Chapter 147: Vaccines and Immunoglobulins

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 52, Vaccines, Toxoids, & Other Immunobiologics.

KEY CONCEPTS

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1. Live vaccines may confer life-long immunity but cannot be administered to immunosuppressed patients.
2. Inactivated and subunit vaccines and toxoids often require multiple doses to protect from infection, and generally booster doses are needed following the primary series.
3. Children less than 2 years of age are unable to mount T-cell–independent immune responses that are elicited by polysaccharide vaccines.
4. Severely immunocompromised individuals should not receive live vaccines, and their responses to inactivated, polysaccharide, toxoid, and recombinant vaccines may be poor.
5. The childhood and adult immunization schedules are updated frequently and published annually. These documents can be used to develop an immunization plan.
6. Immunoglobulin (Ig) provides short-term, rapid postexposure protection from measles, hepatitis A, varicella, and other infections.
7. Ig adverse effects are often secondary to infusion rate. Slowing the IV infusion rate ameliorate chills, nausea, and fever that may develop during administration.
8. Rh_0(D) Ig prevents Rh-negative mothers from mounting an immune response against the Rh(D) antigen on the red blood cells of the fetus that results in hemolytic disease of the newborn.

BEYOND THE BOOK

Devise immunization recommendations for the below mentioned cases.

1. A 56-year-old male with newly diagnosed type 2 diabetes who has not received any vaccines in the past 12 years.
2. A 26-year-old patient who was fully immunized prior to kidney transplant 6 years ago.
3. A 52-year-old male who smokes a pack of cigarettes every day and has not received any vaccines as an adult.
4. A healthy 5 month old child who has not received any vaccines.

Use the immunization schedules found at https://www.cdc.gov/vaccines/schedules

INTRODUCTION

Immunization provides protection from infectious diseases. Immunity to an infectious agent can be acquired by exposure to the disease, by transfer of antibodies from mother to fetus, through administration of immunoglobulin (Ig), and from vaccination. Immunization is the process of introducing an antigen into the body to induce protection against the infectious agent without causing disease. An *antigen* is a substance that induces an immune response. An *antibody* produced by the humoral arm of the immune system usually is the response that is measured as evidence of successful vaccination. However, cellular immune responses, which are more difficult to measure, are also an important aspect of vaccine responses. This chapter introduces the clinical use of vaccines and immunoglobulins. Agents with a limited use, such as agents for bioterrorism or travel, are beyond the scope of this chapter.

PRODUCTS USED TO IMMUNIZE

[1][2][3] Vaccines induce active immunity—that is, immunity generated by a natural immunologic response to an antigen. Vaccines can be live-attenuated or inactivated. Inactivated vaccines may consist of whole or part of the pathogen that induces a protective immune response. Live-attenuated vaccines induce an immunologic response similar to that occurring with natural infection. Because the organisms in live-attenuated vaccines undergo limited replication in the vaccinated individual after administration, they may confer lifelong immunity with one dose (as does a natural infection). Viral vector vaccines are transfected with the gene for the antigen to which immunization is desired. The viral vector which can be further engineered to not replicate, is just the carrier for the gene. The viral vector enters the cell inducing an immune response to the target infection when the inserted gene is expressed during the course of the "infection." With an mRNA vaccine, the mRNA is protected by a liposome from degradation and facilitates its entry into cells, then uses cellular machinery to transcribe the mRNA. Following transcription, the antigen is expressed as a protein on the cell surface which initiates an immune response. Multiple doses of inactivated vaccines usually are needed to induce long-lasting, effective immunity. Additional doses at varying time intervals (booster doses) often are required to maintain immunity. Booster doses of such vaccines elicit memory responses from the B cells that produce immunoglobulin G (IgG). The immune system already has developed an array of antibodies to the antigen. Upon restimulation with a booster dose, the B cells, which produce the most specific antibodies against the antigen, are selected and maintained in the "immunologic memory." Thus, the booster dose results in a rapid, intense antibody response that is long-lasting. Inactivated vaccines can also differ in immunity potential, depending on their composition. For example, polysaccharide vaccines tend to be poorly immunogenic in infants, whereas protein–polysaccharide conjugated vaccines of the same antigen tend to be highly immunogenic (eg, pneumococcal polysaccharide vaccine vs pneumococcal conjugated vaccine). T-cell–independent immune response is made to polysaccharide antigens that stimulate B cells directly.[1] There is no maturation or booster response with a T-cell–independent immune response, and children younger than 2 years cannot make this type of response. Protein–polysaccharide conjugate vaccines stimulate T cells and promote interactions between T cells and B cells when producing the protective immune responses consisting of immunologic memory and high-affinity IgG. Toxoids are inactivated bacterial toxins that stimulate the production of antibodies against the bacterial toxins rather than the infecting bacterial pathogens.

Immunoglobulins (Igs) are sterile solutions containing antibody derived from human (Ig) sources. Igs are derived from donor pools of blood plasma and are processed using cold ethanol fractionation in order to inactivate known potential pathogens. These products are indicated for induction of passive immunity (temporary immunity to infection as a result of administration of antibodies not produced by the host; see other immunoglobulins

below).

In addition to the active component in a vaccine, other active and inert ingredients are often present. Some inactivated vaccines contain adjuvants which are chemicals that stimulate a strong, but short-lived inflammatory response which strengthens the immune response to the antigen. These adjuvants also increase local tissue irritation when injected. Suspending agents, such as water, saline, or complex fluids containing proteins (eg, albumin), are used as the vehicle for the vaccines. Preservatives, stabilizers, and antibiotics may be added to help maintain the integrity of the product. Immunized individuals may respond with allergic reactions not to the agent itself but to the other components of the pharmaceutical preparation. Different manufacturers of the vaccines have different active and inert ingredients or different quantities of these ingredients in their products.

Some vaccines manufactured by different companies are considered interchangeable. Hepatitis A, hepatitis B, and *Haemophilus influenzae* type b (Hib) conjugate vaccines from different manufacturers used for the primary series of three doses are considered interchangeable. It is preferable to use diphtheria, tetanus toxoids, and acellular pertussis (DTaP) vaccine from the same manufacturer to complete the entire primary series. However, immunization should not be delayed if the particular type of vaccine administered for the initial doses cannot be ascertained easily or the vaccine provider does not have the product available.[1]

FACTORS AFFECTING RESPONSE TO IMMUNIZATION

Various factors are known to affect response to vaccines. Viability of the live antigen is an important factor as discussed previously. Total dose also is important because there seems to exist a threshold dose above which no further increase in immune response is seen. The interval between immunization doses, number of doses given, or both may change immune response to an agent. Among hepatitis B vaccine nonresponders, a significant proportion of individuals mount a vaccine response when given additional doses of vaccine.[2] In contrast, additional doses of influenza vaccine are minimally effective in individuals with chronic illness.[3] Generally, intervals longer than those recommended between vaccine doses do not affect immune response.[1]

The route and site of administration of the immunobiologic are important. This is best illustrated by the hepatitis B vaccine, which elicits a satisfactory antibody response when given in the deltoid muscle but not a consistent response when administered in the gluteal area. Injections should be administered at a site with little likelihood of site damage. Vaccines containing adjuvants should be given into a muscle mass because they can cause irritation when given subcutaneously or intradermally.[1]

Host factors influence vaccine response. Immunocompromise, increasing age, underlying disease, and genetic background have been associated with poor response rates.[1–6]

VACCINE ADMINISTRATION

Subcutaneous injections should be administered into the thigh of infants and in the upper arm area over the triceps of older children and adults. A ⅝-in., 25-gauge needle (0.508 mm × 1.6 cm) should be used, taking care not to administer the dose intradermally or intramuscularly (IM). For IM injection, the anterolateral aspect of the upper thigh (infants and toddlers) or the deltoid muscle of the upper arm (children and adults) should be used. Appropriate needle size and length are important to both vaccine immune response and safety (Table 147-1). The buttock should not be used because of the potential for inadequate immunologic response and the potential risk of injury to the sciatic nerve. When the buttock must be used (as for large doses of Ig), only the upper outer quadrant should be used with the needle inserted anteriorly.

The rotavirus vaccines are administered orally. The tube of vaccine should be squeezed inside the infant's mouth toward the inner cheek until the dosing tube is empty. If the infant regurgitates or spits out the vaccine, readministration is not recommended.[7]

TABLE 147-1

Needle Length and Injection Site for Intramuscular Vaccine Administration

Age Group	Needle Length	Injection Site
Neonates (0-28 days)	5/8 in. (16 mm)[a]	Anterolateral thigh
Infants (1-12 months)	1 in. (25 mm)	Anterolateral thigh
Toddlers (1-2 years)	1-1.25 in. (25-32 mm)	Anterolateral thigh[b]
	5/8-1 in. (16-25 mm)	Deltoid muscle
Children (3-10 years)	5/8-1 in. (16-25 mm)	Deltoid muscle[b]
	1-1.25 in. (25-32 mm)	Anterolateral thigh
Children (11-18 years)	5/8-1 in. (16-25 mm)	Deltoid muscle[b]
	1-1.5 in. (25-38 mm)	Anterolateral thigh
Adults (>19 years)		
Men and women <60 kg (130 lb)	1 in. (25 mm)[c]	Deltoid muscle
Men 70-118 kg (152-260 lb)	1-1.5 in. (25-38 mm)	Deltoid muscle
Women 70-90 kg (152-200 lb)		
Men >118 kg (260 lb)	1.5 in. (38 mm)	Deltoid muscle
Women >90 kg (200 lb)		

[a]Skin should be stretched without bunching of subcutaneous tissue.

[b]This table is not intended for determining the correct indications and dosages for using antibody-containing products. Unvaccinated persons might not be fully protected against measles during the entire recommended interval, and additional doses of Ig or measles vaccine might be indicated after measles exposure. Concentrations of measles antibody in an Ig preparation can vary by manufacturer's lot. Rates of antibody clearance after receipt of an Ig preparation also might vary. Recommended intervals are extrapolated from an estimated half-life of 30 days for passively acquired antibody and an observed interference with the immune response to measles vaccine for 5 months after a dose of 80 mg IgG/kg.

[c]Some experts recommend 5/8 in. (16 mm) needle, but skin must be stretched without bunching of subcutaneous tissue.

Adapted from Kroger A, Bahta L, Hunter P. General Best Practice Guidelines for Immunization. Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP).

Live-attenuated influenza vaccine is administered intranasally.[3] A specially designed sprayer is inserted just inside the nostril, and the dose is sprayed by rapidly depressing the plunger of the sprayer. The clip is removed from the plunger so that the second half of the dose can be administered into the other nostril. The vaccinated individual should breathe normally. The dose does not need to be repeated if the individual sneezes during or shortly after administration.

