



Routine Childhood Immunization Series

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LEARNING OBJECTIVES

1. Distinguish the considerations for administering live versus inactivated vaccines.
2. Assess the role of a pharmacist in promoting the vaccination of pediatric patients to reduce the global burden of vaccine-preventable infections.
3. Evaluate the current evidence to educate patients and caregivers about vaccination considerations, including safety, efficacy, and common misconceptions.
4. Justify the role of combination vaccines for the pediatric population.
5. Given a pediatric case, develop a vaccine administration plan using current vaccination recommendations.
6. Distinguish the similarities and differences in childhood vaccine availability, administration, efficacy in disease prevention, adverse effects, contraindications, and warnings.

ABBREVIATIONS IN THIS CHAPTER

ACIP	Advisory Committee on Immunization Practices
DTaP	Diphtheria, tetanus, and pertussis (vaccine)
HepA	Hepatitis A (vaccine)
HepB	Hepatitis B (vaccine)
Hib	<i>Haemophilus influenzae</i> type B
HPV	Human papillomavirus (2-valent, 4-valent, 9-valent vaccine)
IIV	Inactivated influenza vaccine (3-trivalent, 4-quadrivalent)
IPV	Inactivated poliovirus vaccine
LAIV	Live attenuated influenza vaccine
MenACWY	Meningococcal quadrivalent (vaccine)
MMR	Measles, mumps, and rubella vaccine
MMRV	Measles, mumps, rubella, and varicella (vaccine)
PCV	Pneumococcal conjugate vaccine (7-valent, 13-valent)
PPSV23	Pneumococcal polysaccharide vaccine
RIV3	Recombinant influenza vaccine trivalent
RV	Rotavirus vaccine

INTRODUCTION

Vaccines advance health care by dramatically reducing the morbidity and mortality associated with infectious diseases. Vaccines provide protection from infectious agents by promoting an immune response within the body. The first published attempt to induce immunity by inoculation with an infectious agent was by made Edward Jenner in 1798. He found that by introducing small amounts of fluid from cowpox lesions into susceptible people, immunity was developed that could prevent the deadly disease smallpox. Since then, the global burden of many infectious diseases has been dramatically reduced through the development of other effective vaccines. Smallpox has been eradicated globally, and significant reductions in many other various diseases have occurred, including polio, diphtheria, measles, mumps, rubella, pertussis, tetanus, and *Haemophilus influenzae* type B (Hib) (CDC 2011a). Routine immunizations in children are crucial to reduce the risk of an epidemic and prevent the significant morbidity and mortality from vaccine-preventable disease (VPD).

How Vaccines Work

Immunization is the process of generating humoral immunity or providing protection from disease. The immunity conferred can be either active or passive. Active immunization involves provoking the immune system to mount a sustained immune response; passive immunization involves introducing exogenous antibodies to provide temporary, transient protection. Vaccines are an example of active immunization, stimulating the immune system to produce antibodies, cell-mediated

Td	Tetanus and diphtheria (vaccine)
Tdap	Tetanus, diphtheria, and acellular pertussis (vaccine)
VAERS	Vaccine Adverse Event Reporting System
VPD	Vaccine-preventable disease

Table of other common abbreviations.

immunity, or both. When a suspension or fraction of microorganism (the antigen) is administered into the body, it activates antigen-presenting cells; these, in turn, secrete proinflammatory cytokines and chemokines, which recruit other leukocytes in response to the inoculation. T and B lymphocytes are then replicated, differentiated, and stored in large pools of memory cells, which can be quickly stimulated to provide immune

BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

- Concepts on taking a patient history in preparation for assessing appropriateness of vaccines
- General knowledge on interpreting the routine vaccination schedule for healthy children
- Availability, interchangeability and FDA approved indications and ages for vaccines available in the United States.
- Techniques and how to administer vaccines in pediatric patients
- Familiarity with the pathophysiology of vaccine-preventable diseases
- Benefits and risks of assessing data from the Vaccine Adverse Event Reporting System

ADDITIONAL READINGS

The following free resources have additional background information on this topic:

- CDC. [Vaccines & Immunization Topics](#)
- Epidemiology and Prevention of Vaccine-Preventable Diseases. [The Pink Book](#): Course Textbook, 13th Edition (2015)
- Advisory Committee for Immunization Practices. [Vaccine Recommendations](#).
- Infectious Disease Society of America. [2013 Clinical Practice Guideline for Vaccination of the Immunocompromised Host](#)
- American Pharmacist Association. [Immunization Resources](#)

Table of common pediatric laboratory reference values.

protection in subsequent exposures to the same or a biologically similar antigen.

Live vs. Inactivated vs. Toxoid Vaccines

Most vaccines contain a live attenuated organism or killed microorganisms, or a modified bacterial toxin. Live attenuated vaccines consist of a viable microorganism that undergoes limited replication in an individual after administration. The attenuation process decreases the microorganism's virulence while retaining immunogenicity. Because live vaccines more closely mimic natural infection, they often confer life-long immunity. A potential drawback, however, is that a true infection can occasionally develop and lead to morbidity and mortality in immunocompromised hosts. In contrast, inactivated vaccines cannot infect the host because they contain no viable organisms. They tend to be less immunogenic than live vaccines and often must be given in multiple doses to produce lasting immune response. Inactivated vaccines consist of antigens from the organism that can be recognized by the immune system to stimulate an antibody response. Booster doses can further stimulate B cells and antibody response, producing long-lasting immunity.

Inactivated vaccines differ in composition in the resulting immune response. In contrast to protein-containing vaccines, pure polysaccharide vaccines do not generate a T-lymphocyte immune response; they stimulate B lymphocytes directly to produce a solely humoral immune response. In infants and children younger than 2 years, polysaccharide vaccines have poor immunogenicity and are not recommended. Linking or conjugating the polysaccharide to a protein carrier converts it to a T lymphocyte-dependent antigen. Protein-conjugated polysaccharide vaccines can produce a better immune response in infants and young children because of T-lymphocyte involvement (Offit 2002).

Toxoid vaccine contain bacterial toxins that have been inactivated by either chemical or heat treatment. The immunogenicity remains after the inactivation process and stimulates an immune response to the toxin that causes the disease, rather than to the bacteria itself. Examples of toxoid vaccines include tetanus and diphtheria.

Pharmacist Role

Pharmacists should play a role in immunization advocacy by administering vaccines, if permitted; assessing vaccine status for referral; and providing education to families and children. All 50 states, the District of Columbia, and Puerto Rico permit pharmacists to vaccinate in some capacity, with state-specific variances in degrees of scope, type, and autonomy. However, seven states/territories (Connecticut, Florida, Massachusetts, New York, Vermont, West Virginia, and Puerto Rico) still do not allow pharmacists to immunize children. In addition, 12 states limit the types of vaccinations a pharmacist can administer to children (APhA 2015). Efforts to expand the pharmacist's role as a health care provider should include

a focus on authorization to administer all types of vaccines to all ages of children.

Pharmacists practicing in states where pediatric immunizations are not allowed can still provide assessment and referral of children for vaccination. With respect to providing education to families, pharmacists should be able to discuss information about vaccine efficacy and safety, school requirements, risks associated with not vaccinating children, and common misconceptions surrounding vaccines.

VACCINATION SCHEDULES AND ADHERENCE

Publication of Childhood Immunization Schedules

The CDC annually publishes routine and catch-up vaccine schedules for children ages 0–18 years; these schedules are based on recommendations from the Advisory Committee on Immunization Practices (ACIP) and approval from the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Obstetricians and Gynecologists (CDC 2016). Box 1-1 lists available vaccines and brand names.

Pediatric Vaccination Coverage

Failure to routinely vaccinate children increases the risk of an epidemic from VPDs. In 1974, when almost 80% of children in Japan were vaccinated for pertussis, there were 393 cases of pertussis reported and no deaths. By 1976, following rumors that the vaccine was unsafe and not needed, only 10% of infants were vaccinated. In 1979, Japan had a pertussis epidemic, with more than 13,000 cases of pertussis and 41 deaths. In 1981, the number of pertussis cases decreased again after the government reinitiated pertussis vaccination (Gangarosa 1998).

Vaccination rates in U.S. children are monitored and reported in the *Morbidity and Mortality Weekly Report*. For children aged 19–35 months, coverage was stable from 2013 to 2014. Less than 1% of children received no vaccinations; however, other children did not receive the recommended number of injections for each vaccination. Receiving two or more doses of hepatitis A vaccine (HepA) had the worst percentage rate at 57.5%, and receiving three or more doses of inactivated poliovirus vaccine (IPV) had the best percentage rate at 93.3%. Healthy People 2020 coverage targets were reached for four vaccination series (i.e., three or more doses of IPV; one or more dose of measles, mumps, and rubella vaccine [MMR]; three or more doses of hepatitis B vaccine [HepB]; and one or more dose of varicella vaccine). However seven targets did not (i.e., four or more doses of diphtheria, tetanus, and pertussis vaccine [DTaP]; the full series of Hib vaccine; HepB birth dose; four or more doses of pneumococcal conjugate vaccine [PCV]; two or more doses of HepA; the full series of rotavirus vaccine [RV]; and the combined vaccine series) (Hill 2015).

Box 1-1. Available Vaccination Products

Individual Vaccines

DTaP (Daptacel, Infanrix)
Tdap (Adacel, Boostrix)
DT (generic)
Td (Decavac, Tenivac)
TT (generic)
HPV2 (Cervarix)
HPV4 (Gardasil)
HPV9 (Gardasil 9)
MenACWY-CRM (Menveo)
MecACWY-D (Menactra)
Meningococcal polysaccharide (Menomune)
Meningococcal group B (Bexsero, Trumenba)
PCV13 (Prevnar)
PPSV23 (Pneumovax)
MMR (M-M-R II)
V (Varivax)
IIV3 or IIV4 (Afluria, Agriflu, Fluarix, Flucelvax, FluLaval, Fluvirin, Fluzone)
IIV4 (Fluarix, FluLaval, Fluzone)
LAIV4 (FluMist)
HepA (Havrix, Vaqta)
HepB (Engerix-B, Recombivax HB)
Hib (PedvaxHIB, ActHIB, and Hiberix)
IPV (IPOL)
Rotavirus (RotaTaq and Rotarix)

Combination Vaccines

DTaP-IPV/Hib (Pentacel)
DTaP-IPV/HepB (Pediatrix)
DTaP-IPV (Kinrix, Quadracel)
Hib and meningococcal (MenHibrix)
Hib and HepB (Comvax)
HepA and HepB (Twinrix)
MMRV (ProQuad)

Information from: Hamborsky J, Kroger A, Wolfe C, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases (Appendix B-3 and B-4)*. The Pink Book, 13th ed. Washington, DC: Public Health Foundation, 2015.

Among adolescents (ages 13–17 years), recommended vaccination coverage increased in 2013–2014. In teenagers, the 2014 reported rates were 87.6% for tetanus, diphtheria, and acellular pertussis vaccine (Tdap) and 79.3% for first meningococcal quadrivalent vaccine (MenACWY). Ranges varied by state; for example, the rate for the first MenACWY was 46% in Mississippi and 95.2% in Pennsylvania. Moreover, the overall rate for second dose of MenACWY for 17-year-olds was only 28.5%. For the human papillomavirus (HPV) vaccine, only 39.75% of girls and 21.6% of boys completed the three-dose HPV vaccine series (Reagan-Steiner 2015).

