Immunization Practice Update and Recommendations

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Target Audience
This continuing education activity was developed specifically for pharmacists.

Disclosure Statement
The author has indicated that he does not have any conflicts of interest, nor does he have financial relationships with a commercial interest, related to this activity.

Learning Objectives
At the end of this activity, participants should be able to:

- review fundamental concepts associated with immunizations, including adverse reactions and contraindications of vaccine administration.
- describe the proper care, storage, administration and reconstitution of vaccines.
- identify changes in immunization recommendations for each age demographic.

Background
The evidence supporting the use of pharmacists as a primary source for immunizations is increasing every day. A 2012 article from the *Journal of the American Pharmacists Association* focused on the impact pharmacists can have on adult immunization rates in indigent health care settings.\(^1\) The study found that out of 101 patients aged 18-79 years old, 82 (81.2 percent) needed at least one immunization that could be administered by a pharmacist. This means that only 18.8 percent of patients were in compliance with the Centers for Disease Control and Prevention (CDC) vaccine schedule at the beginning, and by the end of the study 38.6 percent were current.\(^1\)

The most recent trends indicate that the number of children receiving the influenza vaccine is increasing yearly, with an overall increase of 12.9 percent from the years 2009-2013. Unfortunately, the rates of adults receiving the flu shot have only increased by 1.1 percent.\(^3\) The community pharmacist has become intrinsic to the increase in vaccination rates. This, coupled with the encouragement of community pharmacy management, has started to reduce the number of individuals who are not current with their recommended vaccination schedule. In 2009, almost every state finally adopted a version of the collaborative practice agreement allowing pharmacists the ability to immunize patients.\(^2\) Currently, there are 45 states that have legislation that allows a pharmacist to administer any U.S. Food and Drug Administration (FDA)-approved vaccine.\(^4\) The pharmacist’s role in immunization has increased, which is helping to provide better patient care.

The consequences of patients being under immunized are being felt across the country. Last year, there were approximately 50,000 deaths attributable to those that were under vaccinated.\(^2\) The incidence of vaccine-preventable diseases that were thought to have been almost eliminated are increasing to levels that have not been seen in decades. This is happening in part because of misguided fear, misinformation and anti-vaccination movements. The pharmacist is still ranked as one of the most trusted and accessible health care professionals.\(^4\) Having the public’s trust offers a great opportunity to help dispel the negatives surrounding vaccinations, and it also affords us the opportunity to get our patients up to date.
Fundamental Concepts Associated with Immunizations

The fundamental concepts are important to remember anytime you receive a question regarding the need for immunizations, the timing and return visits necessary for proper administration, or when dealing with patients who have compromised immune systems. The first set of principles relates to how we distinguish between types of immunity and the methods to which we acquire our immunity. Our immune system is segregated into two different parts. Innate immunity is a collection of barriers and cellular (or molecular) elements that are located throughout our body to quickly respond to an infection. The other part is adaptive immunity, which is in a constant state of flux to meet and destroy the pathogens we are exposed to. The simple explanation for patients is that we have both active and passive immunity. Passive immunity is when a person has antibodies transferred to them by another human or animal. Passive immunity is described as temporary protection that decreases with time. An example of passive immunity is the transfer of antibodies from a mother to her child during pregnancy. Active immunity is protection that is produced by a person’s own body in response to a foreign antigen. This is done by activated B cells that separate into either plasma cells that secrete the antibody to fight infection, or the memory cells that survive for years to quickly recognize and respond to a future presentation of a same antigen. Now the activation of B cells can occur either by natural (antigen exposure) means or by exposure to a vaccination.

Vaccinations are made to activate the B cells within the body. The two major classes of vaccines are live attenuated or inactivated. The live attenuated vaccine (LAV) version is the less common of the two types. The vaccine is created in a controlled laboratory setting and they are weakened to induce a milder response. Unfortunately, immunocompromised patients are unable to handle these vaccinations due to safety concerns. Even in healthy patients, it is possible to have an adverse reaction. There are five vaccinations that are made through the process of live attenuation: tuberculosis (BCG), oral polio virus (OPV), measles, rotavirus and yellow fever. The LAV with the greatest potential for an adverse reaction is the measles vaccine with a 0.3 percent chance of causing febrile seizures. It is possible that a patient can develop either vaccine-associated paralytic poliomyelitis (VAPP) or disease-causing vaccine-derived poliovirus (VDPV), and these are commonly seen with OPV.

