General Immunization Practices

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Recommendations for immunization practices are based on scientific knowledge of vaccine characteristics, biology of immunization, epidemiology of specific diseases, and host characteristics. In addition, experience and judgment of public health officials and specialists in clinical and preventive medi- cine play a key role in developing recommendations that maximize benefits and minimize risks and costs associated with immunization. General guidelines for immunization practices are based on evidence and expert opinion of benefits and risks of vaccinations as they apply to the current epidemi- ology of disease and use of vaccines in the United States. However, many of the principles are universal and are appli- cable to other countries where different public health infra- structures may exist.

# VACCINE STORAGE AND HANDLING

Vaccines must be properly shipped, stored, and handled to avoid loss of their biologic activities. Recommended storage and handling requirements for each vaccine are given in each manufacturer’s product information.1 Correct shipping, storage, and handling practices also are published in recom- mendations of the major vaccine policymaking committees, such as the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC), the Committee on Infectious Diseases of the American Academy of Pediatrics (AAP), and the World Health Organiza- tion (see Chapter 76).2–5 Failure to adhere to these require- ments can result in loss of vaccine potency, leading to an inadequate immune response in the vaccinee. Visible evidence of altered vaccine integrity may not be present. The state/local health department or the manufacturer should be contacted when questions arise about the correct handling of a vaccine. New vaccines or new formulations of an existing vaccine may have different shipping, storage, and handling requirements. The recommended storage practices for the most commonly used vaccines in the United States are described in the Vaccine Storage and Handling Toolkit.6

Refrigerators without freezers and standalone freezers are

usually most effective at maintaining the precise temperatures required for vaccine storage and are preferred to combination refrigerator/freezer units. Freezer storage units may be manual defrost or automatic defrost (“frost-free”). Automatic defrost freezers periodically and transiently increase the freezer tem- perature to reduce the formation of ice. This type of freezer unit is acceptable for storage of vaccines that must be stored in a frozen state (varicella, measles-mumps-rubella-varicella [MMRV], oral polio, zoster).

Exposure to higher or lower temperatures than recom- mended can damage a vaccine. For example, live virus vac- cines, such as oral poliovirus vaccine (OPV), varicella, combination MMRV, and zoster vaccine, are sensitive to tem- peratures above freezing and should be kept frozen until just before administration. Measles-mumps-rubella (MMR without varicella) vaccine may be stored at either refrigerator or freezer temperature. Rotavirus vaccine and yellow fever vaccine should be stored at refrigerator temperature (2–8°C).3,7 Some vac- cines composed of purified antigens or inactivated microor- ganisms, such as hepatitis A, hepatitis B, *Haemophilus influenzae*

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type b (Hib), human papillomavirus (HPV), and inactivated influenza, can lose their potency if frozen and should be kept at refrigerator temperature and never frozen.3,4 Diluents should not be frozen and may be kept at room or refrigerator tem- perature. Maintenance of a “cold chain” from vaccine produc- tion to use helps ensure vaccine potency at the time of administration. Temperature monitoring and control are important for storage and handling of all vaccines, particularly during transport and field use. Temperatures should be moni- tored at least twice a day, using a thermometer that records current, maximum, and minimum temperatures. Whereas maintenance of cold and freezing temperatures may be a problem in tropical climates, data suggest that inappropriate freezing of inactivated vaccines is a problem in maintaining vaccine stability in cold and temperate climates. Shipping con- tainers should be sturdy, the correct size for the amount of vaccine to be shipped, and contain a temperature monitor. Appropriate insulation (e.g., panels and boxes of polystyrene, isocyanurate, or polyurethane) and cold source (e.g., bottles with frozen liquid) should be used to maintain the recom- mended temperature. Dry ice should not be used to transport frozen vaccine, because it might expose the vaccine to tem- peratures lower than recommended for storage. Loose fillers do not provide reliable temperature insulation.3

Vaccines should not be reconstituted until immediately

before use. If not administered within the interval recom- mended by the manufacturer, reconstituted vaccine should be discarded.5 Only the diluent provided by the manufacturer should be used to reconstitute a lyophilized vaccine. With the exception of OPV, live virus vaccines should not be refrozen after thawing.

Certain vaccines are distributed in multidose vials. When opened, the remaining doses from partially used multidose vials can be administered until the expiration date printed on the vial or vaccine packaging unless otherwise specified by the manufacturer, provided that the vial has been stored correctly and that the vaccine is not contaminated.5

# VACCINE ADMINISTRATION

Complete and accurate records documenting administration of all vaccines should be maintained by healthcare providers who administer vaccines and vaccine recipients (or their parents). For each immunization, the following information should be recorded: (a) date of vaccination; (b) product administered, manufacturer, lot number, and expiration date;

(c) site and route of administration; and (d) name, address, and title of healthcare provider administering the vaccine.

