

# Teaching Immunization

*for Medical Education (TIME)*



MULTISTATION CLINICAL TEACHING SCENARIOS

## Influenza Prevention: Facilitator's Answer Key

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**ABBREVIATIONS****Diagnostic Tests**

PCR: Polymerase Chain Reaction

**Vaccines**

TIV: Trivalent inactivated influenza vaccine (TIV)

LAIV: Live, attenuated influenza vaccine (LAIV)

H-D TIV: High-dose trivalent inactivated influenza vaccine

TIV ID: Trivalent inactivated influenza vaccine for intradermal (ID) use

**SOURCES OF INFORMATION ON INFLUENZA VACCINE**

1. Centers for Disease Control and Prevention. Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. – use latest edition ([www.cdc.gov/vaccines/pubs/ACIP-list.htm](http://www.cdc.gov/vaccines/pubs/ACIP-list.htm))
2. Bridges CB, Katz JM, Levandowski RA, Cox NJ. Inactivated influenza vaccines. In: Plotkin SA, Orenstein WA, Offit PA, eds. *Vaccines*. 5th ed. Philadelphia, PA: Elsevier Inc; 2008: 259-290.
3. Belshe RB, Walker R, Stoddard JJ, Kemble G, Maassab HF, Mendelman PM: Influenza vaccine – live. In: Plotkin SA, Orenstein WA, Offit PA, eds. *Vaccines*. 5th ed. Philadelphia, PA: Elsevier Inc; 2008: 291-310.
4. Centers for Disease Control and Prevention. Influenza website. [www.cdc.gov/flu/](http://www.cdc.gov/flu/)
5. Centers for Disease Control and Prevention. Influenza. In: *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Wolfe S, Hamborsky J, eds. 12th ed. Washington, DC: Public Health Foundation, 2011
6. *Shots* Immunization Application for mobile devices and PCs. From the Group on Immunization Education of the Society of Teachers of Family Medicine. Go to [www.ImmunizationEd.org](http://www.ImmunizationEd.org) and click on the *Shots* icon.

**Answers to Questions for Learners – Scenario One**

1. What is the differential diagnosis for his chief complaint?

This case represents secondary bacterial pneumonia following influenza. The differential diagnosis includes primary bacterial pneumonia and spread of an initial bacterial infection of the upper respiratory tract to the lungs. Common organisms include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Legionella*, and *Moraxella catarrhalis*. *Streptococcus* and *Staphylococcus* are gram-positive cocci; gram-positive cocci in clusters are shown in Gram stain, suggesting *Staphylococcus*.

2. What treatment is needed and where should it be administered?

This patient needs hospitalization and supplemental oxygen administration. Treatment should be started quickly, i.e., in the Emergency Department, with intravenous antibiotics. Antivirals are unlikely to be helpful given the amount of time that has passed since onset of influenza symptoms (although some physicians might add them). His pneumonia severity index score is class IV, which indicates a need for hospitalization.

3. Was the diagnosis of influenza appropriate?

Influenza can be diagnosed appropriately upon clinical grounds as long as influenza is known to be occurring in the community. His physician could also have used rapid antigen detection methods or the more accurate PCR or viral culture to diagnose influenza A and B infections on his initial presentation.

4. Before becoming ill, did Mr. Smith have an indication for influenza vaccine? If so, which formulation and what time of year should the vaccine be administered?

Yes, all persons  $\geq 6$  months of age have an indication for influenza vaccine. Diabetes mellitus and renal insufficiency are high-risk indications for inactivated influenza vaccine. Live attenuated influenza vaccine is not recommended for persons with underlying medical illnesses such as diabetes mellitus. Vaccine should be offered as soon as it is available and until, or even after, influenza activity is documented in a community, which peaks January through early March in most seasons.

**Take Home Points:**

Influenza can lead to severe complications and missed opportunities for influenza vaccination can occur.

**Answers to Questions for Learners – Scenario Two**

1. Other than time course and proximity, what evidence supports that their diseases are related?

Each has an age appropriate manifestation of influenza. Influenza has different clinical presentations, depending upon the age of the patient (see Table 1). The incubation period for influenza is 1 to 5 days, which is consistent with the scenario.

