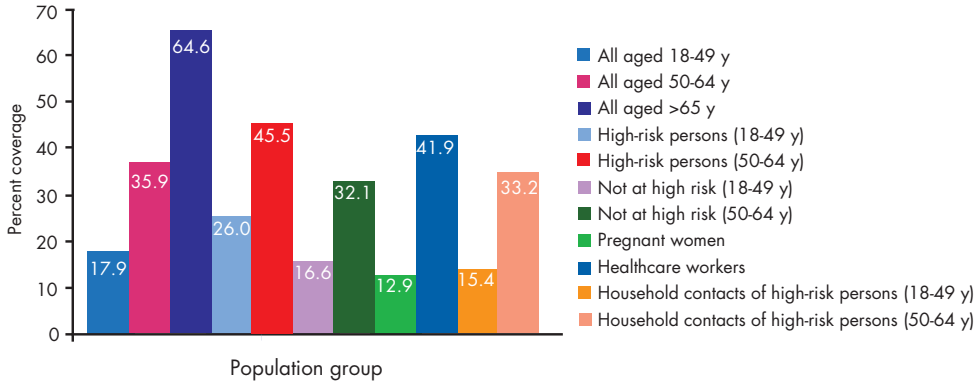
OVERCOMING BARRIERS TO VACCINATION

Healthcare Workers: Vaccination of healthcare workers is a high priority, but only 42% of healthcare workers are immunized each year.[2] Without a universal mandate by law, worksite policies should facilitate access to vaccination by making it more convenient for healthcare workers.[15] This could be done by having a single staff member responsible for vaccinating all the office staff, setting up an immunization booth where staff members clock-in, or using a vaccine cart to deliver vaccine to healthcare workers in their offices. Emphasizing that the primary purpose of vaccinating healthcare workers is to protect patients may help persuade some staff who are otherwise resistant.

Safety Concerns: Parents have reported safety as a concern about influenza vaccination, particularly in developing children.[16] Concern that the small amounts of the mercury-containing preservative thimerosal found in some inactivated influenza vaccines will damage children's nervous systems can reduce pediatric immunization rates. However, there has been no scientific link between the minute amounts of thimerosal in some vaccines with developmental disorders such as autism, and any theoretical risk from thimerosal is outweighed by the benefits from influenza vaccination. Both thimerosal-free and thimerosal-containing vaccines are appropriate for children.

Other patient concerns about safety may also overstate the potential severity; for example, concerns about Guillain-Barré syndrome (GBS), particularly among people who remember the increase in GBS that occurred among recipients of the swine influenza vaccine in 1976 and 1977. However, it is uncertain whether there is a true connection between influenza vaccine and GBS, with most studies showing no or minimal (1/1,000,000) association.[17,18] In addition to these cases being rare,

Figure 2. Influenza vaccination coverage levels among adult target population groups – National Health Interview Survey, United States, 2004[2]



influenza illness itself is associated with central nervous system syndromes, including GBS.

Misconceptions: The belief that influenza vaccination can cause influenza is a barrier to vaccination.[16,19] There is no evidence that either type of vaccine can cause influenza. A minority of people experience minor upper respiratory symptoms (nasal congestion or runny nose) the first time they receive LAIV.[20] In the past, the inactivated vaccine sometimes produced fever and aching because of foreign protein, but the current, more purified, vaccine causes very few side effects.

People use the term "flu" to erroneously refer to a spectrum of upper respiratory infections.[21] Educate patients that respiratory and other illnesses temporally associated with vaccination are not necessarily influenza or related to the vaccine. For example, in one study many parents incorrectly believed that influenza manifests as gastrointestinal symptoms, which may cause parents to think that diarrhea or vomiting temporally associated with vaccination is a sign of vaccine failure or is the result of vaccination.