Questions often arise concerning the simultaneous administration of vaccines. In general, inactivated and live-attenuated vaccines can be administered simultaneously at separate sites. If two or more inactivated vaccines cannot be administered simultaneously, they can be administered without regard to spacing between doses. Inactivated and live vaccines can be administered simultaneously or, if they cannot be administered simultaneously, at any interval between doses. If live vaccines are not administered simultaneously, their administration should be separated by at least 4 weeks. Live viral vaccines may interfere with purified protein derivative response; thus, tuberculin testing should be postponed for 4 to 6 weeks after administration of live-virus vaccine.[1]

Simultaneous administration of Ig and live-attenuated vaccines may interfere with host antibody response. A dose relationship exists between administration of Ig and inhibition of immune response to a vaccine (Table 147-2). Whole blood and other blood products containing antibodies may interfere with the response to the measles, mumps, rubella, and varicella vaccines. In any individual, if vaccination with MMR or varicella is followed by emergency Ig administration, the vaccine can be repeated or seroconversion to viral antigens can be confirmed after sufficient time has elapsed (see Table 147-2). Ig does not interfere with the response to oral vaccines. Inactivated vaccines and Igs may be administered simultaneously using separate anatomical sites.[1]

TABLE 147-2

Recommended Intervals Between Administration of Immunoglobulin and Measles- or Varicella-Containing Vaccine[a]

Product/Indication	Dose, Including mg Immunoglobulin G(IgG)/kg Body Weight	Recommended Interval before Measles or Varicella-containing[b] Vaccine Administration
RSV monoclonal antibody (Synagis®)[c]	15 mg/kg IM	None
TIG	250 units (10 mg IgG/kg) IM	3 months
Hepatitis A Ig		
Contact prophylaxis	0.02 mL/kg (3.3 mg IgG/kg) IM	3 months
International travel	0.06 mL/kg (10 mg IgG/kg) IM	3 months
HBIG	0.06 mL/kg (10 mg IgG/kg) IM	3 months
RIG	20 IU/kg (22 mg IgG/kg) IM	4 months
Measles prophylaxis Ig		
Standard (ie, nonimmunocompromised) contact	0.5 mL/kg (40 mg IgG/kg) IM	6 months
Blood transfusion		
RBCs, washed	10 mL/kg negligible IgG/kg IV	None
RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	3 months

Packed RBCs (Hct 65%) [0.65][d]	10 mL/kg (60 mg IgG/kg) IV	6 months
Whole blood (Hct 35%-50%) (0.35-0.50)[d]	10 mL/kg (80-100 mg IgG/kg) IV	6 months
Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	7 months
Cytomegalovirus IV immunoglobulin (IGIV)	150 mg/kg maximum	6 months
IVIG		
Replacement therapy for immune deficiencies[e]	300-400 mg/kg Iv[d]	8 months
Immune thrombocytopenic purpura treatment	400 mg/kg IV	8 months
Immune thrombocytopenic purpura treatment	1 g/kg IV	10 months
Postexposure varicella prophylaxis[f]	400 mg/kg IV	8 months
Varicella Ig	125 units/kg (60-200 mg IgG/kg) IM maximum 625 units	5 months

HBIG, hepatitis B Ig; RBCs, red blood cells; RIg, rabies Ig; TIG, tetanus Ig.

[a]This table is not intended for determining the correct indications and dosages for using antibody-containing products. Unvaccinated persons might not be fully protected against measles during the entire recommended interval, and additional doses of Ig or measles vaccine might be indicated after measles exposure. Concentrations of measles antibody in an Ig preparation can vary by manufacturer's lot. Rates of antibody clearance after receipt of an Ig preparation also might vary. Recommended intervals are extrapolated from an estimated half-life of 30 days for passively acquired antibody and an observed interference with the immune response to measles vaccine for 5 months after a dose of 80 mg IgG/kg.

[b]Varicella-containing vaccine, as used here, does not include zoster vaccine. Zoster vaccine may be given without regard to antibody-containing blood products.

[c]Contains antibody only to respiratory syncytial virus (RSV).

[d]Assumes a serum IgG concentration of 16 mg/mL (g/L).

[e]Measles and varicella vaccinations are recommended for children with asymptomatic or mildly symptomatic human immunodeficiency virus (HIV) infection but are contraindicated for persons with severe immunosuppression from HIV or any other immunosuppressive disorder.

VACCINE STORAGE

Appropriate storage is critical to maintaining the integrity of vaccines. Refrigerator temperature is defined as between 2°C and 8°C (36°F to 46°F) and freezer temperature as 50°C (–58°F) to –15°C (5°F). Inactivated vaccines are stored refrigerated. Varicella and COVID-19 (Moderna) vaccine must be stored frozen. MMR vaccine can be stored in either the freezer or refrigerator. The Pfizer COVID-19 vaccine requires ultra-cold temperatures (–80°C to –60°C; –112°F to –76°F) for long-term storage. Live-attenuated influenza vaccine is stored in the refrigerator. Specific storage conditions for individual vaccines can be found in the package insert.

IMMUNIZATION OF SPECIAL POPULATIONS

Groups of individuals may have precautions to vaccines. Many precautions are temporary, and vaccines can be administered later.

Infants

The age of the recipient is an important determining factor in vaccine response. In the first few months of life, passively transferred maternal antibodies acquired during the third trimester of gestation protect an infant. However, the maternal antibodies also inhibit the immune response to live vaccines because the circulating antibodies neutralize the vaccine before the infant has the opportunity to mount an immune response. For this reason, MMR and varicella vaccines are not administered until maternal antibodies have waned, generally by infant age 12 months.

Premature infants should be vaccinated at the same chronologic age using the same schedule and precautions for full-term infants. The full recommended doses of vaccines should be used, regardless of age or birth weight. Breastfed infants should be vaccinated according to standard pediatric schedules.

Pregnant Females and Postpartum Immunization

The benefit of most vaccines outweighs the risk for administration to those who are pregnant. As with most drugs, a lack of information regarding risks to the fetus exists rather than any actual known risk.[1] For example, no cases of congenital rubella syndrome from inadvertent administration of rubella vaccine to a pregnant person have ever been reported. Universal influenza immunization is recommended for individuals who will be or are pregnant during influenza season. Tdap should be administered during the late second trimester or third trimester of pregnancy.[8] Although live vaccines generally are avoided because of the theoretical risk of transmission of the vaccine organism to the fetus, inactivated vaccines may be administered when the benefits outweigh the risks.[1] Insufficient evidence is available for the human papillomavirus (HPV) series during pregnancy, so it should be deferred.[1]

Administration of live vaccines, such as rubella or varicella, is deferred until pregnancy is completed and is routinely recommended for those who do not have evidence of immunity prior to hospital discharge. These live vaccines can be administered without regard to administration of Rh_o(D) Ig in the postpartum period. Additionally, Tdap is recommended for all new mothers who have not received a Tdap before because household contacts are frequently implicated as the source of pertussis infection in a young infant.[8]

Immunocompromised Hosts

4 Immunization of individuals with chronic disease, such as immunocompromise, diabetes or connective tissue disease, alcoholism, or those with cancer or HIV disease, must be individualized based on the disease state and its treatment. In general, severely immunocompromised individuals should not receive live vaccines. Administration of other vaccines may be indicated, but responses may be lower than those mounted by healthy individuals, but may still confer protection.[4]

Patients with chronic pulmonary, renal, hepatic, or metabolic disease who are not receiving immunosuppressants can receive both live-attenuated and killed vaccines and toxoids. Generally, immunization should be considered early in the course of the disease in an attempt to induce immunity at a point when the disease is less severe.

Patients with active malignant disease can receive killed vaccines or toxoids but should not be given live vaccines. The MMR vaccine is not

contraindicated for close contacts, however. Live-virus vaccines can be administered to persons with leukemia who have not received chemotherapy for at least 3 months. Vaccines should be timed so that they do not coincide with the start of chemotherapy or radiation therapy.[3] Annual influenza vaccine should be administered 2 weeks prior to chemotherapy or between cycles.[3] If vaccines cannot be given at least 2 weeks before the start of these therapies, immunization should be postponed until 3 months after the therapy has been completed. Passive immunization with Ig can be used in place of active immunization regardless of the history of immunization.

Glucocorticoids may cause suppressed responses to vaccines. For the purposes of immunization, the immunosuppressing dose of corticosteroids is prednisone 20 mg or more daily or 2 mg/kg daily, or an equivalent dose of another steroid, for at least 2 weeks. Patients receiving long-term, alternate-day steroid therapy with short-acting agents, administration of maintenance physiologic doses of steroids (eg, 5-10 mg/day of prednisone) topical, aerosol, intra-articular, bursal, or tendon steroid injections require no special consideration for immunization. If patients have been receiving high-dose corticosteroids or have had a course lasting longer than 2 weeks, then at least 1 month should pass before immunization with live-virus vaccines.[1]

Patients with HIV infection may have suboptimal immune responses to live and inactivated vaccines. The routinely recommended vaccines should be administered to children. MMR should be administered to anyone older than 12 months of age without evidence of immunity and who are not severely immunocompromised (CD4% greater than 15% [or CD4 fraction >0.15] and CD4 count greater than 200 lymphocytes/mm^3 [0.2×10^9/L] for at least 6 months) and repeat MMR series should be considered if vaccinated prior to initiation of combination antiretroviral therapy.[9] Two doses of varicella vaccine separated by 3 months are recommended for those with no evidence of immunosuppression. Adults should receive routinely recommended vaccines. Zoster vaccine may be administered to individuals with HIV infection who do not have clinical manifestations of AIDS and have CD4 counts greater than 200/mm^3 (0.2×10^9/L).[1]

Solid Organ Transplant Patients

Organ transplantation has become routine treatment of end-stage organ disease of many causes. Solid organ transplant patients remain on immunosuppressive regimens for the rest of their lives. These immunosuppressive regimens result in a higher risk of infection and decrease the protection conferred by immunization.[10]

Whenever possible, transplant patients should be immunized prior to transplantation. Live vaccines generally are not given after transplantation. Posttransplantation diphtheria, tetanus, pneumococcal, and influenza vaccine responses are unpredictable. Decreased immune response has been documented following hepatitis B vaccine series.

Patients with Hematopoietic Stem Cell Transplant

Patients with hematopoietic stem cell transplantation receive therapy that almost eliminates hematopoietic cells and may require immunosuppressive medications post-transplant for graft-versus-host disease. Therefore, reimmunization with inactivated vaccines should begin approximately 6 months after hematopoietic stem cell transplantation. Annual influenza immunization may begin as soon as 6 months after successful engraftment. Hematopoietic stem cell transplant recipients are at increased risk for fulminant infection with encapsulated bacteria, so pneumococcal vaccines, meningococcal vaccines, and Hib vaccines are recommended. MMR and varicella vaccines can be administered at 24 months. Immunization of household contacts and healthcare workers also is necessary.[1,11]

CONTRAINDICATIONS AND PRECAUTIONS

There are few contraindications to the use of vaccines except those outlined earlier. The contraindications include a history of anaphylactic reactions to the vaccine or a component of the vaccine. Unexplained encephalopathy occurring within 7 days of a dose of pertussis vaccine is a contraindication to future doses of pertussis vaccines. Immunosuppression and pregnancy are temporary contraindications to live vaccines. An interval of time must elapse based on the dose of Ig before a live vaccine can be administered (see Table 147-2). A personal or family history of seizures is a precaution for receiving the combination MMR–varicella (MMRV) vaccine. Immunizers should use MMR and varicella vaccines separately.[1] Generally, mild-to-moderate local reactions, mild acute illnesses, concurrent antibiotic use, prematurity, family history of adverse events, diarrhea, and lactation or breastfeeding are not contraindications to immunization.