2. What tests are available commonly and when should they be used?

Rapid antigen detection tests, reverse-transcriptase polymerase chain reaction (RT-PCR), and viral culture are commonly available tests for influenza. Diagnostic testing should be used to diagnose the first case when an institutional outbreak of influenza is suspected. Testing should be considered when test results would influence clinical decision making and is recommended for inpatients. For individual patients seen in ambulatory care settings, tests are most useful when they are likely to help with diagnostic and treatment decisions, such as the use of influenza antiviral agents.

Details are available in: Harper SA, Bradley JS, Englund JA, et al. Seasonal influenza in adults and children – diagnosis, treatment, chemoprophylaxis, and institutional outbreak management. Clinical practice guidelines of the Infectious Diseases Society of America 2009;48:1003-32

3. Were these cases preventable?

Annual influenza vaccine is universally recommended for persons  $\geq 6$  months of age. Hence, influenza was potentially preventable in all three persons. Chronic-care visits (e.g., hypertension visit for Jonathan's grandmother) and hospital discharge (e.g.,

following cholecystectomy) are important but often overlooked opportunities to administer vaccinations.

4. Where was influenza most likely to have been contracted initially?

Jonathan most likely contracted influenza in kindergarten. School-aged children have the highest age-specific attack rate and are the primary transmission route for influenza. Because most are healthy, they suffer relatively few serious complications. However, they can transmit influenza to elderly adults who have a higher complication rate. Vaccination of school-aged children protects others in a community and can help prevent an outbreak.

5. Jonathan's grandmother is being seen by her primary care physician one day after her cough started. Should any treatment be given?

The current resistance patterns to antivirals should be considered as patterns vary by year. Generally, zanamivir and oseltamivir are effective against both influenza types A and B; they shorten the duration of symptoms by about 1 day and can be given within 48 hours of the onset of illness. Amantadine or rimantadine can be given therapeutically to persons who contract influenza type A, provided that either drug is started within 48 hours of the onset of symptoms. People who are at high risk of serious complications from influenza may benefit most from antiviral medications. Therefore, in general, people who are in these high-risk groups should be given priority for use of influenza antiviral medications:

- Any person hospitalized for laboratory-confirmed or highly suspected influenza-like illness, within 48 hours of onset; after 48 hours it may be beneficial.
- Any person with laboratory confirmed or highly suspected influenza illness at high risk for serious complications of influenza and who is within the first 2 days of illness onset should be treated with antiviral medications. (Pregnancy category C)

**Take Home Points:**

The signs of influenza vary by age group; missed vaccination opportunities occur frequently; antiviral treatment is indicated for certain groups, particularly for persons at risk for complications.

**Answers to Questions for Learners – Scenario Three**

1. Was the record review important? How good are the influenza vaccination rates in the practice?

Assessment, i.e., the medical record review, is very important because the problem must be quantified before meaningful, well-informed action will occur. Many clinicians do not know the actual vaccination rates in their practices according to record review and they tend to overestimate these rates. The vaccination rates in the scenario are modest; the values given are typical for many practices. Such data may provide motivation for action and a baseline upon which to measure change.

2. Why are the vaccination rates suboptimal?

Possible reasons for low vaccination rates include:

- a. Some people underestimate influenza severity and infectiousness.
- b. Some clinicians have not done quality assurance studies about vaccine rates in their practice; hence, they do not realize that vaccination rates are low.
- c. Missed opportunities occur when clinicians forget to address influenza vaccination when there is an opportunity, e.g., acute and chronic-care visits and hospital discharge.
- d. Clinicians use invalid vaccine contraindications, such as mild acute illnesses, as a reason not to vaccinate.
- e. Patients may not realize their need for vaccination.
- f. Some patients are fearful of adverse events following vaccination.
- g. Some patients do not access healthcare institutions during the vaccination season.
- h. Systems to raise vaccination rates are lacking in some health centers.