## Infection Control and Sterile Injection Technique

Infection resulting from administration of vaccines is unlikely if appropriate precautions are utilized. Hands should be washed with soap and water or cleansed with an alcohol- based waterless antiseptic hand rub before each patient contact to reduce the risk of bacterial contamination and transmission of microorganisms between vaccine recipients and healthcare personnel. In general, use of protective gloves is not necessary when administering vaccines unless the healthcare provider

will have contact with potentially infectious body fluids or has open lesions on the hands.2,5

Failure to follow relevant infection control guidelines can result in transmission of bloodborne pathogens or bacterial infection and abscess formation. Contamination of an injec- tion site can occur from bacteria on the skin at the site of injection. To prevent such contamination, skin at the injection site should be prepared with isopropyl alcohol (70%) or another disinfecting agent and allowed to dry before injection. Transmission of pathogens also can occur if needles, syringes, vaccines, or other equipment used to administer vaccines becomes contaminated. To prevent such contamination, syringes and needles must be sterile. A separate needle and syringe should be used for each injection. Disposable needles and syringes should be discarded after a single use in a labeled, puncture-proof container to prevent inadvertent needle-stick injury or reuse. Because recapping and removing a used needle from a syringe can result in injury to the user, needles should not be recapped after use.5 The needle and syringe should be discarded as a single unit without removing the needle from the syringe. Single-use disposable needles and syringes should not be sterilized and reused.

If only reusable (i.e., nondisposable) needles and syringes

are available, they must be thoroughly cleaned and sterilized after each injection to prevent transmission of bloodborne or other pathogens between patients. Reusable syringes are usually glass rather than plastic. Because of its inert character- istics, glass can be cleaned and sterilized more easily than plastic. Because hypodermic needles enter deep tissues, great care must be taken to ensure that all contaminants are removed from the needle and syringe.8 Liquid germicides alone are insufficient for needle sterilization because of the restricted access of the chemical agent to the lumen of the needle. Strict adherence to the recommended time and temperature for the sterilization procedure used must be observed.

Most vaccines have a similar appearance after they are drawn into a syringe. Cases in which the wrong vaccine was administered often are attributable to the practice of prefilling syringes or drawing doses of a vaccine into multiple syringes before their immediate need.5 The routine practice of prefill- ing syringes should be discouraged because of the potential for such administration errors. To prevent errors, vaccine doses should not be drawn into a syringe until immediately before administration. In certain circumstances in which a single vaccine type is used (e.g., in a community influenza vaccina- tion campaign), filling a small number (10 or fewer) of syringes before their immediate use may be considered. Care should be taken to ensure that the cold chain and sterility are maintained until the vaccine is administered. When the syringes are filled, the type of vaccine, lot number, and date of filling must be labeled accurately on each syringe, and the doses should be administered as soon as possible after filling, by the same person who filled the syringes. Manufacturer prefilled-syringes that are activated (i.e., syringe cap removed or needle attached) but unused should be discarded at the end of the clinic day. Likewise, vaccine drawn into syringes by the user (i.e., not by the manufacturer) should be discarded at the end of the clinic day.

## Route of Administration

One or more routes of administration (e.g., intramuscular, subcutaneous, intradermal, intranasal, and oral) are recom- mended for each vaccine and are listed in the manufacturer’s product label and in published recommendations of immu- nization advisory committees ([Table 9.1](#_bookmark0)).2,5 These routes usually are determined during prelicensure vaccine studies and are based on vaccine composition and immunogenicity.

Vaccines should be administered in sites where they elicit the desired immune response and where the likelihood of local tissue, neural, or vascular injury is minimal.2 To avoid unnec- essary local and systemic adverse events and to ensure the appropriate immune response, people administering vaccines should not deviate from the recommended route of adminis- tration in the product label. A route of administration or anatomic site of injection different from that recommended can result in an inadequate immune response. For example, the immunogenicity of hepatitis B vaccine and rabies vaccine is substantially lower when the gluteal instead of the deltoid vaccination site is used.9,10 The reduced immunogenicity pre- sumably is a result of inadvertent injection into subcutaneous or deep fatty tissue rather than into muscle.