Children enrolled in kindergarten in 2013–2014 had vaccination coverage rates of 94.7% for two doses of MMR, 95.0% for the varying local requirements for DTaP, and 93.3% for two doses of varicella vaccine among states with a two-dose requirement. The median total exemption rate was

1.8%, with a range of less than 0.1% for Mississippi to 7.1% in Oregon. Eleven states had an exemption rate of 4% or greater (Seither 2014).

Among children ages 19–35 months, coverage rates for many vaccines were lower for those living below the federal poverty level than for those at or above the poverty level (Hill 2015). Across all age ranges, vaccination coverage rates varied across states and by vaccine, but there was no consistency across any region (Hill 2015; Reagan-Steiner 2015; Seither 2014).

Reasons for under-vaccination and refusal range from vaccination access to negative patient perceptions; therefore, improving adherence and decreasing exemption requires a multifaceted approach. When data are available, initiatives to improve adherence should be tailored toward local or county vaccination or exemption rate concerns. The [CDC Community Guide](#) lists the recommended methods to increase appropriate vaccination. The programs fall under three themes: (1) enhancing access to vaccination services, (2) increasing community demand for vaccinations, and (3) ensuring provider or system-based interventions.

Public Policy and Risks

Individual states require vaccinations for entry into school and even day care facilities. Each state passes its own regulations, and there is great variance in what qualifies as an exemption. All states allow for medical exemptions, many allow for religious exemptions, and some even permit exemptions because of philosophical beliefs. States also vary in required documentation and enforcement of regulations. During an epidemic, many states forego exemptions and exclude students without the required vaccinations from school (CDC 2015b).

In July 2016, [California State Bill 277](#), one of the strictest school vaccine laws, will go into effect. Allowing only medically necessary exemptions, the bill requires parents who choose not to vaccinate for other reasons to homeschool their children because they will not be allowed to attend school with other students.

Currently, the [CDC's Public Health Law Program](#) is compiling summaries of school exemption information by each state. However, pharmacists should know the pertinent local law so that they can educate parents about the potential impact of vaccination refusal.

Beyond access to school, the risks and consequences of vaccine refusal may affect the health of children and those around them. Pharmacists should educate parents to inform medical staff of their child's vaccination status when they call 911, ride in an ambulance, visit a hospital ED, or visit a physician's office. This information will greatly affect the differential diagnoses because the child could have a VPD. If the child has a VPD, additional precautions (e.g., isolation) must be taken to protect others who have immunocompromise or who may not be vaccinated. In an outbreak, parents must be

able to recognize the signs and symptoms of the VPD and be cognizant that some diseases can be spread by those who are asymptomatic (CDC 2015b).

PATIENT EDUCATION ON VACCINE CONCERNS

Among the many reasons why parents refuse to have their children vaccinated are unfounded misconceptions. To effectively communicate with families refusing to vaccinate, it is important to understand their concerns. Common misconceptions surround four themes: (1) fear that vaccines or their additives are harmful, (2) fear that the vaccine will cause the infection, (3) belief that too many vaccines will overwhelm the child's immune system, and (4) belief that getting the "natural" VPD is healthier (CDC 2015b; Healy 2011).

Because vaccines have reduced the incidence and mortality of disease, firsthand experience of the devastating consequences of VPD is rare today. A lack of familiarity with these consequences had increased the misconception that getting the "natural" disease is healthier than receiving the vaccine (Healy 2011).

Misconceptions of Autism Linkage

The most common misconception about vaccines is that MMR or its additive, thimerosal, can cause autism (AAP 2016; CDC 2015b). The concern with the MMR vaccine and autism began in 1998 with Andrew Wakefield's study published in *Lancet*. His article claimed that the MMR vaccine caused inflammatory bowel disease, which allowed harmful proteins to damage the brain. In 2010, *Lancet* retracted his article for ethical misconduct, and 10 of the 13 authors retracted the findings (AAP 2016; IAC 2013).

Other concerns regarding autism may be caused by the timing of MMR administration; the vaccine is given at age 12–15 months, and the first symptoms of autism usually develop at 15 months (Roberts 2002). However, to date, more than 20 articles have found no association between the MMR vaccine and autism ([healthychildren.org](#) 2015; IAC 2013).

Thimerosal, a preservative that contains mercury, was never used in MMR (CDC 2015b). In the 1990s, it was found in other vaccines but was removed in 1999 as a precautionary safety measure; however, it can still be found in multidose flu vaccines today. To date, studies have found no relationship between early exposure to thimerosal and autism (CDC 2015b; [healthychildren.org](#) 2015).

Other Vaccine Substances

Further vaccine safety concerns surround adjuvants, preservatives, or trace substances such as formaldehyde from the manufacturing process (CDC 2015b). The adjuvant aluminum continues to raise safety concerns because of its potential for negative health consequences. Vaccines in the United States that contain aluminum are HepA, HepB, DTaP, Tdap,

Hib, HPV, and PCV13 (CDC 2015b). The amount of aluminum in each ranges from 0.125 mg to 0.625 mg, which is about 1% of the estimated average daily aluminum intake (30–50 mg) from foods, drinking water, and medicines (CDC 2015b). Because aluminum has been in vaccines for 70 years and is only associated with minor injection-site reactions, there is no current recommendation to remove aluminum adjuvants from vaccines. However, further research is evaluating the toxicology and pharmacokinetics of aluminum adjuvants in infants and children (Eickhoff 2002).

Vaccines as a Disease Cause

Some families may believe that their child will contract the disease from the vaccine (Healy 2011). As discussed earlier, inactivated vaccines cannot cause the illness, and live vaccines only rarely cause disease in healthy children. Occasionally, live vaccines can cause a mild form of the disease that is not harmful (CDC 2015b). For example, less than 5% of children will develop a localized or generalized varicella-like rash 5–26 days after vaccination. Usually, the rash has two to five lesions (IAC 2016). An exception is the patient with immunocompromise, who may develop a more severe form of illness (Kroger 2011). Another exception was the live oral polio vaccine, which was known to rarely cause severe illness even in healthy children. However, the oral polio vaccine is no longer used in the United States (CDC 2015b).

Overwhelming the Immune System

In a national survey, 25% of parents reported believing that too many immunizations can weaken a child's immune system (Gellin 2000). This concern leads to the belief that giving the recommended number of vaccines at pertinent clinic visits is unsafe because “too many” vaccines are given “too soon” (Offit 2009). Children currently receive 14–26 injections by the time they are 2 years old.

Advocates argue that the high antigen exposure from vaccines will weaken the immune system. In reality, children are exposed to around 130 antigens in currently recommended vaccines, compared with the 200 antigens that were in the only vaccine, smallpox, administered in the 1900s (Offit 2002). It has been estimated that, based on the number of circulating B cells in the body, their capacity to respond to antigens, and the number of antigenic epitopes contained in each vaccine, infants have the capacity to respond to 10,000 vaccines at any given time. Thus, giving 11 vaccines concurrently to an infant would use only about 0.1% of the immune system capacity (Offit 2002). The CDC maintains that the immune system will not be overwhelmed by multiple vaccinations, and the recommended immunization schedule provides the best protection from infection (CDC 2015b).

Parents may also believe the infant's immune system is too immature. This belief is not medically justified, because neonates can generate both humoral and cellular immune responses from the time of birth, regardless of gestational age.

The only major deficiency in the immune system of children younger than 2 years is a decreased B-cell response relative to older children and adults. T cell–dependent immunity, however, is robust even before birth. Pure polysaccharide vaccines invoke immune response solely by B-cell stimulation and are thus less effective in children younger than 2 years. To ensure that polysaccharide vaccines are effective in this age group, they are conjugated to a protein so that the child can respond through T cell–dependent mechanisms (Offit 2002).

Alternative Schedules

Concerned parents may request an alternative vaccine schedule. Currently, *The Vaccine Book: Making the Right Decision for Your Child* by Dr. William Sears offers alternative vaccine schedules for concerned parents (Offit 2009). These alternative schedules are not recommended; they lack evidence of efficacy and do not decrease adverse events (Fisher 2009; Offit 2009). In fact, there are risks of following an alternative schedule that spreads out vaccine administration. Children may be unprotected when they are most vulnerable to a VPD. Moreover, there would be a decrease in the benefits of herd immunity and an increase in the number of physician visits for an immunization (Fisher 2009).

Patient Education Resources

Parents and families may have additional concerns about vaccinations. Patient-friendly information specific to each vaccine and vaccines in general can be found on the [CDC website](#). These materials include vaccine basics and benefits, frequently asked questions, and true stories of families negatively affected by VPD. Other patient resources are found in Box 1-2.

INTERPRETATION OF VACCINE SCHEDULES AND ADMINISTRATION CONSIDERATIONS

In addition to patient education materials and the [vaccine schedules](#), the [CDC website](#) provides great resources to aid providers in assessing vaccination status and staying up to date with evolving research and recommendations. It is essential to review the website regularly because the most up-to-date recommendations may change in between annual publication of the standard schedules. For example, in March 2015, the recommendation for HPV vaccination changed to

Box 1-2. Patient-Friendly Immunization Education Resources

- [Parents' Guide to Childhood Immunizations](#)
- [American Academy of Pediatrics](#)
- [Vaccine Education Center at the Children's Hospital of Philadelphia](#)

include the addition of HPV9; this recommendation was not incorporated into the official schedule until the 2016 publication. In addition, when each new vaccine schedule appears, it should be reviewed for updates.

Interpreting the schedule for routine vaccine administration in healthy children is straightforward. The footnotes associated with the schedule provide additional details such as minimal and maximal administration age and intervals between vaccinations. Of note, the minimal administrations interval between live vaccines not given simultaneously is always 28 days. Administering a vaccine before the minimum age or recommended interval will likely result in a suboptimal immune response (Kroger 2011). Factors that lead to a suboptimal immune response if a child is too young include immaturity of the immune system and interference from maternal antibodies (IAC 2016; Chung Wai Ng 2014). If a multi-series dose of a vaccine is given too early, protection to that dose may be reduced because of interference in antibody response between the two doses (CDC 2015a; IAC 2016). However, vaccines administered 4 days or less before the minimal interval or age are still considered valid, though the mandate at the local or state level to count the vaccine as valid may be different. If a dose is administered before the minimal interval, the repeat dose should be spaced appropriately after the invalid vaccine. If a vaccine is given before the minimal age, the dose should be repeated when the child reaches the age limit (Kroger 2011).

Assessing the Need for Vaccines

Assessing vaccine status and appropriateness becomes more challenging in patients who require catch-up vaccines or who have additional considerations (e.g., immunocompromise). The Pink Book Appendix A-15, [Summary of Recommendations for Child/Teen Immunization](#), is an essential resource for assessing the need for vaccination in more complex situations or patients (Hamborsky 2015). However, for full details of all considerations for a specific vaccine, the *Morbidity and Mortality Weekly Report* with [ACIP recommendations](#) should be consulted.

Administering Multiple Vaccines

When patients require several vaccines to catch up, a common question is, “Which vaccines are most important to give at that visit?” The American Academy of Pediatrics and ACIP recommend to give all needed vaccines at the visit and not to delay vaccines. Currently, the number of injections that can be administered at one time is without limit. If possible, intramuscular vaccines should be spaced by at least 1 inch to potentially reduce the risk of overlapping local reactions (IAC 2016).