Inactivated vaccines comprise the majority of all vaccinations. Although these are far safer, caution is still needed when administering these to patients. For the purpose of this discussion, we will focus on the inactivated flu vaccine. Besides an atypical site reaction, a patient could experience an adverse reaction if they have an allergy (eggs are listed as the primary concern because these vaccines are cultured in eggs). Other conditions that put the patient at risk for serious adverse reactions include a previous diagnosis of Guillain-Barre Syndrome (a disease in which the body’s immune system mistakenly attacks the nervous system, causing inflammation) or generalized symptoms of a serious acute illness. Vaccines should be administered with caution to these patients, and the options should be discussed with their physician.

Herd immunity is often a reason that parents cite to justify not getting their children vaccinated. The basis of the herd immunity theory is that if a large enough portion of the population is protected, then the transmission of a disease to an unvaccinated individual is unlikely. The threshold of vaccinated individuals that is required to achieve herd immunity is believed to be in the 70-95 percent range to adequately protect the unvaccinated. There is rarely published data that can accurately assess the vaccination levels of a given population in a snap shot of time. The 70-95 percent range cited previously is well below the national average, and it is safe to conclude that nationally and better yet worldwide it is almost impossible to be protected via herd immunity.

Thimerosal (also spelled thiomersal) is a mercury containing preservative that is both anti-septic and anti-fungal. It is used to help store the vaccines safely and for longer periods. Individuals
without any medical training are publicizing false information. Fabricated statements about thimerosal (the ingredient containing mercury) causing autism have put fear into parents steering them away from vaccinating their children. This herd immunity theory coupled with the fear mongering that often accompanies discussion over the safety of vaccines can confuse and bewilder parents into choosing to trust in the community protection. From 2012-2014, there are more and more areas of the country with vaccine preventable disease breakouts. Pharmacists can help to quell the fears, and protect their patients by helping to dispel the myths.

STOP AND REFLECT

Patient AB presents to your pharmacy asking for a flu vaccination. After filling out the necessary paperwork the patient sits down to wait for your review. Upon reading the questionnaire, you see that the patient is 54 years old, with a history of hypertension, diabetes and tobacco use (one pack a day for 20 years). She has a sulfa allergy, is in no acute distress and presents without any recent illness. After your review, you sit down with the patient and ask her a few prime questions to assess if she is eligible for the vaccination. What are the questions you should ask her and what would be your response?

Proper Handling and Storage of Vaccines

Vaccines can provide several challenges to the community or clinical pharmacy. The most common problem is the receipt and storage of vaccines. First, the pharmacist (or person who receives deliveries) needs to ensure that the vaccine was held at a proper temperature during delivery. The common practice in most pharmacies is to take any medications, including vaccines, that were refrigerated during transport directly to their proper storage place immediately upon arrival. If the temperature during transport is in question, it is better to discard the vaccine and contact your distributor.11

In any pharmacy, an essential tool is a properly maintained refrigerator and freezer. In most states, including Michigan, it is required to maintain a temperature log and the refrigerator must be checked twice a day or more.11 The current standard of practice set by the Michigan Department of Community Health (MDCH) is to check the temperature once when the pharmacy opens and 30-60 minutes before close. The temperature log is required to be kept for at least three years.11

One of the options pharmacies may use to record temperatures is a Data Logger. This automated machine records the temperature in either °F or °C. Temperature ranges recommended by the CDC are as follows:

- °F refrigerator: 34° to 47°
- °F freezer: 6° to -59°
- °C refrigerator: 9° to 1°
- °C freezer: -16° to -51°

The recommended temperature ranges vary slightly from state to state, and in Michigan the ranges are less strict.9 The temperature range average in Michigan is to aim for °F freezer 0° and °F refrigerator 40°. The best option is to adhere to the stricter standards imposed by the state or CDC to avoid any possible problems.11 It is also recommended to store water bottles labeled “Do Not Drink” against the walls and floors of the unit to stabilize the temperatures.10 You can also set the
Data Logger to record temperatures in specified intervals. The current recommendation by the CDC is every 15 minutes or less.\textsuperscript{9} The reason this setting was chosen is that it can be reasonably done with the digital data logger. It is unreasonable to suspect that someone could manually check the temperature every 15 minutes. The Data Logger is mounted to the outside of the unit and the probe is placed inside as close to the corner of the unit door as possible. MDCH recommends using only calibrated thermometers with a Certificate of Traceability and Calibration testing that has not expired.\textsuperscript{10} It is important to note that it is required to have these types of thermometers if you are carrying Vaccines for Children (VFC) or you have been given a “Yellow Fever Stamp.” It is also a recommendation from the MDCH to use the Digital Data Loggers. Other recommendations are to have the probe placed in glycol and centrally located between the vaccines. The receiver must always be on the outside of the unit, and it needs to be plugged into a computer weekly to download the temperature readings.\textsuperscript{10}

There are certain vaccinations that need special care while in transit and after delivery. To make matters more confusing, it also depends on which manufacturer or wholesaler is delivering the medication. A good rule to remember is that every vaccine needs some sort of cooling. The vaccines that need to be protected from light, frozen, shipped with frozen gel packs and received within 72 hours of shipping are varicella, zoster and measles, mumps, rubella and varicella (MMRV). MMRV is unique because, as an example, if it is shipped from McKesson it needs refrigerant and maybe frozen, but if it is shipped from Merck it must be packed with frozen gel packs and cannot be received more than 48 hours after shipment date.\textsuperscript{11} MMRV must also be protected from light.