Deep intramuscular injection generally is recommended for adjuvant-containing vaccines because subcutaneous or intradermal administration can cause marked local irritation, induration, skin discoloration, inflammation, and granuloma formation.5 However, subcutaneous injection can lessen the risk of local neurovascular injury and is recommended for vaccines that are less reactogenic but immunogenic when administered by this route, such as live virus vaccines. Intra- dermal administration is preferred for live bacille Calmette- Guérin (BCG) vaccine and one brand of inactivated influenza vaccine.11

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Aspiration before injection of vaccines or toxoids (i.e., pulling back on the syringe plunger after needle insertion, before injection) is not necessary because there are no large blood vessels at the recommended injection sites. Also, the process of aspiration can be painful, especially for infants.12

## Subcutaneous Injections

Vaccines recommended for subcutaneous injection usually are administered into the thigh of infants younger than 12 months of age and into the upper, outer triceps area of persons 12 months of age or older. Subcutaneous injections also can be administered into the upper, outer triceps area of an infant. A 58 -inch, 23- to 25-gauge needle is recommended in most situations.2,5 The needle is inserted into the tissues below the dermal layer of the skin. To avoid administering the vaccine into a muscle, the skin and subcutaneous tissue should be held gently between the thumb and fingers to raise these tissues from the muscle layer. The needle is inserted into the resulting skinfold at an approximately 45-degree angle.5

## Intramuscular Injections

Selection of the site of injection and needle size is based on the volume of vaccine to be administered, the thickness of the overlying subcutaneous tissue, the size of the muscle, and the desired depth below the muscle surface into which the mate- rial is to be injected.

The quadriceps muscle mass in the anterolateral thigh is most commonly used for intramuscular injection in infants, whereas the deltoid muscle of the upper arm is the usual recommended site for older children and adults. After a child begins to walk, the upper arm is the preferred site.13 By this age, the child’s deltoid muscle is usually large enough to be used for intramuscular injection. Although the anterolateral thigh is also an acceptable site, intramuscular injection into the thighs of 18-month-old children has been reported to cause transient limping.14,15 For infants and younger children, if more than two vaccines are injected in a single limb, the thigh is the preferred site because of the greater muscle mass; the injections should be sufficiently separated (i.e., ≥1 inch) so that any local reactions can be differentiated.13,14

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| **TABLE 9.1** Dose and Route of Administration for Selected Vaccines | | |
| **Vaccine** | **Dose** | **Route** |
| Diphtheria, tetanus toxoids, and acellular pertussis (DTaP); diphtheria and tetanus toxoids (DT); tetanus and diphtheria toxoids (Td); tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) | 0.5 mL | IM |
| DTaP–hepatitis B (HepB)–inactivated poliovirus (IPV) | 0.5 mL | IM |
| DTaP-IPV/*Haemophilus influenzae* type b (Hib) | 0.5 mL | IM |
| DTaP-IPV | 0.5 mL | IM |
| Hib | 0.5 mL | IM |
| Hib-MenCY | 0.5 mL | IM |
| Hepatitis A (HepA) | ≤18 y: 0.5 mL  ≥19 y: 1 mL | IM |
| HepB | ≤19 y: 0.5 mLa  ≥20 y: 1 mL | IM |
| HepA-HepB | ≥18 y: 1 mL | IM |
| Live attenuated influenza vaccine (LAIV) | 0.2 mL divided dose between nares | Intranasal spray |
| Inactivated influenza vaccine (IIV) | 6–35 mo: 0.25 mL  ≥3 y: 0.5 mL | IM |
| IIV intradermal | 18–64 y: 0.1 mL | Intradermal (ID) |
| Measles, mumps, and rubella (MMR) | 0.5 mL | Subcutaneous (SC) |
| MMR and varicella (MMRV) | 0.5 mL | SC |
| Quadrivalent meningococcal conjugate vaccine (MCV4) | 0.5 mL | IM |
| Quadrivalent meningococcal polysaccharide vaccine (MPSV4) | 0.5 mL | SC |
| Serogroup B meningococcal vaccine | 0.5 mL | IM |
| Pneumococcal conjugate vaccine (PCV) | 0.5 mL | IM |
| Pneumococcal polysaccharide vaccine (PPSV) | 0.5 mL | IM or SC |
| Human papillomavirus (HPV; bivalent vaccine, 2vHPV, quadrivalent vaccine, 4vHPV, or 9-valent vaccine, 9vHPV) | 0.5 mL | IM |
| IPV | 0.5 mL | IM or SC |
| Rotavirus (RV1 or RV5) | (1 or 2 mL) | Oral |
| Varicella | 0.5 mL | SC |
| Herpes zoster | 0.65 mL | SC |
| aPersons age 11–15 y may be administered Recombivax HB (Merck), 1 mL (adult formulation) on a two-dose schedule.  *Modified from Immunization Action Coalition:* [*http://www.immunize.org*](http://www.immunize.org/)*.* | | |

Because of the potential risk of injury to the sciatic nerve, the gluteal region is not recommended for routine vaccina- tion.2,5 This recommendation is based primarily on reported cases of sciatic nerve injury resulting from injection of antimi- crobial agents or antiserum into the gluteus.16,17 No reports of direct nerve injury resulting from gluteal injection of current childhood vaccines have been published.