In addition, simultaneous administration of most vaccines has not been shown to increase the incidence of adverse effects or decrease the efficacy of vaccines (Kroger 2011). An exception to this is in children with functional or anatomic

asplenia; these patients should not have PCV13 and Menactra-brand meningococcal conjugate vaccine administered at the same visit. Rather, these vaccines should be separated by at least 4 weeks because Menactra is thought to interfere with the antibody response to PCV13 (CDC 2015a).

Although not recommended or necessary, there may realistically be situations in which a parent or provider is uncomfortable administering the quantity of vaccines required at one visit. At this time, a clinical decision will need to be made in order to determine which vaccines are “most important.” Factors to consider may include, but are not limited to, current outbreaks in the area, prevalence of disease for the recommended vaccines, and common age for severe negative effects if the child contracts the VPD.

Combination Vaccines

Administering vaccines with combination products can help reduce the number of injections at a visit. Currently, in the United States, the only four vaccines that are not available in any combination form for pediatric patients are influenza, PCV13, pneumococcal polysaccharide vaccine (PPSV23), and HepA. Although it is ideal to use combination products in most situations, there are special considerations with certain products, such as ProQuad and febrile seizure risk (as discussed later). Another consideration for combination vaccines is the potential for confusion about the components and which vaccines should be administered for subsequent doses (Kroger 2011).

CONSIDERATIONS PERTAINING TO ALL VACCINATIONS

Contraindications and Precautions

To prevent the risk of an adverse outcome, contraindications and precautions should be assessed before administering a vaccine. For specific contraindications and precautions to each vaccine, see Pink Book Appendix A-15, [Summary of Recommendations for Child/Teen Immunization](#) (Hamborsky 2015). Across all vaccines, the only truly universal contraindication is history of severe anaphylaxis to a component in the vaccine, and the only universal precaution is moderate or severe acute illness with or without fever (CDC 2015a; Kroger 2011). There is no concise definition of moderate or severe acute illness; rather, it is based on subjectivity of the severity of symptoms and the cause of illness. Of note, the use of antibiotics or antivirals does not automatically indicate moderate or severe illness. Mainly, this precaution is meant to prevent confusion between diagnosing the underlying illness and confounding it with a vaccination adverse effect (Kroger 2011). Therefore, it will be up to the provider to determine the appropriateness of withholding vaccines because of illness.

However, many misconceptions cause health care professionals to withhold vaccines unnecessarily (Box 1-3). A full list of common perceived contraindications/precautions by

Patient Care Scenario

A 12-month-old boy with no significant medical history comes to your clinic for a well visit in October. He started his routine vaccinations appropriately but fell out of care because of a lack of health insurance and has received no vaccines since he was 4 months old. His vaccine history is as follows:

HepB	0 months, 2 months
RV	2 months, 4 months
DTaP	2 months, 4 months
Hib (ActHIB)	2 months, 4 months
PCV13	2 months, 4 months
IPV	2 months, 4 months

What vaccinations are best to administer to this patient today?

ANSWER

First, look at figure 1 of the Recommended Immunization Schedule for Persons Aged 0 Through 18 Years to evaluate which vaccines he is behind schedule on, as well as which ones would normally be due at 12 months of age. Then, consult the catch-up schedule in figure 2 of the

Recommended Immunization Schedule for Persons Aged 0 Through 18 Years to determine how to approach the vaccines he has fallen behind on.

The following table describes an evaluation for each vaccine:

Vaccine	Vaccine Indicated?	Notes
HepB	Yes	Administer third dose on schedule now
RV	No	Contraindicated in those > 8 mo
DTaP	Yes	Catch up for third dose now; in 6 mo, give fourth dose
Tdap	No	Not indicated for those < 7 yr
Hib	Yes	Catch up for third dose now; no longer will need fourth dose
PCV13	Yes	Catch up for third dose now; no longer will need fourth dose
PPSV23	No	Not indicated for those < 2 yr
IPV	Yes	Administer third dose on schedule now
IIV	Yes	Administer first dose now; in 4 wk, give second dose
LAIV	No	Contraindicated in those < 2 yr
MMR	Yes	Administer first dose on schedule now
Varicella	Yes	Administer first dose on schedule now
HepA	Yes	Administer first dose on schedule now
HPV	No	Not indicated for those < 9 yr
Meningococcal	No	Only indicated in patients < 11 yr if high risk

This patient currently needs HepB, DTaP, Hib, PCV13, IPV, IIV, MMR, varicella, and HepA. Although it may seem like nine vaccines is a large number to administer in a single visit, ACIP and the AAP recommend giving all needed vaccines at the visit and not to delay vaccines. It is safe to give multiple vaccines at the same visit, whereas deferring some until a later date may expose the child to an unnecessary risk of delayed immunity. The number of injections required may be reduced by offering combination vaccines. Several different combinations of formulations can provide the necessary vaccines in as few as six injections. One example is ProQuad (MMRV) plus IIV plus PCV13 plus Pentacel (DTaP/Hib/IPV) plus HepA plus HepB. Twinrix (HepA/HepB) is not approved in pediatric patients and should be given as a separate HepA and HepB vaccine in this population. If administering

ProQuad, it is recommended to counsel the family on the small increased risk of febrile seizures compared with administering the vaccine as MMR and varicella as two separate injections. If several intramuscular injections are given into the same muscle, they should be administered at least 1 inch apart. Because DTaP and PCV13 are the most likely to cause local injection-site reactions, it may be prudent to give the injections containing these vaccines in separate limbs, if possible.

1. Immunization Action Coalition. [Ask The Experts: Topics](#) [homepage on the Internet].
2. Robinson CL. [Advisory Committee on Immunization Practices recommended immunization schedules for persons aged 0 through 18 years – United States, 2016](#). *MMWR* 2016; 65:86-7.

vaccine can be found in Table 7 of the *Morbidity and Mortality Weekly Report General Recommendations on Immunization*.

Special considerations do exist. Some parents may worry that vaccinating a child with mild acute illnesses will increase

the risk of adverse reactions or overburden the immune system. However, the rates of antibody response and vaccine adverse reactions in children with mild illness are similar to those in healthy children (Offit 2002). Regardless, it would

Box 1-3. Conditions Generally Not Considered Contraindications to Vaccination

- Minor acute illness such as diarrhea and minor upper respiratory tract illnesses (including otitis media) with or without low-grade fever
- Mild to moderate local reactions and/or low-grade or moderate fever after a prior dose of the vaccine
- Current antimicrobial therapy
- Recent exposure to infectious disease
- Convalescent phase of illness
- Pregnant or immunosuppressed person in the household
- Preterm birth
- Breastfeeding
- Allergies to products presumed to be in vaccine, but are not in vaccine

Information from: Kroger AT, Sumaya CV, Pickering LK, et al. Centers for Disease Control and Prevention. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2011;60:1-61; Hamborsky J, Kroger A, Wolfe C, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book*, 13th ed. Washington, DC: Public Health Foundation, 2015.

be important in this situation to appropriately educate and empower parents to decide whether they still want to withhold vaccines until after illness has improved. Prematurity is generally not a contraindication to vaccinations; however, one exception is RV, which should be deferred until discharge for any child who has been in the hospital since birth (Kroger 2011). Waiting to administer RV until a premature infant is clinically stable and no longer in the hospital will outweigh the theoretical risk of an adverse reaction as the result of a lower level of rotavirus maternal antibody in very preterm infants (Cortese 2009).

All children should receive all routine vaccines, including MMR, varicella, and RV, even if there are household or close contacts with immunocompromise. The only exception to this is the smallpox vaccine, which should not be administered if household members have immunocompromise; however, smallpox vaccination is no longer routinely recommended in the United States since the eradication of the naturally occurring disease (Kroger 2011). Inactivated influenza vaccine (IIV) is recommended over live attenuated influenza vaccine (LAIV) for individuals in close contact with a severely immunocompromised person. Because of theoretical transmission of the virus, if LAIV is received, contact should be avoided for 7 days after administration (Grohskopf 2015). Viruses from the MMR vaccine are not transmitted to contacts, and it is rare for varicella to be transmitted (Kroger 2011). To reduce the transmission of rotavirus that is shed during the first weeks after vaccine administration, everyone should wash hands after changing the child's diaper (Cortese 2009).

Box 1-4. Specific Immunodeficiencies

Primary

- Severe antibody deficiencies (e.g., X-linked, agammaglobulinemia and common variable immunodeficiency)
- Less severe antibody deficiencies (e.g., selective IgA deficiency and IgG subclass deficiency)
- Complete T-lymphocyte defects (e.g., severe combined immunodeficiency [SCID] disease, complete DiGeorge syndrome)
- Partial T-lymphocyte defects (e.g., most patients with DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia telangiectasia)
- Persistent complement, properdin, or factor B deficiency chronic granulomatous disease, leukocyte adhesion defect, and myeloperoxidase deficiency

Secondary

- HIV/AIDS
- Malignant neoplasm (leukemia, lymphoma, or generalized malignancy)
- Transplantation
- Immunosuppressive or radiation therapy
- Asplenia
- Chronic renal disease

IgA = immunoglobulin A; IgG = immunoglobulin G.

Information from: Hamborsky J, Kroger A, Wolfe C, eds. [Appendix A-26: Epidemiology and Prevention of Vaccine-Preventable Diseases](#). *The Pink Book*, 13th ed. Washington, DC: Public Health Foundation, 2015.

Immunosuppression

Another controversy in vaccine administration is determining the safety and efficacy of administering vaccines in children with altered immunocompetence. Immunodeficiencies are classified into primary and secondary (Box 1-4). Immunodeficiencies make patients more susceptible to infection, so additional vaccines are often warranted; however, they also increase the risk of complications with live vaccines, so some immunizations may be contraindicated. Even after classification, it is difficult to assess the degree to which a drug or disease causes immunosuppression and whether a vaccine is indicated or should be withheld until later (Kroger 2011). The Pink book appendix [Vaccination of Persons with Primary and Secondary Immune Deficiencies](#) summarizes vaccine efficacy, contraindications, and recommendations by type of immunodeficiency. For example, asplenia makes patients particularly susceptible to infection with encapsulated bacteria, so recommended vaccines are targeted toward these organisms.

Timing of vaccination is important to ensure adequate immunity as well. For planned splenectomies, vaccination at least 14 days before surgery is optimal. For emergency splenectomies when preoperative vaccination is not possible, waiting until at least 14 days after surgery produces the best immune response (Shatz 1998). In some situations,

consultation with an infectious disease or immunology specialist is indicated (Kroger 2011).

From a safety standpoint, risk and benefit must be considered when deciding to administer a vaccine. All inactivated vaccines can safely be administered to children with immunosuppression, who are already at an increased risk of the disease and its complications. Live vaccines may increase the risk of severe complications because of uninhibited replication (Kroger 2011). However, depending on the type of immunodeficiency and degree of immunosuppression, certain live vaccines may be recommended. This includes varicella in patients with HIV infection who are not severely immunocompromised (defined as a CD4+ T-lymphocyte count greater than 200 cells/mm³ for adolescents and a percentage greater than 15 for infants and children (CDC 2015a; Rubin 2014).