When storage units get out of range, it is important to take immediate corrective action. The action should be recorded and the necessary staff members should be notified.\textsuperscript{11} If any of the vaccines are out of range for a significant amount of time, it is important to take the vaccines out and place in a bag clearly labeled “Do Not Use.” Next, you must keep the vaccines in the storage container. The MDCH recommends that you do not discard them, but instead notify the manufacturer.\textsuperscript{11} A good resource for proper storage and handling procedures can be found on the CDC Web site at www.CDC.gov, under storage and handling toolkit.

STOP AND REFLECT
When setting up the refrigerator and freezer in your pharmacy, you decide to use a Digital Data Logger to fully comply with the guidelines in Michigan. What physical setup parameters do you need to be aware of in order to ensure you will properly handle the vaccines?

Proper Reconstitution and Administration Practices
The number of diseases that can be prevented with vaccines continues to increase. With these newfound prevention measures, the procedures of reconstitution and administration are becoming more involved. Vaccines are given orally, intramuscularly, intranasally and subcutaneously. The trend in vaccines is the combination of multiple vaccinations into one administration. It is important for pharmacists to stay current on this evolving field.

Most vaccines have some sort of reconstitution associated with them. The manufacturers usually include the proper diluent along with the vaccination to ensure safety and proper use. The vaccines that commonly come with a diluent include pneumococcal (PCV13); rotavirus RV1 (Rotarix \textsuperscript{*} only); measles, mumps and rubella (MMR); varicella; MMRV; and Zoster.\textsuperscript{12} Certain vaccines need to be administered immediately after reconstitution. These are MMR, RV1,
Menomune® (MPSV4) and Menveo® (MCV4-CRM). The other vaccinations must be administered during a certain timeframe and that information can be found in the guidelines. The best practice recommended by the MDCH is to have a copy of the “Vaccine Preparation and Administration” reference sheet, published by the MDCH and available online at www.Michigan.gov/mdch, posted in the vaccine prep area or on the front of the storage unit.

One of the most challenging parts of keeping patients up to date on their vaccinations is the timing of the doses. For the purpose of simplicity, in this article we will focus on the three most common vaccinations: herpes zoster (Zostavax™), pneumococcal conjugate (PCV13) and influenza (IIV3/IIV4). Schedule information along with important footnotes for all other vaccines can be found on the CDC website at www.CDC.gov.

**Herpes Zoster Vaccine**

One of the more talked about vaccinations on the market is intended to prevent herpes zoster (shingles) infections. Herpes zoster affects 1.2 to 3.4 cases per 1,000 individuals per year, with an increase to 3.9 to 11.8 per 1,000 individuals per year over the age of 65. Zostavax™ is a live attenuated virus vaccine that is shipped and stored frozen until administration. Once a patient is ready to have the vaccine administered, the pharmacist will remove the vial from the freezer and immediately reconstitute with the diluent supplied by the manufacturer. Once this occurs, the solution will appear as an off-white to pale yellow liquid. This is then drawn up and administered subcutaneous into the deltoid region of the upper arm muscle. The vaccine is given as a single dose to those patients that are age 50 years old or greater. The current CDC recommendation is that patients wait until the age of 60 before receiving the vaccine, but other literature indicates the sooner the better. Contraindications are known severe immunodeficiency from hematologic, chemotherapy, immunosuppressant therapy or HIV. Pregnancy is also an absolute contraindication. One of the interesting precaution measures is the stopping of antiviral medications (such as acyclovir, valacyclovir, etc.) for a period of 24 hours before to 14 days after administration. This is because the antiviral medications can possibly destroy the LAV vaccine rendering it ineffective.