If injections are given in the gluteal site, care must be taken to avoid nerve injury. The central region of the buttocks should be avoided. The needle should be inserted into the upper, outer quadrant and directed anteriorly (i.e., not cau- dally or perpendicular to the skin surface). If the gluteal muscle is chosen, injection should be lateral and superior to a line between the posterior superior iliac spine and the greater trochanter or the ventrogluteal site (i.e., the center of the triangle bounded by the anterior superior iliac spine, the tubercle of the iliac crest, and the upper border of the greater trochanter of the femur). These areas are free of major neurovascular structures. Because of the large volume that must be injected and its large muscle mass, the gluteal site

often is used for passive immunization with immunoglobulin preparations.2,5

A 22- to 25-gauge needle is appropriate for intramuscular administration of most vaccines. The ideal needle length may depend on the vaccination technique.18 One technique for intramuscular injections consists of gently bunching the muscle in the free hand while the needle is inserted perpen- dicular to the skin. A second technique consists of using the thumb and index finger to stretch the skin flat over the injec- tion site while inserting the needle perpendicular to the skin and injecting the vaccine.18,19

The subcutaneous tissue and muscle layer thickness of the anterolateral thigh and deltoid region have been determined by ultrasonography.18,20,21 On the basis of the resulting data, a 58-inch (16-mm) needle used according to the second tech- nique described above is estimated to be adequate for intra- muscular injection in the thigh of infants and toddlers and in the deltoid of toddlers.18 However, when using the “bunching” technique described above, a 78 - to 1-inch (22- to 25-mm) needle would be necessary for adequate intramuscular

penetration of the thigh of a 4-month-old infant and of the thigh and deltoid of toddlers and older children.2,5,18,20 For injection into the thigh of children 3 years through 10 years of age, the needle length must be 1- to 1.25-inches in length.22

For adolescents and adults, the ideal needle length for intramuscular injection depends on the weight and sex of the vaccinee. For adolescents the deltoid muscle is preferred; however, the anterolateral thigh may be used, and if used the needle must be 1- to 1.5-inches in length.23 Poland and col- leagues21 reported that women have a greater deltoid fat pad thickness by ultrasonography and a greater deltoid skinfold thickness than men of an equal body mass index. These authors recommended a 1-inch (25-mm) needle for men for all weight ranges studied (i.e., 59–118 kg); a 58 - to 1-inch (16–25-mm) needle is recommended for women weighing less than 60 kg, a 1-inch (25-mm) needle is sufficient for women who weigh 60 to 90 kg, and a 1.5-inch (38-mm) needle is recommended for women who weigh more than 90 kg and men who weigh more than 118 kg.5,21

## Vaccinating Persons With Bleeding Disorders and Persons Receiving Anticoagulant Therapy

Persons with bleeding disorders such as hemophilia and persons receiving anticoagulant therapy can be at increased risk for bleeding after intramuscular injection. If possible vac- cination could be scheduled prior to the use of anticoagulant therapy so that the patients’ risk of bleeding is not increased by their therapeutic action.

A 23-gauge or smaller needle should be used for the vac- cination, and firm pressure without rubbing should be applied to the site for at least 2 minutes following injection. Alterna- tively, vaccines recommended for intramuscular injection could be administered subcutaneously to persons with a bleeding disorder if the immune response and clinical reac- tion to these vaccines are expected to be comparable by either route of injection, such as meningococcal conjugate vaccine and hepatitis A vaccine.2,24,25

## Intradermal Injections

BCG, one influenza vaccine, and smallpox vaccine are the only vaccines in the United States licensed for intradermal admin- istration. Intradermal influenza vaccine is administered near the middle of the upper arm, over the insertion of the deltoid muscle. The intradermal influenza vaccine is administered using a prefilled 350-inch microneedle injector system.

Smallpox (vaccinia) vaccine is administered by the intra-

dermal route using multiple punctures with a unique bifur- cated needle held perpendicular to the skin (see Chapter 33). A successful vaccination results in a pustular lesion (“Jenne- rian pustule”) at the vaccination site 6 to 8 days after primary vaccination. The skin reaction following revaccination may be less pronounced, with more rapid progression and healing, than that after primary vaccination.26

## Oral Administration

For vaccines given orally, the vaccine must be swallowed and retained. A dose of oral polio vaccine (OPV) should be repeated immediately if a patient spits out, does not swallow, or regurgitates a dose within 10 minutes after administra- tion.24 However, readministration of rotavirus vaccine is not recommended if the dose is spat out or regurgitated. No data exist on the benefits or risks associated with readministering a dose of regurgitated rotavirus vaccine. The infant should receive the remaining recommended doses of rotavirus vaccine

following the routine schedule (with a 4-week minimum interval between doses).5,27