Another consideration with altered immunocompetence is vaccine effectiveness. This also depends on the degree of immunosuppression and the type of immunodeficiency. Because they are safe to give, inactivated vaccines are recommended to be given as scheduled, even though there may be a suboptimal immune response. However, patients receiving chemotherapy or radiation will likely have a suboptimal immune response, and inactivated vaccines should be withheld, if possible. If vaccines are administered, both live and inactivated vaccines may potentially require readministration after immune function has improved to ensure adequate immunity, though no specific criteria for revaccination have been established (Kroger 2011)

Drugs Affecting Immune Status

Corticosteroids and certain drugs can cause some level of immunosuppression, although to what degree is not clearly established. Because of safety concerns, the consensus is that live vaccines should be delayed if a patient is receiving high-dose steroids (defined as either 2 mg/kg or more or 20 mg/day or more of prednisone or equivalent) for 14 days or more. Live vaccines can safely be administered 1 month after discontinuing high-dose therapy. Patients receiving chronic maintenance physiologic replacement corticosteroids should not have vaccines deferred. However, doses higher than physiologic maintenance may reduce the immune response (Kroger 2011).

In general, children who are going to receive chemotherapy, other immunosuppressive drugs, or radiation should optimally have all types of vaccines administered at least 14 days before starting therapy. When vaccines are administered less than 14 days before or during therapy, they should be readministered at least 3 months after therapy is discontinued, if immunosuppression has resolved. This recommendation stems from a possible suboptimal response to vaccines and potential safety concerns for live vaccines during this time. One exception is IIV; it should be administered even during immunosuppression and does not need to be repeated (Kroger 2011).

Table 1-1. Intervals Between Administration of MMR or Varicella and Immune Globulin Preparations

Interval (months)	Products
3	<ul style="list-style-type: none"> • RBCs, adenine-saline added blood transfusion • Hepatitis A IG • Hepatitis B IG • Tetanus IG
4	<ul style="list-style-type: none"> • Rabies IG
5	<ul style="list-style-type: none"> • Varicella IG
6	<ul style="list-style-type: none"> • Blood transfusion with packed RBCs • Blood transfusion with whole blood • Botulinum immune globulin intravenous (human) • CMV (cytomegalovirus) IG • Measles IG
7	<ul style="list-style-type: none"> • Blood transfusion with plasma/platelet products
8	<ul style="list-style-type: none"> • IGIV dose 400 mg/kg/dose IV
10	<ul style="list-style-type: none"> • IGIV dose 1000 mg/kg/dose IV

IG = immunoglobulin; IGIV = intravenous immunoglobulin; IV = intravenously.

Information from: Hamborsky J, Kroger A, Wolfe C, eds. [Appendix A-24](#). In *Epidemiology and Prevention of Vaccine-Preventable Diseases*. The Pink Book, 13th ed. Washington, DC: Public Health Foundation, 2015.

Administration of antibody-containing products are thought to interfere with live vaccine replication of the MMR and varicella vaccines (CDC 2015a). Therefore, it is recommended to give the vaccines at least 2 weeks before the antibody product. However, the intervals for administration vary by product (Table 1-1).

Because of the many exceptions and considerations to these recommendations, the guidelines from the Infectious Diseases Society of America and CDC should also be consulted when administering vaccines in children with altered immunocompetence. For example, children may retain immune memory and not require repeat vaccination if they are receiving chemotherapy or radiation for certain malignancies. Inactivated vaccines may also be recommended in patients receiving low-dose intermittent or maintenance therapy of immunosuppressive agents. Moreover, if the benefit of vaccination outweighs the risk, a live vaccine might be indicated in the patient with immunocompromise (Kroger 2011).

General Adverse Effects

Common vaccine-specific adverse effects are discussed in the following. Some adverse effects encompass most

vaccines: these include pain, injection-site reactions, fever or flu-like illness, syncope, and anaphylaxis. Clinically significant adverse effects after vaccine administration should be reported to the [Vaccine Adverse Event Reporting System](#) (VAERS), a national surveillance reporting system (CDC 2015a).

The pain associated with childhood vaccines can lead to long-term negative effects, such as conditioned fear of needles and avoidance of associated procedures. Even though the perception of pain varies from patient to patient, there are methods to reduce the pain associated with vaccination. These measures include breastfeeding, giving sweetened solutions for infants younger than 12 months, injecting the most painful vaccine last, using tactile stimulation in children 4 years and older, using distraction, and applying topical anesthetics (CDC 2015a).

Injection-site reactions usually present as soreness, redness, itching, or swelling at the injection site. If a reaction occurs, the symptoms usually resolve within a few days but may last up to a week. Treatment consists of cold compresses and, depending on the severity of the reaction, analgesics or antipyretics (Rosenblatt 2015; Schmitt 2015). Injection-site reactions can occur with any vaccine and are not associated with specific vaccine components. If a skin reaction (e.g., rash) varies from the typical presentation of an injection-site reaction, the patient should be referred for a follow-up. Many vaccines can cause rare skin reactions that are specific to the vaccine or its components (Rosenblatt 2015).

Fever or flu-like illness is also a common adverse effect. Usually, the fever begins within 24 hours of vaccine administration and resolves in 1–2 days. For live vaccines such as MMR and varicella, fever may be delayed for 1–4 weeks (Schmitt 2015). A fever from vaccines should be approached similarly to any other fever. Children who develop fever from vaccinations have no higher risk of febrile seizures. The only exception is the slight increase risk of febrile seizures within 5–12 days after the first dose of the MMR vaccine or the measles, mumps, rubella, and varicella vaccine (MMRV) (CDC 2015b). When MMR and varicella are administered separately to children 12–47 months of age, about 4 of 10,000 children will have a febrile seizure compared with 8 of every 10,000 children who receive MMRV. It is therefore recommended to discuss this risk with all families before administering MMRV so that they can decide whether the combination MMRV vaccine or separate injections of MMR and varicella are most appropriate, especially if there is a personal or family history of febrile seizures or epilepsy (CDC 2015b).

For all of the previously mentioned vaccines, prophylactic acetaminophen or ibuprofen are not recommended because of insufficient evidence that they reduce discomfort, fever associated with vaccines, or risk of febrile seizures (Kroger 2011; Sullivan 2011). In addition, pretreatment with antipyretics may decrease immune response to the vaccines (Das 2014). Although more studies are needed to determine the

true risk, antipyretics should be reserved for postvaccination treatment of an adverse event (Das 2014).

Syncope after vaccinations is common, especially in those 11–18 years of age. A VAERS report found that 62% of reported fainting episodes occurred in this age range (CDC 2015b). It is recommended to observe patients while they sit or lie down for 15 minutes after vaccinating. In addition, giving patients a beverage or snack may reduce the chance of fainting (CDC 2015b; Kroger 2011).

Anaphylaxis occurs in about 1 of 1.5 million doses of vaccines administered to children and adolescents. If an allergic reaction occurs, the person administering the vaccine should be prepared to care for the patient and have an emergency plan in place. It is also recommended that all individuals administering vaccines be certified in cardiopulmonary resuscitation (CDC 2015a).

INDIVIDUAL VACCINE INFORMATION

Diphtheria, Tetanus, and Pertussis

Overview of Infection Disease

Diphtheria is caused by the bacterium *Corynebacterium diphtheriae*, a gram-positive bacillus, and manifests as an upper respiratory tract infection. *C. diphtheriae* produces a toxin that is responsible for producing the clinical features and complications of the disease. The infection affects mucous membranes, primarily in the tonsils, pharynx, larynx, and nasal mucosa, and can lead to formation of the disease's hallmark, a pseudomembrane. As the pseudomembrane grows in size, it can extend into the airway space and cause respiratory obstruction and subsequently death from asphyxiation. Additional complications of the toxin include myocarditis, neuropathy, paralysis, and pneumonia. Without treatment, about 50% of patients with diphtheria will die; even with proper treatment, the mortality rate remains about 10%. Vaccination is extremely effective in preventing diphtheria. Because of high vaccination rates, fewer than five U.S. cases were reported in the past decade. However, diphtheria remains a significant threat in other areas of the world such as India and Nepal (CDC 2015a; WHO 2015).

Tetanus is disease caused by *Clostridium tetani*; this gram-positive anaerobic bacterium produces a neurotoxin that causes muscles to contract. *C. tetani* enters the body through a wound or cut in the skin and travels throughout the body to manifest its effects on various sites of the CNS. The resulting unopposed muscular contraction can lead to spasms, seizures, and autonomic nervous system dysfunction. The associated death rate, even with appropriate treatment, is 10%–20%. Vaccination has made tetanus uncommon in the United States, with an average of around 30 cases per year, primarily in those who are unvaccinated or not up to date with booster shots (CDC 2015a).

Pertussis (“whooping cough”) is a respiratory disease caused by *Bordetella pertussis*, a gram-negative aerobic

bacterium. Pertussis is known for its paroxysmal coughing spells, which lead to the characteristic high-pitched “whoop” sound on inspiration. Pertussis was a common childhood illness and a major cause of child mortality. From 1922 to 1940, the incidence averaged 150 reported cases per 100,000; this was significantly reduced after introduction of the vaccine in the 1940s, and the incidence was 0.5 cases per 100,000 in 1976 (Faulkner 2015). However, pertussis incidence in the United States has increased during the past 3 decades. The annual number of cases in 2012 was 48,000, up from a low of 1300 in 1981. This can be attributed to more vaccine refusals as well as to the switch to acellular vaccine from whole cell vaccine, which was more immunogenic. In response, the ACIP has expanded its recommendations regarding pertussis vaccination several times since 2010 to combat the growing threat of disease (CDC 2015a).

Recommended Administration Schedule

The DTaP vaccine is given as a five-dose series to children younger than 7 years. Minimal intervals after the first two doses are 4 weeks, with a 6-month interval before each of the last two doses. The Tdap vaccine is recommended for adolescents as a single dose. For children and adolescents 7 years and older who have not completed the primary DTaP series, a three-dose series should be given: one dose of Tdap, followed at least 4 weeks later with a dose of tetanus and diphtheria vaccine (Td) and a second dose of Td at least 6 months after the first. For pediatric patients, the formulations including pertussis should always be used unless there is a contraindication (Robinson 2016).

In 2011, ACIP expanded its pertussis vaccine recommendations to include all individuals 11 years and older who have not received a dose of Tdap, emphasizing the need for this vaccine in adults who will be in contact with infants younger than 12 months. The intent is to protect infants, who are most at risk of pertussis complications, by preventing carrier transmission before they develop adequate immunity from their primary vaccination series (CDC 2011b). In addition, since 2012, Tdap has been recommended for pregnant women during each pregnancy (regardless of the timing of previous vaccinations), preferably between 27 and 36 weeks’ gestation to maximize antibody transfer through the placenta for protection of the infant after birth (CDC 2013b).

Vaccine-Specific Considerations

Arthus reactions have been described for patients receiving vaccines that contain tetanus or diphtheria toxoid. This immune-mediated type III hypersensitivity reaction causes a localized vasculitis at the injection site, leading to severe pain, swelling, induration, and hemorrhage within 4–12 hours after the injection. Arthus reactions are generally self-limiting and resolve without treatment in 1–2 days; however, symptomatic management with analgesics or anti-inflammatory drugs can be considered (Butler 1976). A history of Arthus

reaction after previous vaccination is not a contraindication to further receipt of the Td or Tdap vaccines; however, it is generally recommended to wait at least 10 years between boosters because the severity of the reaction is correlated with the frequency of toxoid exposure.