3. What can be done to improve influenza vaccination rates, given that this is a busy practice with several different providers?

Vaccination rates can be improved by the following interventions:

- a. Setting a target vaccination rate for the practice and monitoring progress; **this is one of the most powerful interventions.**
- b. Comparing vaccination rates of different practices in a competitive spirit and awarding prizes for the highest rates.
- c. Sending reminders to patients using an autodialing telephone machine, electronic messages, or postcards.
- d. Having office staff inquire about vaccination status at registration or during measurement of vital signs. Colored stickers, electronic or paper checklists, EMR alerts, or inked rubber stamps help to communicate this reminder to providers.
- e. Computer-generated "tickler" reminders in the EMR or placed in a patient's chart.
- f. Displaying vaccination messages in the office waiting room by electronic or printed messages.
- g. Issuing standing orders for staff to administer influenza vaccine according to a protocol, without the need for an individual physician order for each patient. This allows an office nurse to deliver vaccination services during influenza vaccine season, allowing a patient to receive vaccinations without seeing a physician. Standing orders has been shown to be a highly effective intervention.
- h. During the late fall, opening an influenza vaccination clinic or express vaccination service that is staffed by nurses.
- i. Participating in mass media campaigns or public service announcements (as a benefit to the practice, these may provide free publicity).

### Take Home Points

Assessment of vaccination rates identifies areas for improvement; setting a goal and monitoring progress and implementing reminder systems and standing orders are powerful interventions to raise rates.

**Answers to Questions for Learners – Scenario Four**

## 1. What treatment should Mrs. Gaither receive?

Mrs. Gaither should receive TIV or H-D TIV and an influenza antiviral agent that is appropriate based on susceptibility patterns of the outbreak. The influenza antiviral agent should be administered for 2 weeks, until antibodies develop from influenza vaccine. Vaccination is indicated because of her age (influenza vaccine is recommended for anyone 6 months of age or older).

Because influenza is in the community, she is at risk for influenza and should be vaccinated even though antiviral agents may protect her from her husband's infection. Because she has chronic renal disease, if oseltamivir is used, it should be reduced to 75mg every other day if the creatinine clearance is 10-30mL/min; it is not recommended if the creatinine clearance is <10mL/min. There is no dose adjustment for zanamavir. Zanamivir and oseltamivir are effective for influenza type A and B infections; oseltamivir is licensed for persons aged 1 year and older. Zanamivir is FDA approved for prophylaxis for persons 5 years old and older and treatment in persons 7 years of age and older.

Based on susceptibility testing, amantadine and rimantadine can be used for prevention or treatment in persons aged  $\geq 1$  year with dosage reductions for renal disease per guidelines.

People who are at high risk of serious complications from influenza may benefit most from antiviral medications. Therefore, in general, people who fall into these high-risk groups should be given priority for use of influenza antiviral medications:

- Persons requiring hospitalization for laboratory confirmed or highly suspected influenza illness, within 48 hours of onset; after 48 hours it may be beneficial.

- Any person at high risk for serious complications of influenza and who is within the first 48 hours of illness onset should be treated with antiviral medications. (Pregnancy category C)

All persons at high risk of serious influenza complications should be given antiviral medications if they are likely to be exposed to others infected with influenza. For example, when a high-risk person is part of a family or household in which someone else has been diagnosed with influenza, the exposed high-risk person should be given chemoprophylaxis.

## 2. Can trivalent inactivated influenza vaccine (TIV) cause “flu”?

Inactivated influenza vaccine cannot cause influenza or "flu" because the viruses have been killed. In adults, systemic symptoms following inactivated influenza vaccination are similar to those of placebo injection (Table 2).

Misconceptions about why individuals report getting the flu from the flu shot may result when individuals are exposed to flu or a virus that causes a flu-like illness before immunity from the vaccine has developed. It generally takes about 2 weeks to develop immunity to influenza following vaccination. Also, influenza vaccine is about 70%-90% effective in preventing disease, so there will be some individuals who will not be protected by the vaccine.

There is a small risk that intranasally administered live attenuated influenza virus (LAIV) vaccine may cause disease in immunosuppressed persons. LAIV vaccine contains a live virus with three traits that distinguish it from wild-type virus and strictly limit the ability of LAIV to cause influenza in healthy persons. First, LAIV is attenuated, such that it produces mild or no signs and symptoms related to influenza virus infection. Second, LAIV is cold-adapted so that it replicates efficiently at the temperature in the human upper airways in order to produce immunity. Finally, LAIV is temperature-sensitive and cannot replicate efficiently at the temperature in the

human lower airways. Therefore, it is unable to cause influenza or "flu" in most people. Since LAIV vaccine contains live viruses, there is a small chance for transmission of these viruses from vaccinees to other persons. If vaccine virus is inadvertently administered to or transmitted to immunosuppressed persons, there is a theoretical risk that LAIV could cause disease.

3. Given that she has an allergy to duck feathers, should she receive TIV?

Allergy to duck feathers, allergic rhinitis, and a family history of convulsions are not valid contraindications to influenza vaccination. However, anaphylaxis to influenza vaccine is a valid contraindication and anaphylaxis to eggs is an indication for referral to an allergist or other physician with expertise in management of allergic conditions for risk assessment regarding influenza vaccination. Starting in 2011, according to the ACIP, persons who have hives after egg exposure can be vaccinated with TIV provided that they are observed for at least 30 minutes for signs of a reaction and that they are vaccinated by a provider who is familiar with manifestations of egg allergy. This is due to the trace amount of egg protein in TIV and demonstrated safety in vaccinating persons with hives after egg exposure. An acute, moderate, or severe febrile illness is a valid reason to postpone vaccination temporarily.

4. What are the chief side effects of antiviral drugs that are used for influenza?

The side effects of zanamivir are reduced FEV1, bronchospasm, respiratory function deterioration, and oropharyngeal or facial edema. The side effects of oseltamivir are nausea and vomiting. The side effects of rimantadine are nausea, insomnia, nervousness, and dizziness; it may increase the risk of seizures in those with a seizure disorder. The side effects of amantadine are nausea, dizziness, confusion, dry mouth, and constipation. Serious reactions to amantadine have been reported such as exacerbation of neurologic or psychiatric disorders (e.g., seizure or suicidal thoughts).

5. Which groups of patients have the highest influenza hospitalization rates?

Persons 65 years of age or older with high-risk medical conditions (e.g., diabetes mellitus, chronic lung disease, hemodynamically significant cardiac disease, chronic renal disease) have the highest hospitalization rates from influenza (Figure 3).

### Take Home Points

Influenza is most severe in those with high-risk conditions and such persons should receive antiviral agents when infected with influenza (when seen within an appropriate time frame). Inactivated influenza vaccine cannot cause influenza disease.

**Answers to Questions for Learners – Scenario Five**

1. What can be done for Mr. Cook? When can he return to work?

Being a healthy 35-year-old, Mr. Cook is not at high risk for influenza complications and, therefore, is not a priority for treatment, but could be considered for therapy if local supplies are sufficient. Mr. Cook can receive an antiviral agent for 5 days. He can return to work when he is no longer contagious and has completed antiviral therapy. For adults, the period of communicability is usually from the day before symptoms begin through approximately 5 days after illness onset. The choice of antiviral agents should be based on susceptibility patterns from the outbreak.

People who are at high risk of serious complications from influenza may benefit most from antiviral medications. Therefore, in general, people who fall into these high-risk groups should be given priority for use of influenza antiviral medications:

- Any person requiring hospitalization for laboratory confirmed or highly suspected influenza illness within 48 hours of onset, after 48 hours it may be beneficial.
- Any person at high risk for serious complications of influenza and who is within the first 2 days of illness onset should be treated with antiviral medications.

(Pregnancy category C)

Antiviral medications can be considered in other situations when the available supply of such medications is locally adequate. Influenza vaccination is recommended for staff of long-term care institutions.