OBTAINING AN IMMUNIZATION HISTORY

An immunization history should be obtained from every patient, regardless of the reason for the healthcare visit. State-based or other public health jurisdiction-based immunization information systems, also called immunization registries, have been developed to improve immunization coverage by allowing healthcare providers access to records at any contact with the healthcare system. If an official written record is not available, patient characteristics (eg, military service, travel history, and occupation) may provide clues to the immunization history. Serologic testing for immunity has a limited role in documenting immunization history but is done in selected circumstances (eg, employment in a healthcare facility). If a written record does not exist, one should be generated at the time of initiation of immunization. Patients without a written record should be considered susceptible, and an immunization program started and completed unless a serious adverse reaction occurs. As a general rule, the risks associated with overimmunization are minimal relative to the risks associated with contracting vaccine-preventable diseases.[1]

Every healthcare visit, regardless of its purpose, should be viewed as an opportunity to review a patient's immunization status and to administer needed vaccines. Immunization is perhaps the most cost-effective health intervention available. Each visit should include assessment of individuals' vaccine needs, administration of indicated vaccines, and documentation of immunization histories. The outcome measurement of what percentage of patients in a particular practice site is completely immunized is extremely important because the benefits of optimal vaccine use extend beyond the individual patient to the public as a whole.

VACCINE SAFETY

The United States has a robust vaccine safety monitoring system. Healthcare providers must report all events requiring medical attention within 30 days of vaccination to the Vaccine Adverse Event Reporting System (VAERS), which serves as a central depot for vaccine-related adverse effects. Only a temporal association between the adverse event and vaccine administration is required. No adverse event rates can be determined because only the number of adverse events reported is known; the number of vaccines administered is not known. This database can be used to survey for changes in the frequencies of adverse events, to evaluate risk factors for adverse events, and to find rare adverse events.[11] VAERS reports can be made online at https://vaers.hhs.gov/reportevent.html. In addition to VAERS, the Vaccine Safety Datalink connects the Centers for Disease Control and Prevention (CDC) and large healthcare systems to actively monitor vaccine safety, and the Clinical Immunization Safety Assessment Project is a partnership between the CDC and academic medical centers to provide expert consultation and conduct research on vaccine safety.[13] The Institute of Medicine is an independent body that studies and reports on vaccine safety.[14]

The National Childhood Vaccine Injury Act of 1986 offers a no-fault alternative means to compensate individuals for injury following vaccination. The program offers liability protection to manufacturers and an efficient means of recovering damages for individuals potentially injured by vaccines. The types of vaccine-related injuries that are considered for compensation are outlined in the Health Resources and Services Administration's Vaccine Injury table (https://vaers.hhs.gov/docs/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf).

USE OF VACCINES

The Advisory Committee on Immunization Practices (ACIP) is composed of medical and public health experts who make recommendations for vaccine use.[15] They consider burden of disease, vaccine efficacy and safety, and cost effectiveness of vaccines. Other professional organizations, for example, the American Academy of Pediatrics, the American Academy of Family Physicians, or the American College of Obstetrics and Gynecology, publish guidelines. Usually, these guidelines are the same as those issued by the ACIP or the groups try to reconcile their recommendations.

5 The latest vaccine schedules can be found at https://www.cdc.gov/vaccines/schedules/hcp/index.html. All states require children to be fully immunized prior to entering elementary school; however, optimal protection is achieved by immunizing at the recommended ages, which requires special attention to children younger than 2 years. Adults and adolescents also require vaccination and often are unaware of this need. An early adolescent preventive health visit at age 11 to 12 years is recommended. This visit is an opportunity to catch up on missed immunizations and to administer meningococcal conjugate, Tdap, and HPV vaccines. Additionally, another visit at age 16 is recommended during which time the second meningococcal conjugate vaccine can be administered and a discussion regarding the need for meningococcal serogroup B vaccine series can occur. All individuals older than 6 months of age should receive an annual seasonal influenza vaccine. Adults should receive routine tetanus–diphtheria (Td) or Tdap boosters and be immune to MMRV by either immunization or history of infection. Adults need zoster vaccine after age 50 years, and

pneumococcal vaccines after age 65 years. Certain individuals with conditions or lifestyles that put them at high risk for vaccine-preventable diseases also should be immunized as described in the following text and outlined in the immunization schedules in the appendices.

VACCINES

Diphtheria Toxoid Adsorbed

Diphtheria is an acute illness caused by the toxin released by a *Corynebacterium diphtheriae* infection. The toxin inhibits cellular protein synthesis, and membranes form on mucosal surfaces. Systemic toxemia can result in myocarditis, neuritis, and thrombocytopenia. Membrane formation can cause respiratory obstruction, and significant toxin absorption can lead to severe illness and death.

Diphtheria toxoid adsorbed is a sterile suspension of modified toxins of *C. diphtheriae* that induces immunity against the exotoxin of this organism. Two strengths of diphtheria toxoid are available in the United States: pediatric strength (D) and adult strength (d), which contains less antigen. The widespread use of diphtheria toxoid essentially has eliminated diphtheria from the United States.

Primary immunization with diphtheria toxoid (D) is indicated for children older than 6 weeks. The toxoid is given in combination with tetanus toxoid and acellular pertussis vaccine (as DTaP or in combination with additional childhood vaccines that have been licensed to decrease the number of injections required to complete the childhood immunization recommendations) at age 2, 4, and 6 months. Additional doses are given at age 15 to 18 months and again at age 4 to 6 years.[8] Booster doses should be given every 10 years.

For unimmunized adults, a complete three-dose series of diphtheria toxoid should be administered, with the first two doses given at least 4 weeks apart and the third dose given 6 to 12 months after the second. One of the vaccine doses in this series should be Tdap. The combined Td preparation is used for adults because it contains less diphtheria toxoid than the pediatric dose and is associated with fewer reactions to the diphtheria component. All adults should receive booster doses of Td or Tdap every 10 years.[8] Adverse effects of diphtheria toxoid include mild-to-moderate tenderness, erythema, and induration at the injection site. Systemic reactions occur rarely.

Haemophilus Influenzae Type b Vaccines

Before 1995, Hib was responsible for thousands of cases of serious illnesses (eg, meningitis, epiglottitis, pneumonia, sepsis, and septic arthritis). The incidence of Hib disease has declined more than 99% since the introduction of the conjugate vaccines based on the organism's capsular substance, polyribosylribitol phosphate (PRP).[16]

Hib conjugate vaccines are indicated for routine use in all infants and children younger than 5 years. Multiple products in various combinations are available for use in infants and children of different ages. The primary series of Hib vaccination consists of a 0.5-mL IM dose at ages 2, 4, and 6 months. The series should not be initiated in an infant younger than 6 weeks. Although use of one product for the entire primary series is desirable, adequate protection is achieved even when different products are used during the initial series. Following the primary series, a booster dose is recommended at age 12 to 15 months. Any of the Hib conjugate vaccines are suitable for the booster dose regardless of which conjugate was used for the primary series of doses.[16]

Schedules are more complex for infants who do not begin Hib immunization at the recommended age or who have fallen behind in the immunization schedule. For infants 7 to 11 months of age who have not been vaccinated, three doses of Hib vaccine should be given: two doses spaced 4 weeks apart and then a booster dose at age 12 to 15 months (but at least 8 weeks since the second dose). For unvaccinated children ages 12 to 14 months, two doses should be given, with an interval of 2 months between doses. In a child older than 15 months, a single dose of any of the vaccine preparations is indicated.[16]

Vaccines for Hib are recommended for routine use only for children up to age 59 months; beyond this age, the incidence of invasive Hib disease is low. Patients with certain underlying conditions (eg, children with HIV infection, sickle cell disease, splenectomy, and hematopoietic stem cell transplants and young children receiving chemotherapy for malignancies) are at higher than normal risk for Hib infection, and use of at least one dose of vaccine in these patients should be considered.[16] Adverse reactions to the Hib vaccine are uncommon. Erythema and induration at the injection site occur in approximately 5% to 30% of children and resolve within 12 to 24 hours. Fever, diarrhea, and vomiting are reported occasionally.[16]

Hepatitis Vaccines

Information on vaccination for viral hepatitis is given in Chapter 58.

Human Papillomavirus Vaccine

HPV infections are the most common sexually transmitted infections, with the highest prevalence of infection in sexually active young adults. Although more than 120 different HPV types have been identified, at least 40 different types of HPV infect the anogenital tract. These 40 different viruses are grouped into low-risk and high-risk types. Low-risk types can cause genital warts and mild abnormalities on Papanicolaou (Pap) tests. Ninety percent of all cases of genital warts and the majority of respiratory papillomatosis are caused by types 6 and 11. As many as 18 types are considered high risk as they have the ability to penetrate the nucleus of an epithelial cell to transform it to a precancerous cell. They cause abnormal Pap test results and may lead to cancer of the cervix, vulva, vagina, anus, penis, or oropharynx. Types 16 and 18 cause about 70% of all cervical cancers. Another 10% of HPV-related cancers are caused by types 31, 33, 45, 52, and 58. Men who have sex with men (MSM) are at a higher risk for infection with HPV, genital warts, and anal cancer.[17] The incidence of cancers associated with HPV is higher among MSM, and the rate of anal cancer among MSM continues to rise. High-risk HPV infections are necessary but not sufficient for the development of cervical cancer and for the majority of other anogenital and oral squamous cell cancers.

A 9-valent HPV vaccine against types 6 and 11 and 16, 18, 31, 33, 45, 52, and 58 is licensed for the prevention of HPV. ACIP recommends HPV vaccine for the prevention of HPV-related disease in individuals aged 9 to 26 years. Individuals who start the HPV series between the ages of 9 and 14 years should receive two doses separated by 6 months. This vaccine is administered as a three-dose series using a schedule of 0, 1 to 2, and 6 months for individuals who start the series at age 15 years or older. The vaccines are recommended for adolescents aged 11 to 12 years and catch-up immunization for individuals aged 13 to 26 years. The ACIP recommended shared clinical decision making for HPV vaccine for individuals aged 27 to 45 years.[17]

The vaccine is well tolerated, with injection-site reactions and systemic reactions (eg, headache and fatigue) occurring as commonly in immunized individuals as in the groups receiving placebo. Although syncope is possible with any immunization, the target population of adolescents and young adults has a higher incidence of syncope, including with administration of the HPV vaccine.[17]

Influenza Virus Vaccine

Information on vaccination for influenza is given in Chapter 131.

Measles Vaccine

Measles (rubeola) is a highly contagious viral illness characterized by rash and high fever. Complications of measles infections include severe diarrhea, otitis media, pneumonia, and encephalitis. Measles results in one to two deaths per 1,000 cases, with a much higher death rate in developing countries. With widespread vaccination, measles has been eliminated from the Western Hemisphere.