Human Papillomavirus

Overview of Infection Disease

Human papillomavirus is a DNA virus that can cause infection in the skin or mucous membranes; spread primarily through contact with infected skin, mucous membranes, or body fluids, it is the most common sexually transmitted infection, affecting most sexually active individuals. An estimated 79 million people in the United States are infected with HPV, with 14 million new infections annually, half of which are in individuals 15–24 years of age (Satterwhite 2013). There are more than 150 serotypes of HPV, many of which cause subclinical infection and go unnoticed. Of primary clinical concern, however, are the infections that can lead to cancer or warts. Human papillomavirus is strongly associated with cancers of the cervix, penis, anus, and oropharynx, with serotypes 16 and 18 being the most common culprits, followed by serotypes 31, 33, 45, 52, and 58. Anogenital warts are also caused by HPV, with more than 90% associated with serotypes 6 and 11 (Markowitz 2014).

Recommended Administration Schedule

As recommended by ACIP, boys and girls should have routine HPV vaccination with a three-dose series beginning at age 11 or 12, with a minimal starting age of 9 years. Female patients 9–26 years of age should be vaccinated with HPV vaccine, with no preference given by ACIP between HPV2, HPV4, and HPV9. Male patients 9–21 years of age, as well as up to age 26 for high-risk patients (i.e., men who have sex with men, those with immunocompromise), should be vaccinated with HPV4 or HPV9. If the formulation of previous doses is unknown, or unavailable, any of the available HPV vaccine formulations may be used to complete the series for female patients; HPV4 or HPV9 is preferred for male patients.

Approved in 2014, HPV9 is a new formulation with expanded serotypes that offers protection against an additional 10%–15% of HPV-associated cancers (Petrosky 2015). However, ACIP has made no recommendations about revaccinating (or restarting the vaccine series) for those who previously received HPV vaccine doses and who desire the additional serotype coverage offered by HPV9. Clinical and pharmaco-economic evidence is currently insufficient to support revaccination of those who have already completed the vaccine series; however, some data suggest that revaccination with HPV9 after completing a series of HPV4 is safe (Petrosky 2015).

Several studies showing the noninferiority of two-dose or even one-dose regimens compared with the full three-dose HPV vaccine series have prompted some organizations to

alter their recommendations (Kriemer 2015; Dobson 2013). For example, WHO now recommends only a two-dose schedule for adolescents who initiate the vaccine series before 14 years of age (WHO 2014). However, ACIP has not altered its recommendations and continues to support completion of a three-dose series.

Vaccine-Specific Considerations

Adherence to recommended vaccination schedules for HPV vaccine has lagged behind that of many other vaccines, with completion of the recommended three-dose series in only around one-half of adolescent girls by age 17 and less than one-fourth of boys by age 17 (Reagan-Steiner 2015). Reasons for the low vaccine uptake include lack of knowledge about the risks of HPV-associated cancer, general concerns about vaccine efficacy and safety, high cost of the vaccine, and unfounded concerns about the vaccines promoting sexual promiscuity (Fernández 2014). Several studies have shown that HPV vaccination does not increase sexual activity among teens and is not associated with an increase in overall sexually transmitted infection rates (Jena 2015; Liddon 2012). Pharmacists can significantly affect the prevention of HPV and related cancers by educating patients and screening for vaccination status. In addition, because most states now allow pharmacists to administer the HPV vaccine, immunization can be performed at the time of assessment in the pharmacy to reduce the risk of lack of patient follow-through on recommendations.

Meningococcus

Overview of Infection Disease

Meningococcal disease is caused by the bacterium *Neisseria meningitidis*, an aerobic gram-negative diplococcus that can cause severe infections including meningitis and bacteremia. *N. meningitidis* strains are classified according to the antigenic structure of their polysaccharide capsule, with serotypes A, B, C, W135, X, and Y causing the most clinically important infections. Disease is spread by transmission of the bacteria from droplets and close contact with an infected or colonized individual. Patients most at risk of the invasive disease are those without a functional spleen, with complement deficiency, or living in crowded housing situations.

The disease generally has a rapid onset of fever, headache, and stiff neck, and patients may also have nausea, vomiting, photophobia, and confusion. Overall rates of meningococcal disease are highest in children younger than 1 year, with a second peak in adolescence associated with close contact with classmates in school and dormitories on college campuses. Most clinical disease in the United States is caused by serogroup B (about 60%), followed by serogroups C and Y (CDC 2015a). Periodic outbreaks have gained public attention in recent years, including several on college campuses (Soeters 2015) and in urban populations of men who have sex with men (MDH 2015; CDC 2013a).

Recommended Administration Schedule

Vaccination with a quadrivalent meningococcal vaccine (MenACWY) is routinely recommended for adolescents as well as younger children who are at high risk of disease, including patients with functional or anatomical asplenia, with complement deficiency, or living in an area of high meningococcal disease prevalence or in outbreak settings (Cohn 2013). The prevalence of meningococcal disease caused by serogroup B has prompted the development and recent U.S. approval of new recombinant vaccines. Additional administration of a vaccine covering serogroup B is recommended in patients at high risk of disease because of the conditions listed earlier or in the setting of an outbreak (Folaranmi 2015). The serogroup B meningococcal vaccine was incorporated into the 2016 vaccination schedule for high-risk groups and non-high-risk groups that may receive the vaccine based on individual clinical decision making.

Vaccine-Specific Considerations

One particularly dangerous drug-related risk factor for meningococcal disease is the monoclonal antibody eculizumab. Eculizumab is used in the treatment of paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome; it works by interfering with complement-mediated hemolysis. The complement deficiency induced by eculizumab has been associated with cases of severe and deadly meningitis from *N. meningitidis* and has prompted the FDA to require a boxed warning and a Risk Evaluation and Mitigation Strategies (REMS) program for this drug. According to the package insert, a main component of the REMS program is administration of the quadrivalent meningococcal vaccine at least 14 days before initiating eculizumab. Although the prescribing information and REMS program do not specifically mention vaccination with the newer serogroup B meningococcal vaccine, it would be prudent to consider adding this vaccine in patients undergoing eculizumab therapy who are at risk of all serotypes of meningococcal infection. In addition, eculizumab increases the risk of infection with other encapsulated bacteria, including *H. influenzae* and *Streptococcus pneumoniae*, so the need for vaccines against those agents should also be assessed.

Pneumococcus

Overview of Infection Disease

S. pneumoniae is a gram-positive aerobic bacterium that causes many types of illnesses, with the most severe morbidity and mortality associated with pneumonia, bacteremia, and meningitis. In the United States, an estimated 900,000 people acquire pneumococcal pneumonia each year, with almost 50% of these patients requiring hospitalization and a mortality rate of 5%–7%. An additional 3700 deaths annually are attributable to bacteremia or meningitis caused by *S. pneumoniae*. Since the introduction of the pneumococcal vaccines, rates of infection and death from *S. pneumoniae*

have decreased substantially, both among the specific serotypes covered by the vaccine and overall. For example, before PCV7, the incidence of PCV7-type invasive pneumococcal disease was 80 cases per 100,000 in children younger than 5 years; this decreased to less than 1 case per 100,000 by 2007 (CDC.gov 2015a).

Recommended Administration Schedule

Vaccination with a four-dose series of PCV13 is universally recommended for all children beginning at 2 months of age. The PPSV is recommended for children 2 years and older with high-risk conditions (e.g., sickle cell disease, anatomic or functional asplenia, chronic cardiac, pulmonary or renal disease, diabetes, CSF leaks, HIV infection, immunosuppression, diseases associated with immunosuppressive and/or radiation therapy, solid organ transplantation, those who have or will have a cochlear implant). In addition, children 6–18 years of age at high risk of pneumococcal disease should receive doses of both PCV13 (unless they have completed the PCV13 series) and PPSV23, separated by at least 8 weeks.

In older children with high-risk conditions, extra attention should be paid to the primary PCV series because these children may or may not have received PCV13, given that until 2010, the routine vaccination consisted of PCV7. See [Pink Book Appendix A-15](#), Summary of Recommendations for Child/Teen Immunization, for details of recommended timing of vaccine administration.

Vaccine-Specific Considerations

In addition to the invasive infections that pneumococcal vaccine was designed to prevent, including meningitis and bacteremia, PCV has a benefit in reducing otitis media caused by *S. pneumoniae* (Fortanier 2014). From a public health standpoint, this is an important benefit, given the frequency of otitis media in young children. However, data cannot be extrapolated to a patient-specific level because many organisms can cause otitis media.

Measles, Mumps, and Rubella

Overview of Infection

Measles virus, a species in the genus *Morbillivirus*, caused disease in almost all children in the pre-vaccine era. Measles, also known as rubeola, spreads by the respiratory route and manifests systemically as the virus spreads throughout the body. Typical early clinical features include a prodrome phase, which begins with a fever followed by the “three Cs” (i.e., cough, coryza, and conjunctivitis). Koplik spots, which are punctate bluish white spots on mucous membranes, are considered pathognomonic for measles. The generalized rash that occurs with measles typically begins at the hair-line of the face and upper neck and then continues downward and outward across the body until it reaches the hands and feet. The rash usually resolves after several days in the same

order in which it appears, beginning at the head and ending in the extremities. Measles is generally self-limiting but can occasionally be severe, leading to complications including pneumonia, encephalopathy, and even death in a small proportion of patients.

The burden of measles has decreased significantly in the United States since the vaccine was introduced in 1963, with the incidence decreasing by more than 95% from its peak. However, several recent outbreaks have brought about a resurgence of measles; in 2014 there were 668 cases across 27 states. Most of the outbreaks were associated with virus that was imported from an endemic area of the world, or by people who traveled to one of those areas. Because measles is highly contagious, a single source can quickly spread disease throughout a community, particularly through patients who are unvaccinated or under-vaccinated (CDC 2015a). The outbreak that garnered the most attention was in Orange County, California, because it was associated with exposure to the virus at a Disney theme park. A total of 125 confirmed measles cases were associated with this outbreak (Zipprich 2015).

Mumps is a virus in the *Paramyxoviridae* family that is spread by the respiratory route. The virus replicates in the nasopharynx and surrounding lymph nodes, then spreads throughout the body in the bloodstream. After an initial prodrome, consisting of nonspecific symptoms of fever, malaise, myalgia, anorexia, and headache, mumps most commonly manifests as parotitis. The inflammation can affect several salivary glands and can be unilateral or bilateral. Orchitis can also occur in up to 50% of postpubescent males infected with mumps, which can lead to further complications including testicular atrophy. Other serious complications, though rare, can also occur, including meningitis, deafness, myocarditis, and death (CDC 2015a). After the introduction of routine vaccination the incidence of mumps declined sharply to less than 1% of previous rates. However, outbreaks have occurred in the past few years, primarily attributed to communities with low vaccination rates or to close contact in crowded settings. Public interest in mumps spiked during a 2014 outbreak that occurred among players and staff in the National Hockey League (Ruderfer 2015).

Rubella virus, also known as German measles, is a viral illness spread by the respiratory route. It manifests primarily as a mild illness with a primary feature of rash that begins on the face and spreads down through the trunk and to the feet and hands, similar to measles. Systemic symptoms of rubella are generally mild and can include low-grade fever, malaise, lymphadenopathy, upper respiratory symptoms, and arthralgias. The biggest concern with rubella, and the primary motivation for vaccination against the virus, is congenital rubella syndrome (CRS). Rubella infection early during a woman's pregnancy can cause severe problems with the fetus and may lead to fetal death, spontaneous abortion, or preterm delivery. If the child survives the infection

and is born alive, CRS can affect all organ systems, with severity and location depending on the stage of gestation when the infection occurred. The most common complication of CRS is permanent deafness, which can often be the sole manifestation of the disease in an infant. Other complications of CRS include eye defects, cardiac defects, bone alterations, liver damage, spleen damage, and mental retardation (CDC 2015a).