As well as believing that influenza-like illness is a side effect of the immunization, parents can have a wide range of misconceptions regarding influenza vaccination, including that:[19,21,22]

- Side effects of the immunization are worse than the illness itself
- Children get more immunizations than necessary ("immunization fatigue"), which could weaken their immune system
- Their child is not at risk from influenza illness or its complications
- Their child's doctor had inadequate vaccine supplies
- Their child being sick interfered with vaccination
- They did not know whether vaccination was recommended for their child
- Children not in day care are not particularly susceptible to influenza
- Children >6 months of age are still too young for vaccination

PCPs can increase vaccination rates among children, who are often the "epicenter" of influenza outbreaks, by educating parents. This includes stressing the real dangers posed by influenza in even healthy young children and emphasizing that the benefits of annual influenza immunization outweigh any risks for almost everybody.[19,21] Studies have shown that a physician recommendation for influenza vaccination is a positive predictor for immunization among both healthy young children and children with chronic medical conditions.[19,21,23,24]

If a patient or parent refuses the influenza vaccination, PCPs should investigate and address any obstacles or misconceptions that they may have. PCPs can also use other rationalizations for giving the vaccine; for example, by asking about family members who are sick, young, or old, and stressing that vaccination will help protect these at-risk populations. There may also be cultural or language barriers to certain patient populations receiving the influenza vaccine. Overcoming this may require a clear explanation of the symptoms of influenza, with no or limited use of jargon, to distinguish influenza from other illnesses, and an emphasis on the benefits of vaccination.

Opportunities to Vaccinate: Family physicians may be responsible for vaccinating the entire family, so if family members are present for a well child visit for example, they should take the opportunity to immunize the entire group whenever possible. But all PCPs can play a role for the whole family by taking an interest in a patient's child and ensuring that he or she will see his or her family physician or pediatrician for vaccination, or vice versa for a pediatrician, by taking an interest in the parents.

Prime Patients: Throughout the year, PCPs can prime the young, the elderly, and any patient with risk factors (eg, diabetes, heart disease, renal insufficiency, chronic obstructive pulmonary disease [COPD], asthma) that they and their family and close contacts will need to be vaccinated in the fall. Every preventive medicine update, regardless of the time of year, is also an opportunity to talk about immunizations.

Visual Reminders: Simple visual reminders can raise patients' awareness and comfort level around influenza vaccination in order to increase vaccination rates. For example, post signs that communicate the importance of preventing influenza; or have the staff members, such as nurses or receptionists, wear a yellow smiley face that says "I've had my flu shot, Have you?" which will also be given to any person who receives the immunization.

Policies: In the elderly community, policies and procedures should be in place to immunize everyone in the nursing home. Standing orders for influenza vaccination of nursing home residents and home health agencies, requirements to document refusals, and

- minimal consent requirements for vaccinations can improve immunization coverage.[2,25] It is equally important to vaccinate caregivers, nurses, nurse assistants, housekeepers, and food service personnel working in nursing homes—these employees often have young children who are usually the first to become ill in an epidemic.[5]

  In the clinic, simple systems can be put into place to increase vaccination rates; for example, preprint a message, "please call our office to schedule your flu vaccination," on statements sent from the office in September or use a stamp on the chart of high-risk patients, so that anyone who sees the patient during the influenza season is aware that influenza vaccination is indicated. Another example is changing the flow sheet for prenatal care of obstetric patients to include influenza vaccination for those who visit during the influenza season, and a reminder to spread similar recommendations to family members of pregnant patients.

  Outreach: PCPs are responsible for reaching out to people who may not come into the clinic and for educating their communities. This can be done by involving people who have an active role in the community (eg, parent-teacher associations, religious leaders) to build awareness and a community ownership around influenza vaccination. In addition to administering vaccine to persons during routine healthcare visits, coverage can be increased by offering vaccination at pharmacies, grocery stores, workplaces, schools, churches, or other locations in the community. It is also helpful to schedule extensive influenza clinic hours, including weekends and evenings. For underserved populations without health insurance, vaccination may be available through state health departments at minimal or no cost.