The measles vaccine is a live-attenuated viral vaccine that produces a subclinical, noncommunicable infection. Approximately 95% of vaccine recipients mount a protective immune response after a single dose, and most individuals are protected for life.[9] Most persons who do not respond to the first dose of measles vaccine will respond after receiving a second dose, and this forms the basis for the two-dose vaccine strategy that was implemented in the United States in 1989.

The measles vaccine is administered subcutaneously as a 0.5-mL dose in the arm (or in the thigh if the patient is younger than 15 months). The vaccine is administered routinely for primary immunization to persons 12 to 15 months of age. Two combinations of measles containing vaccines are available: measles, mumps, rubella (MMR) or measles, mumps, rubella, varicella (MMRV). The measles vaccine is not administered earlier than 12 months (except in certain outbreak circumstances or for travel) because persisting maternal antibody that was acquired transplacentally late in gestation can neutralize the vaccine virus before the vaccinated person can mount an immune response. A second dose of measles-containing vaccine is recommended when children are 4 to 6 years old.[9] The second dose of vaccine results in response in up to 99% of individuals.

Measles-containing vaccine should not be given to pregnant females or immunosuppressed individuals. An exception is HIV-infected patients, who are at high risk for severe complications if they develop measles. Adults with HIV infection who have no evidence of measles immunity should be

immunized as long as they are not severely immunocompromised (CD4 greater than 200 lymphocytes/mm^3 [0.2 × 10^9/L] for at least 6 months). The second dose should be given 1 month later.[8] Children with HIV who are not severely immunocompromised can be immunized according to the childhood immunization schedule at 12 months and 4 to 6 years of age.[9]

Administration of Ig interferes with measles vaccine response, so the recommended interval between the Ig and vaccine is determined by the dose of Ig (see Table 147-2).[1] Live vaccines not administered during the same visit must be delayed for at least 4 weeks following measles or MMR vaccine.[1]

Measles vaccine is indicated in all persons born after 1956 or in those who lack documentation of wild-virus infection by either history or antibody titers. Two doses of a measles-containing vaccine separated by at least one month are required for children, college students, and healthcare workers who were born in 1957 or later.[9]

The measles vaccine has an excellent safety record. The most common side effect following vaccination is fever, which occurs in 5% to 15% of vaccinees. Transient generalized rash may occur in approximately 5% of vaccine recipients. These reactions generally appear 5 to 12 days postvaccination and last 2 to 5 days. Other adverse effects, such as headache, cough, sore throat, eye pain, malaise, and transient thrombocytopenia, occur less frequently.[9]

Meningococcal Vaccines

N. meningitidis is a leading cause of meningitis and sepsis in children and young adults in the United States. Five serotypes, A, B, C, W-135, and Y, cause almost all infections in humans. The infection is transmitted by respiratory droplets from infected individuals and asymptomatic carriers. Symptoms include severe headache, sensitivity to light, stiff neck, nausea and vomiting, and high fever. Mortality occurs in 24 to 48 hours following onset of symptoms in 10% to 13% of infected individuals.[18] Immunization is recommended for high-risk populations, such as those exposed to the infection, those in the midst of uncontrolled outbreaks, travelers to areas with epidemic or hyperendemic meningococcal disease, and individuals who have terminal complement component deficiencies or asplenia.

MenACWY Conjugate

Two meningococcal (MenACWY) conjugate vaccines combining the same serotypes are licensed for use in individuals aged 9 months to 55 years old (Menactra®, Sanofi-Pasteur) or 2 months to 55 years old (Menveo®, Novartis).

The meningococcal conjugate vaccine is recommended for adolescents at ages 11 to 12 years with a second dose at age 16 years. Reimmunization at 5-year interval is recommended for individuals who are at high risk.[18]

Injection-site reactions are the most common adverse effects following administration of either the meningococcal conjugate or polysaccharide vaccine.

MenB vaccines

Meningococcal serogroup B (MenB) vaccines use recombinant antigens from the bacterial capsule, specifically factor H binding protein, Neisseria adhesin A, neisserial heparin binding antigen, and outer membrane vesicles. The ACIP recommends either of the two MenB vaccines, Trumenba® or Bexsero®, for individuals at high risk for invasive meningococcal disease.[17] Additionally, MenB vaccine use should be considered through shared clinical decision-making for adolescents and young adults. Trumenba® requires two or three dose series administered at 0 and 6 months or 0, 2, and 6 month intervals. (The three-dose series should be used for high-risk individuals and during an outbreak.) Bexsero® requires two doses with at least one month between doses. Both vaccines were licensed based upon antibody response studies.[18] The most common adverse events after MenB vaccines are pain at the injection site, fatigue, headache, myalgia, and chills.

Mumps Vaccine

Mumps is a viral illness that classically causes bilateral parotitis 16 to 18 days after exposure. Fever, headache, malaise, myalgia, and anorexia may precede the parotitis. Serious complications are rare but more common in adults.

The mumps vaccine is a live-attenuated vaccine. The vaccine is available in combinations with measles, rubella (as MMR), and varicella (MMRV) vaccines.

The vaccine is administered as a 0.5-mL subcutaneous injection in the upper arm. Dosing recommendations coincide with those for measles vaccine, with the first dose administered at age 12 to 15 months and the second dose prior to the child's entry into elementary school. Two doses of mumps-containing vaccine are recommended for school-aged children, international travelers, students in post–high school educational institutions, and healthcare workers born after 1956.[9] A single dose of vaccine is acceptable documentation of immunity to mumps for other adults considered at lower risk of mumps infection, including adults born after 1956 and those with an uncertain history of wild-virus infection. Mumps vaccine should not be given to pregnant women or immunosuppressed patients.[1] A third dose of mumps vaccine should be considered for individuals at risk for infection during an outbreak.[19]

Serious adverse reactions to the vaccine are reported rarely. Fever, parotitis, rash, and lymphadenopathy occur rarely. Local reactions, including soreness, burning, and stinging, may occur at the injection site.[9]

Pertussis Vaccine

Pertussis is caused by a bacterial infection with *Bordetella pertussis*. The infection starts with signs and symptoms of an acute respiratory infection, called the catarrhal stage. The coughing spells manifest about a week later. Typically, young children will have the characteristic whoop as they struggle to inhale while coughing. Adolescents and adults are more likely to have prolonged periods of coughing. Pertussis can affect any age group, but young infants are at much higher risk for pneumonia, seizures, brain damage, and death. Their rate of hospitalization is much higher than for other age groups. The individual is contagious during the catarrhal stage and the first 2 weeks of the cough.[8]

Acellular pertussis vaccines contain components of the *B. pertussis* organism. All acellular vaccines contain pertussis toxin, and some contain one or more additional bacterial components (eg, filamentous hemagglutinin, pertactin, and fimbriae types 2 and 3). Acellular pertussis vaccine is recommended for all doses of the pertussis schedule at 2, 4, 6, and 15 to 18 months of age. A fifth dose of pertussis vaccine is given to children 4 to 6 years of age.[20] Pertussis vaccine is administered in combination with diphtheria and tetanus (DTaP). Administration of an acellular pertussis-containing vaccine (Tdap) is also recommended for adolescents once between ages 11 and 18 years and a single dose of Tdap should be administered to all adults.[19] Additional doses of acellular pertussis-containing vaccine for adults are acceptable, as the ACIP considers Td and Tdap interchangeable.[20] Special attention is warranted for the immunization of individuals who have close contact with young infants. Tdap should be administered to pregnant individuals in their late second or third trimester of pregnancy. Tdap should also be administered to all close contacts, including household contacts and out of home care providers.[8]

Local administration site reactions are relatively common. Systemic reactions, such as moderate fever, occur in 3% to 5% of vaccinees. Rarely, high fever, febrile seizures, persistent crying spells, and hypotonic hyporesponsive episodes occur following vaccination. Encephalopathy without known cause within 7 days of a pertussis vaccine are contraindications to future doses of this vaccine.[1]

Pneumococcal Vaccines

Streptococcus pneumoniae is a common pathogen with a range of manifestations, including asymptomatic upper respiratory tract colonization, sinusitis, acute otitis media, pharyngitis, pneumonia, meningitis, and bacteremia. Rates of invasive infections are highest in children younger than 2 years and in the elderly.[21,22] The majority of invasive pneumococcal infection deaths occur in the elderly or in those with underlying medical conditions. Four pneumococcal vaccine preparations, PCV13, PCV15, PCV20 and 23-valent pneumococcal polysaccharide vaccine (PPSV23) are available. The vaccines have different indications and are not interchangeable.

Pneumococcal Polysaccharide Vaccine

Pneumococcal polysaccharide vaccine (Pneumovax 23) is a mixture of highly purified capsular polysaccharides from 23 of the most prevalent or invasive types of *S. pneumoniae* seen in the United States. These 23 types represent 85% to 90% of all blood isolates and 85% of pneumococcal isolates from other generally sterile sites. The vaccine is administered IM or subcutaneously as a single 0.5-mL dose.[24]

Pneumococcal Conjugate Vaccine

Pneumococcal conjugate vaccines were initially developed to protect infants and young children from invasive pneumococcal disease. In clinical use, the vaccine is associated with a dramatic decline in invasive disease not only in immunized young children but also in individuals in all age groups. Conjugate vaccines are also used to protect adults with high risk medical conditions and those aged 65 years and older.[23]

Immunization of Children

PCV13 or PCV15 is administered as a 0.5-mL IM injection at 2, 4, and 6 months of age and between 12 and 15 months of age. A single dose of PCV13 or PCV15 should be administered to children aged 6 to 18 years with sickle cell disease or splenic dysfunction, HIV infection, immunocompromising conditions, cochlear implant, or cerebral spinal fluid leak. PPSV23 can be used in conjunction with PCV13 or PCV15. PPSV23 should be administered after age 2 years and at least 2 months after the last dose of PCV13 or PCV15.

Immunization of Adults

The ACIP recommended PCV20 or PCV15 followed by PPSV23 in 8 weeks for adults with immunocompromising conditions (Table 147-3).[25] Either PCV15 or PCV20 should be administered with at least a year interval in those adults for whom it has been recommended and have already received one or more doses of PPSV23.

TABLE 147-3

Pneumococcal Vaccines Use in Adults

Vaccine naive adults PCV15 followed by PPSV23 or PCV20
PCV13-immunized adults Conjugate vaccine should not be repeated
PPSV23-immunized adults PCV15 or PCV 20 at least 1 year after last dose of PPSV23
Indications for PCV20 or PCV15 followed by PPSV23 for adults 19 years and older Immunocompromising conditions* Functional or anatomic asplenia Sickle cell disease or other hemaglobinopathies Congenital or acquired immunodeficiencies HIV infection Chronic renal failure or nephrotic syndrome Leukemias, lymphomas, Hodgkin's lymphoma Generalized malignancy Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids or radiation therapy Solid organ transplantation Multiple myeloma High risk medical conditions** Chronic heart disease Chronic liver disease Chronic lung disease Diabetes mellitus Alcoholism Cigarette smoking

CV20, 20-valent pneumococcal conjugate vaccine; PCV15, 15-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine.