Recommended Administration Schedule

The MMR vaccine is universally recommended for all children as a two-dose series beginning at 12 months of age, or for any child who has not yet completed the primary immunization series. In addition, the MMR vaccine may be given to children as young as 6 months if they will be traveling outside the United States. These children should still subsequently receive the full two-dose series according to the immunization schedule (McLean 2013).

Vaccine-Specific Considerations

Because MMR is a live-attenuated virus vaccine, all the considerations pertaining to immunosuppression and blood products for live vaccines apply. Of note, the vaccine contains gelatin and neomycin, so patients who are allergic to these components should not be vaccinated with MMR (CDC 2015b).

Public concerns about the MMR vaccine causing autism have been shown to be unfounded and based on fraudulent work, as discussed previously (Retraction 2010).

Varicella

Overview of Infection Disease

Varicella (chickenpox) is caused by the varicella zoster virus. This herpesvirus causes a pruritic rash that appears first on the head and trunk and then spreads to the rest of the body. It progresses from macules to papules to vesicles before finally crusting over and healing. It is highly infectious and easily spreads person-to-person through aerosolized virus particles. Among household members and close contacts, an estimated 90% of susceptible individuals will contract the virus after exposure to an infected person.

Initial infection is generally mild, and symptoms resolve without specific treatment, although occasionally, bacterial superinfection can cause severe complications. After initial varicella zoster virus infection, the virus remains dormant in the dorsal root ganglia of the nervous system and can be reactivated later in life to cause herpes zoster (shingles) during periods of stress or decreased immunity. Before the varicella vaccine was introduced in 1995, around 150,000–200,000 cases of varicella disease occurred annually, leading to 100–150 deaths each year. Significant declines of more than 80%–90% in both incidence and mortality from varicella have occurred since widespread vaccination was initiated in the United States in the 1990s (CDC 2015a).

Recommended Administration Schedule

The recommended immunization regimen for varicella virus is a two-dose series that is initiated at 12 months of age. Varivax should not be confused with Zostavax. Zostavax is the zoster vaccine used in adults for shingles prevention and is about 14 times more potent.

Vaccine-Specific Considerations

Because varicella vaccine is a live-attenuated virus, all the considerations pertaining to immunosuppression and blood products for live vaccines apply. Of note, the vaccine contains gelatin and neomycin, so patients who are allergic to these components should not be vaccinated with varicella, MMRV, or shingles (CDC 2015b). Occasionally, a child will develop a mild, localized rash resembling chickenpox after varicella vaccination. When this occurs, concern for transmission exists because the virus, though attenuated, is actively replicating in vivo. In general, if the rash is limited to maculopapular lesions, there is no risk of transmission. If the lesions become open vesicles, it is theoretically possible to transmit disease until they all crust over, although it is still quite rare. However, if vesicles develop after varicella vaccination, a noncontagious vaccine-induced rash cannot be differentiated from a true varicella infection. Therefore, if a rash develops 7–21 days after vaccine administration, contact should be avoided with susceptible individuals or immunocompromised patients who are at risk of severe complications of disease until the rash resolves (IAC 2016).

Some antiviral agents may interfere with the efficacy of the varicella vaccine because, as a live vaccine, it requires active replication to stimulate the immune system; this can be impaired in the presence of antiviral medications active against varicella zoster virus (e.g., acyclovir, ganciclovir). See Pink Book [Appendix A-15](#), Summary of Recommendations for Child/Teen Immunization, for more specific recommendations on timing of antivirals around the vaccine (Hamborsky 2015).

Influenza

Overview of Infection Disease

Influenza is a respiratory illness spread by respiratory droplets after an infected person coughs or sneezes. Generally a seasonal disease that peaks in the winter months, the exact timing and the length of influenza season vary with location and climate. Influenza is characterized by an abrupt onset of severe systemic and respiratory symptoms including, but not limited to, fever, chills, myalgia, headache, malaise, non-productive cough, sore throat, and rhinitis. Uncomplicated influenza generally resolves within 7 days; however, children with comorbid conditions may have more severe or prolonged disease or secondary bacterial infections. These complications and secondary infections can lead to significant morbidity and mortality, particularly from post-influenza pneumonia or respiratory failure. In addition, febrile seizures

have been reported in up to 20% of children hospitalized with influenza (CDC 2015a).

The influenza vaccine varies in efficacy each year because of the variability in influenza strains circulating. Efficacy is generally in the 50%–60% range; however, in some recent years, it has been as low as 23% (CDC 2015a). Although this is much lower than what we have come to expect from many other types of vaccines, influenza vaccination can still play an important role in reducing the burden of influenza morbidity and mortality. A recent Cochrane review found a number needed to vaccinate of 39–71 to prevent one case of influenza or influenza-like illness, whereas adverse effects were similar to placebo (Demicheli 2014). In addition, prevention of influenza can reduce complications of the disease, including pneumonia and associated hospitalizations (Grijalva 2015). However, still less than one-half of eligible patients in the United States receive the influenza vaccine each year, which further limits the vaccine's potential to reduce influenza illness and related complications. Pharmacists can help improve vaccination rates by educating patients and administering vaccinations throughout the influenza season (CDC 2015a).

Recommended Administration Schedule

Annual vaccination against influenza at the beginning of each influenza season is universally recommended for all patients 6 months and older. The vaccine should be administered before the onset of influenza activity in the community. Vaccination should continue to be offered as long as influenza viruses are circulating. No preference is given for quadrivalent or trivalent vaccine, and the 2015–2016 guidelines removed the previous preference for LAIV over IIV in healthy children 2–8 years of age. The guidance now suggests that any product that is available and for which the patient is eligible should be administered. The rationale for this recommendation is to decrease the chance of missed opportunity for vaccination because of waiting for the availability of a preferred product. In addition, evidence is conflicting regarding the previously reported superiority of LAIV that had led ACIP to give it a preferential recommendation in younger children (Grohskopf 2015). A recently published study reports that rates of influenza during the 2013–2014 season were actually higher amongst children who received the LAIV compared to those that received IIV (Chung 2016).

Children 6 months to 8 years of age require a second dose of influenza vaccine at least 4 weeks after the first dose in the first season they are vaccinated to optimize response. Response rate after a single dose improves with age and varies by influenza serotype, but it improves with a second dose for all serotypes in children younger than 9 years (Neuzil 2006). If a child in this age group previously received only a single dose in an influenza season, it is still recommended that the child be given two doses in the current season to ensure optimal response. The only exception to this would be

if the initial vaccine the child received contained exactly the same influenza strains as the current season; then, a single dose would be adequate. However, it is often difficult to determine this with certainty, so it is recommended to err on the side of caution and give the two-dose series to optimize efficacy (Grohskopf 2015).

Vaccine-Specific Considerations

Influenza vaccines have traditionally been grown in chicken eggs; there is therefore a potential risk to patients with severe egg allergy. However, several studies have shown that even patients with documented egg allergies have an extremely low chance of a severe allergic reaction, and even mild allergic reactions to the influenza vaccine are uncommon (Des Roches 2012). Current ACIP recommendations state that children with a history of egg allergy that includes only hives (but not anaphylaxis or angioedema) can be given IIV3 or IIV4 as long as they are monitored for at least 30 minutes after vaccination by an appropriate health care provider. In addition, patients who can tolerate eating lightly cooked eggs are unlikely to have a true allergy and can be administered IIV using the same general precautions. The LAIV formulation has not been extensively studied in egg allergy and should be avoided until further information is available. Alternatively, there is a completely egg-free recombinant vaccine formulation, recombinant influenza vaccine trivalent (RIV3), which can be administered to patients with any severity of egg allergy. However, RIV3 is currently not approved for use in pediatric patients, so any use in children younger than 18 years would be off-label (Grohskopf 2015). Several clinical trials assessing safety and immunogenicity in children have been completed, although the full results are not yet available at the time of writing this chapter (NIH 2015a, 2015b).

A prevalent misconception about the influenza vaccine, and a common reason given for declining to be vaccinated, is the concern that the vaccine can cause influenza illness. The inactivated injectable vaccine is a completely nonviable form of the virus that cannot replicate, so it cannot cause illness. However, the vaccine can cause adverse effects including low-grade fever, headaches, and muscle aches, which patients may falsely attribute to the influenza virus. Some patients may coincidentally contract influenza after vaccination, but not from the vaccine itself. It takes 10–14 days to develop an adequate antibody response to the vaccine to provide protection, so if patients are exposed to the virus during this time, they may develop disease despite receiving the vaccine. Other non-influenza viruses can also present with similar symptoms, which could be mistaken by patients to be influenza disease.

Although LAIV is an attenuated form that theoretically could cause illness, it is a weakened form of the virus and has been adapted to replicate only in the colder temperatures of the nasal passages, so it cannot cause infection in the lungs. Because of the small theoretical risk of causing disease,

however, LAIV is contraindicated in immunocompromised individuals, as are other live virus vaccines (CDC 2015a).

Hepatitis A

Overview of Infection Disease

Hepatitis A is an RNA virus in the *Picornaviridae* family that is transmitted by the fecal-oral route and causes an inflammatory disease of the liver. Unlike some other hepatitis viruses, hepatitis A virus is generally self-limiting and does not progress to a chronic long-term infection. Symptoms of the disease include nausea, anorexia, fever, malaise, and abdominal pain. Patients may also present with jaundice, scleral icterus, and elevated transaminases. Primary sources of infection are close contact with an infected household member or sex partner. In addition, outbreaks can occur in the food industry when a food handler has the infection and spreads the virus through raw or undercooked foods.

Vaccination has significantly reduced the burden of hepatitis A disease, with an annual incidence of 25,000–35,000 cases before universal vaccination, decreasing to less than 2000 cases annually in recent years (CDC 2015a).

Recommended Administration Schedule

The HepA vaccine is universally recommended for all children beginning at 12 months of age, followed by a second dose at least 6 months later. Older children who have not yet been vaccinated should follow the catch-up schedule to receive adequate protection against the virus (CDC 2015a).

Vaccine-Specific Considerations

The HepA vaccine is preferred for postexposure prophylaxis in healthy patients 1–40 years of age who have been exposed to the virus in the previous 2 weeks. Immunocompromised patients, those with preexisting liver disease, or those who have contraindications to the vaccine must still use immune globulin rather than vaccination for postexposure prophylaxis because of decreased response to the vaccine. Children who have previously received immune globulin should still receive the routine HepA vaccine as recommended (CDC 2015a).

Hepatitis B

Overview of Infection Disease

Hepatitis B virus causes an inflammatory disease of the liver. It is a double-stranded DNA virus in the *Hepadnaviridae* family that is transmitted by blood or body fluids, most often through sexual contact or sharing needles with infected individuals. Some people clear hepatitis B virus after initial infection, but some will develop a long-term, chronic infection. The frequency of developing a chronic infection declines with age and occurs in about 90% of infants infected with hepatitis B virus compared with 2%–6% of adults. Chronic hepatitis B can cause significant morbidity, including cirrhosis or hepatocellular carcinoma. The incidence of hepatitis B

has declined since the vaccine was introduced. At its peak in the 1980s, the annual number of reported cases in the United States was greater than 25,000, compared with around 3000 cases in recent years. True incidence is estimated to be 10-fold higher than these reported numbers because many people asymptotically have the infection chronically (CDC 2015a).