**Pneumococcal Conjugate Vaccine (PCV)**

Pneumococcal disease is the most dangerous vaccine preventable illness in the United States, claiming more than 4,000 lives in 2007 alone. It takes more lives than all other vaccine preventable illnesses combined. The pneumococcal conjugate vaccine (PCV13) and pneumococcal polysaccharide vaccine (PPSV23) are used to try and prevent complications. The dosing age range for PCV13 is first dose at two months, second at four months, third at six months, and the final dose between the ages of 12 months and 18 months. If no dose of PCV13 was ever given to a patient, it is permissible to administer a catch-up regimen, as dictated in the CDC vaccination schedules at www.CDC.gov. The PCV13 vaccine is administered in stages. If there is no prior history of administration and a risk factor is present, the first dose is given between 19 years old and 64 years old and a second dose at 65 years old or greater. The PPSV23 is administered only after the patient has been given PCV13 and is the patient is diagnosed with a high-risk condition. High-risk conditions include HIV, immunosuppression, chronic obstructive pulmonary disease and others. It is important to always read the footnotes included with the vaccination schedules when deciding on a proper vaccination regimen. Both the PCV13 and PPSV23 vaccines are given intramuscular, and the PPSV23 can also be given subcutaneous if the patient prefers.

**Influenza Vaccine**

The influenza vaccinations are by far the most administered vaccines. They are identified as either inactivated (IIV*) or live attenuated (LAIV). The IIV* can either be trivalent (IIV3) or
quadrivalent (IIV4). The difference is a single strain that is not indicated to be one of the most likely seen during the upcoming flu season. It is included in the IIV4 vaccine as a precaution in case the IIV3 is less effective due to a higher prevalence of the fourth strain.\textsuperscript{17} The IIV* types of influenza vaccines are indicated yearly for anyone six months or older. There is only one widely used LAIV, and that is the nasal spray FluMist\textsuperscript{TM}. This is a great alternative for patients that are not comfortable with needles. Unfortunately, FluMist\textsuperscript{TM} can only be used in patients aged two to 49 years old. The flu vaccine, IIV* type, is highly recommended in pregnant women, children six months to six years old, and all persons over the age of 50. In addition, patients with certain chronic illness (i.e., respiratory illnesses) or who are immunocompromised should receive only the IIV* type of vaccine as well.

Along with the common types, there are two other influenza vaccinations. The first is the recombinant influenza vaccine (RIV), also known by its brand name FluBlok\textsuperscript{TM}. The advantage of the RIV formulation is that it’s a great alternative if a patient has had a prior allergic reaction to eggs. RIV is not cultured in eggs; instead, it is formulated in another way. The second type is similar to the IIV* types, but instead it is a ccIIV, which means that it is made from cell culture, rather than from egg cultures. The brand name is Flucelvax\textsuperscript{TM}. The ccIIV formulation is also recommended for those people with prior egg allergies.

Conclusion

Vaccinations are becoming one of the more complicated areas of the pharmacy profession. Many community pharmacists will tell you that the flu season is the most stressful part of the year. Quotas, time goals and similar metrics should never cause you to sacrifice the necessary amount of due diligence that is required to administer vaccines safely. The fundamental concepts will help you explain why vaccinations are important to your patients. Part of the due diligence associated with vaccine safety is understanding how to receive, store, reconstitute and administer vaccines. In the hospital setting, it is important that when you are doing case reports and assessing a patient’s needs, that you keep the vaccine schedule in the back of your mind. In the community pharmacy, the pharmacist has to actively make the choice to raise awareness, dispel fear and encourage those in need to take the time to invest in their own preventative health.
Continuing Education Self-assessment Questions

1. Which of the following statements is correct?
   a. Innate immunity is in a constant state of flux.
   b. Adaptive immunity has cellular molecules located throughout the body to respond efficiently to an infection.
   c. Passive immunity is derived from another living organism.
   d. Active immunity is acquired during birth when the mother “activates” the mechanism unknowingly.

2. Which of the following statements is incorrect?
   a. Sulfa allergies can potentially also include egg allergies, which are dangerous in RIVs.
   b. Vaccines are made to potentiate B cells within the body.
   c. It is possible that certain vaccines can exacerbate an immune system disorder.
   d. The majority of vaccinations are inactivated.

3. Which of the following answers indicates the correct grouping of vaccines that need to be delivered within three days?
   i. MMRV  iv. Zostavax™
   ii. BCG  v. Varicella
   iii. OPV  vi. Yellow fever
   a. i,ii,vi
   b. iv,iii,v
   c. ii,iii,iv
   d. v,iv,i

4. Which of the following statements is correct?
   a. PPSV23 is always given before PCV13.
   b. A 66–year-old woman with COPD with a prior PCV13 vaccination can be given PPSV23.
   c. The final dose of PCV13 should be given between 12-18 years of age if the correct course was started at birth.
   d. It is permissible to catch-up a patient at any time without regard to age.

5. Which of the following statements is correct?
   a. The LAIV FluMist™ can be used for people aged 1-49 years old.
   b. FluBlok™ and the ccIIV formulation can never be used on patients with sulfa or egg allergies.
   c. Patients with chronic bronchitis should only receive IIV* types of flu vaccines.
   d. Pregnant women should never receive the IIV* formulations.
References: