Health Maintenance and Public Health

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Learning Objectives

1. Recommend appropriate first aid therapy for common scenarios, including initial patient positioning, bleeding, asthma, anaphylaxis, seizures, musculoskeletal injuries, chest pain, burns, thermal and heat injuries, and ocular injuries.
2. Develop and execute a plan to deliver appropriate cardiopulmonary resuscitation according to guideline recommendations.
3. Use knowledge of the patterns of drug poisoning, including implicated drugs and patient characteristics, to recommend strategies to prevent and treat opioid overdose.
4. Recommend drugs to prevent infection from exposures to category A bioterrorism threats.
5. Using knowledge of vaccines that are routinely administered, including their route of administration, number of doses, indication, contraindications, and common adverse effects, assess a patient's vaccine history and recommend the necessary vaccines.
6. Develop a process to design and implement interventions for addressing nonadherence, and integrate these interventions into pharmacy practice.
7. Integrate knowledge of complementary and alternative medicines to educate patients and make appropriate recommendations for their use.

Self-Assessment Questions

Answers and explanations to these questions can be found at the end of the chapter.

1. What age group is at highest risk of death from foreign-body airway obstruction?
   A. Younger than 5 years
   B. Five to 10 years
   C. Eleven to 16 years
   D. Seventeen years and older

2. Based on national trends, what drug class is most likely to cause overdose drug deaths in the next year?
   A. Anticoagulants
   B. Tricyclic antidepressants
   C. Benzodiazepines
   D. Opioids

3. What element of disaster preparedness is most likely to lead to an effective disaster response?
   A. Flexible plan based on type of disaster
   B. Availability of on-call pharmacists
   C. Collaborative practice agreement for vaccine administration by pharmacists
   D. Surge supply of doxycycline and ciprofloxacin

4. Which of the following vaccines should not be given to a pregnant woman because of a theoretical risk of infection in the fetus?
   A. Inactivated influenza vaccine (IIV)
   B. Meningococcal conjugate vaccine (MenACWY-D)
   C. Measles, mumps, and rubella (MMR)
   D. Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap)

5. Which of the following statements best represents the medication possession ratio (MPR) measure?
   A. The duration of time from initiation to discontinuation of therapy
   B. Sum of days' supply of a medication during a defined period
   C. The value is increased proportionately to a patient's failure to fill a medication
   D. The degree of a patient's ability to demonstrate understanding of health information to make a health decision

6. Which of the following statements is correct regarding the Dietary Supplement Health and Education Act (DSHEA) of 1994?
   A. Supplements are categorized as drugs and must go through the new-drug approval process before being sold in the marketplace.
   B. Dietary supplements must be proved safe and effective and submitted for U.S. Food and Drug Administration (FDA) approval.
   C. Dietary supplement manufacturers may claim that the product may affect body structure or function.
   D. Labeling must contain a seal of approval to demonstrate safety testing has occurred for the product.

I. FIRST AID

A. Evidence and Recommendations
   1. Where available, the size of treatment effect and level of evidence (LOE) are included according to the American Heart Association methodology (Circulation 2010;122:S657-64).
      a. Class I: Benefit >>> risk (should be done)
      b. Class IIa: Benefit >> risk (reasonable to do)
      c. Class IIb: Benefit ≥ risk (may be considered)
      d. Class III: Risk ≥ benefit (may be harmful)
      e. Level of evidence
         i. A: Several randomized trials or meta-analyses
         ii. B: Single randomized trial or nonrandomized studies
         iii. C: Limited evaluations available (case reports, standard of care, expert opinion)
   2. Recommendations for first aid are based on the First Aid: 2010 American Heart Association and American Red Cross Guidelines for First Aid.
   3. Recommendations for cardiopulmonary resuscitation (CPR) are based on the Adult and Pediatric Basic Life Support guidelines.

B. General First Aid Principles
   1. Obtain help by contacting emergency medical services (EMS) (i.e., call 911) when indicated.
   2. In cases of poisoning, the poison center should also be contacted by dialing 1-800-222-1222 (see Section II for more details).
   3. Positioning: In general, individuals should not be moved. Situations in which a specific position is recommended are listed in the following text.
      a. Potential spinal injury—In general, a person should not be moved if there is any suspicion of a spinal injury.
         i. Secondary injury from moving or manipulating a patient can occur because the spinal cord is unprotected.
         ii. Most spinal injuries are caused by motor vehicle collisions and falls.
         iii. Spinal injury should be suspected if any of the following risk factors are present after a traumatic injury:
            (a) The person is 65 years or older.
            (b) Involved in a motor vehicle or bicycle crash
            (c) Fall greater than standing height
            (d) Pain or tenderness in the neck or back
            (e) Paresthesia symptoms in the extremities
            (f) Upper extremity or torso weakness
            (g) Altered level of consciousness
            (h) Sustained other injuries causing pain in the head or neck
            (i) Children 2 years or older with trauma involving the head or neck
         iv. The head should be stabilized to restrict motion and prevent secondary injury by manually restricting head and neck movement (Class IIb, LOE C).
      b. If there is evidence of shock, the legs should be raised 6–12 inches while the person is supine (Class IIb, LOE C).
         i. Raising the legs may increase blood pressure by shifting volume.
         ii. Evidence of shock may include altered level of consciousness, decreased urine output, cool or mottled skin, weak/rapid pulse, nausea/vomiting, and hypotension. Not all of the preceding signs will be present, and some may be difficult to assess (e.g., decreased urine output) in first aid situations.

iii. If there is pain when the legs are raised, there could be internal trauma, and no further efforts to raise the legs should be made.

c. The individual should be put in the High Arm IN Endangered Spine (HAINES) position (one arm is extended, and the person's head is rested on the arm) (Class IIb, LOE C). The person's legs are bent, and the person is placed on his or her side, when any of the following conditions are present:
   i. Difficulty breathing because of vomiting or secretions
   ii. The individual is unresponsive and should be left alone while help is hailed.

d. The individual is found in a prone position (face down) and is unconscious and should be placed in the supine position (face up).

C. Specific Emergencies and First Aid Recommendations

1. Asthma
   a. Clinical features of a severe asthma attack that can be assessed by a bystander
      i. The person is only able to speak in words or phrases
      ii. Prefers to sit forward (tenting)
      iii. Agitation
      iv. Increased respiratory rate
      v. Peak flow less than 40% of predicted (may be difficult to obtain in some situations)
   b. Help patients administer their rescue inhalers according to physician prescription (Class IIa, LOE C).
   c. Management of asthma exacerbations at home (Expert Panel 3 recommendations)
      i. May decrease length and severity of exacerbation
      ii. Initial treatment is a short-acting β-agonist (e.g., albuterol), using a metered-dose inhaler (MDI) (2–6 puffs) or nebulizer.
      iii. Up to two treatments are recommended, separated by 20 minutes.
      iv. Physician follow-up is recommended in all cases, based on severity (contact physician to emergency department [ED] transport).
      v. All patients should have a written action plan.
2. Anaphylaxis
   a. Clinical features
      i. Rapid onset: Symptoms start in less than 1 minute to several hours after exposure to an allergen.
      ii. Life-threatening respiratory or cardiovascular collapse
      iii. Systemic symptoms
         (a) Skin involvement is reported in up to 90% of cases. Urticaria (i.e., hives), rash, swelling, pruritus (lips, tongue, uvula, ears, genitals, palms of the hands, soles of the feet, periorbital)
         (b) Respiratory involvement in up to 70% of cases. Signs of upper airway involvement may include swelling, pruritus, hoarseness, dysphonia, dysphagia, or stridor. Lower-respiratory signs and symptoms may include shortness of breath, chest tightness, or wheezing.
         (c) Nasal symptoms may be the earliest signs and include rhinorrhea and sneezing.
         (d) The gastrointestinal tract is involved in up to 45% of cases. Symptoms include nausea, vomiting, diarrhea, and abdominal pain.
         (e) The cardiovascular system is involved in up to 45% of cases. Symptoms may include chest pain, tachycardia, bradycardia, hypotension, and shock. A fluid shift of up to 50% from the intravascular compartment can occur in 10 minutes.
   b. Treatment
      i. Treatment recommendations for the first aid provider include administering an epinephrine autoinjector or helping patients self-administer their own epinephrine autoinjector (Class IIb, LOE B).

ii. Administration and dosing of self-injectable autoinjectors
   (a) Inject into the anterolateral aspect of the thigh, and hold for 10 seconds; autoinjector can be administered through clothing.
   (b) Use caution to avoid inadvertent administration into digits and hands.
   (c) Dosing is weight based in children. A child weighing less than 30 kg will be prescribed the 0.15-mg product, and others weighing 30 kg or more will be prescribed the 0.3-mg product.

3. Seizures
   a. The primary treatment for patients experiencing a seizure is to prevent potential injuries.
   b. Avoid restraining patients because this may contribute to muscle or soft tissue injury. Ease patients to the ground, and clear the area around them.
   c. Do not try to place items in the patient's mouth because this can cause damage to the patient's teeth or to the bystander (Class IIa, LOE C).
   d. A postictal state (confusion, decreased level of consciousness, or unresponsiveness) is a common and expected finding after seizures.
4. Chest pain or pressure
   a. Presumed to be cardiac until proved otherwise so the EMS should be activated. Patients should not be transported by private vehicle.
   b. The chest discomfort may radiate down the left jaw or arm; it may be described as pain or pressure, and it can be accompanied by symptoms such as diaphoresis and shortness of breath.
   c. Aspirin 162–325 mg is recommended if there are no allergies or other contraindications (e.g., active bleeding, acute stroke) and aspirin is readily available (Class IIa, LOE A).
      i. Early aspirin administration (within 24 hours) decreases mortality.
      ii. The patient should chew and swallow the dose (use chewable aspirin if available).
      iii. Enteric-coated products should be avoided.
   d. Nitroglycerin sublingual can be administered to patients for whom it is prescribed.
      i. Do not use someone else's nitroglycerin.
      ii. It can be administered every 3–5 minutes up to three doses.
5. Bleeding
   a. The best treatment is direct and manual pressure over the area that is bleeding. To be effective, the manual pressure must be firm and held for a significant amount of time. Gauze should be placed over the affected area and more added, if necessary. No attempt should be made to remove old gauze.
   b. An alternative to manual pressure is using elastic bandages over gauze, but this may not be as effective.
   c. Tourniquets are not generally recommended unless control of bleeding cannot be achieved or is not possible with manual pressure.
      i. Improperly placed tourniquets can lead to secondary injury of muscles and nerves, and to limb ischemia. Limb ischemia can contribute to electrolyte aberrations, leading to cardiac arrhythmias, metabolic acidosis, shock, and death.
      ii. If they are used, the time they were applied should be conspicuously noted and communicated to health care professionals taking over care.
   d. Using pressure points (indirect pressure at a distal location) is less effective than other techniques and should not be used routinely.
6. Wounds and abrasions
   a. Wash with warm soap and water while removing foreign matter from the wound (Class I, LOE A). Although cold and warm water are equally effective, warm water is more comfortable.

b. Superficial injuries should be covered with a topical antibiotic cream or ointment and a dressing to keep the wound moist (Class IIa, LOE A).
   i. Consider potential allergies to antibiotics before application.
   ii. Wounds have less infection risk when covered.

7. Thermal burns
   a. Thermal burns should be cooled with cool to room-temperature (not cold) tap water as soon as possible after the injury (Class I, LOE B).
      i. Treat burns within 30 minutes to help reduce pain, edema, depth of injury, and need for grafting procedures.
      ii. Ice or ice water should not be used because it can cause secondary injuries, including tissue ischemia.
   b. Blisters caused by burns should be left intact, and no attempt should be made to remove or drain them. Place a sterile dressing over the blister to help speed healing and decrease pain (Class IIa, LOE B).
8. Electrical injuries
   a. Electric current traveling through the body can cause a variety of injuries of differing severities, including a tingling sensation, burns, respiratory arrest, and life-threatening cardiac arrhythmias. Prolonged exposure can occur when sufficient current travels through the individual and causes tetany and an inability to let go of the electrical source.
   b. The first step for treating the injured person is to ensure the power is turned off at the source (e.g., breaker box). Failure to do this may contribute to the bystander's injury. Use of other materials (e.g., wooden board) is not recommended to move electric wires from the injured person or to move the person from the electrical source because there is still a risk of electrical conduction through the board.
   c. Do not touch the injured person while the power is on (Class III, LOE C).
   d. After the power has been turned off, the individual has to be assessed and CPR efforts initiated, if indicated. Do not move the injured person unless there is immediate danger.
   e. People who have received an electrical shock should be assessed for nonapparent injuries in a health care setting such as an ED.
9. Ocular injuries
   a. If the eye is exposed to chemicals
      i. Remove contact lenses.
      ii. Irrigate for 10–15 minutes with copious amounts of water with an eyewash station (Class I, LOE C).
      iii. If an eyewash station is not immediately available, the eyelid can be retracted and water poured onto the eye by using a drinking cup.
   b. Mechanical injuries to the globe or foreign objects embedded in the eye are treated initially by covering the affected eye, if possible, and the patient is then referred to an ophthalmologist. No attempt to remove foreign objects should be made.
10. Temperature-related emergencies
   a. Hypothermia caused by exposure to cold is treated by rewarming the affected individual.
      i. The initial treatment is to remove all wet clothing and wrap exposed body parts with blankets or other articles of clothing.
      ii. If there is a delay in medical care
         (a) The person with hypothermia should be actively rewarmed (warm environment, immersion in warm water) (Class IIa, LOE B).
         (b) Frozen parts of the body can be rewarmed by placing them in warm water (e.g., body temperature) for 20–30 minutes (Class IIb, LOE C).

(c) Do not use chemical warmers directly on frostbite because they can cause burns (Class III, LOE C).
(d) If there is a chance of refreezing, rewarming should not be attempted (Class III, LOE C). Any potential benefit is replaced by potential harm if refreezing occurs.

iii. Benefits of rewarming include return of venous circulation and decreased tissue loss.

b. Heat-related injuries include cramps, heat exhaustion, and heat stroke.
   i. Heat cramps are muscle spasms affecting the legs, arms, abdominal muscles, and muscles of the back. Treatment recommendations are to have the affected person rest, cool off, and drink an electrolyte- and carbohydrate-based drink, if available. Massage and stretching are other strategies that can be used in combination with rehydration and cooling.
   ii. Heat exhaustion is characterized by nausea, muscle cramps, dizziness, headache, diaphoresis, and fatigue. The affected person should be moved to a cool, shaded place with clothing removed. External cooling using cool water sprays can also be used. Similar to a person who has had heat cramps, the person who has had heat exhaustion should be encouraged to drink electrolyte- and carbohydrate-based solutions.
   iii. Heat stroke includes exhaustion-related effects in addition to more severe central nervous system involvement, including syncope, altered mental status, and seizures. Because of the severity of the injury, people with heat stroke should be placed in cold water up to their chin, with EMS transport to an ED.

11. Musculoskeletal trauma
   a. Sprains and strains should be treated with external cooling because it decreases pain, swelling, and healing time. The best method to use is a plastic bag filled with ice water covered with a thin towel (Class IIb, LOE C). Refreezable ice packs are less effective. To prevent secondary injury, no more than 20 minutes per application should be used. Heat is inferior to cold and is not recommended.
   b. Bone fractures should be suspected when there is injury to any extremity. No attempt should be made to reduce or straighten bone fractures (Class III, LOE C). There is no evidence of better outcomes such as decreased pain or deformity. Splinting the injured extremity may decrease pain and prevent secondary injury until definitive therapy (Class IIa, LOE C). The injured person should avoid bearing weight on the extremity.
   c. If the extremity is blue or pale, the EMS should be activated because it may indicate a more severe injury requiring prompt medical attention.

Patient Cases

1. A scouting troop is hiking on a trail along a mountainside. One of the adolescent boys slips and falls about 6 feet onto a rocky ledge. He has pain in his left leg. There is obvious injury, including several abrasions and a likely fracture to both the tibia and the fibula. Which is the most appropriate first aid therapy for his apparent fracture?
   A. Try to set his leg manually to decrease pain.
   B. Splint his leg with available materials.
   C. Encourage ambulation to maintain circulation.
   D. Apply ice to the fracture to decrease pain.

2. At the ambulatory care clinic, an adult patient known to have a seizure disorder falls to the floor from a seated position. The patient appears to be having tonic-clonic muscle contractions consistent with a generalized seizure. Which action is best to take?
   A. Try to place a wallet or other object in the patient's mouth to help the patient avoid biting his or her tongue.
   B. Ensure the area is clear of obstacles that could cause secondary injury.
   C. Try to hold the patient still, and speak words of reassurance.
   D. Try to administer the patient's antiseizure medication.

D. Cardiopulmonary Resuscitation
   1. In out-of-hospital arrests, CPR should be initiated unless the following occurs:
      a. There are signs of obvious irreversible death (e.g., rigor mortis, decomposition).
      b. The person performing CPR would be in physical danger.
      c. The patient has an advanced directive indicating that he or she does not wish to receive resuscitative efforts.
   2. Sequence for rescuers: Verify that the patient is unresponsive and not breathing normally.
      a. Patient is not moving or does not respond after tapping on the shoulder and shouting at the patient.
      b. A patient with gasping breaths or absent breathing is assumed to be in cardiac arrest (Class I, LOE C).
   3. If one person is present at an arrest
      a. Adults: Activate the emergency response system (ERS), and obtain an automated external defibrillator (AED) if easily accessible.
      b. Infants and children: Perform 2 minutes of CPR; then activate the ERS.
   4. If more than one person is present at an arrest
      a. One person should activate the ERS and obtain an AED.
      b. One person should initiate CPR (see Table 1).
   5. After activating the ERS
      a. Compressions, then airway, then breathing (CAB) is the preferred sequence (see Table 1).
      b. If a rescuer is untrained or unwilling to provide ventilations, compression-only CPR is recommended.

Table 1. Initial Sequence of Actions After a Person Collapses

	Lay Rescuer	Health Care Provider
Unresponsive adult	1. Activate ERS, and obtain an AED if immediately available 2. Provide 30 chest compressions at a rate of at least 100/minute OR continuously at a rate of at least 100/minute if rescuer is untrained in giving rescue breaths 3. Open the airway, and give two breaths if rescuer is trained in giving rescue breaths 4. Repeat steps 2 and 3 5. Use the AED, when available	1. Activate ERS, and obtain an AED 2. Check pulse (no more than 10 seconds) 3. Provide 30 chest compressions at a rate of at least 100/minute 4. Open the airway, and give two breaths 5. Repeat steps 3 and 4 6. Use the AED, when available Note: If the cause of the collapse is respiratory (e.g., drowning), the health care provider should perform CPR with an emphasis on rescue breathing
Unresponsive infant or child	1. Provide 30 chest compressions 2. Open the airway and give two breaths (omit if rescuer untrained or unwilling) 3. Repeat steps 1 and 2 for a total of five cycles (about 2 minutes) 4. Activate ERS, and obtain an AED if available	1. Check pulse (brachial for infants and carotid or femoral in a child; no more than 10 seconds) 2. Provide 30 chest compressions 3. Open the airway, and give two breaths 4. Repeat steps 2 and 3 for a total of five cycles (about 2 minutes) 5. Activate ERS, and obtain an AED if available

AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; ERS = emergency response system.