Recommended Administration Schedule

Vaccination with HepB is universally recommended for all children as a three-dose series beginning at birth. Of note, this is the only vaccine that is routinely recommended in neonates. All doses administered before 6 weeks of age should be the monovalent HepB rather than combination products with any other vaccines. For catch-up vaccination in children who did not receive the initial vaccination series, the adult formulation with a higher amount of HepB antigen than the pediatric vaccine may be used in children 11 years or older (CDC 2015a).

Vaccine-Specific Considerations

For infants born to hepatitis B virus antigen-positive mothers, hepatitis B immune globulin should also be administered within 12 hours of birth plus the original required vaccine. In these patients, postvaccination testing should be performed 1–2 months after the completion of at least three doses of HepB to ensure immunity (CDC 2015a).

The HepB vaccine can also be used for postexposure prophylaxis in children who have potentially been exposed to the virus and lack documented immunity. The vaccine can be given with or without immune globulin, depending on the hepatitis B status of the source and the vaccination status of the patient (Mast 2006).

H. influenzae Type B

Overview of Infection Disease

H. influenzae is a gram-negative coccobacillus that commonly colonizes the respiratory tract and can cause invasive infections including pneumonia, bacteremia, meningitis, and epiglottitis, as well as relatively superficial infections including otitis media and cellulitis. There are six strains of *H. influenzae* with a polysaccharide capsule (types a–f), as well as nonencapsulated (non-typeable) strains. Historically, Hib has been associated with the most invasive infections and the greatest morbidity and mortality. Invasive Hib is associated with a mortality rate of 3%–6%, and Hib meningitis can cause long-term sequelae, including hearing loss and neurologic deficits in up to 20% of survivors. Before the introduction of the Hib vaccine, the annual incidence of Hib disease was around 20,000 cases. The vaccine has dramatically decreased the incidence by more than 99% since its introduction in the late 1980s. Most *H. influenzae* infections in the United States are now from non-typeable strains that are not covered by the vaccine (CDC 2015a).

Recommended Administration Schedule

The Hib vaccine is universally recommended for all children beginning at age 2 months, with catch-up vaccination routinely recommended for unimmunized children up to age 5 years. The number of total doses and schedule varies depending on the specific vaccine formulation used. ActHIB, MenHibrix, and Pentacel require a three-dose primary series followed by a booster dose of any Hib-containing vaccine. PedvaxHIB and COMVAX require a two-dose series followed by a booster dose of any Hib-containing vaccine. The different number of doses required is because of the varying levels of immunogenicity to the vaccines with different carrier proteins in their formulation (Kelly 2004). Select high-risk children older than 5 years should also be given the Hib vaccine if they are not already immune, including patients with asplenia or HIV (Briere 2014).

Vaccine-Specific Considerations

Although it is generally recommended to complete a vaccination series with the same vaccine formulation, if the same formulation is not available for subsequent doses, any other Hib-containing vaccine may be administered and still be considered valid. An exception is the Hiberix vaccine, which is only indicated for use as a booster dose in children 12 months to 4 years of age who have already received at least one prior dose of Hib-containing vaccine (CDC 2015a).

Polio

Overview of Infection Disease

Polio is a potentially fatal infection that has historically caused significant morbidity and mortality throughout the world. Polio is an RNA enterovirus in the *Picornaviridae* family that is spread by the fecal-oral route. Most infections are asymptomatic or subclinical; however, in around 5% of infections, manifestations such as fever, pharyngitis, gastroenteritis, and flu-like symptoms occur. In addition, in a smaller percentage of patients (0.5%), polio can invade the CNS, resulting in irreversible paralysis by damage to dorsal root ganglia and motor and autonomic neurons of the spinal cord and gray matter of the brain. The neuronal damage can manifest as flaccid paralysis of the extremities, respiratory failure, and neurogenic bladder (CDC 2015a).

Before the introduction of polio vaccine, the virus was responsible for more than 15,000 cases of paralysis annually in the United States. Because of diligent vaccination efforts, endogenous polio was eradicated from the United States in 1979. Vaccination continues to be recommended because of the existence of polio disease in other parts of the world that can potentially be brought into the country through travelers. The overall incidence of polio disease has declined by more than 99% since the launch of global polio eradication efforts in 1988 (CDC 2015a). Several hundred cases still occur annually throughout the world, primarily

concentrated in Pakistan and Afghanistan, with sporadic cases still occurring in other parts of the Middle East and Africa (Global Polio 2015).

Recommended Administration Schedule

The IPV is universally recommended as a four-dose series beginning at age 2 months and as a catch-up vaccine for anyone younger than 18 years who has not completed the series (CDC 2015b). The IPV is the only polio vaccine product that has been available in the United States since 2000. However, the oral polio vaccine is used in areas of the world where endemic polio is still circulating (CDC 2015a).

Vaccine-Specific Considerations

Of note, although IPV protects the recipient from developing polio disease, if a child immunized with IPV travels to an area of the world where polio is endemic and is exposed, the virus may still be able to actively replicate in the intestinal tract and be passed on to others. General precautions, including good hand hygiene, should be taken on return from travel to polio-endemic areas (CDC 2015a).

Rotavirus

Overview of Infection Disease

Rotavirus commonly causes intestinal disease in pediatric patients, particularly infants and young children. Infection with rotavirus manifests as severe watery diarrhea, often with vomiting, fever, and abdominal pain. Complications from rotavirus are primarily because of dehydration from excessive diarrhea and vomiting. Rotavirus is spread by the fecal-oral route and is most prevalent during the winter and spring months (CDC 2015a).

Recommended Administration Schedule

The RV is universally recommended for all children beginning at 2 months of age. If using RotaTeq, three doses are necessary, whereas Rotarix requires only two doses. No preference for one formulation or the other is given by ACIP, and both are effective at preventing disease. It is acceptable to use a different formulation on subsequent administrations, but if a RotaTeq product is used for any of the doses, a total of three doses of RV should be given. Of note, the RV series should not be initiated after age 15 weeks. The maximal age for the final dose of the series is 8 months, after which no further doses should be given even if the series has not been completed (Cortese 2009).

Vaccine-Specific Considerations

The RV is generally well tolerated, with GI upset being most prevalent adverse effect. A rare but serious complication of RV is intussusception. This complication occurred more commonly with a previous formulation of RV, RotaShield, which was removed from the market in 1999. Current vaccines pose a much lower risk (CDC 1999).

CONCLUSION

Infections with VPDs remain a significant cause of morbidity and mortality in the United States and throughout the world. Improvement in vaccine coverage will continue to reduce the burden of, and in some cases eliminate, VPDs. Pharmacists' impact on routine pediatric immunizations will continue to evolve as authorization to vaccinate children expands across state laws and regulations. With this increasing role comes the added responsibility of assessing the appropriateness of vaccines according to recommended CDC schedules and determining risks and benefits among all vaccines regardless of patient complexity. In states that do not permit them to vaccinate children, pharmacists should still assess and refer all patients for appropriate vaccines. Sustaining proper adherence to vaccine schedules is a continuous public health problem; pharmacists should educate families about the importance of vaccination and be able to address concerns and dispel misconceptions that may lead to vaccine refusal.

Practice Points

Infectious diseases have been a source of great morbidity and mortality throughout history. The introduction of vaccines to prevent infections has proven to be one of the greatest medical achievements to date. Pharmacists should be familiar with the scientific, social, and political issues related to vaccines and public health:

- Vaccines induce protection from disease by provoking an immune response by administration of microorganisms, or fractions of microorganisms, into the body.
- Vaccines can be classified in various ways, including live versus inactivated versus toxoid and polysaccharide versus protein conjugated. Each type differs in its considerations regarding the mechanism of provoking an immune response, number of doses required, duration of immunity, and patient eligibility criteria.
- Pharmacists play several important roles related to pediatric immunization, including administering vaccines, assessing vaccine eligibility, and providing patient education, provider guidance, and legislative advocacy.
- Recommended pediatric immunization schedules are published annually by the CDC according to the best available evidence regarding the efficacy and safety of available vaccines.
- Adherence to these recommended schedules is the best way to reduce the burden of VPDs.
- Pharmacists play a critical role in educating the public about vaccinations and clarifying myths and misconceptions that patients may have.
- Pharmacists should be able to interpret immunization schedules and recommend appropriate vaccines according to patient-specific factors.
- In addition to general considerations that pertain to all vaccines, each individual vaccine has specific considerations related to efficacy, safety, formulation, immunization timing, and technique.

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Self-Assessment Questions

1. A 12-year-old boy with no significant medical history comes to your clinic for a routine checkup. After reviewing his medical chart and immunization history, you recommend that he be given tetanus, diphtheria, and acellular pertussis vaccine (Tdap), human papillomavirus 9 vaccine (HPV9), and meningococcal quadrivalent vaccine (MenACWY-D) today. His mother states that he needs the Tdap and MenACWY-D vaccines but not the HPV9 vaccine because he is not yet sexually active. Which one of the following is the best response to give this patient's mother?
- A. Recommend vaccination with HPV2 today and recommend returning for HPV9 when he is sexually active.
 - B. Emphasize the importance of giving MenACWY-D at the same time as the HPV vaccine for optimal efficacy.
 - C. Recommend that the HPV9 vaccine be given today because of the importance of developing immunity to HPV early.
 - D. Emphasize that all recommended vaccines should be given today because that is what the vaccine schedule recommends.

Questions 2 and 3 pertain to the following case.

M.M. is 10-year-old boy who is up to date on all of his routine childhood vaccinations, including pneumococcal conjugate vaccine 7 (PCV7). He is brought to the ED after being in a motor vehicle crash. The physician determines that there is internal organ damage and decides M.M. needs an emergency splenectomy.

2. Which one of the following vaccines and timing of vaccination is best to recommend for M.M.?
- A. Meningococcal, pneumococcal, and *Haemophilus influenzae* type B (Hib) as soon as possible
 - B. Meningococcal and pneumococcal as soon as possible
 - C. Meningococcal, pneumococcal, and Hib at least 14 days after surgery
 - D. Meningococcal and pneumococcal at least 14 days after surgery
3. Which one of the following is best to recommend for pneumococcal vaccination administration in M.M.?
- A. PCV13 only
 - B. PCV13 first, followed by PPSV23 8 weeks later
 - C. PPSV13 first, followed by PCV23 12 weeks later
 - D. PPSV23 only

4. A 4-year-old girl (weight 15 kg) with asthma presents to your clinic for a checkup. She is on day 4 of her second 5-day course of prednisolone solution (30 mg/day) for an asthma exacerbation. The pediatrician plans to administer the vaccines recommended for 4-year-olds but has concerns about possible contraindications to live vaccines, including the measles, mumps, and rubella (MMR) and varicella vaccines. Which one of the following is best to recommend for this patient?
- A. Wait 1 month after completion of prednisone, then administer MMR and V vaccines separately.
 - B. Wait 1 month after completion of prednisone, then administer MMRV combination vaccine.
 - C. Administer MMR and varicella vaccines separately today.
 - D. Administer MMRV combination vaccine today.