## Intranasal Route

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Live attenuated influenza vaccine (LAIV) is licensed for healthy nonpregnant persons 2 through 49 years of age and is the only vaccine administered by the intranasal route. The administra- tion device is a nasal sprayer with a dose-divider clip that allows introduction of one 0.1-mL spray into each naris. The tip should be inserted slightly into the naris before administra- tion. Even if the person coughs or sneezes immediately after administration or the dose is expelled any other way, the vaccine dose need not be repeated. Introduction of low levels of vaccine viruses into the environment likely is unavoidable when administering LAIV; however, no cases have been reported of illness or attenuated vaccine virus infections among inadvertently exposed healthcare providers or immu- nocompromised patients. The risk for acquiring vaccine viruses from the environment is unknown but is likely low; in addition, vaccine viruses are cold-adapted and attenuated and unlikely to cause symptomatic influenza. Severely immuno- suppressed persons should not administer LAIV. However, other persons at higher risk for influenza complications can administer LAIV. These include persons with underlying medical conditions placing them at higher risk or who are likely to be at risk, including pregnant women, persons with asthma, and persons 50 years or older.28

## Needle-Shielding/Needle-Free Devices

Bloodborne diseases (e.g., hepatitides B and C and HIV) are occupational hazards for healthcare providers. In November 2000, to reduce the incidence of needlestick injuries among healthcare providers and the consequent risk for bloodborne diseases acquired from patients, the Needlestick Safety and Prevention Act was signed into law in the United States. The act directed the U.S. Occupational Safety and Health Admin- istration (OSHA) to strengthen its existing bloodborne patho- gen standards. Those standards were revised and became effective in April 2001.29 These federal regulations require the use of engineering and work practice controls to eliminate or minimize employee exposure to bloodborne pathogens.30 “Engineering controls” mean controls (e.g., sharps disposal containers; self-sheathing needles; and safer medical devices, such as sharps with engineered sharps injury protections and needleless systems) that isolate or remove the bloodborne pathogens hazard from the workplace.31 Work practice con- trols mean procedures followed by employers and workers to control hazards in the workplace (e.g., good housekeeping practices; closed transfers/containers/processes; and hygiene procedures).

Needle-shielding or needle-free devices that might satisfy

the occupational safety regulations for administering paren- teral injections are available in the United States and are listed at multiple websites.33 Additional information regarding implementation and enforcement of these regulations is avail- able at the OSHA website.29

## Jet Injectors

Jet injectors (JIs) are needle-free devices that drive liquid medi- cation through a nozzle orifice, creating a narrow stream under high pressure that penetrates skin to deliver a drug or vaccine into intradermal, subcutaneous, or intramuscular tissues.35,36 JIs have the potential to reduce the frequency of needlestick injuries to healthcare providers and to overcome the improper reuse and other drawbacks of needles and

syringes in economically developing countries.37,38 JIs have been reported safe and effective in administering different live and inactivated vaccines for viral and bacterial diseases.39 The immune responses generated are equivalent to, and occasion- ally greater than, immune responses induced by needle injec- tion. However, local reactions or injury (e.g., redness, induration, pain, blood, ecchymosis, and transient neuropa- thy at the injection site) can be more frequent when vaccines are delivered by JIs compared with needle injection.39

In the 1990s, a new generation of JIs was introduced with disposable cartridges serving as dose chambers and nozzle. With the provision of a new sterile cartridge for each patient and correct use, these devices avoid safety concerns for multiple-use–nozzle devices. These devices should be used in accordance with their labeling for intradermal, subcutaneous, or intramuscular administration. One brand of inactivated influenza vaccine has been approved by the U.S. Food and Drug Administration for use with a JI device.40,41

# ALLEVIATION OF PAIN AND DISCOMFORT ASSOCIATED WITH VACCINATION

Several methods have been reported to reduce pain and dis- comfort associated with vaccination injection, but they have not been tested widely.39 Pretreatment with topical lidocaine- prilocaine emulsion cream or patch can decrease the pain of diphtheria and tetanus toxoids and pertussis (DTP and DTaP) vaccination in infants by causing superficial anesthesia.42–44 This product does not interfere with the immune response to MMR43 or to inactivated vaccines.45

Evidence does not support use of antipyretics before or at the time of vaccination; however, antipyretics can be used for treatment of fever and local discomfort that might occur fol- lowing vaccination. Studies of children with previous febrile seizures have not demonstrated antipyretics to be effective in the prevention of febrile seizures.46