2. What should be done for the nursing home residents and other employees with whom Mr. Cook was working?

All persons who live in long-term care facilities should be given antiviral medications for chemoprophylaxis in the event of an institutional outbreak. When vaccine is available, newly vaccinated staff should receive chemoprophylaxis only for the 2-week period following vaccination. Vaccinated and unvaccinated residents should

receive chemoprophylaxis for 14 days or for 7 days after the onset of symptoms in the last person infected. Unvaccinated staff and residents should be offered vaccination; appropriately aged residents may receive either TIV or H-D TIV. Antiviral medications should be used for chemoprophylaxis for staff who cannot receive influenza vaccine or in whom the vaccine is expected to be ineffective.

Influenza tests should be used as soon as possible to confirm influenza as the cause of outbreaks. However, treatment and chemoprophylaxis should be initiated if influenza is strongly suspected and test results are not yet available. Other outbreak control efforts such as cohorting of infected persons and practicing good respiratory and hand hygiene should be implemented. Persons developing compatible symptoms > 72 hours after implementation of chemoprophylaxis or on previously unaffected institutional units should be tested.

### 3. Could this episode have been prevented?

The entire episode could have been prevented or limited in the following ways:

- Medical personnel and others in contact with high-risk persons, including staff of long-term care facilities, should receive influenza vaccine on a yearly basis as part of standard protocol.
- The nursing home should implement a standard protocol wherein all residents are vaccinated each year unless they have a valid contraindication. For instance, part of standard admission orders could include influenza vaccine administration in the fall.
- The nursing home should have a contingency plan for prompt administration of an influenza antiviral agent in the event of an outbreak.

### Take Home Points

Healthcare workers should be vaccinated against influenza annually. In institutional outbreaks, staff and residents should receive antiviral chemoprophylaxis and unvaccinated persons should be vaccinated. Staff vaccination can save patient lives.

**Answers to Questions for Learners – Scenario Six**

1. Is influenza vaccine recommended for any family members?

Influenza vaccine is recommended for all family members, in fact for all persons  $\geq 6$  months of age.

Scott will benefit from inactivated influenza vaccination because of his lung disease. His father will benefit from inactivated vaccine due to IgA deficiency. High-dose trivalent inactivated influenza vaccine is licensed for persons  $\geq 65$  years of age and is an option for the grandfather.

2. Given that Scott and Isabelle have never received influenza vaccine, if they were to be vaccinated, how many doses would be needed? What type of vaccine can each receive?

Children younger than 9 years old should receive two doses of influenza vaccine in the first year that they are vaccinated. The doses should be separated by 4 weeks. Those who received seasonal influenza vaccine for the first season last year and received only one dose, should generally receive 2 doses of influenza vaccine this year; however, in specific years, additional guidance is given by ACIP at [www.cdc.gov/flu](http://www.cdc.gov/flu). For instance, for the 2011-12 season, those less than 9 year old who had a dose of vaccine in 2010-11 season only need one dose in the 2011-12 season because the vaccine strains are identical. Children aged 6 months to 1 year should receive TIV and healthy non-pregnant persons aged 2-49 years can receive either TIV or LAIV. Since Scott and Isabelle have never received influenza vaccine and are younger than 9 years, they should receive 2 doses.

3. Can influenza vaccine be administered simultaneously with other vaccines?

Influenza vaccines can be administered simultaneously with other vaccines. There appears to be an increased risk of febrile seizures when PCV13 and influenza vaccines are co-administered but this is not a contraindication but an information point.

**Take Home Points**

Influenza vaccination is recommended for all persons aged  $\geq 6$  months; children and adults with chronic medical conditions should receive inactivated vaccine; healthy non-pregnant persons aged 2 to 49 years can receive either inactivated or live attenuated vaccine. High-dose TIV is an option for individuals 65 years of age and older.

**INFLUENZA SAMPLE TEST**

This test was developed originally using expert knowledge and a psychometric method for the construction of criterion referenced tests. It may be used as a sample test.

1. In the elderly, the most common symptom(s) of influenza is (are)
  - a. Cough and fever
  - b. Vomiting only
  - c. Vomiting and diarrhea
  - d. Cough, aches, headache, sore throat, and fever
  - e. Rhinorrhea and vomiting
  
2. Which of the following is true?
  - a. Any infant is a candidate for influenza vaccine
  - b. Healthy children 2 to 18 years can receive either TIV or LAIV
  - c. Allergy to erythromycin is a valid contraindication to influenza vaccine
  - d. The first trimester of pregnancy is an absolute contraindication to influenza vaccine
  - e. Anaphylaxis to duck feathers is a valid contraindication to influenza vaccine
  
3. Which of the following is true?
  - a. A family history of grand mal convulsions is a valid contraindication to influenza vaccine
  - b. Unopened influenza vaccine vials from the preceding year can be used in the following season
  - c. Elderly persons with influenza usually display symptoms similar to those of young adults
  - d. Children who are younger than 9 years old and receiving influenza vaccine for the first time should receive 2 doses, 4 weeks apart
  - e. A family history of allergies is a valid contraindication to influenza vaccine

4. Influenza is characterized by the following
  - a. Highest incidence is in children.
  - b. Highest case-fatality rates are found in the elderly for seasonal influenza.
  - c. Highest incidence is in the elderly.
  - d. B and C are correct.
  - e. A and B are correct.
  
5. The risks from inactivated influenza vaccine are less than from actual influenza because
  - a. The vaccine has been used safely in HIV patients
  - b. The vaccine is administered intramuscularly
  - c. The vaccine contains inactivated, killed virus
  - d. Amantadine is administered simultaneously
  
6. Which is the most important to increase influenza vaccination rates for a practice?
  - a. Postcard about influenza sent to patients
  - b. Public service announcements
  - c. Provider (e.g., physician) sets a target goal for the vaccination rates in his practice and monitors progress
  - d. Antiviral samples and literature
  - e. Poster in the waiting room about influenza.
  
7. At office visits in the fall for mild acute afebrile illnesses, influenza vaccine should
  - a. Be postponed until the patient has recovered
  - b. Be administered unless the potential recipient had allergy to duck feathers.
  - c. Be administered unless patient has anaphylactic hypersensitivity to influenza vaccine or other valid contraindications, thereby preventing a missed opportunity.
  - d. Not be administered because it is temporally contraindicated.

8. Mike, a 5-year-old with asthma, is coughing and has clear rhinorrhea. Influenza-like illnesses have been documented in Mike's community. Two days after Mike's illness started, his 31-year-old father had symptoms of cough, generalized myalgia, sore throat, and headache.
- Their illnesses are related and are most likely due to *Corynebacterium diphtheriae*.
  - Their illnesses are most likely unrelated because the symptoms are so different.
  - Their illnesses are related and are most likely due to *Streptococcus*.
  - Their illnesses are related and preventable by vaccination.
  - Their illnesses are likely due to *Legionella*.
9. Mary, a 26-year-old graduate student, was diagnosed with influenza; an outbreak of influenza type A is occurring in the community. She is staying at her grandmother's house. Her grandmother has chronic obstructive lung disease. Her grandmother should
- Receive influenza vaccine only
  - Receive an antiviral agent if her renal function is excellent.
  - Receive an antiviral agent and influenza vaccine
  - Receive an antiviral agent and, if she is not allergic to penicillin, influenza vaccine
  - Receive an antiviral agent but not pneumococcal vaccination
10. John, a 45-year-old insulin-dependent diabetic, has symptoms of mild fever, myalgia, sore throat, and chills that began yesterday (January 3). Influenza type A is in the community. He should
- Receive an antiviral agent and inactivated influenza vaccine.
  - Not receive an antiviral agent because he may have renal failure secondary to diabetes
  - Not receive an antiviral agent because his illness has started
  - Not receive an antiviral agent because of its interaction with insulin.
  - Not receive influenza vaccine because it is too late in the season.

**INFLUENZA TEST ANSWER KEY**

1. A
2. B
3. D
4. E
5. C
6. C
7. C
8. D
9. C
10. A