6. Compression-only CPR
    a. Compression-only CPR is superior to no CPR.
    b. The recommended chest compression rate is at least 100/minute.
    c. Instructions can be given by telephone by emergency medical dispatchers, even for people untrained in giving CPR (Class I, LOE B).
    d. Survival rates with conventional CPR compared with compression-only CPR are similar.
    e. Indicated for lay rescuers responding to a person in presumed adult cardiac arrest. Asphyxial (e.g., drowning) causes for arrest and pediatric arrests should include rescue breaths (Class I, LOE B).
7. Effective chest compressions
    a. Ensure the patient is lying on his or her back (supine) on a hard surface.
    b. Correct rate is *at least* 100 compressions per minute for all patients—Push fast (Class IIa, LOE B).
    c. Minimize interruptions (Class IIa, LOE B). Time performing chest compressions should be at least 80%.
    d. Allow complete chest recoil after each compression (adults: Class IIa, LOE B; pediatric: Class IIb, LOE B).
        i. Incomplete chest recoil is associated with increased intrathoracic pressure.
        ii. Decreased cerebral and coronary perfusion occurs with higher intrathoracic pressures.
        iii. As rescuers become fatigued, incomplete chest recoil is more common because rescuers lean over the patient.
    e. Infants (younger than 1 year)
        i. Lay rescuers and lone health care providers: Two fingers on the sternum just below the nipple line (Class IIb, LOE C)
        ii. Compression/ventilation ratio 30:2

iii. Two health care providers should use the two-thumb encircling technique; compression/ventilation ratio 15:2.
iv. Depth should be about 1½ inches (one-third the depth of the chest); push hard.

f. Children (1 year of age until puberty)
i. Puberty: Hair under the arms for male individuals and breast development in female individuals
ii. Lay rescuers and lone health care providers: One or two hands over the sternum between the nipples
iii. Compression/ventilation ratio 30:2
iv. Two health care providers: One or two hands over the sternum between the nipples; compression/ventilation ratio 15:2
v. Depth should be about 2 inches (one-third of the depth of the chest); push hard.

g. Adults (at and beyond puberty)
i. Lay rescuers and health care providers should use two hands over the sternum between the nipples (Class IIa, LOE B).
ii. Compression/ventilation ratio 30:2
iii. Depth should be at least 2 inches; push hard (Class IIa, LOE B).
iv. Compression and relaxation times should be equal (Class IIb, LOE C).

Table 2. Chest Compression Techniques

	Chest Compression Technique	Landmarks	Depth of Compressions, inches
Infant (Younger than 1 year)	Two fingers over sternum Two-thumb encircling if two health care rescuers	Just below nipple line	About 1½
Child (1 year to prepubescent)	Heel of one hand or heel of one hand with the other hand on top, as for adults	Over sternum at nipple line	About 2
Adult (postpubescent)	Heel of one hand with the other hand on top	Over sternum at nipple line	At least 2

8. Rescuer role change
a. Fatigue can cause deterioration in the quality of CPR in both ventilations and chest compressions.
b. Change ventilator and chest compression roles every 2 minutes to prevent fatigue (Class IIa, LOE B).
c. Role changes should take no more than 5 seconds.

9. Airway and breathing
a. Open the airway (for lay rescuers): Head tilt–chin lift for the injured and uninjured individuals (Class IIa, LOE B).
b. Open the airway (for health care providers).
i. Head tilt–chin lift for individuals without suspected head or neck trauma (Class IIa, LOE B)
ii. Jaw thrust for patients with suspected head or neck trauma (Class IIb, LOE C). If the jaw thrust maneuver fails, the head tilt–chin lift should be used (Class I, LOE C).
c. Evaluate effective ventilations by ensuring a visible chest rise with each breath (Class IIa, LOE C). Ineffective breaths may require repositioning the airway and reattempting ventilations.
d. Ventilatory techniques
i. Mouth-to-mouth for child and adult
ii. Mouth-to-mouth-and-nose for infant. If unable to ventilate, then use mouth-to-mouth or mouth-to-nose (Class IIb, LOE C).

iii. Face shield (i.e., plastic film that acts as a barrier)
iv. Face mask: Contains a one-way valve to allow air to flow from the rescuer to the person in cardiopulmonary distress and diverts the person's exhaled air from the rescuer
v. Bag-mask
(a) Contains a reservoir and a mask designed to cover the mouth and nose
(b) Adult and pediatric sizes are available.
(c) If oxygen is available, provide 100% at a rate of 10–12 L/minute.
(d) Most effective with two rescuers
vi. Each breath should be delivered during 1 second to avoid excessive ventilation leading to complications (Class IIa, LOE C).
(a) Increased intrathoracic pressure, which leads to decreased venous return and decreased perfusion
(b) Increased risk of aspiration and regurgitation of gastric contents
(c) Barotrauma

e. If gasps of breath are present, the patient should be treated in the same way as if he or she were not breathing.
f. Even if a patient has a pulse, rescue breaths may be required.
i. Infant or child—Twelve to 20 breaths/minute (one breath every 3–5 seconds)
ii. Adult—Ten to 12 breaths/minute (one breath every 5–6 seconds) (Class IIb, LOE C)
g. Complications of improper ventilation: Gastric inflation that can cause regurgitation and aspiration and restrict lung compliance

10. An AED is the most likely source of externally applied electricity outside a hospital environment.
a. The efficacy of a single shock is greater than 90%.
b. Use as soon as it is available (Class IIa, LOE C). The time from discontinuing CPR for a shock should be minimized. The shorter the time between the shock and CPR, the more likely the shock is to be successful.
c. CPR should be started immediately with chest compressions after a shock.
d. AEDs: Available in public areas (e.g., casinos, airports, sports facilities, shopping malls)
e. AEDs provide voice and visual prompts to aid in the successful use of the AED.
f. Infants
i. A manual defibrillator is preferred (initial dose 2 J/kg; second dose 4 J/kg).
ii. A pediatric attenuator on an AED can be used if a manual defibrillator is unavailable.
iii. If neither a manual defibrillator nor a pediatric attenuator system on an AED is available, a standard AED can be used (Class IIb, LOE C).
g. Children 1–8 years of age
i. Use a pediatric attenuator system, if available.
ii. Use adult systems if pediatric attenuator system is unavailable.
h. Children older than 8 years and adults: Use an adult pad system.
i. The first step to using an AED is to turn it on; then follow the audio and visual prompts.
j. Pad placement: Pads should be placed on the right upper chest (sterno-lateral position) and the left lateral chest. If medication patches are present, they should be removed and the medication wiped from the skin to maximize the electricity delivered to the heart. If an implanted device is felt or visualized beneath the skin (e.g., an internal cardiac defibrillator), the pad should be placed no closer than 1 inch to the device.

11. Foreign-body airway obstruction
a. Children younger than 5 years are at highest risk of death caused by foreign-body airway obstruction.
i. This age group accounts for 90% of deaths from foreign-body airway obstruction.
ii. Common causes include balloons, small objects, food (e.g., hot dogs, grapes, nuts, candy).

b. Mild airway obstruction – Audible sounds are noted.
c. Severe airway obstruction – No sounds are heard, and no cough is evident.
d. The person choking may show the universal choking sign (two hands encircling the neck).
e. Verbally ask the patient whether he or she is choking.
f. Intervention should be done only for severe choking.
    i. An audible cough that becomes silent
    ii. Respiratory difficulty
    iii. The person choking becomes unconscious.
g. Activate the ERS for severe choking.
h. Perform abdominal thrusts (i.e., Heimlich maneuver) until the foreign body is expelled or the person becomes unresponsive.
i. Abdominal thrusts should not be used in the following groups:
    i. Infants (younger than 1 year)
    ii. A woman in the late stages of pregnancy
    iii. The rescuer is unable to encircle his or her arms around the patient (e.g., in obesity).
    iv. Apply rapid abdominal thrusts until the foreign body is relieved or the patient becomes unconscious.
    v. Chest thrusts can be considered if abdominal thrusts are ineffective.
    vi. Abdominal thrusts can cause internal injury, and survivors may need to be assessed by a physician to determine any extent of injuries.
j. Chest thrusts
    i. Use for patients for whom abdominal thrusts are contraindicated (infants, women in the late stages of pregnancy, people who are too obese for the rescuer to encircle his or her arms around the person's abdomen).
    ii. Infants: Five back blows are alternated with five chest thrusts.
    iii. Consider using if abdominal thrusts fail
k. If the patient becomes unconscious
    i. Ensure the ERS has been activated.
    ii. Begin CPR.
    iii. Examine the mouth for evidence of foreign bodies that can be removed before each series of rescue breaths.

12. Rescuers
    a. The person delivering a shock must ensure all personnel stay clear of the patient while a shock is being delivered.
    b. Careful coordination is necessary to minimize interruptions in good-quality CPR.

E. Pharmacist Roles
1. Become trained and maintain certification in providing CPR.
2. Recognize and manage the pitfalls of CPR.
    a. Chest compressions that are too slow, that are too shallow, or that do not allow complete recoil
    b. Too much time without CPR being performed (e.g., when the defibrillator pads are being applied or the defibrillator is being charged)
    c. CPR that does not start immediately after a shock
    d. Chest compressor fatigue
    e. Excessive or ineffective ventilation

F. Guidelines: Available at www.circulationaha.org

Patient Cases

3. A 71-year-old man well known to the hypertension clinic presents for his follow-up appointment. While in the lobby, he tells the clerk about the pressure he feels in his chest and appears pale and somewhat diaphoretic. Just before coming to the clinic, he took all of his morning medications, including aspirin 162 mg, metoprolol 100 mg, lisinopril 20 mg, atorvastatin 20 mg, and glipizide 5 mg orally. The clerk goes to get help from the pharmacist, and when they arrive in the lobby, they see the patient become unresponsive. The pharmacist instructs the clerk to call 911 and obtain the AED. Which is the most appropriate action for the pharmacist to take next?
   A. Wait for the AED to arrive.
   B. Cycle 30 chest compressions with two rescue breaths.
   C. Cycle one rescue breath with 15 chest compressions.
   D. Start chest-compression-only CPR.

4. At the scene of a car crash, an adult man is unresponsive and not breathing. There is concern about a cervical spine injury. Emergency medical response is already en route, and another bystander (a nurse, trained in CPR) offers to help with the airway. After initiating chest compressions, the nurse is unable to open the airway with a jaw thrust. Which is the best action to take?
   A. Try opening the airway with the jaw thrust until successful.
   B. Continue with chest-compression-only CPR.
   C. Try to open the airway with the head tilt–chin lift maneuver.
   D. Increase ventilation efforts by blowing more forcefully.

II. TOXICOLOGY

A. Poison Control Centers
   1. More than 50 poison control centers exist, covering all 50 states, as well as American Samoa, Micronesia, Guam, Puerto Rico, and the U.S. Virgin Islands.
   2. Single telephone number routes to the poison control center serving that area: 1-800-222-1222
   3. All information from calls is logged and ultimately captured in the National Poison Data System.
      a. Real-time database that can help disseminate public health concerns as they unfold (e.g., contaminated food)
      b. An annual report is published that summarizes data related to calls to poison centers.
   4. Patients undergo initial management on the telephone, with appropriate triage for further evaluation and treatment at a medical facility, if necessary.
      a. Poison control centers are staffed 24 hours per day.
         i. Board-certified medical toxicologist available
         ii. Nurses and pharmacists who are specialists in poison information must pass a national certification examination every 7 years.
      b. Serve as a resource for medical professionals

B. National Toxicology Statistics
   1. The top five drug classes most commonly implicated in overdoses are listed in the following text.
      a. Opioids: 75.2%
      b. Benzodiazepines: 29.4%
      c. Antidepressants: 17.6%
      d. Antiepileptic and antiparkinson drugs: 7.8%
      e. Systemic and hematologic drugs: 7.2%
   2. Opioids were also commonly implicated in pharmaceutical-related deaths when combined with drugs from other classes. The data that follow describe the percentage of cases in which opioids were also involved. For example, 77.2% of deaths involving benzodiazepines also involved the use of opioids.
      a. Benzodiazepines: 77.2%
      b. Antiepileptic and antiparkinson drugs: 65.5%
      c. Antipsychotic and neuroleptic drugs: 58%
      d. Antidepressants: 57.6%
      e. Other analgesics, antipyretics, and antirheumatics: 56.5%
   3. Most (50%–80%) people who die of prescription opioid overdoses have a history of chronic pain.
   4. Opioids
      a. Detection of opioids is commonly done with the use of immunoassays that detect the class of drugs.
      b. Morphine, codeine, and related drugs such as hydrocodone are detected. However, sensitivity differs between them such that detection of hydrocodone requires higher concentrations to produce a positive result.
      c. Oxycodone is also poorly detected.
      d. Some opioids are not detected by the assay because they do not contain a phenanthrene ring (e.g., fentanyl and methadone).
      e. For these reasons, specific rules as to how long an opioid is detectable will vary by drug, dose, and timing. If additional information is necessary about urine detection of a particular opioid, specific assays (qualitative or quantitative) can be obtained.
   5. Substance Abuse and Mental Health Services Administration (SAMHSA) recommended strategies to combat opioid-related deaths (http://store.samhsa.gov/shin/content//SMA13-4742/Overdose_Toolkit_2014_Jan.pdf).
      a. Education for providers, patients, family members, and other individuals at high risk of opioid overdose
         i. Providers should be educated by using evidence-based practices to prevent and manage overdose.
         ii. Others should be educated about potential drug interactions (e.g., alcohol, benzodiazepines), safe storage, signs of overdose, and proper disposal.
      b. Treatment access for those with substance abuse disorders
      c. Access to naloxone
      d. Bystanders of suspected opioid overdose should be encouraged to call 911.
      e. Use prescription drug monitoring programs.
   6. Naloxone
      a. Several laws have been enacted that allow laypersons access to this drug and address liability issues for prescribers and bystanders. The most up-to-date information on laws by jurisdiction is available through www.lawatlas.org.
      b. Pharmacology: Pure opioid antagonist that displaces opioids from binding sites (e.g., μ receptors)
      c. Overdose is classically characterized by respiratory depression, altered mental status, miosis (pinpoint pupils), and decreased bowel motility.
      d. Traditionally, given by intravenous or intramuscular routes in emergency departments

e. Kits containing injectable naloxone and mucosal atomization devices have been used for intranasal drug administration.
   i. Advantages include decreased risk of needlestick injuries and ease of administration.
   ii. Using 2-mg doses, intranasal and intramuscular administration produce similar response rates within 10 minutes; however, duration may be shorter for the intranasal route, requiring more supplemental naloxone doses.

f. Commercially available naloxone intramuscular autoinjector was approved by the U.S. Food and Drug Administration (FDA) in April 2014, and commercially available nasal spray was approved by the FDA in November 2015 and is expected to be marketed in early 2016.
   i. Tradename: Evzio
   ii. Each carton for dispensing contains two autoinjectors and one training device.
   iii. Each autoinjector contains 0.4-mg naloxone. Similar to other autoinjectors, it can be administered through clothing. After actuation, the device should be held in place for 5 seconds.
   iv. Autoinjectors have electronic voice instructions when activated.

7. Public health implications
   a. Providers need to be aware of the effect of pharmaceuticals on health care utilization because of misuse, abuse, and deaths from overdose.
   b. Health care professionals should be aware of and use prescription drug monitoring databases in their state to detect potential abuse.
   c. Pharmacists should play an active role in the care of patients to ensure they are receiving safe and optimal care, especially with opioids. Organizations such as the American Pain Society have issued recommendations for the long-term use of opioids in noncancer pain. Recommendations include proper patient selection and risk stratification, management plans, and monitoring for intended and adverse effects.
   d. Opioid overdose prevention strategies are multipronged, and naloxone is an emerging strategy. With the expansion of naloxone use, providers should be aware of naloxone intranasal kits and naloxone autoinjectors.

C. Pediatric Toxicology (Am J Prev Med 2009;37:181-7)
   1. Pediatric patients (18 years and younger) presenting to the ED with poisoning (medication overdose or overexposure to a nonpharmaceutical consumer product) predominate in the young (5 years or younger).
      a. The most common medications, listed in descending order, causing ED visits because of unsupervised ingestion are listed in the following text.
         i. Acetaminophen
         ii. Opioids and benzodiazepines
         iii. Cough and cold preparations
         iv. Nonsteroidal anti-inflammatory drugs
         v. Antidepressants
      b. The results of this investigation highlight the need for pharmacists to educate patients who are around children on the importance of poison prevention strategies and the need for close supervision of children.
   2. Flow restrictors may be another layer of safety for pediatric medications (J Pediatr 2013;1134:39).

D. Poison Prevention Strategies: May reduce unintentional poisonings from drugs and household products
   1. Child-resistant packaging (e.g., caps on medication containers and poisons)
   2. Identify all poisons around the house and maintain them in a locked cabinet.
   3. Keep all potential poisons in their original containers.
   4. Never store food with poisons.

5. Keep plants away from animals and children.
6. Have poison control number easily accessible.
7. Use carbon monoxide detectors.

III. BIOTERRORISM/NATURAL DISASTERS

A. Emergency Response Starts Locally: The most effective response is through advanced preparation and through disaster drills.
   1. Pharmacists are essential and highly accessible health care providers.
   2. Incidents are first managed locally.
      a. Additional government support is used as required by the effects of the disaster.
      b. Facilities should prepare disaster plans, including contact lists, calling trees, backup communication, medication storage (if applicable), recordkeeping, and emergency supplies.
      c. Disaster plans are facility specific, but many have common themes, including the ability to flex according to the situation. Examples of plans:
         i. Community pharmacy: J Am Pharm Assoc 2013;53:432-7
         ii. Hospital pharmacy: CJHP 2007;September/October:6-15
      d. Personal disaster plans should be made as well. A useful resource for guiding individuals in this process is available at www.ready.gov.
   3. The pharmacist will be faced with critical issues during a disaster, including the following:
      a. Limited formulary
      b. Increased need for therapeutic substitution
      c. Management of adverse effects caused by medication changes
      d. Disruption in continuity of care
      e. Patient's ability to store medications properly is diminished.
      f. How to keep records if there is disruption in electronic and Internet connectivity
      g. Communication disruptions
   4. Role of the pharmacist
      a. American Society of Health-System Pharmacists (ASHP) statement on the role of health-system pharmacists in emergency preparedness includes the following recommendations:
         i. Pharmaceutical control and distribution, including planning efforts
         ii. Management of drug therapy for patients during disasters
         iii. Assist with developing guidelines for the diagnosis and treatment of affected individuals.
         iv. Help select pharmaceuticals and supplies for local, regional, and national stockpiles.
         v. Ensure proper storage, packaging, labeling, and handling of pharmaceuticals.
         vi. Ensure pharmaceutical deployment.
         vii. Educate individuals who receive pharmaceuticals.
         viii. Advise public health officials about appropriate messages related to pharmaceuticals to be shared with the public.
         ix. Collaborate with prescribers in the management of patients.
      b. Other roles identified through experience (Public Health Rep 2009;124:217-23)
         i. Prevention of ED overcrowding by caring for patients with nonemergency needs through collaborative protocols that allow pharmacists to refill limited supplies of medications for chronic therapy
         ii. Assess patients for appropriate level of care through triage activities.

iii. Provide care for minor injuries and other health needs with over-the-counter medications and appropriate use of vaccinations.
iv. Partner with a doctor of pharmacy educational program as a source of additional personnel.

c. Pharmacists with clinical responsibilities can be broadly classified into one of three general categories.
i. Ambulatory readiness pharmacists: Practice in the community setting; the patients they serve include those with low-acuity conditions and chronic diseases.
ii. Pharmacotherapy readiness pharmacists: Practice in the hospital setting and help care for patients with moderate acute conditions and chronic diseases
iii. Critical care readiness pharmacists: Practice in the hospital setting, delivering intensive care to patients with high-acuity medical conditions

5. Locations where pharmacists may serve during a disaster
a. Usual place of work is most likely, but may also include shelters, clinics, hospitals, other outreach sites, or temporary medical centers
b. Points of distribution
i. Mass distribution of prophylactic medications or vaccines
ii. Locations include schools, shopping malls, schools, community centers, and stadiums.
iii. To be effective, patient flow, triage, staffing, recordkeeping, and medication dispensing or immunization administration must be considered.