*If PCV15 is used for immunocompromising conditions, administer PPSV23 8 weeks later.

**If PCV15 is used for those with high risk medical conditions, administer PPSV23 12 months later.

Data from Reference 23.

For adults aged 65 years and older who are not immunocompromised, either PCV20 or PCV15 followed by PPSV23 in one year is recommended. If PCV15 is used for an individual aged 65 years or older who is immunocompromised (Table 142-3), PPSV23 should be administered 8 weeks later.[23]

Poliovirus Vaccines

Poliomyelitis is a contagious viral infection that usually causes asymptomatic infection; however, in its serious form it causes acute flaccid paralysis. Poliovirus is spread via the fecal–oral route. The virus replicates in the upper respiratory tract, GI tract, and local lymphatics. The vast majority of polio infections are subclinical and asymptomatic. Polio has been eliminated from the United States since 1979, and the last case in Western Hemisphere was reported in 1991. Global eradication efforts are entering the final stages, and the eradication of polio should be accomplished in the next few years.

An inactivated vaccine developed by Jonas Salk was licensed for use in 1955. In 1987, an enhanced-potency inactivated polio vaccine (IPV) was introduced and that replaced the original inactivated vaccine. A live-attenuated oral polio vaccine (OPV) was developed by Albert Sabin in 1962. OPV was the primary immunizing agent for poliovirus infection. Widespread OPV use is responsible for the elimination of wild-type polio in most of the world. However, with no poliovirus circulation in the United States for years, IPV is the recommended vaccine for the primary series and booster dose for children.[26] OPV will continue to be used in areas of the world that have circulating poliovirus. The CDC maintains a stockpile of OPV to be used only in case of an outbreak.

The IPV series is administered routinely to children at ages 2, 4, and 6 to 18 months, and 4 to 6 years.[26] Primary polio immunization is recommended for all children up to age 18 years. Primary immunization of adults over age 18 years is not recommended routinely because a high level of immunity already exists in this age group, and the risk of exposure in developed countries is exceedingly small. However, unimmunized adults who are at increased risk for exposure because of travel, residence, or occupation should receive IPV series.

No serious side effects are attributable to IPV. Pregnant women should be given IPV only if there is a clear need, such as women who will be traveling or living in an area with endemic or epidemic poliovirus.

Rabies Vaccine and Immunoglobulin

Rabies is a virtually universally fatal infection in humans. Although all mammals are susceptible to rabies, carnivorous mammals are reservoirs of the virus and responsible for persistence of the virus in nature. In the United States, most human cases of rabies are from exposure to rabid bats, but raccoons, foxes, skunks, and coyotes are also associated with possible exposure. Worldwide, canines are the primary vectors. Transmission of rabies can occur via percutaneous, permucosal, or airborne exposure to the rabies virus. Circumstances favoring such transmission include animal bites and attacks and contamination of scratches, cuts, abrasions, and mucous membranes with saliva or other infectious material (brain tissue). Unprovoked attacks and daytime attacks by nocturnal animals are considered highly suspect. A few cases of person-to-person transmission have been reported.

Symptoms of rabies are nonspecific during the prodromal stage—fever, headache, malaise, irritability, nausea, and vomiting. The acute neurologic phase is characterized by hyperexcitability, hyperactivity, hallucinations, salivation, a fear of water, and air. Patients die within 5 days of presentation with these neurologic symptoms.

Human diploid cell vaccine, and purified chick embryo cell rabies vaccine are killed vaccines used for preexposure and postexposure rabies virus prophylaxis. Preexposure indications for rabies vaccine include persons whose vocation or avocation place them at high risk for rabies exposure, such as veterinarians, animal handlers, laboratory workers in rabies research or diagnostic laboratories, cavers, wildlife officers where animal rabies is common, and anyone who handles bats. Travelers who will be in a country or area of a country where there is a constant threat of rabies, whose stay is likely to extend beyond 1 month, and who may not have readily available medical services (eg, Peace Corps workers and missionaries) should be considered for preexposure prophylaxis. Rabies immunization of immunocompromised individuals should be postponed until the immunosuppression has resolved, or activities should be modified to minimize the potential exposure to rabies. If the vaccine is used in immunocompromised persons, antibody titers should be checked postimmunization. Pregnancy is not a contraindication if the risk of rabies is great. Both vaccine preparations can be administered for preexposure prophylaxis as a three-dose series of 1 mL IM on days 0 and 7 and once between days 21 and 3 years later.[26] Individuals with ongoing risk of exposure—either continuous risk (eg, research laboratory staff or those involved in rabies biologics production) or individuals with frequent exposures (eg, those involved with rabies diagnosis, spelunkers, veterinarians, animal control workers, and wildlife workers in rabies-enzootic areas)—should undergo serologic testing every 6 months and 2 years, respectively, to monitor rabies antibody concentrations. A booster dose is recommended if the complete virus neutralization is less than 1:5 serum dilution by the rapid fluorescent focus inhibition test.[27]

Preexposure prophylaxis does not eliminate the need for postexposure therapy. Persons previously immunized with rabies vaccine or those who previously received postexposure prophylaxis should receive two 1-mL IM doses of rabies vaccine on postexposure days 0 and 3.[27] Rabies Ig should not be given to this group.

Postexposure prophylaxis should be given after percutaneous or permucosal exposure to saliva or other infectious material from a high-risk source. Each case must be considered individually. Consideration needs to be given to the geographic area, species of animal, circumstances of the incident, and type of exposure. Local or state health departments should be contacted for assistance. Thorough cleansing of the wound with soap and water followed by irrigation with a virucidal agent such as povidone–iodine solution is an extremely important part of the management of rabies-prone

wounds. Individuals who have not been immunized previously should receive the recommended regimen of rabies Ig (see Rabies Immunoglobulin below) and four doses of rabies vaccine 1 mL IM on days 0, 3, 7, and 14 after exposure. However, a fifth dose in a series should be considered if the exposed individual is immunocompromised. Vaccine response for these immunocompromised individuals should be checked.[28] Rabies vaccine must be administered in the deltoid muscle in adults and in the anterolateral thigh in children. The gluteal region should not be used.[1,27]

Adverse reactions to rabies biologicals are less common and less serious with the currently available vaccines compared with previously used preparations. Local or mild systemic symptoms can typically be managed with anti-inflammatory medications or antihistamines. Systemic allergic reactions ranging from hives to anaphylaxis occur in a small number of subjects. Given the lack of alternative therapy and the fact that rabies infection is almost always fatal, persons exposed to rabies who do have adverse reactions should continue the vaccine series in a setting with medical support services.[27]

Human rabies Ig is used in conjunction with rabies vaccine as part of postexposure rabies management for previously unvaccinated individuals. The product is derived from plasma obtained from donors who have been hyperimmunized with rabies vaccine and have high titers of circulating antibody.

In persons who previously have not been immunized against rabies, rabies Ig is given simultaneously with rabies vaccine to provide optimal coverage in the interval before immune response to the vaccine occurs. The efficacy of this regimen has been clearly demonstrated as it provides virtually complete protection from rabies when administered with the vaccine series promptly following exposure.[27] Rabies Ig does not interfere with vaccine-induced antibody formation. Its use is not recommended beyond 8 days after initiation of the vaccine series nor in persons previously immunized to rabies.

Human rabies Ig is administered in a dose of 20 international units/kg (0.133 mL/kg). If anatomically feasible, the entire dose should be infiltrated around the wound(s). Any remaining volume should be administered IM at a site distant from the rabies vaccination site. This product should never be administered by the IV route. Because other antibodies in the rabies Ig may interfere with the response to live-virus vaccines (MMR and varicella), it is recommended that these immunizations be delayed for 3 months.[1]

Side effects are rare but may include local soreness at the wound or IM injection site and mild temperature elevations. Pregnancy is not a contraindication to its use.

Rotavirus Vaccine

Rotavirus infection is virtually universal by age 5 years. Rotavirus can cause severe dehydrating diarrhea primarily among children aged 4 months to 23 months. The virus is usually transmitted fecal-orally and has a seasonal pattern with infection most likely in winter. In the pre-vaccine era, about 50% of hospitalizations for diarrhea among children were attributed to rotavirus.

Two vaccines for infants are available in the United States. A pentavalent human-bovine reassortment vaccine is administered orally at ages 2, 4, and 6 months. The monovalent human rotavirus vaccine is administered orally at ages 2 and 4 months. If brands of vaccines are changed during the series, a three-dose series should be used. The infant should be younger than 15 weeks of age for dose 1, and the maximum age for the last dose of the vaccine is 8 months.[7]

Rotavirus vaccination confers a small increased risk of intussusception following vaccine administration. Intussusception is a condition in which the bowel folds in itself in a telescoping fashion which can lead to inflammation, ischemia, or bowel obstruction. A history of intussusception is a contraindication to rotavirus vaccine. Severe combined immunodeficiency is also a contraindication.[28]

Rubella Vaccine

Rubella (German measles) is characterized by an erythematous rash, lymphadenopathy, arthralgia, and low-grade fever. The most important consequence of rubella infection occurs during pregnancy, particularly during the first trimester. Congenital rubella syndrome is associated with auditory, ophthalmic, cardiac, and neurologic defects. Rubella infection during pregnancy can also result in miscarriage or stillbirth. The primary goal of rubella immunization is to prevent congenital rubella syndrome. Rubella is no longer endemic in the United States, but high immunization rates are necessary to prevent rubella outbreaks from imported cases.[9]

Rubella vaccine contains live-attenuated rubella virus. The vaccine is available in combinations with measles and mumps (as MMR), or varicella (MMRV) vaccines.

Rubella vaccine induces antibodies that are protective against wild-virus infection. A second dose is recommended, at the same time measles vaccine is administered (as a second dose of MMR). The vaccine is indicated for children older than 1 year of age. Individuals born before 1957 are assumed to be immune to rubella except for females who could become pregnant. Therefore, all females of childbearing potential should have documentation of receiving at least one dose of a rubella-containing vaccine or laboratory evidence of immunity. The vaccine should not be given to immunosuppressed individuals, although MMR vaccine should be administered to individuals with HIV infection without evidence of immunity (see section "Measles Vaccine").[9] Adverse effects of the rubella virus vaccine tend to increase with the age of the recipient. Mild symptoms are similar to wild-virus infection and include lymphadenopathy, rash, urticaria, fever, malaise, sore throat, headache, myalgias, and paresthesias of the extremities. These symptoms occur 7 to 12 days after vaccination and last 1 to 5 days. Joint symptoms occur more often in susceptible postpubertal females. Arthralgia occurs in 25% of vaccinees, and 10% have arthritis-like symptoms. These symptoms usually begin 1 to 3 weeks after vaccination, persist for 1 day to 3 weeks, and rarely recur.[9]

The rubella vaccine has never been associated with congenital rubella syndrome, but its use during pregnancy is contraindicated. However, routine pregnancy testing prior to vaccination is not recommended. Females should be counseled not to become pregnant for 4 weeks following vaccination.[9]

Tetanus Toxoid Adsorbed and Tetanus Immunoglobulin

Tetanus is a severe acute illness caused by the exotoxin of *Clostridium tetani.* Tetanus is the only vaccine-preventable disease that is not contagious as it is acquired from the environment. Tetanus toxin interferes with neurotransmitters that promote muscle relaxation, leading to continuous muscle spasms that are characteristic of tetanus. Death can be due to the tetanus toxin itself or secondary to a complication such as aspiration pneumonia, dysregulation of the autonomic nervous system, or pulmonary embolism.