Questions 5 and 6 pertain to the following case.

J.K. is a 34-year-old woman who is 30 weeks pregnant with her second child. She has gestational diabetes but no other significant medical history. Her husband, R.K., and 3-year-old son, A.L., accompany her to her clinic visit in October. R.K. is a 37-year-old man with a medical history of hypertension and hypercholesterolemia. A.L. is up to date with his vaccinations and has a history of egg allergy, but he can eat scrambled eggs. J.K. and R.K. currently live alone with their son, but R.K.'s mother (G.M.) will be moving in with them to help care for the child when it is born. G.M. is a 74-year-old woman with osteoarthritis, hypertension, heart failure, and chronic obstructive pulmonary disease.

5. The most recent tetanus-containing vaccine received by each of the family members is as follows: J.K. Tdap 9 years ago and 3 years ago; R.K. tetanus and diphtheria (Td) 4 years ago; G.M. Td 10 years ago; and A.L. diphtheria, tetanus, and pertussis (DTaP) 2 years ago. Which one of the following is best to recommend regarding who in this family should receive Tdap at this time?
- A. J.K., R.K., and G.M.
 - B. J.K. and G.M.
 - C. R.K. and G.M.
 - D. G.M. only.
6. Which one of the following is the most appropriate influenza vaccine for A.L. today, assuming all are readily available in the clinic?
- A. Inactivated influenza vaccine trivalent (IIV3)
 - B. Inactivated influenza vaccine quadrivalent (IIV4)
 - C. Live attenuated influenza vaccine (LAIV4)
 - D. Recombinant influenza vaccine trivalent (RIV3)

7. For which one of the following patients would it be best to withhold varicella vaccine?
 - A. A 2-year-old girl with asthma who received the MMR vaccine 14 days ago
 - B. A 4-year-old girl currently receiving amoxicillin/clavulanate for otitis media
 - C. A 6-year-old boy with chronic kidney disease and a glomerular filtration rate of 30 mL/minute/1.73 m²
 - D. A 12-year-old boy with HIV and a CD4⁺ count of 600 cells/mL (25%)
8. For community pharmacists in states that do not permit pharmacists to vaccinate pediatric patients, which one of the following strategies would have the most immediate effect on increasing vaccination coverage among their patients?
 - A. Organize a petition to lobby the state legislature to expand the age group of patients that pharmacists are allowed to vaccinate.
 - B. Evaluate each child's profile to evaluate which vaccines should be administered and communicate this information to the parent and pediatrician.
 - C. Place informational brochures about vaccine-preventable illnesses in every prescription bag that is dispensed from the pharmacy.
 - D. Play informational videos in the waiting area of the pharmacy with guidance on recommended immunization schedules.
9. An 18-month-old girl is brought to the clinic by her mother for a routine checkup in late September. You determine that the child is due for vaccination with hepatitis B vaccine (HepB), DTaP, inactivated polio vaccine (IPV), IIV, and hepatitis A vaccine (HepA). Which one of the following is best to administer to this patient today?
 - A. Pediarix (DTaP-IPV-HepB), IIV, and HepA vaccines
 - B. Kinrix (DTaP-IPV), IIV, and Twinrix (HepA-HepB) vaccines
 - C. Pediarix (DTaP-IPV-HepB) and HepA vaccines; advise the mother to return after November 1 for IIV
 - D. DTaP, IPV, HepB, IIV, and HepA vaccines
10. An outbreak of hepatitis A is reported in a local pizza shop related to a cook who was infected with the virus. A 7-year-old boy attended a birthday party and ate lunch at the restaurant 5 days ago. He is brought in by his mother, who requests postexposure prophylaxis. The boy has never received the HepA vaccine. Which one of the following recommendations is best for this patient?
 - A. Do not give postexposure prophylaxis.
 - B. Give immunoglobulin for hepatitis A and HepA vaccine.

- C. Give immunoglobulin for hepatitis A only.
- D. Give HepA vaccine only.

Questions 11 and 12 pertain to the following case.

B.B. is in the clinic for his 4-month-old checkup. The boy's medical history includes prematurity (born at 28 weeks) and a complex neonatal ICU (NICU) stay. Currently, B.B. is stable and has diagnoses of bronchopulmonary dysplasia (BPD) (on budesonide), gastroesophageal reflux disease (on lansoprazole), and developmental delay. B.B. received HepB at birth, but his mother refused 2-month vaccines during the NICU stay. The mother again refuses vaccines at this visit because she is concerned that receiving all the vaccines at once will overwhelm B.B.'s immune system and he will end up in the hospital.

11. Which one of the following approaches would best ensure B.B. receives all the recommended vaccines?
 - A. Provide his mother with educational materials and honor her vaccine refusal.
 - B. Recommend an alternative vaccine schedule so that he can receive vaccines over an extended period rather than all at once.
 - C. Administer DTaP and PCV13 because he is less likely to be protected from these diseases through herd immunity.
 - D. Educate the mother about her misconceptions and reinforce that it is safe and effective to give all the recommended vaccines at this visit.
12. If B.B.'s mother agrees to receive all vaccines today and future vaccines on schedule, which one of the following would be the best recommendation for when B.B. should return for catch-up vaccines and which vaccines should be given?
 - A. 8 weeks to receive DTaP, IPV, Hib, HepB, rotavirus vaccine (RV), and Prevnar
 - B. 4 weeks to receive DTaP, IPV, Hib, RV, and Prevnar and 8 weeks to receive HepB
 - C. 4 weeks to receive DTaP, IPV, Hib, HepB, and Prevnar
 - D. 4 weeks to receive DTaP, IPV, Hib, and Prevnar and 8 weeks to receive HepB
13. An infant girl was born at 24 weeks gestation; she is now aged 7 weeks and 5 days and is stable in the NICU. Her current diagnoses include BPD. She receives budesonide, chlorothiazide, and potassium chloride. Which one of the following is best to recommend regarding this patient's vaccines?
 - A. Hold all vaccines until she is corrected to full term.
 - B. Hold all vaccines until she is 2 months old.
 - C. Give DTaP, IPV, Hib, HepB, RV, and Prevnar.
 - D. Give DTaP, IPV, Hib, HepB, and Prevnar.

14. A 48-month-old boy with a history of febrile seizures is to receive DTaP-IPV, MMR, and varicella today. Which one of the following is best to recommend for this patient?

- A. Give prophylactic acetaminophen, and give MMRV combination.
- B. Give prophylactic acetaminophen, and give MMR and varicella as separate vaccinations.
- C. Do not give prophylactic acetaminophen, and give MMRV combination.
- D. Do not give prophylactic acetaminophen, and give MMR and varicella as separate vaccinations.

15. A 15-month-old girl received the MMRV vaccine 10 days ago. Two days ago, she developed a rash on her trunk that consists of five or six vesicular lesions. Her mother calls the clinic and asks if she should be concerned about infection and if they should take any precautions. Which one of the following is the best response to this inquiry?

- A. MMRV cannot cause infection, so the rash is likely an allergy. Give your daughter diphenhydramine, apply 1% hydrocortisone cream, and the infection should improve.
- B. The rash is likely a low-level infection caused by the weakened measles virus in the vaccine. No cases of disease transmission from a rash like this have been reported, so no extra precautions are needed.
- C. The rash is likely a low-level infection caused by the weakened varicella virus in the vaccine. No cases of disease transmission from a rash like this have been reported, so no extra precautions are needed.
- D. It is impossible to distinguish a non-contagious vaccine-induced rash from a true varicella infection. Keep her isolated from susceptible individuals until the vesicular lesions crust over.

16. A 4-year-old boy is in your clinic in late July for a routine checkup. His medical history is significant for asthma, which is controlled with montelukast and as-needed albuterol. He received rabies immune globulin and vaccine in early May after being exposed to a raccoon at the family cabin in the woods. His mother asks which vaccines he should receive today to prepare him for attending prekindergarten this fall. She states that he has kept on schedule with all of his routine vaccinations to date. His vaccine history shows the following:

HepB	0 months, 2 months, 6 months
RV	2 months, 4 months
DTaP	2 months, 4 months, 6 months, 15 months
Hib	2 months, 4 months, 6 months, 15 months

PCV13	2 months, 4 months, 6 months, 15 months
IPV	2 months, 4 months, 15 months
MMRV	15 months
HepA	15 months, 24 months

Which one of the following vaccines is best to recommend for this patient to receive today?

- A. DTaP, IPV, MMRV, PPSV23
- B. DTaP, IPV, MMRV
- C. DTaP, IPV, PPSV23
- D. DTaP, IPV

17. You wish to advocate for expansion of pharmacist authorization to administer vaccines in pediatric patients. In which one of the following age ranges would pharmacists be most likely to demonstrate the greatest effect on vaccination adherence rates?

- A. 0–18 months
- B. 19–35 months
- C. 4–6 years
- D. 13–17 years

18. A 4-year-old girl (DOB August 3, 2011) is about to start kindergarten. Her parents come to the office on September 8, 2015, because the school called to say that the girls can't attend until she receives her 4-year-old vaccines. The mother is irate and states that the girl already received them. The state law does not count vaccines valid if they are administered any earlier than the recommended minimum age or interval by the CDC schedule. A review of the patient's record shows the following:

10/4/11	Pediarix, Comvax, Prevnar, RV
12/8/11	Pediarix, Comvax, Prevnar, RV
2/6/12	Pediarix, Prevnar, RV
8/20/12	Prevnar, HepA, MMR, varicella
12/5/12	Hib, DTaP
8/8/13	HepA
8/1/15	Varicella, Kinrix
8/28/15	MMR

Which one of the following would best resolve this issue?

- A. Tell the parents that you will call the school and inform them the vaccines she received are still efficacious and she can return to school.
- B. Apologize to the parents and administer the Kinrix today, and follow school policy for filling out a temporary medical exemption for MMR.
- C. Apologize to the parents and administer the Kinrix today, and follow school policy for filling out a temporary medical exemption for Varicella.
- D. Apologize to the parents and administer the Kinrix today, and follow school policy for filling out a temporary medical exemption for MMR and varicella.

19. A 13-year-old boy who has no significant medical history and is not sexually active is in the clinic for an initial checkup. On questioning, the parents report that the child is up to date and was vaccinated by the previous pediatrician, but the office permanently closed, and the vaccination record is unavailable. The parents do not want to repeat vaccines and only consent to six vaccines being given at one time. Which one of the following vaccines would be best to administer to this patient today?
- A. Give Tdap, HPV, Menactra, HepB, MMR, and varicella.
 - B. Give Tdap, Menactra, HepB, HepA, IPV, and MMR.
 - C. Give Tdap, IPV, Menactra, HPV, Twinrix, and MMRV.
 - D. Give no vaccines and rely on the parents' history that he is up to date.
20. A 12-month-old boy is brought to the pharmacy by his parents. Eight hours earlier, the boy received his routine vaccines (Pevnar, HepA, MMR, and varicella). Now, his parents report that the child's temperature is 101°F and that he is sleeping more than usual. The parents also state that they think his arms hurt, because he whines when they touch his arms. Which one of the following is the best action to take for this patient?
- A. Report these adverse effects to VAERS and send the child to his physician for workup.
 - B. Report these adverse effects to VAERS and recommend ibuprofen or acetaminophen.
 - C. Do not report to VAERS and recommend ibuprofen or acetaminophen.
 - D. Do not report to VAERS and send the child to his physician for further workup.