6. National coordination
a. The National Incident Management System was established under the Homeland Security Presidential Directive (HSPD)-5: Management of Domestic Incidents
i. Nationwide template to coordinate efforts, including preparation, response, and recovery
ii. Provides the basis for the National Response Framework (NRF)
b. National Response Framework
i. Part of the National Preparedness System, which was mandated by Presidential Policy Directive (PPD)-8: National Preparedness
ii. The NRF is a document that addresses response to a disaster, which is one of the five mission areas—prevention, protection, mitigation, response, and recovery—defined by PPD-8.
iii. Fourteen core capabilities are defined that must be addressed to respond to any incident.
(a) Planning
(b) Public information and warning
(c) Operational coordination
(d) Critical transportation
(e) Environmental response/health and safety
(f) Fatality management services
(g) Infrastructure systems
(h) Mass care services
(i) Mass search and rescue
(j) On-scene security and protection
(k) Operational communications
(l) Public and private resources
(m) Public health and medical services
(n) Situational assessment

iv. The NRF uses emergency support functions (ESFs) to manage resources and deliver core capabilities. Each ESF may address several core capabilities.
(a) Fifteen ESFs: Transportation; Communications; Public Works and Engineering; Firefighting; Information and Planning; Mass Care; Emergency Assistance, Temporary Housing, and Human Services; Logistics; Public Health and Medical Services; Search and Rescue; Oil and Hazardous Materials Response; Agriculture and Natural Resources; Energy; Public Safety and Security; External Affairs
(b) Pharmacists are most likely to be involved with the Public Health and Medical Services (ESF8) because one of the main core capabilities is public health and medical services.
(c) ESF8 is primarily coordinated by the Department of Health and Human Services (HHS), but local, state, and tribal officials retain primary responsibility for health and medical needs. Medical care is just one of the many functions of ESF8.
(d) There are several areas where pharmacists may serve on the federal level. Disaster medical assistance teams and national pharmacy response teams incorporate pharmacists into emergency response, including mass chemoprophylaxis or immunizations. In addition, the U.S. Public Health Service Ready Reserve Corps was established in 2010. In time of national need, those in the Reserve Corps may be deployed on short notice (www.usphs.gov). While deployed, pharmacists are considered federal employees, are paid a government salary, are reimbursed for travel and other expenses, and are provided liability coverage while practicing outside their state. During national emergencies when these teams are activated, licensure in one state is recognized by all states.

7. Strategic National Stockpile (SNS)
a. Local and regional supplies are used initially, but these may become exhausted, necessitating the utilization of the SNS.
b. Managed by HHS, with the Centers for Disease Control and Prevention (CDC) as the agency in charge of the SNS
c. Repository of medications, including antibiotics, antitoxins, antidotes, and other drugs to support an ill-defined threat
d. Deployment of SNS assets includes a 12-hour push pack and vendor-managed inventory. SNS assets are deployed in response to a request by the state governor's office to HHS or CDC.
e. Twelve-hour push package
i. First line of support
ii. Can be delivered anywhere in the United States within 12 hours of the decision to deploy
iii. Contains pharmaceuticals and medical supplies
iv. Personnel are also deployed to ensure efficient receipt and deployment of assets at the site.
v. Located at 12 strategic and secure locations within the United States
f. Vendor-managed inventory is a secondary source of supplies, including medications that are tailored according to continued needs.

B. Weapons of Mass Destruction
1. Bioterrorism
a. The CDC classifies bioterrorism agents as categories A, B, or C, according to their threat to national security.
b. Category A diseases: Category A agents are the highest priority because they can be easily disseminated or transmitted from person to person, are associated with high mortality rates with public health impacts, can cause public panic/social disruption, and require public health preparedness efforts.

These include anthrax (*Bacillus anthracis*), botulism (*Clostridium botulinum*), plague (*Yersinia pestis*), smallpox (*Variola major*), tularemia (*Francisella tularensis*), and viral hemorrhagic fevers (Filoviruses and arenaviruses). Table 3 highlights the clinical characteristics of the diseases and postexposure prophylaxis for category A agents when many individuals are affected.

c. Category B diseases are moderately easy to disseminate and have moderate morbidity but low mortality rates, requiring enhanced disease surveillance and diagnostics; they include diseases mediated by *Clostridium perfringens* toxin, brucellosis, food safety (e.g., *Salmonella, Shigella*), glanders, Q fever, ricin poisoning, melioidosis, typhus fever, equine viral encephalitis, and waterborne diseases (e.g., *Vibrio*).

d. Category C diseases can be engineered for mass dissemination with the potential for high morbidity and mortality; they can cause a major health impact and include Nipah virus infection, hantavirus infection, tick-borne viral infections, yellow fever, and multidrug-resistant tuberculosis.

Table 3. Summary of High-Priority Bioterrorism Agents with Recommendations for Postexposure Prophylaxis

Clinical Manifestations	Adult Postexposure Prophylaxis	Pediatric Postexposure Prophylaxis
Anthrax *(B. anthracis)*		
Inhalational form: Starts with flulike symptoms; then respiratory symptoms progressively worsen; death ensues within 5–7 days but can take up to 2 months	Postexposure prophylaxis for pneumonic (i.e., inhalational) anthrax is most effective when antimicrobials and vaccines are used in combination The vaccine uses a protein to induce immunity and does not contain any dead or live bacteria; it is in limited supply and is only available through CDC	
Cutaneous form: Typically occurs from a break in the skin; pruritic rash and edema at infection site that forms a black eschar; 1–7 days from exposure Gastrointestinal form: Rare, but may occur in conjunction with inhalational form, causing abdominal pain and ulcerations; can also occur from raw/undercooked meats; 1–7 days after exposure No person-to-person transmission Spores may germinate for up to 60 days after exposure, so prophylaxis for many patients may be necessary for up to 60 days	Ciprofloxacin 500 mg PO q12h Or Doxycycline 100 mg PO q12h Or Amoxicillin 500 mg PO tid if the strain is sensitive to penicillin Duration: 60 days Because of the severity of the disease, pregnant women and those who are immunocompromised should receive the same therapy Anthrax vaccine adsorbed is recommended for all adults (18–65 years), including pregnant woman, as a three-dose subcutaneous series; the first dose is administered no later than 10 days after exposure, and the remaining doses are given 2 and 4 weeks after the initial dose	Ciprofloxacin 10–15 mg/kg PO q12h Or >8 years and >45 kg: Doxycycline 100 mg PO q12h ≤8 years or ≤45 kg: Doxycycline 2.2 mg/kg PO q12h (not to exceed 100 mg/dose) Duration: 60 days Although fluoroquinolones and tetracyclines are usually avoided in children, their use is indicated because of the severity of the disease Vaccine recommendations are made when the event occurs

Table 3. Summary of High-Priority Bioterrorism Agents with Recommendations for Postexposure Prophylaxis *(continued)*

Clinical Manifestations	Adult Postexposure Prophylaxis	Pediatric Postexposure Prophylaxis
Botulism *(C. botulinum)*		
Portal of entry is through the ingestion of contaminated food, or it is inhalational, with the earliest onset of symptoms at 6 hours; however, it can be delayed by more than a week The toxin inhibits the release of acetylcholine; symptoms include visual difficulties and trouble with speech, swallowing, breathing, and muscle control No person-to-person transmission	An antitoxin is available through the CDC and may halt clinical progression and shorten disease duration; limited supply of the antitoxin may limit its use in postexposure prophylaxis when many patients may require therapy	
Plague *(Y. pestis)*		
Fleas are the vector to spread natural disease; they cause disease in small rodents and humans through bites; in cases of bioterrorism, aerosolization and resultant inhalation will cause disease Pneumonic form: Caused by primary inhalation or hematogenous spread; the clinical course includes a severe pneumonia with high fevers, chills, malaise, cough that progresses to respiratory failure and death; even with treatment, mortality is around 60% Pneumonic plague can be transmitted from person to person; droplet precautions should be used for infected individuals Bubonic form: High fevers, malaise, buboes (painful and swollen lymph nodes), may progress to bacteremia, sepsis, or pneumonia; with treatment, mortality is around 5%	Preferred Doxycycline 100 mg PO q12h Ciprofloxacin 500 mg PO q12h Or Alternative Chloramphenicol 25 mg/kg PO qid Duration: 7 days Indicated only for pneumonic form	Preferred More than 45 kg: Doxycycline 100 mg PO q12h 45 kg or less: Doxycycline 2.2 mg/kg PO q12h (not to exceed 100 mg/dose) Ciprofloxacin 20 mg/kg PO bid (up to 1 g/day) Or Alternative Chloramphenicol 25 mg/kg PO qid Duration: 7 days Indicated only for pneumonic form

Table 3. Summary of High-Priority Bioterrorism Agents with Recommendations for Postexposure Prophylaxis *(continued)*

Clinical Manifestations	Adult Postexposure Prophylaxis	Pediatric Postexposure Prophylaxis
Smallpox *(Variola DNA virus)*		
Prodrome of illness includes headache, malaise, myalgia, and a temperature of over 102°F (38.9°C); lesions first appear in the mouth and then spread to the skin; the rash (macules, papules, and vesicles) progressively spreads from the hands, face, and forearms to the trunk and lower extremities; lesions have a more dense appearance on the extremities and face; lesions eventually crust over and leave pitted scars; unlike chickenpox, smallpox lesions are commonly found on the palmar aspect of hands and the soles of the feet High person-to-person transmission through close contact, and possible airborne spread Early vaccination can prevent or decrease the severity of disease if given within 4 days of exposure	Vaccine indications • Exposure to the virus • Close contact (less than 2 m) with a person with confirmed or suspected smallpox, including those with medical or public health responsibilities • Laboratory personnel who may come in contact with clinical specimens from patients with known or suspected smallpox Vaccine administration • Bifurcated needles are inserted into the vial • A droplet is suspended between the prongs and is the required dose • The needle is used to puncture the skin 15 times over the deltoid muscle • Patients are evaluated 6–8 days after vaccine administration to ensure an immune response with a lesion at the injection site • The CDC website contains detailed administration instructions (http://emergency.cdc.gov/agent/smallpox/vaccination/vaccination-method.asp) In cases of high exposure to smallpox, including acts of bioterrorism, the benefits of the vaccine outweigh risks, and therefore no absolute contraindications exist in this setting	
Tularemia *(F. tularensis)*		
The mode of delivery for bioterrorism is likely to be aerosolization Symptoms include fever, chills, rigors, headache, myalgia, sore throat, with progression to pneumonia; other organs can also be affected, including spleen, liver, and kidney Untreated, mortality is 30%–60% No person-to-person transmission	Ciprofloxacin 500 mg PO q12h Or Doxycycline 100 mg PO q12h Duration: 14 days	Ciprofloxacin 15 mg/kg PO q12h Or More than 45 kg: Doxycycline 100 mg PO q12h 45 kg or less: Doxycycline 2.2 mg/kg PO q12h (not to exceed 100 mg/dose) Duration: 14 days

bid = twice daily; CDC = Centers for Disease Control and Prevention; PO = orally; qid = four times daily; q12h = every 12 hours; tid = three times daily.

Patient Cases

5. Aerosolization of an unknown bioterrorism category A agent occurred in a large metropolitan area. Initial symptoms of individuals exposed to this agent have been primarily respiratory and pneumonialike after several days. The only people who seem to be affected are those who were in the original area. Family members who were not primarily exposed did not seem to contract illness after contact with their loved ones who were exposed. This category A agent is most likely to cause which of the following diseases?
   A. Botulism
   B. Plague
   C. Smallpox
   D. Tularemia

6. A man presents to the chemoprophylaxis point-of-dispensing tent after confirmed inhalational exposure to anthrax. He has no known allergies to medications. Which postexposure prophylaxis regimen is best?
   A. Single vaccine dose in addition to oral ciprofloxacin for 60 days
   B. Vaccination today and then in 2 and 4 weeks
   C. Oral doxycycline for 60 days
   D. Oral ciprofloxacin for 60 days plus vaccination today, with two additional doses at 2 and 4 weeks

2. Chemical agents
   a. The CDC categorizes chemical agents into various categories, mostly according to the primary signs/symptoms humans would experience. Following are the main categories and representative examples.
      i. Biotoxins: Ricin, digitalis, strychnine, nicotine, tetrodotoxin
      ii. Blister agents/vesicants: Nitrogen and sulfur mustards, lewisite, phosgene oxime
      iii. Blood agents: Arsine, carbon monoxide, cyanide
      iv. Caustics: Hydrogen fluoride, hydrogen chloride
      v. Pulmonary agents: Ammonia, chlorine, bromine, phosphorus
      vi. Incapacitating agents: 3-Quinuclidinyl benzilate, opioids
      vii. Long-acting warfarins: "Super warfarin"
      viii. Metals: Arsenic, mercury, barium
      ix. Nerve agents: Sarin, soman, tabun, VX
      x. Organic solvents: Benzene
      xi. Riot control: Bromobenzylcyanide, chloroacetophenone
      xii. Toxic alcohols
   b. Patient presentation and treatment depend on the causative agent. Specific information regarding recognition, testing, and treatment can be found at www.bt.cdc.gov.

C. Useful Resources
   1. Healthcare Ready (www.healthcareready.org): An online tool that can be used to locate the closest open pharmacy during an emergency, find information about supply-chain issues, and print wallet cards for patients that contain basic medical information, including medications
   2. Emergency preparedness and response (https://emergency.cdc.gov): An extensive CDC resource that reviews issues related to planning and response to disasters
   3. Federal Emergency Management Agency (FEMA) (www.fema.gov): Content important for planning and responding to disasters. The approach is very broad and includes all aspects of disasters. The NRF and details of each emergency support function can be found at this website.

4. Emergency preparedness (www.fda.gov/Drugs/EmergencyPreparedness/default.htm): A resource for consumers and health professionals that details important issues related to the preparation and response to natural and man-made threats

IV. IMMUNIZATIONS

Guidelines

Kim DK, Bridges CB, Harriman KH. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older: United States, 2015. Ann Intern Med 2015;162:214–23.

Centers for Disease Control and Prevention. Advisory Committee on Immunization Practices (ACIP). Recommended Adult Immunization Schedule—United States, 2015. Available at www.cdc.gov/vaccines/schedules/hcp/adult.html.

Centers for Disease Control and Prevention. Advisory Committee on Immunization Practices (ACIP). Recommended Immunization Schedules for Persons Aged 0 Through 18 Years—United States, 2015. Available at www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html.

A. Definitions
   1. Immunity: The ability of the body to detect material endogenous to itself and to eliminate foreign materials
   2. Antigen: A live or inactivated substance capable of producing an immune response
   3. Antibody: Protein molecules produced by B lymphocytes to help eliminate an antigen
   4. Two basic mechanisms for acquiring immunity
      a. Passive: The transfer of antibody produced by animal or human and transferred to another human (e.g., injection or from mother to infant through the placenta or breast milk)
      b. Active: The stimulation of the immune system to produce an antigen-specific antibody
      c. Methods
         i. Survive infection: Memory B cells remember the antigen and, when exposed to it again, replicate and produce antibodies.
         ii. Vaccination: The injection of a small amount of antigen to produce an immune response

B. General Recommendations
   1. Live, attenuated: Contains modified and weakened live virus
      a. Produces an immune response similar to a natural infection by replicating in a vaccinated person
      b. Immune response is produced after the first dose for most people; however, some patients may need more than one dose to provide a high level of immunity.
      c. Can cause adverse effects (e.g., fever, malaise, myalgias), such as the disease being vaccinated against but typically not as severe
      d. Contraindicated in immunosuppressed patients because of the risk of causing uncontrolled replication
      e. Contraindicated in pregnancy because of concern about infecting the fetus
      f. Children younger than 1 year cannot develop an immune response to live vaccines.
      g. Live, attenuated vaccines
         i. Virus
            (a) Measles, mumps, and rubella (MMR)
            (b) Varicella
            (c) Zoster

(d) Yellow fever
(e) Rotavirus
(f) Intranasal influenza
(g) Oral polio – Not available in the United States

ii. Bacteria—Oral typhoid

2. Inactivated: Contains virus that has been inactivated by heat and/or chemicals
   a. Not alive; therefore, cannot replicate in the body
   b. Usually requires several doses to prime the immune system and then to produce response
   c. Examples of inactivated vaccines
      i. Polio (injection only)
      ii. Hepatitis A/B
      iii. Influenza (injection only)
      iv. Human papillomavirus (HPV)
      v. Rabies
      vi. Pneumococcal conjugate or polysaccharide
      vii. Meningococcal conjugate or polysaccharide
3. Polysaccharide vaccines: Inactivated vaccines that contain long chains of sugar molecules that make up the surface capsule protein of the bacteria
   a. Pure polysaccharide
      i. Immune response does not require T-helper cells; is mediated through B cells
      ii. Children younger than 2 years are unable to form an immune response by this method because of immaturity of the immune system.
      iii. Types of pure polysaccharide vaccines
         (a) Pneumococcal polysaccharide vaccine (PPSV23)
         (b) Meningococcal polysaccharide vaccine (MPSV4)
   b. Conjugate polysaccharide
      i. A polysaccharide vaccine combined with protein that changes the response to a T cell–mediated response
      ii. Allows children younger than 2 years to form an immune response
      iii. Types of conjugate polysaccharide vaccines
         (a) *Haemophilus influenzae* type B (Hib)
         (b) Pneumococcal conjugate vaccine (PCV13)
         (c) Meningococcal vaccine (MenACWY)
4. Recombinant vaccines
   a. Produced by inserting part of the gene of the antigen into the gene of another cell (e.g., a yeast cell)
   b. Types of recombinant vaccines available
      i. Human papillomavirus
      ii. Hepatitis B
      iii. Live typhoid vaccine (attenuated *Salmonella typhi)*
      iv. Egg-free influenza
5. Timing and spacing
   a. Antibody-vaccine interactions
      i. Live, attenuated vaccines may be affected by circulating antibodies.
         (a) Vaccine given first: Wait 2 weeks before administering antibody.
         (b) Antibody given first: Wait 3 months before administering vaccine. (Exception: Zoster vaccine is not known to be affected by circulating antibody at any time before or after receipt of antibody-containing blood product.)
      ii. Does not apply to inactivated vaccines

b. Simultaneous administration
    i. There is no limit to the number of vaccines that can be administered in one visit.
    ii. Live, attenuated injectable vaccines not given during the same visit must be separated by at least 4 weeks.
        (a) If administered too closely together, the first vaccine given could interfere with the immune response of the second.
        (b) Does not apply to oral live, attenuated vaccines (i.e., rotavirus)
        (c) Does not apply to inactivated vaccines
c. Interval between multidose vaccines
    i. Increasing the interval between multidose vaccines will not diminish the effect of the vaccine.
    ii. Decreasing the interval between multidose vaccines may interfere with the immune response.
    iii. Exception: Vaccines may be given up to 4 days before the next scheduled dose.
d. Age requirements: Vaccines should not be given earlier than the minimum age requirement for the vaccine.
    i. Exception: During a measles outbreak, the MMR vaccine may be given before 12 months of age; however, this dose will not count toward the series.
    ii. Exception: Vaccines may be given up to 4 days before the minimum age because doing so is unlikely to result in a decreased immune response.

6. Number of doses
    a. Live, attenuated vaccine
        i. Provides an immune response after one dose
        ii. A second dose, if recommended, is usually given to ensure 100% immunity.
    b. Inactivated vaccines
        i. Usually require two or three doses before an immune response is complete
        ii. Immune response may wane over time, thus requiring a booster dose.
7. Certain vaccines are recommended for people traveling outside the United States: The CDC's Yellow Book is the definitive reference for recommended vaccines (wwwnc.cdc.gov/travel/yellowbook/2016/table-of-contents).
8. Adverse reactions
    a. Local injection site reactions: Most common and least severe
        i. Pain, redness, and swelling at the injection site
        ii. Occur within 4 hours of injection
        iii. More common with inactivated vaccines
    b. Systemic
        i. Generalized symptoms of fever, rash, headache, malaise, myalgias, and/or loss of appetite
        ii. More common with live, attenuated vaccines because the immune response takes on a mild form of the disease vaccinated against
        iii. Manifests within 7–21 days
    c. Allergic: Least common and most severe
        i. Life threatening; seek medical assistance immediately
        ii. May be caused by vaccine itself or one of its components (i.e., eggs, neomycin, latex)
        iii. Rate: Fewer than 1 in 500,000
        iv. Symptoms may occur within seconds of exposure or may be delayed an hour or more after exposure.
    d. Reporting adverse reactions
        i. Vaccine Adverse Event Reporting System (VAERS), a subunit of the CDC
        ii. Report any clinically significant adverse event
        iii. Access website online at http://vaers.hhs.gov/esub/index.

9. Precautions
    a. Definition—Condition in a recipient that might increase the chance or severity of a serious adverse reaction or might compromise the ability of the vaccine to produce immunity
    b. Risk-benefit assessment before administration
        i. Pertussis-containing vaccines—Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine only
            (a) Temperature greater than 105°F within 48 hours of a dose and no other identifiable cause
            (b) Collapse or shocklike state within 48 hours of a dose
            (c) Persistent, inconsolable crying lasting more than 3 hours within 48 hours of a dose
            (d) Seizure without fever within 3 days of a dose
        ii. Guillain-Barré syndrome within 6 weeks of a vaccine
            (a) DTaP; tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap); tetanus and diphtheria (Td) vaccines: Should receive if benefits outweigh risks
            (b) Influenza vaccine: Benefits of receiving likely outweigh risks
            (c) Meningococcal conjugate vaccine – Avoid, except in individuals with high risk of contracting meningitis.
    c. Temporary—Those who may receive a vaccine when conditions improve or change
        i. Moderate to severe acute illness
        ii. Recent receipt of antibody-containing blood products (applies only to MMR, rotavirus, and varicella-containing vaccines)
10. Contraindications
    a. Permanent—Those who should avoid vaccination with a specific vaccine
        i. Severe allergic reaction after a previous dose (e.g., anaphylaxis)
        ii. Encephalopathy not attributable to another cause occurring 7 days after a pertussis vaccine
    b. Temporary contraindications to live, attenuated vaccines—Those who may receive a vaccine once conditions improve or change
        i. Pregnancy
            (a) Live, attenuated vaccines should not be given because of the theoretical risk of infection to the fetus (documented only with vaccinia).
            (b) Inactivated vaccines cannot replicate; therefore, they cannot cause fetal infection and are safe to give (exception: HPV because its safety has not been studied).
        ii. Immunosuppression
            (a) Live, attenuated vaccines should not be administered because of the risk of uncontrolled replication.
            (b) Inactivated vaccines may be given; however, the immune response may be diminished, and revaccination when immune competence is regained is recommended.
            (c) Chronic therapy with high-dose oral steroids: Defined as prednisone 20 mg/day (or greater than or equal to 2 mg/kg/day) for more than 14 days; is contraindicated with live, attenuated vaccines (may vaccinate once discontinued for more than 1 month)
            (d) Aerosolized, topical steroids or short-term steroid bursts are not a contraindication to live, attenuated vaccines.
            (e) Live, attenuated vaccines can be given 3 months after the cessation of chemotherapy or at least 2 weeks before the initiation of immunosuppressive therapy.
    c. Household contacts of individuals with altered immunocompetence may be given live vaccines, if indicated. An exception to this: Contacts of severely immunocompromised patients requiring care in a protective environment.
11. Invalid contraindications
    a. Mild illness
    b. Antimicrobial therapy

c. Disease exposure
d. Household contact with pregnant or immunosuppressed person
e. Breastfeeding
f. Preterm birth
g. Family history of adverse events
h. Many simultaneous vaccines
i. Current administration of tuberculin skin test

Patient Case

7. H.H. is a 4-year-old boy who presents with a runny nose. He does not have a fever today. Medical history is significant for asthma exacerbation 3 months ago. Which combination of vaccines will most likely be given to H.H. at this visit?

A. Live, attenuated influenza vaccine (LAIV), MMR vaccine
B. Inactivated influenza vaccine (IIV), varicella vaccine
C. LAIV and HPV vaccine
D. IIV and MenACWY

C. Influenza Vaccine
1. Influenza infection
   a. Usually results in a respiratory illness
   b. Incubation: 1–4 days
2. Virus types
   a. Type A: Moderate to severe illness that affects all age groups (human and animal virus origins)
   b. Type B: Typically, milder illness that affects children only (human-only virus)
   c. Type C: Rarely seen, never attributed to epidemics
3. Common clinical features include fever, chills, body aches, malaise, and sore throat.
4. Vaccine composition
   a. Contains different influenza viruses, based on surveillance forecasts by the World Health Organization (WHO) of the viruses likely to be prevalent in the coming year
      i. LAIV is available as a quadrivalent vaccine.
         (a) Two influenza type A strains
         (b) Two influenza type B strains
      ii. Inclusion of two influenza type B lineages should increase the likelihood of providing antibodies against a higher number of circulating types.
      iii. IIV is available in the quadrivalent or trivalent inactivated influenza vaccine composition.
   b. Vaccine development takes about 6 months; therefore, decisions must be made in January to have a vaccine available by October.
5. Types of influenza vaccine
   a. Inactivated influenza vaccine
      i. Administered intramuscularly
         (a) 0.25 mL for children 6–35 months of age
         (b) 0.5 mL for children 3 years and older
      ii. Grown in chicken embryos
      iii. Available in multidose vials or in preservative-free, single-dose vials
      iv. Immunity after administration is generally less than 1 year

v. Adverse reactions
(a) Local injection site reactions (15%–20%)
(b) Systemic reactions are uncommon.
(c) Immediate hypersensitivity is usually associated with a component of the vaccine.

b. Live, attenuated influenza vaccine
i. Administered as 0.1-mL spray per each nostril
ii. Grown in chicken embryos
iii. Available in a single-dose, preservative-free sprayer unit
iv. Indicated only for individuals 2–49 years of age
v. Contraindications and precautions
(a) Pregnant women
(b) Patients receiving immunosuppressive therapy
(c) Patients with chronic medical conditions
(d) People with history of egg allergy
(e) Children 2–4 years of age with asthma or wheezing episode documented in past 12 months
(f) People who take antiviral medication within past 48 hours
(g) People who care for severely immunocompromised individuals who require a protective environment
vi. Adverse reactions are localized and/or may present as mild influenza-type symptoms.

c. High-dose IIV
i. Administered intramuscularly
ii. Grown in chicken embryos
iii. Available in multidose vials or in preservative-free, single-dose vials and syringes
iv. Contains 4 times the amount of antigen compared with IIV
v. Approved for use in individuals older than 65 years
vi. Developed to increase immunogenicity in older populations because the ability to form an immune response wanes with age
vii. The CDC does not give this vaccine preference over IIV because of the lack of clinical efficacy data.

d. Intradermal influenza vaccine
i. Administered by intradermal route
ii. Grown in chicken embryos
iii. Available in a single-dose, prefilled microinjection system
iv. Approved for use in individuals 18–64 years of age
v. Preservative free

e. Recombinant influenza vaccine (RIV3) (egg free)
i. Trivalent vaccine administered intramuscularly
ii. Flu shot produced without using chicken eggs was approved by the FDA in 2013.
iii. May be administered to patients with true severe hypersensitivity reactions to eggs
iv. Preservative free; approved for individuals 18 years of age and older

6. Recommendations
a. Influenza vaccine administration should begin before onset of influenza activity (by October, if possible).
b. All individuals 6 months or older should get a yearly influenza vaccine.
c. Individuals at high risk of complications should be certain to get the vaccine.
i. Pregnant women (IIV only)
ii. Children younger than 5 years, especially children younger than 2 years

iii. Adults 50 years and older (IIV only)
iv. Individuals of any age with certain medical conditions (IIV only)
(a) Diabetes
(b) Asthma
(c) Chronic obstructive pulmonary disease
(d) Neurologic and neurodevelopmental conditions
(e) Cystic fibrosis
(f) Heart disease (congenital heart disease, congestive heart failure, coronary artery disease)
(g) Kidney and liver disorders
(h) Weakened immune system
(i) Morbid obesity
(j) Individuals younger than 19 years receiving chronic aspirin therapy
v. Individuals in close contact with those at high risk of complications
(a) Health care workers
(b) Household contacts of high-risk individuals
(c) Household contacts and caregivers of children younger than 6 months (i.e., those who cannot receive the vaccine)

d. With the advent of RIV3, all patients with severe egg allergies can receive the influenza vaccine with RIV3. Those with a hives-only reaction may receive IIV or RIV3.
e. All children 6 months to 8 years of age who are receiving their first influenza vaccine should receive a total of two doses, at least 4 weeks apart.

D. Pneumococcal Vaccine
1. Pneumococcal infection
a. Usually results in pneumococcal pneumonia (less commonly, otitis media or meningitis)
b. Incubation period is 1–3 days for pneumonia.
2. Caused by the bacterium *Streptococcus pneumoniae*
a. Ninety known serotypes, but only a few account for severe disease
b. Encapsulated bacteria
3. Clinical features of pneumonia commonly include fever, chills, productive cough, dyspnea, and tachypnea.
4. Pneumococcal vaccine
a. Inactivated vaccine
b. Administration route
i. Pneumococcal polysaccharide may be administered intramuscularly or subcutaneously.
ii. Pneumococcal conjugate may be administered intramuscularly.
c. Types of vaccine
i. Pneumococcal conjugate vaccine (PCV13)
(a) Contains polysaccharide, conjugated antigen for 13 serotypes of pneumococcal bacteria
(b) Available only in single-dose, preservative-free syringes
(c) Previously contained seven serotypes (PCV7); however, changed to PCV13 because of an increased incidence of infections with serotypes outside those contained in PCV7
(d) FDA approved for use in patients aged 6 weeks to 5 years (four-dose series), 6–17 years (single dose), and 50 years and older (single dose)
ii. Pneumococcal polysaccharide vaccine (PPSV23)
(a) Contains purified capsular polysaccharide antigen from 23 serotypes of pneumococcal bacteria
(b) Available in single prefilled syringes and single-dose and multidose vials

(c) Accounts for about 88% of pneumococcal disease
(d) Around 80% of patients will develop antibodies after one dose.
(e) FDA approved for individuals 2 years of age and older and adults 50 years of age or older

d. No information regarding safety in pregnancy—It is best to give the vaccination to women of childbearing age at high risk of pneumococcal disease before conception.
e. Adverse reactions are usually localized injection site reactions. Systemic reactions are rare.

5. Recommendations
   a. Pneumococcal conjugate vaccine (PCV13)
      i. All children younger than 2 years
         (a) Series of four doses
         (b) Given at 2, 4, 6, and 12–15 months
      ii. Children 2–5 years of age should receive one dose of PCV13 if three or four doses of PCV7 were received, and two doses of PCV13 at least 8 weeks apart if fewer than three doses of PCV7 were received, if they have chronic heart disease, diabetes mellitus, chronic lung disease, sickle cell disease, asplenia, human immunodeficiency virus (HIV) infection, chronic renal failure, or diseases treated with immunosuppressive therapy or radiation.
      iii. Children and adolescents 6–18 years of age who are PCV13 naive and asplenic with cochlear implants, or who have chronic renal failure, HIV infection, diseases treated with immunosuppressive therapy or radiation, or cerebrospinal fluid (CSF) leaks, or who are immunocompromised receive one dose.
      iv. Adults 65 years of age and older
         (a) Receive one dose of PCV13 followed by one dose of PPSV23, 6–12 months later
         (b) Adults who have not previously received PCV13 and who have previously received one or more doses of PPSV23 should receive one dose of PCV13 at least 1 year after receipt of the most recent PPSV23.
   b. Pneumococcal polysaccharide vaccine (PPSV23)
      i. When PCV is also indicated, PCV13 should be given first
      ii. All patients 65 years and older
      iii. Patients between 2 and 64 years of age with the following conditions should receive one dose:
         (a) Chronic lung disease
            (1) Asthma—Children and adolescents 2–18 years of age who are using high-dose oral corticosteroids or adults 19 years and older
            (2) Chronic obstructive pulmonary disease
            (3) Emphysema
         (b) Chronic heart disease
         (c) Diabetes mellitus
         (d) Chronic renal failure or nephrotic syndrome
         (e) Anatomic or functional asplenia
         (f) Cochlear implants
         (g) CSF leak
         (h) Immunocompromising conditions
         (i) HIV infection
      iv. All patients 19–64 years of age (in addition to those previously included)
         (a) Smoke cigarettes
         (b) Reside in nursing homes or long-term care facilities
         (c) Chronic liver disease
         (d) Alcoholism

v. Revaccination
(a) Individuals receiving one or two PPSV23 doses before age 65 years should receive another dose at age 65 years or in 5 years, whichever is longer.
(b) Individuals with chronic renal failure, functional/anatomic asplenia, immunocompromising conditions, sickle cell disease, HIV infection, or nephrotic syndrome should receive a one-time revaccination 5 years after the initial dose.
(c) No further doses are needed if patients were vaccinated at or after age 65 years.

c. Recommendations for adults 19 years and older with immunocompromising conditions, functional or anatomic asplenia, CSF leaks, or cochlear implants
i. Pneumococcal vaccine–naive individuals
(a) PCV13 first
(b) PPSV23 at least 8 weeks later with revaccination as previously outlined
ii. Previous vaccination with PPSV23
(a) PCV13 at least 1 year after PPSV23
(b) Revaccination with PPSV23 should occur 5 years after original vaccination with PPSV23 and at least 8 weeks after vaccination with PCV13.

Patient Case

8. L.D. is a 40-year-old man with HIV infection. He received one dose of PPSV23 5 years ago. Which pneumococcal vaccine would be best to give him currently?
A. Give one dose of PCV13.
B. Give one dose of PPSV23.
C. Either vaccine is appropriate.
D. Neither vaccine is recommended.

E. Meningococcal Vaccine
1. Meningococcal infection
a. Typically presents as meningococcal meningitis
b. Incubation period is 2–10 days.
2. Caused by the bacterium *Neisseria meningitidis*—Encapsulated bacteria
3. Common clinical features include fever, headache, and neck stiffness (may progress to sepsis)
4. Meningococcal vaccine
a. Inactivated vaccine
b. Two-dose series; minimal interval between doses is 8 weeks
c. Types of meningococcal vaccine
i. Meningococcal polysaccharide vaccine (MPSV4 [Menomune])
(a) Quadrivalent vaccine that contains serogroups A, C, Y, W
(b) Administered subcutaneously
ii. Meningococcal conjugate vaccine (MenACWY-D [Menactra] and MenACWY-CRM [Menveo])
(a) Contains four *N. meningitidis* serogroups conjugated to either a diphtheria toxoid (MenACWY-D) or a CRM197 (MenACWY-CRM)
(b) Administered intramuscularly
(c) Available in single-dose, preservative-free vials
(d) Is the preferred formulation of the vaccine because it provides a better immune response than MPSV4

(e) MenACWY-D is approved for individuals 9 months–55 years of age, whereas MenACWY-CRM is used in children as young as 2 months and through age 55 years.

iii. Combination vaccine also available—Meningococcal groups C and Y and *Haemophilus* b tetanus toxoid conjugate vaccine (Hib-MenCY-TT) (MenHibrix)

d. Adverse reactions

i. Local injection site reactions

ii. Systemic reactions: Fever (fewer than 3%), headache, and malaise

iii. There have been some case reports of Guillain-Barré syndrome occurring after the administration of meningococcal conjugate vaccine, but the association with the vaccine is unclear.

5. Recommendations

a. Meningococcal conjugate vaccine

i. High-risk children with functional/anatomic asplenia (including sickle cell)

(a) For children younger than 19 months, administer four-dose series of Menveo or MenHibrix at 2, 4, 6, and 12–15 months of age.

(b) For children 19–23 months of age with incomplete series of MenHibrix or Menveo, ensure completion of series with two doses at least 3 months apart.

(c) For children 24 months or older with incomplete series, administer two-dose series at least 2 months apart. If MenACWY-D is given, wait until 2 years of age and at least 4 weeks after completion of PCV13.

ii. High-risk children with persistent complement component deficiency

(a) For children younger than 19 months, administer four-dose series of Menveo or MenHibrix at 2, 4, 6, and 12–15 months of age.

(b) For children 7–23 months with complement component deficiency and no vaccination

(1) If MenACWY-CRM is given, a two-dose series should be given with the second dose after 12 months of age and at least 3 months after the first dose.

(2) If MenACWY-D is given at 9–23 months of age, a two-dose series should be given with the second dose at least 3 months after the first dose.

(c) For children 24 months or older with complement component deficiency with incomplete vaccination, give two doses of either MenACWY-D or MenACWY-CRM at least 2 months apart.

iii. For children who travel to high endemic areas, administer the age-appropriate formulation and series.

iv. Administer one dose of MenACWY-D or MenACWY-CRM to all children 11–12 years of age and one booster dose at 16 years.

v. Administer one dose of MenACWY-D or MenACWY-CRM at age 13–18 years, if not previously vaccinated.

(a) If first dose is given at 13–15 years of age, a booster dose should be given at 16–18 years.

(b) If first dose is given when older than 16 years, a booster dose is not necessary.

vi. Unvaccinated college freshmen living in a dormitory through age 21 years

vii. Individuals 2–55 years of age at increased risk of meningococcal disease

(a) Microbiologists routinely using *N. meningitidis* isolates (single dose)

(b) Military recruits (single dose)

(c) Patients traveling to countries with *N. meningitidis* epidemics (single dose)

(d) Patients with terminal complement component deficiency (two doses administered at least 2 months apart)

(e) Patients with anatomic or functional asplenia or complement component deficiencies (two doses administered at least 2 months apart)

(f) Patients at risk during an outbreak because of a vaccine serogroup

viii. For adults 56 years and older.
(a) MenACWY (either option) is preferred if previously vaccinated with MenACWY and have indication for revaccination.
(b) Multiple doses are anticipated.
ix. Infection with HIV is not an indication for a routine MenACWY vaccination; but if a vaccination is given, two doses of MenACWY should be administered 2 months apart.

b. Meningococcal polysaccharide vaccine (MPSV4)
i. Acceptable alternative for patients 2–55 years of age, if the conjugate vaccine is unavailable
ii. Preferred vaccine in patients 56 years and older who have not received MenACWY previously and require a single dose

c. Revaccination every 5 years is recommended for patients who remain at high risk.

Patient Case

9. A.J. is a 17-year-old female adolescent who is planning to attend college next fall. Her admission process requires documentation of completed vaccination history. A.J. received her most recent vaccine when she was 13 years of age. Which vaccine option would be best to give to A.J. today?

A. Give one dose of MenACWY-D.
B. Give one dose of Hib-MenCY-TT.
C. A.J. is not a candidate for the vaccine because she already received the necessary vaccines.
D. A.J. is not a candidate for the vaccine because she does not meet the age requirements.

F. Varicella Vaccine
1. Varicella infection
a. Caused by the varicella zoster virus—Has the ability to lie dormant in the nervous system
i. Primary infection: Chickenpox with incubation period of 14–16 days
ii. Secondary infection: Herpes zoster (shingles)
b. Clinical features include rash, fever, and pruritus.
2. Varicella vaccine
a. Live, attenuated vaccine
b. Administered subcutaneously as a series of two doses
c. Approved for use in patients 12 months and older
d. Contains a small amount of neomycin
e. Among patients 12 months to 12 years of age, 97% develop an immune response; however, in those 13 years and older, two doses are necessary to achieve a similar response.
f. Adverse reactions
i. Local injection site reactions
ii. Varicellalike rash at injection site
g. Contraindications/precautions
i. Avoid in those who are severely immunocompromised or pregnant.
ii. Avoid use in those receiving an antiviral (e.g., acyclovir, famciclovir) 24 hours before vaccination.
iii. Avoid use of antiviral agents for 14 days after vaccine administration.
3. Recommendations
a. Children younger than 13 years
i. First dose should be given to all children 12–15 months of age.

ii. Second dose should be given to all children 4–6 years of age. Second dose may be administered before age 4 years if 3 months have elapsed since first dose. If second dose is administered at least 4 weeks after the first dose, it may be accepted as valid.

b. Adolescents and adults 13 years and older
   i. Should be given if there is no history of varicella immunity, defined as follows:
      (a) U.S. citizens born before 1980 are considered immune (exceptions: health care personnel and pregnant women).
      (b) Documentation of two varicella vaccinations, at least 4 weeks apart
      (c) History of diagnosis confirmed by a health care provider
      (d) History of herpes zoster diagnosis confirmed by a health care provider
      (e) Laboratory diagnosis
   ii. Should give special consideration to those who have close contact with individuals at high risk of severe disease or of exposure or transmission

c. Pregnant women should be assessed for varicella immunity and, if not immune, they should receive the first dose after completion of pregnancy and the second dose 4–8 weeks later.

d. Postexposure prophylaxis—Can be 70%–100% effective in preventing disease if given within 3 days of exposure to varicella virus; especially useful in controlling outbreaks in hospitals, schools, and day care centers

G. Herpes Zoster Vaccine
1. Herpes zoster infection
   a. Caused by reactivation of a latent varicella zoster virus associated with aging and immunosuppression
   b. Clinical features include unilateral lesions on trunk or trigeminal nerve, pain, and paresthesia.
2. Herpes zoster vaccine
   a. Live, attenuated vaccine
   b. Administered subcutaneously
   c. Contains the same antigen as the varicella vaccine, but is at least 14-times more potent
   d. Available in a preservative-free powder for reconstitution
   e. Contains neomycin
   f. Use of the vaccine can decrease the incidence of herpes zoster infection by 50%—Efficacy is best in those 50–59 years of age and decreases with increasing age.
   g. The duration of protection from herpes zoster infection is currently unknown.
   h. Adverse reactions—Local injection site reactions
      i. Contraindications
         (a) Avoid use in pregnancy.
         (b) Severe hypersensitivity to neomycin or other vaccine component
         (c) Avoid in severely immunocompromised individuals, including those taking high-dose prednisone (or equivalent) of 20 mg or more for more than 14 days.
      ii. Precautions
         (a) Avoid use in those receiving an antiviral (e.g., acyclovir, famciclovir) 24 hours before vaccination.
         (b) Avoid use of antiviral agents for 14 days after vaccine administration.
3. Recommendations
   a. All individuals 60 years and older regardless of their history of chickenpox or herpes zoster infection
   b. The herpes zoster vaccine was approved for use in patients 50 years and older by the FDA. The CDC has not changed its recommendations to date.

H. Tetanus, Diphtheria, and Pertussis Vaccines
   1. Tetanus
      a. Caused by the neurotoxic exotoxin tetanospasmin, which is produced by *Clostridium tetani,* gram-negative anaerobe in soil
      b. Enters the body through open wounds, with an incubation period of 3–21 days
      c. Common clinical features include lockjaw (trismus), neck stiffness, difficulty swallowing, abdominal muscle rigidity, fever, and sweating.
   2. Diphtheria
      a. Caused by a toxin produced by *Corynebacterium diphtheriae* that commonly presents as pharyngeal/tonsillar diphtheria
      b. Incubation period is 2–5 days.
      c. Common clinical features in pharyngeal diphtheria include malaise, sore throat, fever, exudative pharyngitis, and anorexia.
   3. Pertussis (whooping cough)
      a. Caused by *Bordetella pertussis*
      b. Incubation period is 7–10 days.
      c. Clinical features present in progressive stages of respiratory infection, starting with runny nose, fever, and mild cough and progressing to rapid, prolonged coughing spells, often causing cyanotic episodes and vomiting.
      d. Immunity after disease is not always permanent.
   4. Types of vaccine
      a. Inactivated vaccine
      b. Available in combination vaccines (composition and age indicated are shown in Table 4)
      c. Uppercase letters signify a full-strength dose; lowercase letters signify a partial dose.
      d. Pertussis is found in its acellular form within the vaccine because the whole-cell vaccine was previously associated with severe adverse reactions.
      e. Adverse effects
         i. DTaP/diphtheria-tetanus (DT)
            (a) Local injection site reaction (increase in severity with each dose)
            (b) Temperature as high as 101°F (38.3°C)
            (c) Swelling of the entire leg/arm where the vaccine was administered; seen after fourth or fifth dose
         ii. Tdap/Td vaccine
            (a) Local injection site reactions
            (b) Mild fever
            (c) Headache
            (d) Tiredness
            (e) Swelling of the entire leg/arm where the vaccine was administered

Table 4. Formulations of Vaccines Containing Diphtheria, Tetanus, and Pertussis

Vaccine	Diphtheria	Tetanus	Pertussis	Age
DTaP	7–8 Lf-units	5–12.5 Lf-units	2–25 mcg	Birth to 7 years
DT	7–8 Lf-units	5–12.5 Lf-units	–	Birth to 7 years
Td	2–2.5 Lf-units	5 Lf-units	–	7 years and older
Tdap	2–2.5 Lf-units	5 Lf-units	2.5–8 mcg	7 years and older

DT = diphtheria-tetanus; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; Lf = limit of flocculation unit; Td = tetanus and diphtheria vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

5. Recommendations
    a. Children, birth to 6 years—Total of five doses of DTaP
        i. Given at 2, 4, 6, and 15–18 months and at 4–6 years
        ii. Fourth dose may be given at 12 months as long as 6 months have elapsed between doses 3 and 4.
        iii. DT may be substituted if child does not tolerate pertussis portion of the vaccine (including inconsolable crying, temperature greater than 105°F (40.6°C), or seizures).
    b. Adolescents, 11–12 years of age
        i. One dose of Tdap
        ii. Then, one dose of Td every 10 years as a booster vaccine
    c. Adults, 18 years and older
        i. One dose of Tdap if not already received
        ii. Then, one dose of Td every 10 years as a booster vaccine
    d. Pregnant women
        i. One dose of Tdap with each pregnancy, regardless of Tdap/Td history
        ii. Preferably between 27 and 36 weeks of gestation
        iii. Recommended to protect the infant because the first dose of DTaP is not given until 2 months of age, and the full series is not completed until 5–6 years
    e. Adults 65 years and older
        i. One dose of Tdap if not already received
        ii. Then, one dose of Td every 10 years as a booster vaccine

Patient Case

10. K.T. is a 45-year-old man who presented with a laceration to his arm after a car accident. He is unsure of the date of his most recent tetanus booster, but believes it was more than 10 years ago. Which form of vaccine would be best to give this patient today?

    A. DTaP
    B. DT
    C. Td
    D. Tdap

I. HPV Vaccine
    1. Human papillomavirus
        a. Most common sexually transmitted infection in the United States, with 20 million reported infections
            i. Current estimates show that 80% of women will be infected by age 50 years.
            ii. Up to 20% prevalence in heterosexual men
        b. More than 100 types of HPV have been isolated.
            i. Types 6 and 11 have been associated with benign cervical cell abnormalities, genital warts, and laryngeal papillomas.
            ii. Types 16 and 18 together account for 70% of cases of cervical cancer.
        c. Clinical features are generally asymptomatic, but patients may have anogenital warts and cervical cancer precursors.
        d. High-risk sexual behavior is the only verifiable risk factor for HPV disease.
    2. HPV vaccines
        a. Recombinant, inactive vaccine
        b. Intramuscular injection in single-dose, preservative-free syringes and vials

c. Dosing schedule of three doses, with second dose administered 4 to 8 weeks after first dose and third dose administered at least 12 weeks after second dose and at least 24 weeks (6 months) after first dose
d. Infection with a specific type of HPV before vaccination will not decrease the effectiveness of the vaccine to the other types contained within the vaccine.
e. Vaccine will not help treat previous HPV infection.
f. Not studied in pregnancy and therefore not recommended
g. Three vaccine types available
    i. Quadrivalent vaccine (Gardasil, HPV4)
        (a) Contains proteins of HPV types 6, 11, 16, and 18
        (b) Approved for use in male and female individuals 9–26 years of age
    ii. 9-Valent vaccine (Gardasil 9)
        (a) Contains proteins of HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58
        (b) Approved for use in male individuals 9–15 years of age and female individuals 9–26 years of age
    iii. Bivalent vaccine (Cervarix, HPV2)
        (a) Contains proteins of HPV types 16 and 18
        (b) Approved for use in female individuals 9–25 years of age
h. Adverse reactions
    i. Local injection site reactions
    ii. Systemic reactions: Nausea, dizziness, myalgia, and malaise
    iii. To avoid syncope, it is recommended that patients be observed in the clinic for 15–20 minutes after vaccination.

3. Recommendations
    a. Female recipients
        i. All girls should receive vaccine (quadrivalent, bivalent, or 9-valent) at 11 or 12 years of age.
        ii. All female individuals 13–26 years of age if not previously vaccinated
    b. Male recipients
        i. All should receive the quadrivalent vaccine at 11 or 12 years.
        ii. All male individuals 13–21 years of age if previously unvaccinated or whose three-dose series was incomplete
        iii. All men 22–26 years of age may also receive the vaccine.

Patient Case

11. Which of the following individuals is a candidate for the HPV vaccine?
    A. 32-year-old health care worker
    B. 27-year-old pharmacy school student
    C. 40-year-old woman not in a monogamous relationship
    D. 13-year-old male adolescent

J. MMR Vaccine
    1. Measles
        a. Caused by a paramyxovirus
        b. Incubation period is 14–18 days.
        c. Clinical features are the progression of a prodrome of high-grade fever and cough to blue-white Koplik spots on mucous membranes, hairline rash spreading downward/outward, and diarrhea.

2. Mumps
    a. Caused by a paramyxovirus acquired through the nasopharynx by respiratory droplets
    b. Incubation is 14–18 days.
    c. Clinical features are the progression of a prodrome of low-grade fever, headache, and malaise to unilateral or bilateral parotitis.
3. Rubella (German measles)
    a. Caused by a togavirus
    b. Incubation period is 14 days.
    c. Clinical features are the progression of a prodrome (not seen in children) of a low-grade fever, malaise, and upper respiratory symptoms to a rash starting on the face and spreading to the rest of the body (symptoms are more faint than those of measles).
4. MMR vaccine
    a. Live, attenuated vaccine
    b. Administered subcutaneously
    c. About 2%–5% may not respond (especially to measles and mumps viruses) to full immunity after the first dose; therefore, two doses are recommended.
    d. Grown in chick embryo fibroblast culture but has been given to egg-allergic patients without incident
    e. Adverse events
        i. Local injection site reactions
        ii. Systemic reactions: Fever, rash, joint pain
5. Rubella vaccine
    a. RA 27/3 (Meruvax II)
    b. Live, attenuated vaccine
    c. Only one dose is necessary to confer immunity.
    d. Use of the single agent is not recommended.
6. Recommendations
    a. All children should receive the MMR vaccine (two-dose series).
        i. First dose is given at 12 months or older.
        ii. Second dose is usually given at 4–6 years but can be given as soon as 28 days after first dose.
        iii. Administer one dose at age 6–11 months before departure from the United States for international travel. Revaccinate with two doses with first dose starting at 12 months or older and second dose at least 4 weeks later.
    b. Adults not receiving MMR as a child should be given at least one dose of the vaccine unless they were born before 1957 (considered immune).

K. Hepatitis A Vaccine
1. Hepatitis A infection
    a. Caused by the hepatitis A virus
    b. Acquired through fecal-oral transmission
    c. Replicates in the liver and is detected in the blood and excreted in the feces by the biliary system within 10–12 days; however, symptoms do not present until about 28 days after infection and resolve in about 2 months
    d. Clinical features include fever, malaise, jaundice, dark urine, abdominal pain, and nausea.
2. Types of vaccine
    a. Inactivated whole-cell virus vaccine
    b. Havrix and Vaqta are available with no preference given to one vaccine over the other.
        i. Havrix is a two-dose series given at 0 and 6–12 months.

ii. Vaqta is a preservative-free vaccine given at 0 and 6–18 months.
iii. Twinrix is a three-dose, combination hepatitis A and hepatitis B vaccine given at 0, 1, and 6 months.
c. Pediatric versions approved for individuals 12 months to 18 years of age
d. Adult versions approved for individuals 19 years and older
e. Seroconversion is 100% after two doses.
f. Adverse reactions
i. Local injection site reactions
ii. Systemic symptoms include malaise, fever, and fatigue.
3. Recommendations
a. Since 2005, it has been recommended that all children 12–23 months of age receive this vaccine.
b. All patients at high risk of the disease
i. Travelers to countries with a high rate of the disease or close contact with international adoptee
ii. Men who have sex with men
iii. Illicit drug use
iv. Patients with chronic liver disease
v. Patients who are treated with clotting factor concentrates
vi. Patients who work with hepatitis A–infected animals or in a hepatitis A research laboratory
c. Given as a two-dose series, at least 6 months apart

L. Hepatitis B Vaccine
1. Hepatitis B infection
a. Caused by the hepatitis B virus (HBV)
b. Clinical feature is a progression from a prodrome of malaise, nausea/vomiting, fever, right upper quadrant pain, rash, dark urine to the ictal phase of jaundice, and hepatomegaly to potentially chronic hepatitis.
c. Most HBV infections result in complete elimination of the hepatitis B surface antigen (HBsAg) from the body and replacement with HBV antibodies.
2. Types of vaccine
a. Two available vaccines
i. Recombivax HB
(a) Pediatric formulation: Can be used for any age group
(b) Adult formulation: Can be used for any age group
(c) Single-dose vials (preservative free)
ii. Engerix-B
(a) Pediatric formulation: Approved for use in patients 20 years and younger
(b) Adult formulation: Approved for use in patients 11 years and older
(c) Does not contain thimerosal as a preservative, but does contain it as a residual from the manufacturing process
b. Recombinant, inactive vaccine administered as a three-dose injection series
c. After three doses, up to 95% of patients 19 years and younger develop an immune response, and up to 90% of adults develop an immune response. This effect wanes over time, with a significant drop-off in patients older than 60 years.
d. Adverse reactions
i. Local injection site reactions
ii. Systemic: Fatigue, headache, irritability, and fever

3. Recommendations
    a. All children at birth, 1–2 months, and 6–18 months. Unlike most vaccines, the recommended period between doses 2 and 3 is at least 8 weeks for optimization of anti–hepatitis B antigen titers.
    b. All children at 11–12 years (and up to 18 years as catch-up), if not vaccinated as an infant
        i. Given at baseline, 1 month, and 6 months
        ii. Alternative (only with Recombivax vaccine): Baseline and 4 months later only in patients 11–15 years of age
    c. Adults at high risk of HBV if not previously vaccinated
        i. High-risk patients
            (a) Individuals with diabetes as soon as diabetes is diagnosed, up to age 60 years; after age 60 years, they may be vaccinated at the discretion of the primary care provider
            (b) Sexual partners of HBsAg-positive individuals
            (c) Sexually active people not in a mutually monogamous relationship
            (d) Men who have sex with men
            (e) Current or recent illicit intravenous drug users
            (f) Household contacts of HBsAg-positive individuals
            (g) Health care workers
            (h) Individuals with end-stage renal disease
            (i) Travelers to places where hepatitis B infection is prevalent
            (j) Those infected with HIV
        ii. Usually given at baseline, 1 month, and 6 months

Patient Case

12. C.C. is a 33-year-old woman who will be traveling to Beijing to manage a start-up manufacturing company. Which of the following recommendations would you offer C.C. regarding vaccination against hepatitis A?
    A. C.C. is not a candidate for this vaccine because of her age.
    B. C.C. should receive a three-dose series of hepatitis A vaccine because she will be moving to a country with a high rate of the disease.
    C. C.C. should receive a two-dose series of hepatitis A vaccine because she will be moving to a country with a high rate of the disease.
    D. C.C. will not be at high risk of hepatitis A, and her risks in receiving the vaccine outweigh the benefit.

M. Hib Vaccine
1. Hib infection
    a. Caused by the encapsulated bacterium *H. influenzae* by entering the body through the nasopharynx, where it can be dormant for several months before causing disease
    b. Disease is not very common in children older than 5 years.
    c. Common clinical feature of meningitis (common manifestation) include fever, decreased mental status, and stiff neck.
    d. Risk factors for disease
        i. Household crowding
        ii. Large household size
        iii. Day care attendance
        iv. Low socioeconomic status
        v. Low parental education
        vi. School-aged siblings

2. Hib vaccine
    a. Polysaccharide vaccine was removed from the market in 1988 because a more useable conjugate vaccine was developed.
    b. Polysaccharide-protein conjugate vaccines
        i. Approved for use in children 6 weeks and older
        ii. Clinical efficacy is 95%–100% after two or three doses.
        iii. Types
            (a) Polyribosylribitol phosphate chemically conjugated to tetanus toxoid (PRP-T)
            (b) *Haemophilus* B conjugate, conjugated to meningococcal group B outer membrane protein (PRP-OMP)
    c. Adverse reactions—Local injection site reactions
3. Recommendations
    a. All children should start the vaccine series at 2 months.
        i. PRP-T: Intramuscular
            (a) Ideally, should be used only as the final (booster) dose in children 12 months to 4 years of age with one dose of Hib vaccine
            (b) Otherwise, series of three doses at 2, 4, and 6 months with one booster dose at 12–15 months
        ii. PRP-OMP: Intramuscular
            (a) Series of two doses at 2 and 4 months
            (b) One booster dose at 12–15 months
    b. The two vaccines are interchangeable because they are equally efficacious. If using a combination of both vaccines, a total of three doses should be given.
    c. If the vaccination series is started late, not all doses may be necessary; the number of doses can be determined by using Table 5.
    d. Patients with asplenia or sickle cell disease and those undergoing splenectomy should receive one dose.
    e. Patients who receive a hematopoietic stem cell transplant should receive three doses 6 months after transplantation with at least 4 weeks between doses.
    f. Hib vaccination is not recommended for adults with HIV infection because the risk of infection is low.

Table 5. Dosing Schedule for Haemophilus influenzae Type B Vaccines

Vaccine	Age at First Dose, months	Primary Series	Booster
PRP-T	2–6	Three doses, 2 months apart	12–15 months
	7–11	Two doses, 2 months apart	12–15 months
	12–14	One dose	2 months later
	15–59	One dose	Unnecessary
PRP-OMP	2–6	Two doses, 2 months apart	12–15 months
	7–11	Two doses, 2 months apart	12–15 months
	12–14	One dose	2 months later
	15–59	One dose	Unnecessary

PRP-OMP = *Haemophilus* B conjugate; PRP-T = polyribosylribitol phosphate chemically conjugated to tetanus toxoid.

N. Polio Vaccine
   1. Poliomyelitis
      a. Caused by the polio virus that enters by mouth and attaches to the throat; within 1 week, it invades the lymph nodes and, eventually, the bloodstream.
      b. It may then infect the central nervous system, causing replication in motor neurons, resulting in cell destruction and clinical symptoms of the disease.
      c. Clinical features of infection are usually asymptomatic but, in rare cases, may result in symptoms of meningitis (1%–2%) or paralytic symptoms (fewer than 1%).
   2. Types of vaccine
      a. Oral poliovirus vaccine
         i. Live, attenuated vaccine that contains all three serotypes of poliovirus
         ii. No longer used in the United States because of limited cases of vaccine-associated paralytic poliomyelitis
      b. Inactivated poliovirus vaccine
         i. Contains all three serotypes of poliovirus
         ii. Administered subcutaneously or intramuscularly
         iii. Available in a multidose vial, containing 2-phenoxyethanol as a preservative
         iv. Contains trace amounts of neomycin, streptomycin, and polymyxin B
         v. Considered 99% effective after three doses
         vi. Adverse reactions—Localized injection reactions
   3. Recommendations for inactivated poliovirus vaccine
      a. Vaccinate all children starting at age 2 months.
      b. Series of four doses given at 2 months, 4 months, 6–18 months, and 4–6 years

O. Rotavirus Vaccine
   1. Rotavirus infection
      a. Enters the body through the mouth and replicates directly in the small intestine, resulting in severe gastroenteritis caused by rotavirus (usually more severe in infants)
      b. Incubation period of around 2 days
      c. Clinical features typically include watery diarrhea with or without fever/vomiting.
      d. Infection with rotavirus seldom leads to immunity from the disease, but subsequent infections are less severe.
   2. Rotavirus vaccine
      a. Live oral vaccine
      b. Types
         i. RV5 (RotaTeq)
            (a) Contains five strains of rotavirus suspended in a buffer solution
            (b) Administered as three doses at 2, 4, and 6 months (completed by 32 weeks)
            (c) Contains trace amounts of bovine fetal serum but is preservative free
            (d) In studies, has been up to 74% effective in decreasing any gastroenteritis symptoms and 98% effective in decreasing severe gastroenteritis symptoms
         ii. RV1 (Rotarix)
            (a) Contains one strain of rotavirus
            (b) Two doses at 2 and 4 months (completed by 24 weeks)
            (c) Available as a lyophilized powder for reconstitution that must be used within 24 hours of reconstitution
            (d) Latex rubber in packaging
   3. Virus can shed in the feces up to 15 days after administration.

4. Immunity duration is unknown; has been studied for 2 consecutive years, with waning protection in the second year
5. Adverse reactions
    a. Intussusception, which occurred in previously marketed rotavirus vaccine; however, this has occurred as often as with placebo in the current vaccines
    b. Vomiting
    c. Diarrhea
    d. Irritability
    e. Fever
6. Recommendations
    a. The Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Practice have no preference for the use of one vaccine over the other.
    b. The vaccines should be administered routinely at 2 months but can be initiated as early as 6 weeks, with at least 4 weeks between doses.
    c. Infants receiving a diagnosis of rotavirus before or during vaccine administration should still complete the full treatment recommendations.
    d. It is not recommended to re-dose if part of dose, or the entire dose, is spit out.

P. Summary of Vaccine Recommendations

Table 6. Childhood Immunization Schedule, Birth to 6 Years

Vaccine	Birth	1 mo	2 mo	4 mo	6 mo	12 mo	15 mo	18 mo	19–23 mo	2–3 yr	4–6 yr
Hepatitis B	1st dose	2nd dose			3rd dose						
Rotavirus			1st dose	2nd dose	3rd dose[a]						
DTaP/DT			1st dose	2nd dose	3rd dose		4th dose				5th dose
Hib			1st dose	2nd dose	3rd dose[b]	3rd or 4th dose[b]					
PCV/PPSV			1st PCV	2nd PCV	3rd PCV	4th PCV				PPSV[c]	
IPV			1st dose	2nd dose	3rd dose						4th dose
Influenza					Annually (IIV only)					Annually (IIV or LAIV)	
MMR					d	1st dose					2nd dose
Varicella						1st dose					2nd dose
Hepatitis A						2-dose series[e]				[f]	
Meningococcal			Give only if high risk								

Recommended for all individuals in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection.

Recommended if some other risk factor is present.

[a]If RV5 or unknown, give third dose.

[b]If PRP-OMP is given at 2 and 4 months, a dose at 6 months is not indicated. Only a booster at 12–15 months of age.

[c]Only if at high risk.

[d]Administer one dose to infants aged 6–11 months before departure from the United States for international travel.

[e]Give the second dose 6–18 months after the first dose.

[f]May give if immunity desired.

DTaP/DT = diphtheria and tetanus toxoids and acellular pertussis vaccine/diphtheria-tetanus; Hib = *Haemophilus influenzae* type B; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus vaccine; LAIV = live, attenuated influenza vaccine; MMR = measles, mumps, and rubella; mo = month(s); PCV/PPSV = pneumococcal conjugate vaccine/pneumococcal polysaccharide vaccine; PRP-OMP = *Haemophilus* B conjugate, conjugated to meningococcal group B outer membrane protein; RV5 = rotavirus vaccine; yr = years.

Table 7. Childhood Immunization Schedule, 6–18 Years

Vaccine	7–10 Years	11–12 Years	13–18 Years
Tdap		Tdap	
Human papillomavirus		Three-dose series	
Meningococcal		First dose	Booster[a]
Influenza	One dose annually		
Pneumococcal	One or two doses[b]		
Hepatitis A	Two doses[b]		

[a]Booster dose at 16 years.

[b]If at high risk and not previously vaccinated.

Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

Table 8. Adult Immunization Schedule

Vaccine	19–21 Years	22–26 Years	27–49 Years	50–59 Years	60–64 Years	65 Years or Older
Influenza	1 dose annually					
Tdap/Td	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 years					
Varicella	2 doses[a]					
HPV	3 doses					
Zoster					1 dose	
MMR	1 or 2 doses[a]					
PCV13	1 dose[b]					1 dose
PPSV23	1 or 2 doses[c]					1 dose
Meningococcal	1 or more doses[c]					
Hepatitis A	2 doses[c]					
Hepatitis B	3 doses[c]					
Hib	1 to 3 doses[d]					

Recommended for all individuals in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection.

Recommended if some other risk factor is present.

[a]Without evidence of immunity.

[b]Only in immunocompromising conditions, functional or anatomic asplenia, CSF leaks, or cochlear implants.

[c]Only in at-risk individuals and those not previously vaccinated.

[d]Only in functional or anatomic asplenia, sickle cell disease, elective splenectomy, or hematopoietic stem cell transplant.

CSF = cerebrospinal fluid; Hib = *Haemophilus influenzae* type B; HPV = human papillomavirus; MMR = measles, mumps, and rubella; PCV = pneumococcal conjugate vaccine; PPSV = pneumococcal polysaccharide vaccine; Td = tetanus and diphtheria; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

Q. Vaccine Storage

1. Most vaccines need to be stored at refrigerator temperatures of 35.6°F–46.4°F (2°C–8°C) and not frozen. Exception: Varicella-containing vaccines should be kept frozen until reconstituted.
2. Multidose vials may be used until the expiration date on the package unless otherwise stated in the manufacturer's product information.

R. Pharmacists as Immunizers
   1. Authority
      a. Pharmacists may administer the influenza vaccine in every state.
      b. The authority to administer other vaccines varies greatly by state.
      c. To administer a vaccine, a pharmacist must have an order from a physician or other provider to do so. This varies among states and is usually a standing order and/or a written prescription.
   2. Certificate programs
      a. Most states require pharmacists to have completed a certificate program to administer vaccines.
      b. Most state pharmacy boards allow immunization training in college of pharmacy curricula to be used in place of a formal certificate program.
      c. Several immunization delivery continuing education programs exist for pharmacists.
         i. Most notable is a program through the American Pharmacists Association
         ii. www.pharmacist.com/pharmacy-based-immunization-delivery

S. Safety
   1. Clinical Laboratory Improvement Amendments (CLIA) waiver
      a. All places that perform diagnostic tests are considered a laboratory.
      b. Laboratories that perform only tests with an insignificant risk of erroneous results may apply for a CLIA waiver.
      c. A CMS-116 form may be completed to obtain this waiver.
      d. An alphabetized list of waived laboratory tests is available at www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfClia/analyteswaived.cfm.
   2. Bloodborne pathogen safety
      a. All bodily fluids should be considered hazardous—All employees with exposure to bodily fluids should be provided with, and use, personal protective equipment (PPE) appropriate to the task (e.g., gloves, gowns, laboratory coats, face shields or masks, eye protection, mouthpieces, resuscitation bags, pocket masks, or other ventilation devices).
      b. Gloves should always be worn when it can be reasonably anticipated that the employee will have hand contact with blood, other potentially infectious materials, mucous membranes, and nonintact skin (does not apply to administering vaccines). The employer should make running water accessible for employees to wash their hands immediately after removing PPE. If running water is not immediately available, an antiseptic cleaner is an appropriate alternative as long as employees can eventually get to running water.
      c. Sharps/needles should not be bent, recapped, or clipped after use.
      d. Sharps/needles should be disposed of in a container that is puncture-resistant, red, leakproof, and closeable for transport.
      e. Food and drink should not be kept in the same location (refrigerator, freezer, countertops) where potentially hazardous materials are kept.
      f. Employers shall make the hepatitis B vaccine available to all employees with potential exposure to bloodborne pathogens. This shall be provided at no cost to the employee. The employee has the right to decline this vaccine but must sign a statement attesting to his or her refusal.

V. ADHERENCE

Guidelines

World Health Organization. Adherence to Long-term Therapies: Evidence for Action. Available at www.who.int/chp/knowledge/publications/adherence_full_report.pdf.

The American College of Preventive Medicine. Medication Adherence: Improving Health Outcomes Time Tool: A Resource from the American College of Preventive Medicine. Available at www.acpm.org/?page=MedAdhereTTProviders.

A. Definitions
   1. Adherence: The extent to which a person's behavior (taking medication, following a diet, or making healthy lifestyle changes) coincides with recommendations from a health care provider
   2. Medication adherence: The patient's conformance with the provider's recommendation with respect to timing, dosage, and frequency of medication-taking during the prescribed length of time
      a. Primary nonadherence is when a prescription is written but the patient does not fill the prescription.
         i. Harder to quantify because of a lack of claims data
         ii. Now able to identify never-filled prescriptions because of electronic prescriptions
      b. Secondary nonadherence is when a prescription is filled but the patient does not continue to conform to the provider's recommendation.
   3. Compliance: Patient's passive following of provider's orders
   4. Persistence: Duration of time a patient takes medication, from therapy initiation to discontinuation
   5. Measuring adherence
      a. Medication possession ratio (MPR)
         i. Historically, the most common way for measuring adherence using claims data
         ii. Defined as the summation of a medication days' supply across a defined interval
         iii. Does not account for actual patient discontinuation of medication
         iv. Varying definitions of the numerator and denominator
         v. May overestimate adherence, depending on defined intervals
         vi. In general, a patient is considered adherent if the MPR is greater than 80%.
      b. Proportion of days covered (PDC)
         i. Method of assessing adherence using claims data
         ii. Defined as the number of days with drug on hand divided by the number of days in a specified time interval. It may be multiplied by 100 to yield a percentage.
         iii. The denominator does not use a simple summation of days' supply as MPR, which ensures that the calculation is both more conservative and more consistent (e.g., if the measurement period is 365 days, and if the patient's first fill of the medication is on day 20 of the year, then the denominator period is 345 days (365 – 20 = 345).
         iv. In general, a patient is still considered adherent if the PDC is greater than 80%.
      c. Comparison of MPR and PDC
         i. PDC and MPR result in similar results when examining adherence to a single drug.
         ii. PDC will be a more conservative estimate to adherence when examining adherence to a class of drugs that is prone to frequent switching and concomitant therapy with several drugs within a class.

B. Burden of Nonadherence
   1. Nonadherence rate
      a. 2003 report by the WHO estimates adherence rates to be about 50%.
         i. Adherence rates tend to significantly decline after 6 months.
         ii. After 1–2 years, nonadherence rates may reach up to 75% with some medications.

b. Primary nonadherence has been estimated to be up to 24% across medication classes.
c. Adherence rates among various medication classes
    i. Primary nonadherence
        (a) Antihyperlipidemic medications between 13% and 34%
        (b) Antidiabetic medications between 11% and 32%
        (c) Antihypertensive medications between 7% and 28%
    ii. Secondary nonadherence
        (a) Antihyperlipidemic medications up to 39%
        (b) Antidiabetic medications up to 28%
        (c) Antihypertensive medications up to 34%
        (d) Rates with medications continue to decline over time and may reach up to 50%.

2. Outcomes related to nonadherence
    a. Estimated costs to the health care system are thought to be $290 billion annually.
    b. Associated with as many as 40% nursing home admissions
    c. 5.4 times increase of hospitalizations, rehospitalizations, or premature death in patients with high blood pressure
    d. 2.5 times increased risk of hospitalization for patients with diabetes

C. Reasons for Nonadherence
1. Sources contributing to nonadherence
    a. Provider and health care system factors
        i. Ineffective communication
        ii. Failure to recognize health literacy issues and/or cultural beliefs
        iii. Lack of positive reinforcement
        iv. Continuity or access to care
    b. Medication- and condition-related factors
        i. Complexity of administration
        ii. Number of medications
        iii. Therapy duration or frequent changes in therapy
        iv. Fear of or experienced adverse effects
        v. Lack of immediate benefits
        vi. Asymptomatic disease
        vii. Social stigma with certain medications
        viii. Cost of medications
    c. Patient-related factors
        i. Lack of knowledge about the disease state, medications, and outcomes
        ii. Cost of medication, copayment or both
        iii. Social support
        iv. Health literacy
        v. Physical
            (a) Blind, deaf, cognitive impairment
            (b) Dysphagia
        vi. Cultural
2. Characteristics related to nonadherence with cardiovascular medication
    a. Cost
    b. Concerns about medication adverse effects
    c. Lack of belief in benefits of medications
    d. Lack of knowledge about the severity of a cardiovascular-related disease

e. Sex—Male individuals tend to have a higher occurrence.
f. Ethnicity—Nonwhite race
g. Age—Younger

3. The National Community Pharmacists Association identified six predictors of adherence in a recent analysis.
   a. Personal connection with pharmacist or staff
   b. Cost
   c. Continuity of care
   d. Patients' beliefs about the importance of the medication
   e. Patients' knowledge about their disease state(s)
   f. The risk of adverse effects

D. Strategies and Interventions to Improve Adherence
   1. Strategies should be multifactorial and address characteristics of nonadherence.
      a. Patient interventions
         i. Pillboxes
         ii. Visual aids
         iii. Electronic reminder systems
         iv. Education about medication and disease state(s)
         v. Financial assistance programs
      b. Provider or health care systems intervention
         i. Introduce team-based care with pharmacists or nurses.
         ii. Improve communication.
         iii. Improve access to care (i.e., telemedicine).
         iv. Use of technology to improve monitoring of adherence
         v. Use of generic or preferred formulary medications
      c. Policy-based interventions (i.e., cost coverage for certain disease states)
   2. Interventions have been difficult to design for broad-spectrum approaches to address adherence and improve clinical outcomes.
   3. Population-based interventions for improving adherence to cardiovascular medications
      a. Collaboration, education, decision aids all have low or insufficient methods for assessing adherence and outcomes.
      b. Pharmacist-led hypertension clinics
         i. Improved blood pressure control
         ii. Improved adherence to hypertension medications
         iii. Long-term outcomes lacking
      c. Improving the cost of cardiovascular medications
      d. Blister packaging
         i. Improvement in adherence and persistence
         ii. Widespread applicability difficult to judge because limited trials exist
      e. Use of interactive voice response system
         i. Improved first fill compared with usual care
         ii. Outcomes too early to predict, as is long-term persistence with medications

E. Integrating Adherence into Pharmacy Practice
   1. Use of mnemonics to help aid with assessing and addressing nonadherence
      a. SIMPLE technique by the American College of Preventive Medicine
         i. S – Simplify the regimen.
         ii. I – Impart knowledge.
         iii. M – Modify patient beliefs and behavior.
         iv. P – Provide communication and trust.
         v. L – Leave the bias.
         vi. E – Evaluate adherence.
      b. B-SMART
         i. B – Barriers
         ii. S – Solutions
         iii. M – Motivation (necessary only if not ready for change)
         iv. A – Adherence tools
         v. R – Relationship
         vi. T – Triage

Table 9. Examples of Addressing Adherence Issues Through SIMPLE and B-SMART

SIMPLE	B-SMART
Simplifying Regimen -Adjusting medication frequency, dosage, and timing with patient activities -Customized packaging -Use of adherence aids	Barriers (questions to identify barriers) -During the past week, how many days have you missed taking any of your medications? -Have you stopped or started taking any of your medications on your own? -Have you experienced any problems or had any adverse effects while taking your medication?
Impart Knowledge -Involving the patient's family or caregiver -Helping to cope with medication costs -Providing instructions in writing and verbally	Solutions -Use of devices to address individual concerns -Education on the benefits and risks of not taking medication -Tips to reduce adverse effects -Referral to financial services -Use of interpreter lines -Simplify regimen
Modify Patient Beliefs and Behavior -Self-management -Shared decision-making -Addressing fears and concerns -Ensuring comprehension of risks with nonadherence -Asking patients to restate the positives and negatives	Motivation (necessary only if the patient is unwilling to change) -Assessing the patient's willingness to change (determined in barrier identification) -Ask additional questions to confirm adherence -Discern if related to not taking the medication at all -Guide the discussion -Validate self-efficacy and self-management -Convey hopefulness

Table 9. Examples of Addressing Adherence Issues Through SIMPLE and B-SMART *(continued)*

SIMPLE	B-SMART
Provide Communication and Trust -Listen -Interview patients -Use plain language -Work with the patient	Adherence Tools -Using solutions identified and offering individualized solutions -Collaborate with the patient, provider, and family -Ensure understanding -Ask the patient to restate (active participation)
Leave the Bias -Understand health literacy -Communicate in a patient-centered manner	Establishing Relationships -Eye contact -Active listening and being nonjudgmental -Communicate in an open adult-to-adult style -Seek to understand -Be on time, and follow up
Evaluate Adherence -Ask patients at each encounter -Periodically review patient's refill history -Use medication adherence scales	Triage -Refer for case management -Behavior and social medicine/social services -Health education classes -Community programs -Physician follow-up

Patient Case

13. W.M. is a 57-year old man with a diagnosis of hypertension who was given a prescription for lisinopril. After 1 week, he stopped taking the medication because he was too dizzy to function at work. He presents today asking for a blood pressure check. His blood pressure reading is 175/95 mm Hg. After discussing goals, W.M. demonstrates understanding and has been implementing other lifestyle behaviors to improve blood pressure. Which barrier to adherence have you identified?

    A. Financial
    B. Concerns about medication adverse effects
    C. Social support
    D. Health literacy

2. Tools available for patients and providers
    a. Addressing forgetfulness or complex medication regimens
        i. Calendars
            (a) MyMedSchedule (www.mymedschedule.com [free—Need to register])
            (b) Use of Microsoft Office programs
            (c) Wallet cards
        ii. Pillboxes
            (a) Inexpensive to moderately priced
            (b) Readily available
            (c) E-Pill—Calendar and pillbox (www.epill.com/chart.html)
        iii. Alarms

b. Addressing physical concerns
    i. Talking Rx (www.talkingrx.com)
        (a) Attaches to the bottom of a pill vial
        (b) Allows a pharmacist or caregiver to leave a 60-second recorded message
    ii. Prodigy diabetes devices that are fully audible (www.prodigymeter.com)
c. Financial Support
    i. Online resource: www.needymeds.org, www.rxassist.org, www.pparx.org, www.benefitscheckup.org
    ii. Medicare plan resource: www.medicare.gov
d. Organizational tools and support
    i. American Heart Association (http://scriptyourfuture.org/file/4dc82ede7ea0a.pdf)
        (a) Medicine management tool
        (b) Worksheet to keep track of patient's daily medicines, glucose readings, and blood pressure
    ii. American College of Cardiology (www.cardiosmart.org/Tools/Med-Reminder)
        (a) CardioSmart Med Reminder (mobile application)
        (b) The CardioSmart Med Reminder is to be used for educational purposes only.
    iii. American Society of Consultant Pharmacists Foundation (www.adultmeducation.com)
        (a) Focus on improving medication adherence in older adults
        (b) Tools for assessing medication knowledge and readiness for change
        (c) Consumer information (i.e., Questions You Should Ask About Your Medicines)
e. Improving health literacy
    i. Agency for Healthcare Research and Quality's (AHRQ's) Health Literacy Universal Precautions Toolkit (www.ahrq.gov/literacy)
    ii. National Council on Patient Information and Education (www.talkaboutrx.org)

VI. COMPLEMENTARY AND ALTERNATIVE MEDICINE

A. Definitions
    1. Complementary and alternative medicine (CAM)—Diverse group of medical and health care systems, practices, and products not considered part of conventional medicine
    2. Complementary—Used together with conventional medicine
    3. Alternative—Used in place of conventional medicine
    4. Dietary supplement—Intended to supplement the diet
        a. Contains vitamin, mineral, herb/botanical, amino acids, enzymes, metabolite as replacements, and other ingredients intended to supplement the diet
        b. Does not meet definition of food

B. Types of CAM
    1. Natural products
        a. Botanicals
        b. Animal-derived extracts
        c. Vitamins, minerals, fatty acids, amino acids, and proteins
        d. Prebiotics and probiotics
    2. Mind and body practices (i.e., tai chi, medication, hypnosis)
    3. Manipulative/body based (i.e., chiropractic manipulation, massage therapy)
    4. Energy medicine (i.e., acupuncture, cupping)

C. Dietary Supplement Regulations
   1. Before 1994, dietary supplements were subject to same regulatory requirements as other foods under the FDA.
   2. The Dietary Supplement Health and Education Act (DSHEA) of 1994
      a. Dietary supplements can be marketed without FDA approval.
      b. Manufacturer responsible for safety and efficacy but not required to submit to the FDA
      c. The FDA monitors for adverse events once on the market, but no regulations are designated before postmarketing surveillance period.
      d. Must follow good manufacturing practices for foods
      e. May make three types of claims
         i. Health claims—The FDA authorizes scientific-based literature.
         ii. Structure/function claims—Not subject to FDA review or authorization
         iii. Nutrient content claims—Describes the level of substance in the product
   3. Label requirements
      a. Must contain supplement facts
      b. Legislation requires supplement manufacturers to have substantiation of label claims carry a disclaimer: "This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease."
      c. Supplement seal of approval to ensure additional testing and safety by manufacturer
         i. Not required, but ideal because it ensures additional testing
         ii. U.S. Pharmacopeia (USP) Convention
         iii. NSF International (formerly known as National Sanitation Foundation)
         iv. Consumer laboratories

D. Concerns with CAM
   1. Estimated that only 33%–45% of patients report CAM use to a health care professional
   2. Those more likely to use CAM
      a. Women
      b. Higher income
      c. Self-assessed good health
      d. Higher education levels
      e. Former smokers
      f. Hospitalized in the past year
      g. Access to health care (insured)
   3. Few studies have critically evaluated some of the most common CAM agents.
      a. Most CAM agent interactions remain largely unknown.
      b. The most common supplements studied for interactions include the following:
         i. Garlic
         ii. Gingko
         iii. Ginseng
         iv. St. John's wort
   4. It is estimated that up to 60% of patients do not report adverse events associated with CAM, and many do not recognize that the adverse events they experience are associated with the CAM product.

E. Examples of Dietary Supplements
   1. The National Health Interview Survey in 2007 surveyed more than 20,000 U.S. citizens on supplement use.
      a. The top five supplements used were the following:
         i. Glucosamine/chondroitin—For joint pain
         ii. Fish oil/omega-3 fatty acid supplements—For cholesterol and cardiovascular health
         iii. Echinacea—For immunity
         iv. Flaxseed oil—For cholesterol
         v. Garlic—For cholesterol
      b. In the 2002 survey, both ginseng and gingko biloba were in the top 5 in place of flaxseed and fish oil.
   2. Management of dyslipidemia with herbal supplements
      a. Fish oil/omega-3 fatty acid supplements
         i. Indication: Hypertriglyceridemia, cardiovascular protection
         ii. Mechanism
            (a) Lower triglycerides (TGs) by decreasing hepatic secretion of very-low-density lipoprotein (VLDL), increasing VLDL clearance, and reducing TG transport
            (b) Anti-inflammatory and antithrombotic effects because they compete with arachidonic acid in the cyclooxygenase and lipoxygenase pathways
         iii. Dose
            (a) Average dose required is between 2 and 4 g/day of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).
            (b) Typical fish oil capsule contains 120 mg of DHA and 180 mg of EPA.
         iv. Adverse effects
            (a) Fishy aftertaste, stomach upset, belching, heartburn, halitosis
            (b) Doses greater than 3 g/day may increase bleeding risk in some individuals.
            (c) Some reports exist that fish oil may worsen glycemic control in diabetes.
         v. Interactions
            (a) Antiplatelets—Increased bleeding risk
            (b) Antihypertensives—May lower blood pressure
         vi. Effectiveness
            (a) Hypertriglyceridemia
               (1) Decreased TG values by 20%–50% in a dose-dependent manner
               (2) Doses of 4 g/day do not seem to be as effective as gemfibrozil 1200 mg/day.
            (b) Cardiovascular protection
               (1) A recent 2012 meta-analysis showed no benefit of fish oil for secondary prevention in patients with existing cardiovascular disease.
               (2) Likely because of the widespread use of statins now as compared with when fish oil was first studied
               (3) This new study conflicts with previous information regarding the overall cardioprotective benefits of fish oil.
      b. Flaxseed oil
         i. Indication—Cardiovascular disease, hypercholesterolemia
         ii. Mechanism
            (a) Hypercholesterolemia
               (1) Contains high content of α-linolenic acid, which is a precursor to omega-3 fatty acids
               (2) Possibly affects the synthesis of bile acids from cholesterol
               (3) Overall, not well understood
            (b) Cardiovascular disease: May increase systemic arterial elasticity, which may improve circulatory function

iii. Dose
  (a) Ground flaxseed up to 50 g/day (for hypercholesterolemia)
  (b) Flaxseed oil 1.2–3.6 g/day (for hypercholesterolemia and cardiovascular disease)
iv. Adverse effects—Diarrhea, allergic reactions, questionable increased risk of prostate cancer
v. Interactions—Antiplatelets with increased risk of bleeding
vi. Effectiveness
  (a) Hypercholesterolemia—Some research shows that flaxseed oil significantly reduces cholesterol or TG values in patients with or without baseline elevations. Other research does not.
  (b) Cardiovascular disease—Some evidence suggests benefit in combination with a low-fat diet. However, it has not been well studied, and overall studies assessing outcomes are lacking.

c. Garlic
i. Mechanism: Inhibits hepatic cholesterol synthesis through the active ingredient allicin
ii. Dose: 0.4–1.2 g/day of dried garlic powder; 2–5 mg of garlic oil; 300–1000 mg of garlic extract
iii. Adverse effects: Stomach upset, garlic breath, reports of bleeding, and body odor
iv. Interactions
  (a) Increased international normalized ratios (INRs) with warfarin
  (b) Mixed evidence on the impact of the cytochrome P450 (CYP) isoenzyme system
v. Effectiveness
  (a) Meta-analysis of 13 randomized, double-blind, placebo-controlled studies with a statistically significant reduction of 5.8% in total cholesterol (TC) in favor of garlic
  (b) Systematic review of studies for at least 4 weeks with a decrease in TC by 17.1 mg/dL and a decrease in low-density lipoprotein cholesterol (LDL-C) by 6.2 mg/dL

d. Other supplements for high cholesterol
i. Plant sterols/stanols
  (a) Indication: Hypercholesterolemia
  (b) Mechanism: Inhibits the absorption of dietary and biliary cholesterol
  (c) Dose: From 800 mg to 6 g per day
  (d) Adverse effects: Nausea, indigestion, diarrhea, constipation
  (e) Interactions: Ezetimibe may reduce stanols/sterols values up to 41%.
  (f) Effectiveness
    (1) Significantly reduces TC and LDL-C values
    (2) Recommended as part of lifestyle modification in American Diabetes Association's (ADA's) Standards of Medical Care in Diabetes—2015
ii. Red yeast rice (several products contain lovastatin)
  (a) Indication: Hypercholesterolemia
  (b) Mechanism: Inhibits endogenous cholesterol synthesis (like statins)
  (c) Dose—600 mg twice daily to 2400 mg once or twice daily
  (d) Adverse effects
    (1) Stomach discomfort, heartburn, flatulence, headache, and dizziness
    (2) Concerns about myopathy and liver toxicity exist because it contains lovastatin.
  (e) Interactions
    (1) Statins—Duplicate therapy
    (2) CYP 3A4 inhibitors (e.g., clarithromycin, ketoconazole, protease inhibitors)
    (3) Gemfibrozil—Increased risk of myopathies
  (f) Effectiveness
    (1) Some research has shown decreases in TC of up to 20% and in LDL-C of up to 26%.

(2) However, these products provided up to about 10 mg daily of statins.
(3) The FDA has tried to remove red yeast rice products from the market, yet they remain available, despite containing variable amounts of prescription medications.

iii. Soy, fiber, policosanol, and krill oil may also be widely used by patients for potential cholesterol-lowering effects with varying levels of evidence and impact on hypercholesterolemia.

Patient Case

14. R.T. is a 58-year-old man with coronary artery disease, hypertension, obesity, and impaired fasting glucose. Current medications include aspirin, metoprolol, lisinopril, and pravastatin. The lipid panel is as follows: TC 152 mg/dL, LDL 59 mg/dL, TG 349 mg/dL. R.T.'s primary care provider has recommended that R.T. start taking fish oil. Which of the following counseling points will you offer R.T.?

A. Omega-3 fatty acids increase intestinal cholesterol absorption.
B. Recommend ginseng instead of fish oil to improve triglycerides.
C. Avoid over-the-counter fish oil products because of the risk of hepatotoxicity.
D. Improved triglyceride benefits are associated with a fish oil product containing EPA and DHA at 2–4 g/day.

3. Glucosamine/chondroitin
   a. Indication: Osteoarthritis
   b. Mechanism
      i. Glucosamine sulfate—Stimulates the metabolism of chondrocytes in cartilage and of synovial cells in the synovium
      ii. Chondroitin sulfate—Protects cartilage from degradation by inhibiting leukocyte elastase, decreasing migration of polymorphonuclear leukocytes, and increasing synthesis of proteoglycans and hyaluronic acid
   c. Dose
      i. Glucosamine: 1500 mg once daily or divided three times daily
      ii. Chondroitin: 1000–1200 mg once daily or divided two or three times daily
   d. Adverse effects
      i. Glucosamine: Mild stomach concerns
      ii. Chondroitin: Mild stomach concerns
   e. Interactions
      i. Glucosamine
         (a) May induce resistance to etoposide, teniposide, and doxorubicin
         (b) Doses greater 3000 mg/day may enhance the effects of warfarin.
      ii. Chondroitin: Doses greater than 2400 mg/day may enhance the effects of warfarin.
   f. Effectiveness—A recent 2-year study showed that, during a 2-year period, glucosamine and chondroitin alone or in combination showed no clinically significant benefit on pain or function scales, compared with placebo.
4. Echinacea
   a. Indication—Treatment and prevention of the common cold and other upper respiratory infections
   b. Mechanism—Activates phagocytosis and increases the number of circulating lymphocytes
   c. Dose
      i. Capsules containing freeze-dried extract: 100 mg three times daily
      ii. Herbal compound tea: 5–6 cups of tea the first day; then 1 cup daily for 5 days
      iii. Liquid: Use 20 drops every 2 hours for the first day; then three times daily for up to 10 days

d. Adverse effects—Allergic reactions, fever, stomach disturbances, dry mouth, sore throat, tingling and numb tongue, mouth ulcers
e. Interactions
    i. Possible CYP3A4 inhibitor
    ii. May interfere with immunosuppressants
f. Effectiveness—Several randomized placebo-controlled trials showed no difference in symptoms.

5. Other significant supplements
    a. Ginseng
        i. Indication—Mental performance/memory, immunity
        ii. Mechanism
            (a) May work against stress by affecting the hypothalamic-pituitary-adrenal axis
            (b) Seems to increase serum cortisol concentrations and stimulate adrenal function
        iii. Dose—100–200 mg once or twice daily
        iv. Adverse effects—Insomnia, tachycardia, mania, Stevens-Johnson syndrome
        v. Interactions
            (a) May lower blood glucose values and may enhance hypoglycemic effects of some antidiabetes medications
            (b) May enhance effectiveness of anticoagulants, causing reduction of blood coagulation
        vi. Effectiveness
            (a) Mental performance/memory
                (1) Several studies report improvement in reaction time, concentration, learning, math, and logic.
                (2) Most studies are small and not well designed.
                (3) In addition, a small amount of negative evidence
            (b) Immunity
                (1) A few studies suggest ginseng stimulates T lymphocytes and neutrophils.
                (2) Improves the effectiveness of antibiotics in acute bronchitis and enhances the body's response to influenza vaccine
            (c) If patients use it, recommend short-term use (less than 3 months).
    b. Gingko biloba
        i. Indication: Claudication, dementia, tinnitus
        ii. Mechanism: Protects tissues from oxidative damage
        iii. Dose: 40–80 mg three times daily
        iv. Adverse effects—Stomach disturbances, headache, dizziness, palpitations, vertigo, allergic skin reactions, spontaneous bleeding
        v. Interactions
            (a) Anticonvulsants—May lower seizure threshold
            (b) Antiplatelets—Increased bleeding risk
            (c) Aminoglycosides—Increased ototoxicity
            (d) Thiazide—Increased blood pressure
        vi. Effectiveness
            (a) For dementia
                (1) Studies lasting 3 months to 1 year show stabilization or improvement in some cognitive and social functioning measures in many types of dementia.
                (2) Improvement appears to be less than that found with prescription drugs.
            (b) For claudication
                (1) May increase pain-free walking distance

(2) Most studies used ginkgo 120 mg/day divided in two or three doses for 6 months, which may increase the risk of adverse effects.
(3) Additional studies are needed to compare the use of gingko with exercise therapy and prescription medications.

c. St. John's wort
  i. Indication—Depression, anxiety
  ii. Mechanism—Serotonin receptor antagonist (serotonin-3 and serotonin-4)
  iii. Dose—300 mg three times daily
  iv. Adverse effects—Photosensitivity, insomnia, vivid dreams, restlessness, anxiety, diarrhea, fatigue, dry mouth
  v. Interactions
    (a) Induces CYP3A4, CYP2C9, CYP1A2, and P-glycoprotein
    (b) Marginal effect on CYP2D6
    (c) Antidepressants—As it works on similar neurochemicals
  vi. Contraindications—Should be avoided during pregnancy or lactation
  vii. Effectiveness
    (a) St. John's wort extract is likely as effective as the selective serotonin reuptake inhibitors.
    (b) Short-term response rates appear to be between 65% and 100%, but long-term rates appear to be closer to 60%–69%.
    (c) Although beneficial outcomes exist, drug interactions likely preclude the use of this supplement; moreover, there is a need for provider management of depression and mood disorders.

d. Black cohosh
  i. Indications—Hot flashes, premenstrual syndrome, painful menstruation
  ii. Mechanism—Estrogenlike effects by an unknown mechanism, possibly some serotoninergic-type effects
  iii. Dose—20–40 mg twice daily (according to manufacturer, 20 mg provides results similar to 40 mg)
  iv. The use of black cohosh should not exceed 6 months' period because of the lack of safety data.
  v. Adverse effects—Stomach upset, rash, headache, dizziness, weight gain, cramping, hepatotoxicity
  vi. Interactions
    (a) Mixed evidence that black cohosh inhibits CYP2D6
    (b) Hepatotoxic drugs—Because of case reports of liver toxicity, caution is needed when using black cohosh with other agents with potential hepatotoxicity (e.g., isoniazid, methotrexate, acetaminophen), and liver function test monitoring is recommended.
    (c) Avoid use in patients with breast cancer—Although relatively unknown, best to avoid in patients with breast cancer because of unknown risks of possible estrogenlike effects.
  vii. Effectiveness
    (a) Studies funded by the German manufacturer of Remifemin, a branded form of an alcohol extract of black cohosh, found this specific product helpful in reducing the frequency of hot flashes and in alleviating mood disorders with no difference in liver function test findings.
    (b) Several meta-analyses since then have failed to provide consistent evidence that black cohosh provides symptomatic improvement in the management of menopausal symptoms.
    (c) Liver function test monitoring is recommended because of increased case reports of hepatotoxicity.

e. Saw palmetto
  i. Indication—Benign prostatic hypertrophy (BPH)

ii. Mechanism—Noncompetitively inhibits 5-α-reductase types 1 and 2, and prevents conversion of testosterone to dihydrotestosterone
iii. Dose—160 mg twice daily or 320 mg once daily
iv. Adverse effects
  (a) Mild and comparable with placebo
  (b) Impotence rate similar to placebo and less than with finasteride
  (c) High doses may cause stomach upset and diarrhea.
v. Interactions—None specifically proved
vi. Effectiveness
  (a) Research on saw palmetto is inconsistent for treating BPH, with some positive results and others showing no difference compared with placebo.
  (b) Positive studies suggest a 25% improvement in nocturia.
  (c) Other studies show effects of saw palmetto comparable with those of finasteride in improving peak and mean urine flow and residual volume.
  (d) α-Adrenergic blockers appear more effective in head-to-head trials.
  (e) May take up to 1–2 months to show effectiveness

f. Melatonin
i. Indication—Sleep disorders (e.g., circadian rhythm, insomnia, jet lag)
ii. Mechanism—Shifts circadian rhythm by increasing the binding of GABA (γ-aminobenzoic acid) to its receptors
iii. Dose
  (a) For jet lag: 0.5–5 mg at bedtime on arrival of the destination day and continuing for 2–5 days
  (b) For insomnia: 0.3–5 mg at bedtime in either immediate-release or extended-release form
iv. Adverse effects—Daytime sleepiness, dizziness, and headache, but no different from placebo
v. Interactions
  (a) Anticoagulants—Some case reports of minor bleeding with melatonin and warfarin
  (b) Fluvoxamine—May increase bioavailability of exogenous melatonin by up to 20 times; may be beneficial in difficult-to-treat insomnia
  (c) Immunosuppressants (e.g., cyclosporine, tacrolimus, azathioprine)—Melatonin stimulates immune function and may interfere with therapy; avoid using in combination.
vi. Effectiveness
  (a) Insomnia
    (1) Research on melatonin is inconsistent for treating insomnia.
    (2) Some studies report decreased sleep latency onset time by 4–7½ minutes, with clinical significance being a reduction of 5–10 minutes.
    (3) On average, melatonin significantly increases total sleep duration by about 13 minutes.
    (4) Other studies fail to show changes in objective measurements.
  (b) Jet lag
    (1) Most evidence shows melatonin can positively improve alertness and psychomotor performance.
    (2) Traveling westward: May take melatonin 0.5 mg on the night of arrival during the second half of the night until adapted (shifts body clock to later time)
    (3) Traveling eastward: May take melatonin 0.5–3 mg on the night of arrival at local bedtime until adapted (shifts body clock to earlier time)
    (4) The American Academy of Sleep Medicine recommends the use of melatonin in conjunction with other methods as a viable treatment option.

Patient Case

15. C.B. is a 56-year-old woman who presents to the pharmacy after watching a daytime talk show. She is excited to learn about the menopausal management options available over the counter to help alleviate hot flashes. She asks about black cohosh and whether there is any information she should know about before taking this product. What is the best recommendation that you will give to C.B.?
    A. It is as effective as a selective serotonin reuptake inhibitor.
    B. This product should not be used by patients with a history of asthma.
    C. Recommend to discontinue use after 6 months.
    D. This product may be safely recommended for patients with a history of breast cancer.

F. Counseling Tips for CAM
    1. Encourage open communication between patient and health care providers.
    2. Target one medical problem.
    3. Assess regularly.
    4. Avoid in pregnancy and lactation.
    5. Avoid combination or proprietary blend products.
    6. Stop dietary supplements 2–3 weeks before elective surgery.
    7. Same potential as prescription drugs for adverse effects and drug interactions

G. Tools for Evaluating CAM

Table 10. Overview of Tools for Evaluating CAM

	Monograph Components	Rating Scales	Additional Pearls
Natural Medicines Comprehensive Database[a]	-Safety -Effectiveness -Adverse reactions -Dosage/administration -Interactions with drugs, herbs, food, laboratory tests, and diseases -Interactions with herbs -Mechanism of action -Editor's comments -Patient handout	**Safety** -Likely safe -Possibly safe -Possibly unsafe -Likely unsafe -Unsafe **Efficacy** -Effective -Likely effective -Possibly effective -Possibly ineffective -Likely ineffective -Ineffective	-Evidence based, links provided to references within monograph—Clinical Management Series (CE presentations) -Links to Pharmacist's Letter -USP-verified products -Subscription necessary http://naturaldatabase.therapeuticresearch.com/

Table 10. Overview of Tools for Evaluating CAM *(continued)*

	Monograph Components	Rating Scales	Additional Pearls
AltMedDex	-Overview -Dosing information -Dosage forms, drug storage plus stability, adult and pediatric doses -Pharmacokinetics -Cautions/ contraindications -Adverse reaction -Pregnancy and lactation -Drug interactions -Clinical applications -Monitoring guidelines -Place in therapy -Mechanism of action -Comparative -References	Not categorized by effectiveness or safety **Variables not defined**	-Evidence based, but WITHOUT links to references within monograph—More detailed efficacy information provided in monograph without having to look up the article -AltMedDex protocols -Part of the Micromedex resources (www.micromedex.com/ products/) -Subscription necessary
Natural Standard[a]	-Historical/theoretical uses -Dosing/toxicology -Precautions -Contraindications -Adverse effects -Interactions -Mechanism of action -History -Evidence table -Evidence discussion -Products studied	-Safety -Similar to natural medicines -Efficacy **A:** Strong scientific evidence **B:** Good scientific evidence **C:** Unclear/conflicting scientific evidence **D:** Fair negative scientific evidence **F:** Strong negative scientific evidence **-Lack of evidence**	-Three available monographs -Professional monograph – Bottom Line Monograph (available in Spanish) -Flashcard (specifically for patients) -News items -Interactive tools -www.naturalstandard.com -Subscription required
Quackwatch.com *(founded 1996)*	-Rather than individual product monographs, topics are presented in the format of articles	-No standardized categories for evaluating effectiveness or safety of individual alternative therapies	-Lists of Quackwatch-recommended and sources of health advice are available on this website (www.quackwatch.com/) -Free weekly e-mail newsletter -A health fraud discussion list is available -Quackwatch Web pages are also available in German, French, and Portuguese

CAM = complementary and alternative medicine; CE = continuing education; USP = U.S. Pharmacopeia.

[a]Natural Medicines Comprehensive Database and Natural Standard were recently merged into a product called Natural Medicines.

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ANSWERS AND EXPLANATIONS TO PATIENT CASES

1. Answer: B

The American Heart Association and American Red Cross guidelines for first aid recommend splinting potential fractures (Answer B is correct). Answer A is incorrect because setting bone fractures may induce more pain, and there is no evidence that it will decrease pain or deformity. Ambulation is not recommended; in fact, any weight bearing should be avoided until further evaluation and treatment (Answer C is incorrect). Ice is recommended when there is a sprain or strain, but the priority is to immobilize the leg with splints (Answer D is incorrect).

2. Answer: B

According to first aid guidelines, the initial management of a patient with a seizure is to prevent injury, which includes keeping the area clear (Answer B is correct). Although the lay public might think of placing an object such as a wallet into the patient's mouth to prevent tongue biting, the risk of being bitten and of causing harm to the patient outweighs any potential benefit (Answer A is incorrect). Holding the patient still is not recommended, and, in fact, the patient should not be restrained because of potential secondary injuries (Answer C is incorrect). Although this patient probably requires adjustment in his or her seizure medications, administering a dose acutely is not recommended because it would probably be an oral medication, and the patient is unlikely to be able to swallow (Answer D is incorrect).

3. Answer: B

When an AED is immediately available, it should be used as rapidly as possible, but the clerk will be slightly delayed as he or she calls 911 and grabs the AED; waiting for it to arrive will decrease the chances for survival (Answer A is incorrect). This situation involves a man with a witnessed arrest, when an AED and immediate CPR are most likely to be effective. While the pharmacist waits for the AED to be obtained and set up, CPR can be initiated with chest compressions and ventilations in the correct ratio (Answer B is correct). Answer C is not the correct ratio for any CPR effort, according to the most recent guidelines. Chest-compression-only CPR would be appropriate for a non–health care rescuer to provide if an AED was unavailable (Answer D is incorrect).

4. Answer: C

In this case, two rescuers are providing health care, allowing the nurse to focus on the airway. The best choice to open the airway if the jaw thrust is not effective is to open the airway with the head tilt–chin lift maneuver (Answer C is correct). Continuing with the jaw thrust might prevent secondary injury by limiting neck movement, but guidelines recommend rescue breaths with the head tilt–chin lift procedure if the jaw thrust is unsuccessful (Answer A is incorrect). Chest-compression-only CPR can be used for witnessed arrests when a bystander is not trained in rescue breaths; however, two health care providers are responding, so this is not the best choice (Answer B is incorrect). Increased pressure would lead to gastric distention and a risk of aspiration and vomiting (Answer D is incorrect).

5. Answer: D

Many of the category A agents, when aerosolized, can cause pneumonialike illnesses. Botulism is less likely because there was no mention of associated symptoms affecting the muscles (Answer A is incorrect). Smallpox would also cause skin lesions and is highly contagious (Answer C is incorrect). Pneumonic plague can be transmitted from person to person by droplets; however, because none of the family members developed the illness after exposure to the affected individuals, the likelihood of plague is diminished (Answer B is incorrect). The most likely disease is tularemia (Answer D is correct).

6. Answer: D

The best choice for postexposure prophylaxis against inhalational anthrax is a combination of antibiotics and the vaccine. The recommended vaccine schedule is a three-dose series (Answer D is correct). The regimen in Answer A is not optimal because it does not constitute a full vaccine schedule and is limited to a single dose. Answers C and D are not optimal because these regimens are inferior to using the combination of antibiotic and vaccine in this setting.

7. Answer: B

Answer A is not the correct choice because although H.H. is a candidate for MMR vaccine, he is not a candidate for LAIV. Patients 2–4 years of age with a documented wheezing episode in the past 12 months should not

receive LAIV. In addition, the HPV vaccine will not be offered until the patient is 11 years of age (Answer C is incorrect). The IIV is more appropriate for this patient. He should receive all vaccines as recommended. He is eligible to receive both his MMR and varicella vaccines at this visit (Answer B is correct). This patient should not receive the meningococcal vaccine until his 11-year checkup (Answer D is incorrect).

8. Answer: A

This patient has a diagnosis of HIV and is considered an immunocompromised person. This makes him a candidate for both PPSV23 and PCV. Although this patient has already received the first dose of PPSV23, the patient should receive one dose of PCV13 now and then one dose of PPSV23 at least 8 weeks after receiving the dose of PCV13. The patient will be eligible for a third dose of PPSV23 at age 65 years (Answer A is correct; Answers B, C, and D are incorrect).

9. Answer: A

A.J. should receive one booster dose when possible before college entry (Answer C is incorrect). One booster dose is recommended because her first dose was administered before her 16th birthday (Answer D is incorrect). Either type of meningococcal conjugate vaccine (MenACWY-D or MenACWY-CRM) would be appropriate for her to receive (Answer A is correct). Hib-MenCY-TT is not indicated at her age (Answer B is incorrect).

10. Answer: D

Until 2005, guidelines stated that Td vaccine was necessary only when administering tetanus boosters after the 11- to 12-year checkup. Because of recent pertussis outbreaks, guidelines have changed to include a one-time revaccination with Tdap vaccine to booster pertussis immunity. It is likely that this patient received Td vaccine with his most recent booster dose; thus, he requires Tdap vaccine today (Answer C is incorrect; Answer D is correct). The DTaP and DT vaccines are not recommended because they are approved only for patients younger than 7 years (Answers A and B are incorrect).

11. Answer: D

The quadrivalent HPV vaccine may be administered to both male and female individuals aged 9–26 years. The bivalent vaccine is administered to female individuals 9–25 years of age. Although other vaccines may be appropriate, the 32-year-old health care worker and the 40-year old woman reporting a nonmonogamous relationship are not candidates for this vaccine (Answers A and C are incorrect). The 27-year-old pharmacy school student (Answer B) would not be a candidate for this vaccine, if just starting the vaccine series. If the series was started before the student reached 27 years of age, the vaccine series may be completed. However, the best choice is Answer D. The HPV vaccine series should be initiated at the 11- or 12-year checkup before onset of sexual activity.

12. Answer: C

The Advisory Committee on Immunization Practices (ACIP) states that susceptible people traveling to or working in countries that have high or intermediate hepatitis A endemicity are at increased risk of hepatitis A virus infection and should be vaccinated before departure. Hepatitis A vaccine is a two-dose series. (Answer C is correct; Answers A, B, and D are incorrect.)

13. Answer B

W.M. discontinued his medication because of the adverse effects that he was experiencing (Answer B is correct). He does come with the request to check his blood pressure, understands goals, and has implemented lifestyle changes. These actions demonstrate his understanding of the importance to manage the hypertension (Answer D is incorrect). W.M. does not mention financial concerns, and, from the information provided, it seems that he has means to access the prescribed medication (Answer A is incorrect). The case does not identify any social concerns (e.g., unstable living conditions, low health literacy, inability to access pharmacy) and is not the best answer choice (Answer C is incorrect). The next step to assist W.M. is to contact his provider and discuss appropriate options and an action plan to resolve adverse reactions.

14. Answer: D

Omega-3 fatty acids improve hyperlipidemia by decreasing intestinal cholesterol absorption (Answer A is incorrect). Ginseng is an herbal product that may be used for mental performance or memory (Answer B is incorrect). Fish oil is typically not associated with hepatotoxicity, unlike red yeast rice (Answer C is incorrect). Fish oil is a source of omega-3 fatty acids, primarily EPA and DHA, which are used to lower triglycerides and improve cardiac health. The recommended dose for triglyceride lowering is 2–4 g/day in divided doses (Answer D is correct).

15. Answer: C

The North American Menopause Society recommends that if black cohosh is selected for management of mild vasomotor symptoms, the product should be used on a short-term trial. Adverse effects of black cohosh include gastrointestinal disturbances, headache, rash, and weight gain. Because of the number of case reports of acute hepatitis with black cohosh, the Dietary Supplement Information Expert Committee recommended that a cautionary statement be included on products, alerting consumers to the potential for hepatotoxicity. The use of black cohosh is not recommended beyond a 6-month period because of the lack of safety data (Answer C is correct). Answer A is not correct because there is no current evidence to support that black cohosh is as effective as selective serotonin reuptake inhibitors (SSRIs) in the management of hot flashes. A few studies have shown SSRI therapy to be effective in reducing hot flash symptoms (JAMA 2003;289:2827-34, J Clin Oncol 2002;20:1578-83, JAMA 2011;305:267-74); however, the efficacy of black cohosh has not been well established and has not been compared with the efficacy of SSRIs. Answer B is not correct because there is no warning to the use of black cohosh in patients with a history of asthma. It is unclear how black cohosh may interact with estrogen or progesterone therapy. The safety of black cohosh for patients with a medical history significant for breast cancer is controversial. To date, studies have been inconclusive to support efficacy and safety; therefore, Answer D is not the best recommendation that can be offered to patients.

ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. Answer: A

Although foreign-body airway obstruction can occur at any age (Answers B–D), deaths occur most commonly in those younger than 5 years of age (Answer A is correct).

2. Answer: D

All of the listed drugs are commonly implicated in overdose. However, the overwhelming majority of overdose deaths are caused by opioids (Answer D is correct). Anticoagulants fall under the systemic and hematologic drug category, which accounts for about 7% of drug deaths (Answer A is incorrect). Tricyclic antidepressants are a class within the antidepressant category that accounts for fewer than 20% of drug-related overdose deaths (Answer B is incorrect). Benzodiazepines are the second leading cause of overdose deaths caused by drugs (Answer C is incorrect).

3. Answer: A

All of the elements listed are important for an effective disaster plan. Pharmacists will invariably be required as part of the plan, but they may not need to be "on call" because a disaster may require use of calling trees and other mechanisms to engage important personnel (Answer B is incorrect). Each disaster will be specific. Although vaccinations and antibiotic supplies are important, they are only applicable to a subset of disasters (Answers C and D are incorrect). The most important element is flexibility of the plan to allow an effective local response (Answer A is correct).

4. Answer: C

Live, attenuated vaccines are not recommended in pregnant women because of the theoretical risk of infection to the fetus. Of the vaccines listed, the only live, attenuated vaccine is the MMR vaccine. Therefore, Answers A, B, and D are incorrect, and Answer C is the best answer. In fact, the Tdap (Answer D) vaccine is now recommended for administration to women between weeks 27 and 36 of pregnancy to protect the infant, because the first dose of DTaP is not given until 2 months of age, and the full series is not completed until 5–6 years of age. Whereas live, attenuated influenza vaccine should be avoided in pregnant women, IIV (Answer A) does represent a vaccine that pregnant women should receive if pregnant during the usual period for annual influenza vaccination.

5. Answer: B

Medication possession ratio is defined as the sum of days' supply of a medication for a defined period (Answer B is correct). A patient is considered adherent if MPR is 0.8 (80%) or higher; therefore, a higher MPR value is an indication of a patient's adherence to prescribed therapy. Answer C is not correct because the MPR value is increased proportionally to a patient's refills. If a patient fails to refill a medication, the MPR would decrease over time. The duration of time from start to end of a medication regimen is defined as persistence (Answer A is incorrect). Health literacy is defined by the patient's ability to interpret and understand health information to make an informed decision regarding his or her health (Answer D is incorrect).

6. Answer: C

The DSHEA of 1994 defines dietary supplements as food, not drugs (Answer A is incorrect). DSHEA does not require that the safety or efficacy of supplements be established before they are marketed, nor is this requirement mandated by the FDA (Answer B is incorrect). Three types of claims may be made: health claims, structure/function claims, and description of the contents in the product (Answer C is correct). A supplement may be certified for quality by a third party certifier, although this is not required under DSHEA rules. Products that undergo this additional testing will include a quality "seal" authorized by the certifier (Answer D is incorrect).