- Registries can be used to improve vaccination levels by identifying patients at risk for influenza-related complications in order to mail postcard reminders or place telephone calls to those identified.[26] The implementation of a computerized reminder system has been shown to increase rates of vaccination among children with asthma (from 5% to 32% in one study, and by 80% in another).[11-14] However, electronic health records are not required to develop a registry; basic computer software or even a simple card system can be used to identify high-risk patients prospectively.

ANTIVIRAL AGENTS

Four antiviral agents have been available for the prophylaxis and therapy of influenza as adjuncts to vaccination. The M2 inhibitors, amantadine and rimantadine, are effective against influenza A virus isolates, but have no activity against influenza B virus. However, their use has been limited by side effects and by the frequent emergence of influenza A variants with reduced sensitivity to these agents.[27] The resistant viruses are readily transmissible, cause influenza illness, and are frequently more virulent than the original virus.[28] The ACIP recommends that neither amantadine nor rimantadine be used to treat or chemoprophylax influenza A because of the widespread resistance until susceptibility has been re-established among circulating influenza A viruses.[2]

More recently, 2 neuraminidase inhibitors against influenza A and B viruses have been available, oral oseltamivir and inhaled zanamivir. These agents are associated with less toxicity than the adamantanes and are far less likely to promote the development of drug-resistant influenza strains.[29]

CHEMOPROPHYLAXIS

Although influenza vaccination remains the cornerstone for the control of influenza, antiviral medications are an important adjunct to vaccine in some situations. Several large controlled studies have demonstrated that oseltamivir and zanamivir are effective in preventing clinical influenza when the drugs are used either as prophylaxis after exposure for close contacts, such as household members, or as seasonal prophylaxis in the community.[29-34]

Who to Chemoprophylax: There is not total consensus of which populations should receive seasonal chemoprophylaxis for a period of weeks with an expensive antiviral agent in limited supply. These could include individuals who are allergic to eggs, some immunocompromised hosts unable to illicit an immune response to the vaccine (eg, hematopoietic stem cell transplant recipients), and other high-risk individuals who should not receive vaccine.

People with significant comorbidities (eg, diabetes, COPD, acquired immunodeficiency disorder, aged ≥65 years with senescent immunologic systems) that predispose them to serious complications of influenza resulting in hospitalization, would probably benefit most from targeted chemoprophylaxis with neuraminidase inhibitors to prevent influenza. In noninstitutionalized populations, chemoprophylaxis should be started when there is documented influenza

in the local community. It can be problematic to get the drug to people living at home within a short period; one solution is to preposition the drug with the target patients, who will be notified to take it in the event that there is documented influenza in the community.

Because the vaccine is not totally effective in older individuals, a proportion of nursing home residents are expected to develop influenza despite immunization. A study that examined the use of oseltamivir for the chemoprophylaxis of influenza in a frail older population, 80% of who had been vaccinated, found that oseltamivir for 6 weeks was 92% effective in preventing influenza illness after 2 index cases of documented influenza.[35] Oseltamivir chemoprophylaxis was also associated with a significant reduction in the incidence of secondary complications.[35] Inhaled zanamivir has also been demonstrated to be effective in chemoprophylaxis of influenza in a highly vaccinated long-term care population.[36] However, the eye-hand coordination required for this inhaled agent can make it difficult to use in the elderly.

Therefore, when 2 confirmed index cases of influenza occur, chemoprophylaxis directed at everyone in the nursing home (regardless of their vaccination status) to reduce the spread of virus, including the index cases and the staff, should be implemented immediately based on standing orders. Chemoprophylaxis should continue for a minimum of 2 weeks until 1 week after the end of the outbreak.[2]

Short-term targeted postexposure prophylaxis can be used in a family setting where an index case has occurred and the other family members have not been vaccinated or are at high risk. In one study, zanamivir was approximately 80% effective in preventing influenza A and B within households where the index patient was not treated.[32]

ANTIVIRAL TREATMENT

Even in a totally vaccinated population there will be 20% to 30% vaccine failure and cases of influenza. The neuraminidase inhibitors reduce the median time to improvement in infected subjects by 1 to 1.5 days, decrease the duration of viral shedding, and reduce complications requiring antibiotic treatment. In one study, zanamivir provided early symptom relief and a reduced duration of illness in adults; the benefits were particularly marked in patients who were aged ≥50 years, who had underlying illnesses, who were considered high risk, or who were more severely ill at the beginning of therapy.[37]

Antiviral therapy of a child with influenza will decrease morbidity in terms of hospitalization and secondary infections. Oseltamivir in children over the age of 1 year decreased the incidence of otitis media by 44% and reduced the use of antibiotics.[38] In addition, because children excrete virus for a longer period than adults, treatment with a neuraminidase inhibitor significantly shortens the duration of viral shedding, therefore reducing the possibility of infecting contacts.

Antiviral agents must be instituted within 48 hours of symptom onset for maximal benefit. They should be used when the probability of infection with influenza and the expected benefit are both high, because supplies of these medications are limited. These populations primarily include those at risk from complications of influenza illness.

To increase the appropriate use of antiviral agents in the treatment of influenza illness, patients should be educated that an effective treatment is available, but they must contact their provider within the 48-hour window after symptom onset required for it to be effective. Because it is particularly difficult to get community dwelling elderly people whose vaccine did not protect them into the office and on antiviral treatment within the 48-hour window, consider prepositioning at-risk patients with an antiviral agent at home for use if they develop symptoms.

INFECTION CONTROL

Adults can be infectious from the day before symptoms begin through approximately 5 days after illness onset, children can be infectious for more than 10 days after onset of symptoms, young children can shed virus before their illness onset, and severely immunocompromised patients can shed virus for weeks or months.[2]

Influenza is primarily transmitted from person to person via large respiratory droplets that are generated when infected persons cough, sneeze, or talk; these large droplets can then be directly deposited onto the mucosal surfaces of the upper respiratory tracts of susceptible persons who are near (±3 feet) the droplet source. Transmission also may occur by direct (person-to-person) or indirect (person-fomite-person) contact. Airborne transmission can also occur via the smaller droplet nuclei; for example, on a grounded plane, but this route is probably less important than person-to-person spread by respiratory droplets.

PCPs should educate patients about basic infection control measures during the influenza season that will also help protect them from all kinds of viruses. The first is restricting contact between sick people and well people to prevent transmission. Persons who are sick should not go to a nursing home, whether as a healthcare worker or visitor. In addition, persons who are sick should not be in the workplace, particularly if a healthcare worker. Hand washing hygiene and cough etiquette should be encouraged.

Mechanical precautions to prevent disease spread can also help protect high-risk patients from influenza, particularly in an institutional setting such as a nursing home.[5] These include cohorting affected residents, particularly those who are not able to practice good cough etiquette, and assigning the same staff to take care of them.[5] Residents with respiratory illness should be encouraged to wear masks when they leave their rooms, and staff should wear masks and wash their hands frequently if they are taking care of symptomatic residents.[5]

SUMMARY

Many patients perceive pandemic influenza as a great threat, but pay minimal attention to seasonal influenza. However, seasonal influenza causes a predictable level of morbidity and mortality in the United States each year. By directing patients' anxiety about pandemic influenza to awareness about seasonal influenza, PCPs can impact their patient populations right away through education, vaccinating the recommended groups, and identifying those who will benefit from chemoprophylaxis or chemotherapy of influenza.

Preventing influenza is the priority, and vaccination is the cornerstone of prevention, but remains underutilized. It is the PCP's responsibility to educate patients and communities about the natural history of influenza and why annual vaccination is necessary for both high-risk patients and their family members and close contacts, including healthcare workers. This education can start at any time of year, whether by priming high-risk patients during routine visits or by setting up a patient registry, for example. Chemoprophylaxis and antiviral therapy are not substitutes for vaccination, although they are important adjuncts in preventing and controlling influenza.

CONCLUSION

In order to prevent the morbidity and mortality associated with influenza, PCPs have a role that goes far beyond the traditional medicine model where patients come to the office for one-on-one care. PCPs are now responsible for reaching out to their patients who do not come to the office or clinic during the influenza season, to educate their communities about the importance of vaccination, and to advocate for universal guidelines for vaccination in order to improve outcomes.

PRACTICAL APPROACHES TO SEASONAL INFLUENZA IN PRIMARY CARE SETTINGS

Patient education:

- Stress the real dangers posed by influenza.
- Explain the benefits of influenza vaccination for high-risk patients and their family or close contacts.
- Take the time to identify and eliminate patient beliefs and fears that are barriers to vaccination; eg:
  - Influenza vaccine causes influenza.
  - Children get too many immunizations.
  - Language or cultural barriers.
- Put overstated safety concerns into context; eg, thimerosal containing vaccines for children, GBS.

Develop protocols to increase rates of vaccination; eg:

- Preprint a message on statements sent to patients.
- Standing orders in nursing homes.
- Prime target patients at any time during the year (eg, a diabetic on diagnosis or at a follow-up well or ill visit).
- Use visual reminders such as posters or a "smiley face" to raise patient's consciousness.
- Vaccinate family members who accompany the patient (eg, for a well-child visit).
- Add influenza vaccination to patients' flow sheet.

Increase vaccination rates among the office/clinic staff; eg:

- Assign a single staff member to be responsible for vaccinating all staff.
- Use vaccine carts to bring the vaccine to the staff.

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1. Identify key populations at high risk, and triage those populations for vaccination and other preventative measures?	☐	☐	☐
2. Develop a vaccination program, and effectively vaccinate patients for influenza?	☐	☐	☐
3. Differentiate flu symptoms from similar presentations, and appropriately counsel patients on treatment options?	☐	☐	☐
4. Investigate office systems changes with the potential to improve or enhance vaccination and treatment program, including patient registries?	☐	☐	☐
5. Incorporate new vaccinations and pharmacologic agents for the treatment of influenza?	☐	☐	☐

Please rate the monograph for:	Yes	No	Somewhat
It was understandable and easy to read	☐	☐	☐
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Posttest Questions Answer Grid

Mark only one answer for each question.

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3. [a] [b] [c]
4. [a] [b] [c] [d]
5. [a] [b] [c] [d]
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Post-test Questions:

1. Among healthy adults aged < 65 years, the inactivated influenza vaccine prevents seasonal influenza in what proportion of recipients?

    a. 30%-50%
    b. 50%-70%
    c. 70%-90%
    d. > 90%

2. Which of the following are currently recommended for postexposure chemoprophylaxis of high-risk patients?

    a. Amantadine and rimantadine
    b. Influenza vaccines
    c. Oseltamivir and zanamivir

3. In infected individuals, neuraminidase inhibitors are not able to:

    a. Reduce the median time to improvement by 48 hours
    b. Reduce the duration of viral shedding
    c. Decrease complications requiring antibiotic treatment

4. To be of benefit, antiviral agents must be instituted within:

    a. 24 hours
    b. 36 hours
    c. 48 hours
    d. 72 hours

5. When influenza is circulating in the community, the positive predictive value for influenza in adults with influenza-like illness who have both cough and fever within 48 hours of symptom onset is:

    a. 60%
    b. 70%
    c. 80%
    d. 90%

6. Influenza is primarily transmitted by:

    a. Large respiratory droplets
    b. Small droplet nuclei
    c. Direct (person-person) or indirect (person-fomite-person) contact

7. The cornerstone of the management of seasonal influenza is:

    a. Annual vaccination
    b. Chemoprophylaxis
    c. Antiviral therapy

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