Tetanus toxoid is an adjuvanted suspension of the toxoid derived from *C. tetani.* A series of three 0.5-mL doses of tetanus toxoid elicits protection in virtually all individuals. Primary vaccination provides protection for at least 10 years.[8] Additional doses of tetanus toxoid (combined with diphtheria toxoid, ie, Td) are recommended as part of wound management if a patient has not received a dose of tetanus toxoid within the preceding 5 years. For minor or clean wounds, no dose is given (Table 147-4). Tetanus Ig should be given to individuals who have received fewer than three doses of tetanus toxoid and have more serious wounds. It can be administered with tetanus toxoid, provided that separate syringes and separate injection sites are used.

TABLE 147-4

Tetanus Prophylaxis

Vaccination History	Clean, Minor Wounds		All Other Wounds	
	Td[a]	TIG	Td or Tdap[a]	TIG
Unknown or fewer than three doses	Yes	No	Yes	Yes
Three or more doses	No[a,b]	No	No[a,c]	No

[a]A single dose of Tdap should be used for the next dose of tetanus–diphtheria toxoid for individuals aged >10 years.

[b]Yes, if more than 10 years since the last dose.

[c]Yes, if more than 5 years since the last dose.

Data from Reference 8.

In children, primary immunization against tetanus usually is offered in conjunction with diphtheria and pertussis vaccination (using DTaP or a combination vaccine that includes other antigens used to decrease the number of injections to complete the childhood immunization schedule) at age 2, 4, 6, and 15 to 18 months.[8] In children 7 years and older and in adults who have not been immunized previously, a series of three 0.5-mL doses of a tetanus toxoid-containing vaccine is administered IM initially. The first two doses are given 1 to 2 months apart, and the third dose is recommended at 6 to 12 months after the second dose. Boosters are recommended every 10 years, and unless there is contraindication to diphtheria toxoid, Td or Tdap should be used.[8]

Adverse reactions to tetanus toxoid include mild-to-moderate local reactions at the injection site, such as warmth, erythema, and induration. Occasionally, a nodule at the injection site develops and remains for a few weeks. This type of reaction is indicative of high preexisting antibody concentrations, and additional doses of toxoid should not be given any sooner than 10 years. Local reactions do not limit the use of the toxoid for further dosing.

Tetanus Ig is a sterile, concentrated, nonpyrogenic solution of Igs prepared from hyperimmunized humans. It is used to provide passive immunity to tetanus after the occurrence of traumatic wounds in nonimmunized or suboptimally immunized persons (see Table 147-4).[8] A dose of 250 to 500 units IM should be administered. When administered with tetanus toxoid, separate sites for administration should be used. Tetanus Ig also is used for treatment of tetanus. In this setting, a single dose of 3,000 to 6,000 units IM is administered.

Adverse effects of tetanus Ig include pain, tenderness, erythema, and muscle stiffness at the injection site, which may persist for several hours. Systemic reactions occur rarely. IV administration has been associated with severe adverse reactions and is not recommended.

Varicella and Zoster Vaccines

Varicella is a highly contagious disease caused by varicella-zoster virus. The clinical illness is characterized by the appearance of successive waves of pruritic vesicles that rapidly crust over. Malaise and fever are common and last for 2 to 3 days. The virus remains dormant in the dorsal ganglia and reactivates as herpes zoster, also known as *shingles.* Although the exact stimulus for reactivation is unknown, a decrease in varicella-specific cell-mediated immunity associated with age or immunosuppression appears to be necessary but not sufficient for reactivation.

Varicella Vaccine

Live-attenuated varicella vaccine contains the Oka/Merck strain of varicella virus. Varicella vaccine must be kept frozen and protected from light. Once reconstituted, it must be administered subcutaneously within 30 minutes.[29] The varicella vaccine is recommended for all children at 12 to 15 months of age, with a second dose prior to entering school between ages 4 and 6 years.[29] Two doses separated by 4 to 8 weeks should be administered to anyone who lacks immunity to varicella. Because the varicella vaccine is a live vaccine, it is contraindicated during pregnancy and in immunocompromised individuals. An exception is children with asymptomatic or mildly symptomatic HIV infection, who should receive two doses of varicella vaccine 3 months apart. In addition, children with humoral immune deficiencies may be immunized. Persons who have received blood, plasma, or Ig products in the recent past should not receive varicella vaccine because of concern that passively acquired antibody will interfere with response to the vaccine. The recommended time interval between antibody-containing products and varicella vaccine depends on the dose of Ig (see Table 147-2).[1] Although no adverse events associated with salicylate use after vaccination have been reported, salicylates should be avoided for 6 weeks after vaccination because of the association of salicylate use and Reye syndrome following varicella infection.[35]

Common adverse events include local swelling, and erythema at the injection site occur in up to 32% of patients and fever in 10% to 15%. A varicella-like rash occurs in approximately 4% of vaccinees, accompanied by few, if any, systemic symptoms. The rash may be localized at the injection site or generalized. Lesions usually are few in number (2-10) and often papular rather than vesicular. Transmission of vaccine virus to susceptible close contacts has occurred but is rare and believed to occur only when the vaccinee develops a rash. Because the risk of vaccine virus transmission is low and primary infection can be severe, vaccination of household contacts of immunocompromised patients is recommended to prevent introduction of varicella into the household.[29] Varicella vaccine is contraindicated in immunosuppressed individuals and those who are pregnant. Aspirin should be avoided for 6 weeks following varicella vaccine administration because of its association with Reye syndrome. Also, a caution in those with a personal or family history of seizures exists for the use of MMRV. Consider using the MMR and varicella vaccines separately.[29]

Zoster Vaccine

After the primary infection with varicella-zoster virus manifested as chicken pox, the virus remains latent in the dorsal ganglia. Herpes zoster, also called *shingles*, occurs upon reactivation of varicella-zoster virus associated with waning cellular immunity to the virus. Herpes zoster can occur at any age, but the incidence dramatically increases with age. The rate of disease increases sharply after age 50 years. The disease rate in individuals older than 80 years of age is 15 cases per 1,000 person-years. Patients with HIV, cancer, or other conditions associated with immunosuppression are at increased risk for disease.[30]

The clinical presentation of herpes zoster usually is a vesicular eruption limited to one dermatome. The most common complication is postherpetic neuralgia, which is pain that persists for weeks to years after the skin lesions have healed. The risk of postherpetic neuralgia increases with age. Virtually no risk of developing postherpetic neuralgia with herpes zoster exists prior to age 50 years, but the risk increases to 50% to 75% after ages 60 and 75 years, respectively.[31]

A recombinant zoster vaccine (RZV) with an adjuvant is recommended by the ACIP for use in individuals aged 50 years and older and immunocompromised individuals aged 19 years and older as a two-dose series at 0 and 2 to 6 months.[30] The vaccine is approximately 91% effective for the prevention of zoster in those aged 50 years and older though effectiveness is lower in immunocompromised populations.[41] Although the incidence of serious adverse effects were similar in the vaccine and placebo groups, the incidence of injection site and systemic adverse events were much higher in the vaccine group. Almost 80% of those who receive RZV report injection site pain with 9% of those reporting injection site reactions that interfere with their normal activities. No difference in the incidence of injection site reactions were found when comparing dose 1 to dose 2.[30]

Varicella-Zoster Immunoglobulin

Varicella-zoster Ig is used after exposure to varicella for passive immunization of susceptible immunodeficient patients or other susceptible individuals at particularly high risk for complications of varicella infection. Postexposure prophylaxis with varicella-zoster Ig is indicated for the following susceptible individuals: (a) immunocompromised patients without evidence of immunity, (b) neonates whose mothers develop varicella within 5 days before or 2 days after delivery, (c) hospitalized premature infants (more than 28 weeks of gestation) whose mothers have no evidence of immunity, (d) hospitalized preterm infants (less than 28 weeks' gestation or weight less than 1,000 g), and (e) susceptible pregnant individuals.[29] If varicella is prevented, vaccination should be offered at a later date. Exposure to varicella is defined as direct indoor contact for more than 1 hour with an infectious person. A negative history of clinical disease is not a reliable indicator of varicella susceptibility. Most people with a negative clinical history will have detectable antibody on laboratory testing.

For maximum effectiveness, varicella-zoster Ig must be given as soon as possible and not more than 10 days following exposure.[29] Because this agent may only attenuate infection, patients who receive varicella-zoster Ig still may have a period of communicability, and varicella-zoster Ig may prolong the incubation period to 28 days. Antiviral therapy can be initiated if signs and symptoms of varicella infection become apparent.

Administration of varicella-zoster Ig is by the IM route at doses of 125 plaque-forming units per 10 kg of body weight up to 625 units (five vials) for patients weighing more than 40 kg. The dose for newborn infants is 125 units.[29]

OTHER IMMUNOBIOLOGICS

Immunoglobulin

Ig is available as both intramuscular immunoglobulin (IMIG) and IV immunoglobulin (IVIG) preparations. These products contain a wide spectrum of IgG antibodies to the pathogens prevalent in the area from which the donors were obtained. IMIG typically contains 15% to 18% protein and not less than 90% IgG. A number of IVIG preparations are available commercially in the United States. Generally, these preparations contain greater than 90% IgG monomers and trace to small amounts of IgA. Because different processes are used in the preparation of IMIG and IVIG products, they are not interchangeable.

When administered either IV or IM, Ig distributes in approximately 5% of the body weight of the recipient. The plasma half-life of Ig ranges from 18 to 32 days. This range of half-life probably is attributable to the variation in the half-life of IgG subclasses. Peak serum concentrations occur immediately with IVIG but within 2 days with IMIG. After the initial period of equilibration, circulating IgG levels are superimposable between IV and IM equivalent dosages. No dosage adjustment is necessary in patients with renal insufficiency, hepatic insufficiency, or both, dialysis patients, or geriatric patients.

Ig is indicated in a wide variety of circumstances to provide passive immunity to individuals. The indications for IMIG differ from those for IVIG. IMIG is indicated for providing passive immunity in patients with hepatitis A infections in those for whom IMIG is recommended in addition to immunization, hepatitis B exposures (however, hepatitis B Ig is significantly more effective), measles, varicella, and primary immunodeficiency diseases. Although IMIG is indicated for the treatment of primary immunodeficiency, IVIG is better tolerated and is more effective. IMIG is not indicated for prevention of rubella, mumps, or poliomyelitis. **Table 147-5** lists the suggested dosages of IMIG for prevention or attenuation of various infectious diseases.

TABLE 147-5

Indications and Dosage of Intramuscular Immunoglobulin in Infectious Diseases

Primary immunodeficiency states	1.2 mL/kg IM then 0.6 mL/kg every 2-4 weeks
Hepatitis A exposure	0.02 mL/kg IM within 2 weeks if <1 year or >39 years of age
Hepatitis A prophylaxis	0.02 mL/kg IM for exposure <3 months' duration
	0.06 mL/kg IM for exposure up to 5 months' duration
Hepatitis B exposure	0.06 mL/kg (HBIG preferred in known exposures)
Measles exposure	0.5 mL/kg (maximum dose 15 mL) as soon as possible

There are many licensed indications, as well as off-label uses, for IVIG.[43] The therapeutic dose of IVIG is set empirically at 2 g/kg, often given as five daily doses of 400 mg/kg each. Mechanisms of IVIG action for treatment of these conditions have been hypothesized.

1. *Primary Immunodeficiency States.*[32,33] In primary immunodeficiency states, monthly doses of between 100 and 800 mg/kg are administered; the average dose is 200 to 400 mg/kg. The immunodeficiency states for which IVIG is indicated include both antibody deficiencies and combined immune deficiencies. Significant reactions can occur in patients with low intrinsic levels of IgA given IVIG with greater amounts of IgA. An IVIG product with low amounts of IgA should be used for these patients.

2. *Immune Thrombocytopenia.*[34] For the treatment of hemorrhage associated with immune thrombocytopenia (ITP), doses of 1 g/kg daily for 2 to 3 days plus high-dose methylprednisolone are indicated. Adults tend to respond less well to IVIG than do children. IVIG is acceptable for treatment of both chronic and acute ITP, and IVIG has been used for ITP associated with pregnancy without adverse effects on the fetus. Corticosteroids remain the drugs of choice for adult ITP. In thrombotic thrombocytopenia purpura, IVIG is reported to be effective in patients who do not respond to plasmapheresis. Other platelet disorders in which IVIG may be useful include neonatal immune thrombocytopenia, perinatal autoimmune thrombocytopenia, drug-induced thrombocytopenia, thrombocytopenia secondary to infection, and transfusion-refractory thrombocytopenia; however, the data supporting these uses are minimal.

3. *Chronic Lymphocytic Leukemia.*[35] IVIG is used as a prophylactic measure in patients with chronic lympocytic leukemia who have had a serious bacterial infection.

4. *Kawasaki Disease.*[36] This disease, which generally occurs in children, carries the hallmark of development of coronary artery abnormalities. Generally, the American Academy of Pediatrics recommends that if the strict criteria for Kawasaki disease are met, an IVIG dose of 400 mg/kg/day for four consecutive days be used or, preferably, 2 g/kg as a single dose. The dose should be administered within 10 days of disease onset. Aspirin therapy also should be initiated.

5. *Pediatric HIV infection.*[37] IVIG prevents serious bacterial infections in children with HIV infection. However, in the era of highly active anti-retroviral therapy, its use has waned.

6. *Allogeneic bone marrow transplantation.*[38]

7. *Chronic inflammatory demyelinating polyneuropathy.*[38] This disabling neuropathy often responds to corticosteroids, IVIG, or plasmapheresis.

8. *Multifocal motor neuropathy*[39] IVIG is considered first-line therapy.

9. *Kidney transplantation involving a recipient with high antibody concentrations or an ABO-incompatible donor.*[40] Some transplant recipients have antibody concentrations that present an immunological barrier to transplantation. Desensitization can be accomplished using IVIG.

Many other uses of IVIG have been identified. These uses are off-label but may be generally accepted in the medical community for routine treatment.[32]

7 Adverse effects of Ig vary with the route of administration. Following IMIG, pain, tenderness, and muscle stiffness persisting for hours or days are common. Repeat courses may cause sensitization with resulting allergic reactions. Chills, fever, nausea, and vomiting often are related to the rate of the infusion.[41] Infusion should be given at a rate of 0.01 to 0.02 mL/kg/min for 30 minutes. If no reactions occur, then the rate can be increased to 0.02 to 0.04 mL/kg/min. If reactions do occur, the infusion should be stopped for 30 minutes and restarted at a lower rate. Although recommendations for infusion rate vary slightly depending on the preparation, the guidelines presented can be followed for the various IV preparations.

Most adverse reactions are mild and transient. Arthralgia, myalgia, fever, pruritus, nausea, vomiting, chest tightness, palpitations, diaphoresis, dizziness, pallor, and respiratory distress have been reported. Rarely, aseptic meningitis has occurred from a few hours to 2 days after high-dose infusion. The syndrome resolves within days without sequelae. Acute renal failure has been reported, primarily in individuals with underlying renal dysfunction, diabetes, sepsis, volume depletion, or other nephrotoxic drugs or in patients older than 65 years. To minimize the risk, ensure adequate hydration prior to infusion and choose an IVIG product that does not contain high-sucrose concentrations for individuals at high risk.[41]

Ig products are derived from human blood. Precautions such as donor screening and fractionation procedures and solvent–detergent treatment during the manufacturing process render the IVIG products free of HIV and hepatitis B and C viruses. Although no manufacturing process can guarantee no viral contamination, the potential infection risk from Ig preparations is very small.

$Rh_o(D)$ Immunoglobulin

8 Second only to the ABO blood group system, Rhesus antigen D [$Rh_o(D)$] is an important antigen in human blood. The $Rh_o(D)$ locus encodes this antigen, but this locus is absent in approximately 15% of the population. Individuals lacking the $Rh_o(D)$ locus are $Rh_o(D)$ negative and have the potential to mount an antibody response to erythrocytes with the $Rh_o(D)$ present. $Rh_o(D)$ incompatibility during pregnancy can lead to sensitization of the mother. The maternal antibodies developed following normal fetal leakage of erythrocytes to the mother can cause hemolytic disease of the newborn during subsequent pregnancies.

$Rh_o(D)$ Ig is a sterile solution of Igs prepared from human sera with high titers of $Rh_o(D)$ antibody. $Rh_o(D)$ Ig suppresses the antibody response and formation of anti-$Rh_o(D)$ in $Rh_o(D)$-negative individuals exposed to $Rh_o(D)$-positive blood. Administration of $Rh_o(D)$ Ig prevents hemolytic disease of the newborn in subsequent pregnancies with a $Rh_o(D)$-positive fetus. When administered within 72 hours of delivery of a full-term infant, $Rh_o(D)$ Ig reduces active antibody formation from 1% to about 0.2%. The reduction in antibody formation is lower when $Rh_o(D)$ Ig is given beyond 72 hours postpartum. Smaller doses of $Rh_o(D)$ Ig are used after abortion, miscarriage, amniocentesis, or abdominal trauma. In addition, $Rh_o(D)$ Ig is used in the case of a premenopausal female who is $Rh_o(D)$ negative and has inadvertently received $Rh_o(D)$-positive blood or blood products.[42]

The dosage of $Rh_o(D)$ Ig varies with the indication. A standard dose of 300 mcg is given within 72 hours of a term delivery. Occasionally, when the fetus is known to be $Rh_o(D)$ positive, a 300-mcg dose is given at 28 weeks' gestation and within 72 hours after delivery. For postpregnancy termination occurring up to 13 weeks' gestation, one microdose (50 mcg) vial is given within 72 hours. For pregnancy termination after 13 weeks, one standard dose (300 mcg) is given within 72 hours. In other circumstances, such as in abdominal trauma, amniocentesis, or transfusion accidents, the dosage (number of standard dose vials) is based on the estimated packed red blood cell volume of fetal/maternal hemorrhage divided by 15. $Rh_o(D)$ Ig is administered IM only.

Adverse reactions to Rh_o(D) Ig include injection-site tenderness and fever. Rh_o(D) may minimally interfere with response to rubella or varicella vaccine. Rubella- or varicella-seronegative females should be immunized with MMR or MMRV at hospital discharge even if they received Rh_o(D) Ig postpartum.[1]

Vaccine Hesitancy

Vaccine confidence is the trust that individuals and providers have in recommended vaccines, in those who administer vaccines, and the policies and processes by which vaccines are developed, manufactured, licensed, and recommended.[43] Vaccine hesitancy is a global threat to protection conferred by strong immunization programs. A variety of justifications for choosing not to vaccinate exist. The Strategic Advisory Group of Experts (SAGE), a working group under the World Health Organization (WHO), defined three overarching drivers for vaccine hesitancy: complacency, convenience, and confidence.[44] This "3 Cs Model" defined complacency as a low perceived risk of contracting vaccine-preventable diseases, and therefore low necessity to receive vaccines. Convenience is based on socioeconomic factors such as availability, accessibility, affordability, and ability to understand, such as language barriers or low health literacy. Confidence stems from trust in various aspects of healthcare, such as the vaccine itself, healthcare professionals administering vaccines, or policy-makers who advocate for vaccination and determine their need.

Communication is key to relaying a vaccine message starting with empathy and understanding. Healthcare providers should assume that individuals want to be vaccinated and make a strong recommendation for vaccines. Healthcare workers must be prepared to share facts that address misinformation and respond to patient questions. An active discussion of expected side effects is associated with patient confidence. Finally, the conversation can be concluded by encouraging the individual to take action to get the vaccine.[45]

VACCINE INFORMATION RESOURCES

The field of vaccinology is developing rapidly, with numerous changes in recommendations for vaccine use made each year. Keeping up to date with the current recommendations can be a challenge. The childhood and adult immunization schedules are updated frequently and published annually. Recommendations for the use of influenza vaccine are issued annually. Healthcare providers involved in primary care and immunization delivery must keep themselves abreast of these changes in a systematic way. Reading electronic newsletters and browsing reliable websites are efficient methods for obtaining information (Table 147-6). Although several excellent, reliable, and timely websites exist, hundreds of sites with misleading and incorrect information also exist. Many of these sites are targeted at parents.

TABLE 147-6

Web Resources for Vaccine Information

Recommended Internet Sites for Vaccine Information	
http://www.cdc.gov/vaccines/	Vaccines & Immunizations
	Centers for Disease Control and Prevention
www.immunize.org	Immunization Action Coalition
www.nfid.org/	National Foundation for Infectious Diseases
www.cdc.gov/mmwr/	Morbidity and Mortality Weekly Report
http://www.nationalacademies.org/hmd/	The National Academies of Sciences, Engineering, and Medicine. Health and Medicine Division
http://www.hrsa.gov/vaccinecompensation/	Vaccine Injury Compensation Program
http://www.chop.edu/centers-programs/vaccine-education-center/	Vaccine Education Center
	Children's Hospital of Philadelphia
https://vaers.hhs.gov/index.html	Vaccine Adverse Event Reporting System
Recommended Electronic Newsletters	
www.immunize.org/express	The Immunization Action Coalition's newsletter
www.cdc.gov/mmwr/	Morbidity and Mortality Weekly Report

Parents and patients often have questions regarding vaccine safety. The Vaccine Education Center at the Children's Hospital of Philadelphia has several documents that may answer those questions (http://www.chop.edu/centers-programs/vaccine-education-center). The CDC is another source of information for parents (https://www.cdc.gov/vaccines/parents/vaccine-decision/index.html). Vaccines are the only class of medications to which nearly every patient is exposed. Knowledge of these agents is critical to providing pharmaceutical care. Dramatic progress in public health has been made through the appropriate use of immunization. Additional improvements in quality of life and mortality can be made through continued increases in vaccination coverage with careful attention to this aspect of care by all healthcare providers.

ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
CDC	Centers for Disease Control and Prevention
DTaP	diphtheria, tetanus toxoids, and acellular pertussis
Hib	*Haemophilus influenzae* type b
HPV	human papillomavirus
Ig	immunoglobulin
IMIG	intramuscular immunoglobulin
IPV	inactivated polio vaccine
ITP	idiopathic (immune) thrombocytopenic purpura
IVIG	IV immunoglobulin
MenB	meningococcal serogroup B
MMR	measles, mumps, rubella vaccine
MMRV	measles, mumps, rubella, varicella vaccine
MSM	men who have sex with men
OPV	oral polio vaccine
PCV	pneumococcal conjugate vaccine
PPSV23	23-valent pneumococcal polysaccharide vaccine
Td	tetanus–diphtheria
Tdap	tetanus, diphtheria, acellular pertussis
TIG	Tetanus immune globulin
VAERS	Vaccine Adverse Event Reporting System

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SELF-ASSESSMENT QUESTIONS

1. Which of the following is an example of a situation in which vaccine-induced immune response would be poor?

   A. Meningococcal conjugate vaccine administered to a healthy 12-year-old child.

   B. Hepatitis B vaccine administered with a 1.5-in. (3.8 cm) needle to a 22-year-old woman who weighs 125 kg.

   C. Third dose in the inactivated polio vaccine series administered to a 12-month-old child.

   D. Measles, mumps, rubella vaccine administered to a 4-month-old infant.

2. Which of the following is the most likely adverse effect of IVIG use in a patient with immune thrombocytopenia purpura and congestive heart failure?

   A. Anaphylaxis associated with native IgM antibodies

B. Kawasaki disease

C. Volume overload

D. Chronic renal failure

3. Michael is a 5-year-old boy who presents for his well-child visit prior to entering kindergarten. His past medical history is unremarkable except for an anaphylactic reaction to amoxicillin 4 days ago when he was being treated for a tooth abscess. He was seen in the emergency room and given prednisone 40 mg daily for 5 days and azithromycin for 5 days. Although he was up-to-date on his childhood immunization at age 36 months, he now presents for routine immunizations prior to entering school. Which of the following strategies is recommended to accomplish administration of all needed vaccines as soon as possible?

A. Administer DTaP, MMRV, IPV today

B. Administer DTaP, IPV today, and postpone MMRV until he has been off prednisone for 3 months

C. Administer no immunizations until he has been off prednisone for 3 months

D. Administer DTaP and IPV today and postpone MMRV until he has been off antibiotics for 2 weeks

4. Which of the following describes the rationale for Rh_o(D) antibody treatment?

A. Administered to an Rh-negative infant to prevent it from developing antibodies to its red blood cells

B. Administered to an Rh-positive mother to prevent her from developing antibodies to her Rh-negative infant

C. Administered to an Rh-negative mother to prevent her from developing antibodies that may cause her to become anemic

D. Administered to an Rh-negative mother to prevent her from developing antibodies to Rh-positive red blood cells that may cause anemia in the fetus in future pregnancies

5. Which of the following infections is pooled human immunoglobulin useful in preventing?

A. Measles

B. Diphtheria

C. Yellow fever

D. Guillain-Barré syndrome

6. A vaccine for a hypothetical viral infection that is particularly problematic in young infants has been developed. The vaccine is a whole virus inactivated preparation that is administered by the intramuscular route. Which of the following is likely true about its use?

A. Children younger than 2 years of age will not likely mount an immune response to it.

B. Its administration should be separated from the administration of hepatitis B immunoglobulin by 4 months.

C. Multiple doses will be required to induce a protective immune response

D. A single dose will induce long-term protection

7. Justin is a 22-year-old male who had significant contact with a raccoon deemed to have rabies. The patient received rabies immunoglobulin and began the inactivated rabies vaccine series (doses on days 0, 3, 7, 14, and 28) in the emergency room yesterday. He now presents for follow-up with employee health service. Upon review of his health record including his immunization record, a second dose of a measles-containing vaccine is recommended because he is a healthcare worker. Which of the following strategies is recommended for the second dose of MMR vaccine?

A. Administer an MMR vaccine now

B. Administer the MMR vaccine in 4 weeks

C. Administer an MMR vaccine in 4 months

D. Administer an MMR vaccine in 6 months

Use this case for the next two questions.

Sarah is a 24-year-old elementary school teacher who is 14 weeks pregnant. This is her first pregnancy. She was noted to be rubella seronegative on routine prenatal screening laboratory panel. She was age-appropriately immunized as a child.

8. Which of the following recommendations is appropriate for the administration of a dose of rubella-containing vaccine?

A. Vaccinate postpartum at hospital discharge.

B. Vaccinate now to prevent possible congenital rubella syndrome.

C. Vaccinate 3 months postpartum.

D. No rubella vaccine should be given as she received the MMR as a child.

9. Which of the following vaccines are recommended for Sarah during her pregnancy?

A. Tdap and inactivated influenza vaccines.

B. Rubella and live-attenuated influenza vaccines.

C. Td and inactivated influenza vaccines.

D. No vaccines should be administered during pregnancy.

10. Mr. Olden is a 46-year-old man who has just been diagnosed with type 2 diabetes. He has not received any immunizations as an adult that he can remember and has not seen a physician since his military physical. Which of the following vaccines are recommended?

A. Hepatitis A series, hepatitis B series, PPSV23, annual inactivated influenza, Tdap

B. PPSV23, annual inactivated influenza, Tdap, hepatitis B series

C. Hepatitis A series, hepatitis B series

D. PCV13, annual influenza, Tdap

11. For which of the following individuals would you recommend PPSV23 revaccination?

A. A 72-year-old man with COPD who was vaccinated 5 years ago

B. A 66-year-old woman with diabetes who was vaccinated when she was 62

C. A 44-year-old man with HIV who was vaccinated at the time of HIV diagnosis 5 years ago

D. A 62-year-old kidney transplant patient who was vaccinated prior to her transplant 3 years ago

12. What action is recommended if the interval between doses of human papillomavirus vaccine is longer than the recommended interval?

A. Add one additional dose

B. Restart the series from the beginning

C. Continue the series, ignoring the prolonged interval

D. Perform a serologic test to determine if a vaccine response has been mounted

13. Mr. North is a 48-year-old male who is being seen for a pre-anesthesia physical prior to a planned uncomplicated hernia repair scheduled in two weeks. He smokes a pack of cigarettes daily. He is otherwise healthy, on no medications, and has not been immunized as an adult. Which of the following vaccines are recommended?

A. MMR, Td, annual live-attenuated influenza

B. Td, annual live-attenuated influenza, *Haemophilus influenza* type b, meningococcal, PCV 13 followed by PPSV23 in 8 weeks

C. Tdap, annual inactivated influenza, PPSV23, zoster

D. Tdap, annual inactivated influenza, PPSV23

14. Which of the following describes the procedure for administering an intramuscular immunization to an adult?

A. Insert the needle at a 45° angle

B. Use a 21- to 23-gauge needle in a length of 5/8 in. (1.6 cm)

C. Use a 25-gauge needle in a length of 1 to 1.5 in. (2.5-3.8 cm)

D. Use the deltoid muscle or the gluteus maximus for the injection site

15. Which of the following describes an advantage of the VAERS?

A. All vaccine adverse events that occur in the United States are reported.

B. Only common adverse events are collected.

C. Adverse event rates can be calculated.

D. Risk factors for adverse events can be evaluated.

SELF-ASSESSMENT QUESTION-ANSWERS

1. **D.** Young children must be at least 12 months old before the measles, mumps, rubella vaccine is administered as maternal antibody can neutralize the live vaccine viruses before the child has a chance to mount an immune response to the vaccine. Meningococcal conjugate vaccine is indicated for a 12-year-old child, and the third dose of inactivated polio vaccine is recommended for a 12-month-old child. An appropriately long needle is being used for administration of a dose of hepatitis B vaccine to an obese 22-year-old female.

2. **C.** The dose of IVIG for treatment of immune thrombocytopenia purpura is 1 g/kg daily for 2 or 3 days. The volume associated with those infusions is large and may result in volume overload, particularly in an individual at risk, such as someone with congestive heart failure.

3. **A.** This child can be vaccinated without regard to his current antibiotic therapy or short prednisone burst. He can receive DTaP, MMRV, and IPV today as recommended for a child aged 4 to 6 years.

4. **D.** The Rh-negative mother may mount an immune response to her Rh-positive fetus. Rho(D) antibody is administered to the mother to prevent her from developing antibodies to Rh-positive red blood cells that may cause anemia in the fetus during future pregnancies.

5. **A.** Pooled human immunoglobulin can be used for postexposure prophylaxis of measles. It is not useful for the prevention of diphtheria or yellow fever. IVIG is used as a treatment option for Guillain-Barré syndrome.

6. **C.** Because the hypothetical vaccine is an inactivated vaccine, multiple doses will likely be needed to induce immunity in young infants. Immunoglobulin administration and long-term protection are typically properties of live-attenuated vaccines.

7. **C.** MMR is a live vaccine so its administration must be separated from immunoglobulin containing products. Using Table 147-2, the recommended interval between RIG and MMR vaccine is 4 months.

8. **A.** Live vaccines (MMR) are not recommended for administration to pregnant females so the vaccine should be administered at the completion of the pregnancy—postpartum at hospital discharge.

9. **C.** Tdap should be administered late in the second or during the third trimester to females during each pregnancy. Pregnant females are at particularly high risk for hospitalization or death from influenza infection so seasonal inactivated influenza vaccine is recommended.

10. **B.** This individual needs adult vaccines (Tdap, annual inactivated influenza vaccine) and other vaccines indicated because he has type 2 diabetes (PPSV23 and hepatitis B series).

11. **C.** PPSV23 is repeated after a 5-year interval for individuals who are at particularly high risk for invasive pneumococcal disease, such as the individual with HIV infection. A single dose is administered after age 65 years.

12. **C.** As for most vaccine series, the prolonged interval can be ignored and the series completed with the recommended number of doses.

13. **D.** This individual needs adult vaccines (Tdap, annual inactivated influenza vaccine) and vaccines indicated because he is a smoker (PPSV23).

14. **C.** Intramuscular vaccines are administered using a 23- to 25-gauge needle that is inserted at a 90° angle to the skin into the deltoid.

15. **D.** The VAERS is a passive system that allows healthcare providers and patients to report adverse events following immunization. The system allows risk factors for adverse events to be considered, but adverse event rates cannot be determined as the number of vaccines administered (the denominator) is not known. Also, consider that not all adverse events are reported.