A topical refrigerant spray can reduce the short-term pain associated with injections and can be as effective as lidocaine- prilocaine cream.46,47 Oral administration of sweet-tasting fluid just before injection may cause a calming or analgesic effect in some infants.48 Breastfeeding is a potent analgesic intervention for infants during blood collection and may, by extrapolation, help decrease injection pain during immuniza- tion. Distraction techniques such as listening to music or “blowing away pain” also may help children cope with the discomfort associated with vaccination.49,50 Swaddling and slow lateral swaying also help as comfort measures.51

# AGES FOR ADMINISTRATION OF IMMUNOBIOLOGICS

Recommendations for the age and timing of vaccination are based on multiple considerations and may vary in different countries. Optimal response to a vaccine depends on a number of factors, including the nature of the vaccine and the age and immune status of the recipient. Recommendations for the age at which vaccines are administered are influenced by age- specific risks for disease and complications, ability of persons of a certain age to respond to the vaccine, and potential inter- ference with the immune response by passively transferred maternal antibody or previously administered antibody- containing blood products. Vaccines usually are recommended for members of the youngest age group at risk for experiencing the disease for whom efficacy and safety have been demon- strated. These principles are demonstrated with the following examples.

The optimal timing for administration of measles vaccine depends on the rate of disappearance of passively acquired maternal antibody and the risk of exposure to measles virus. At birth and through the first 6 months of life, most infants have passive immunity to measles because of transplacentally acquired maternal measles antibodies. These antibodies inter- fere with the immune response to live virus measles vaccine by limiting vaccine virus replication. In many developing countries, where measles is highly endemic and frequently affects infants, routine measles vaccination is recommended at 9 months of age (see Chapter 21).52 However, in the United States, where measles is less common and measles among infants is infrequent, measles vaccine is recommended rou- tinely at 12 through 15 months of age, ages at which almost all infants will have no residual maternal antibody.2,53

Another example is the recommended age of pertussis vac-

cination. Early infancy is the time of greatest risk of serious complications from pertussis, but infants who are younger than 1 month of age do not respond as well immunologically to whole-cell pertussis vaccine (and presumably acellular vac- cines) as do older infants.54–56 Initiation of routine immuniza- tion with pertussis vaccine in the United States is recommended at 2 months of age.57,58 This scheduling represents a compro- mise between factors affecting the immune response and the epidemiology of the disease necessitating early protection against pertussis. Tdap (tetanus, diphtheria, and pertussis) given to pregnant women will stimulate the development of maternal antipertussis antibodies, which will be transferred to the fetus by the placenta, likely providing the newborn with protection against pertussis in early life.59 Tdap also will protect the mother from pertussis around the time of delivery, making her less likely to become infected and transmit pertussis to her infant.59 Vaccination too early in life also may affect the immune response to subsequent doses of vaccine. For example, neonatal administration of diphtheria and tetanus toxoids (DT) may result in suppression of antibody responses to subsequent doses of Hib conjugate vaccines covalently linked to forms of those toxoids.60 When children who receive measles vaccine before the age of 1 year are revaccinated, they develop vaccine- induced immunity against disease but may have a somewhat diminished antibody response compared with children vacci- nated initially after their first birthday.61,62

In the United States, the recommended childhood, adoles-

cent, and adult immunization schedules are revised annually and are approved by the ACIP, the AAP (for the childhood and adolescent schedule), the American Academy of Family Physi- cians, the American Congress of Obstetricians and Gynecolo- gists, the American College of Physicians (for the adult schedule), and the American College of Nurse Midwives (for the adult schedule).63,64 A recent U.S. childhood vaccination schedule is shown in [Fig. 9.1](#_bookmark2).63 The most current vaccination schedules for children and adults are available from the CDC Vaccines and Immunizations website ([http://www.cdc.gov/](http://www.cdc.gov/vaccines/schedules/index.html) [vaccines/schedules/index.html](http://www.cdc.gov/vaccines/schedules/index.html)).65 [Table 9.2](#_bookmark3) lists the recom- mended and minimum ages and recommended and minimum acceptable intervals between doses of vaccines used in the United States. Other vaccination schedules are discussed in Chapters 74, 75, and 76.

# SPACING OF VACCINE DOSES

## Spacing of Multiple Doses of the Same Vaccine

Although administration of one dose of some vaccines may induce a protective antibody response, most vaccines require administration of multiple doses in a primary series for devel- opment of immunity. Examples of the former are rubella and yellow fever vaccines; examples of the latter are poliovirus,

hepatitis B, and pertussis vaccines. In addition, periodic revac- cination (“booster doses”) with certain vaccines may be neces- sary to maintain immunity. Examples are typhoid vaccines and tetanus and diphtheria toxoids.

Because of immunologic memory, intervals longer than routinely recommended between doses do not impair the immunologic response to live and inactivated vaccines that require more than one dose to achieve primary immunity. Similarly, delayed administration of recommended booster doses does not adversely affect the antibody response to such doses.2,5 As a result, interruption of a recommended primary series or an extended interval between booster doses does not necessitate reinitiation of the entire vaccination series. For example, lengthening the interval between two doses of inac- tivated poliovirus vaccine (IPV) may increase the antibody response to the second dose.66 In the case of oral typhoid (Ty21a) vaccine, an exception has been proposed. The impact of a lapse in the series of oral typhoid vaccine is not known. However, as a rule of thumb for Ty21a, if fewer than 3 weeks

have passed since the last dose, the series may be completed with the missing dose or doses. If more than 3 weeks have passed, the full series should be repeated.

Vaccination providers should strive to adhere as closely as possible to recommended childhood, adolescent, and adult immunization schedules. Clinical studies confirm that recom- mended ages and intervals between doses of multidose anti- gens provide optimal protection or have the best evidence of efficacy. [Table 9.2](#_bookmark3) lists recommended intervals between doses of commonly used vaccines.

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In certain circumstances, administering doses of a multi- dose vaccine at shorter than the recommended intervals might be necessary. Examples include when a person is behind schedule and needs to be brought up-to-date as quickly as possible and cases of impending international travel. In these situations, an accelerated schedule with intervals between doses shorter than intervals recommended for routine vaccina- tion can be used.63 Although the effectiveness of all accelerated

*Text continued on p. 10ł*

#### Recommended immunization schedule for persons aged 0 through 18 years – United States, 2016.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded.

Vaccine

Birth 1 mo 2 mos 4 mos 6 mos 9 mos 12 mos 15 mos 18 mos

19–23

mos

2–3 yrs 4–6 yrs 7–10 yrs 11–12 yrs 13–15 yrs 16–18 yrs

Hepatitis B1 (HepB)

1st dose 2nd dose

3rd dose

Rotavirus2 (RV) RV1 (2-dose series); RV5 (3-dose series)

Diphtheria, tetanus, & acellular pertussis3 (DTaP: <7 yrs)

*Haemophilus influenzae* type b4 (Hib)

Pneumococcal conjugate5 (PCV13)

Inactivated poliovirus6 (IPV: <18 yrs)

1 dose

st

See

1st dose

2 dose footnote 2

2nd dose 3rd dose

nd

4th dose

5th dose

1 dose

st

2 dose footnote 4

nd

See

3rd or 4thdose, See footnote 4

1 dose

st

2 dose 3 dose

nd rd

4th dose

1st dose

2 dose

nd

3 dose

rd

4 dose

th

Influenza7 (IIV; LAIV)

Annual vaccination (IIV only) 1 or 2 doses

Annual vaccination (LAIV or Annual vaccination (LAIV or IIV)

IIV) 1 or 2 doses 1 dose only

Measles, mumps, rubella8 (MMR) See footnote 8 1st dose 2nd dose

Varicella9 (VAR)

1st dose

2nd dose

Hepatitis A10 (HepA)

2-dose series, See footnote 10

Meningococcal11 (Hib-MenCY

6 weeks; MenACWY-D 9 mos; MenACWY-CRM 2 mos)

Tetanus, diphtheria, & acellular pertussis12 (Tdap: 7 yrs)

Human papillomavirus13 (2vHPV: females only; 4vHPV, 9vHPV: males and females)

See footnote 11

1st dose

2nd dose

(3-dose series)

Meningococcal B11

See footnote 11

Pneumococcal polysaccharide5 (PPSV23)

Range of recommended ages for all children

Booster

Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

Range of recommended ages during which catch-up is encouraged and for certain high-risk groups

Not routinely recommended

This schedule includes recommendations in effect as of January 1, 2016. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at [**http://www.cdc.gov/vaccines/hcp/acip-recs/index.html.**](http://www.cdc.gov/vaccines/hcp/acip-recs/index.html)Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online ([**http://www.vaers.hhs.gov**)](http://www.vaers.hhs.gov/) or by telephone (**800-822-7967**). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online ([**http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm**)](http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm)) or by telephone (**800-CDC-INFO**

[**800-232-4636**]).

This schedule is approved by the Advisory Committee on Immunization Practices ([http//www.cdc.gov/vaccines/acip),](http://www.cdc.gov/vaccines/acip))

the American Academy of Pediatrics ([http://www.aap.org),](http://www.aap.org/) the American Academy of Family Physicians ([http://www.aafp.org),](http://www.aafp.org/) and the American College of Obstetricians and Gynecologists ([http://www.acog.org).](http://www.acog.org/)

**NOTE: The above recommendations must be read along with the footnotes of this schedule.**

**Figure 9.1.** Immunization schedules. Available at [www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html](http://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html). *Continued*

#### Catch-up immunization schedule for persons aged 4 months through 18 years who start late or who are more than 1 month behind —United States, 2016.

The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child’s age. Always use this table in conjunction with Figure 1 and the footnotes that follow.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Children age 4 months through 6 years** | | | | | |
| Vaccine | Minimum age for dose 1 | Minimum interval between doses | | | |
| Dose 1 to Dose 2 | Dose 2 to Dose 3 | Dose 3 to Dose 4 | Dose 4 to Dose 5 |
| Hepatitis B1 | Birth | 4 weeks | 8 weeks *and* at least 16 weeks after first dose. Minimum age for the final dose is 24 weeks. |  |  |
| Rotavirus2 | 6 weeks | 4 weeks | 4 weeks2 |  |  |
| Diphtheria, tetanus, and acellular pertussis3 | 6 weeks | 4 weeks | 4 weeks | 6 months | 6 months3 |
| *Haemophilus influenzae*  type b4 | 6 weeks | 4 weeks  if first dose was administered before the 1st birthday.  8 weeks (as final dose)  if first dose was administered at age 12 through 14 months.  No further doses needed  if first dose was administered at age 15 months or older. | 4 weeks4  if current age is younger than 12 months **and** first dose was administered at younger than age 7 months, **and** at least 1 previous dose was PRP-T (ActHib, Pentacel)  or unknown.  8 weeks *and* age 12 through 59 months (as final dose for healthy children)4  if current age is younger than 12 months **and**  first dose was administered at age 7 through 11 months (wait until at least 12 months old);  OR  if current age is 12 through 59 months **and**  first dose was administered before the 1st birthday, **and** second dose administered at younger than 15 months; OR  if both doses were PRP-OMP (PedvaxHIB; Comvax)  **and** were administered before the 1st birthday (wait until at least 12 months old).  No further doses needed  if previous dose was administered at age 15 months or older. | 8 weeks (as final dose) This dose only necessary for children age 12 through 59 months who received  3 doses before the 1st birthday. |  |
| Pneumococcal5 | 6 weeks | 4 weeks  if first dose administered before the 1st birthday.  8 weeks (as final dose for healthy children)  if first dose was administered at the 1st birthday or after.  No further doses needed  for healthy children if first dose administered at age 24 months or older. | 4 weeks  if current age is younger than 12 months and previous dose given at <7months old.  8 weeks (as final dose for healthy children) if previous dose given between 7–11 months (wait until at least 12 months old);  OR  if current age is 12 months or older and at least 1 dose was given before age 12 months.  No further doses needed  for healthy children if previous dose administered at age 24 months or older. | 8 weeks (as final dose)  This dose only necessary for children aged 12 through 59 months who received  3 doses before age  12 months or for children at high risk who  received 3 doses at any age. |  |
| Inactivated poliovirus6 | 6 weeks | 4 weeks6 | 4 weeks6 | 6 months6  (minimum age 4 years for final dose). |  |
| Measles, mumps, rubella8 | 12 months | 4 weeks |  |  |  |
| Varicella9 | 12 months | 3 months |  |  |  |
| Hepatitis A10 | 12 months | 6 months |  |  |  |
| Meningococcal11  (Hib-MenCY >6 weeks;  MenACWY-D >9 mos;  MenACWY-CRM >2 mos) | 6 weeks | 8 weeks11 | See footnote 11 | See footnote 11 |  |
| **Children and adolescents age 7 through 18 years** | | | | | |
| Meningococcal11  (Hib-MenCY >6 weeks;  MenACWY-D >9 mos;  MenACWY-CRM >2 mos) | Not applicable (N/A) | 8 weeks11 |  |  |  |
| Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis12 | 7 years12 | 4 weeks | 4 weeks  if first dose of DTaP/DT was administered before the 1st birthday.  6 months (as final dose)  if first dose of DTaP/DT or Tdap/Td was administered at or after the 1st birthday. | 6 months  if first dose of DTaP/DT was administered before the 1st birthday. |  |
| Human papillomavirus13 | 9 years | Routine dosing intervals are recommended.13 | | | |
| Hepatitis A10 | N/A | 6 months |  |  |  |
| Hepatitis B1 | N/A | 4 weeks | 8 weeks **and** at least 16 weeks after first dose. |  |  |
| Inactivated poliovirus6 | N/A | 4 weeks | 4 weeks6 | 6 months6 |  |
| Meningococcal11 | N/A | 8 weeks11 |  |  |  |
| Measles, mumps, rubella8 | N/A | 4 weeks |  |  |  |
| Varicella9 | N/A | 3 months if younger than age 13 years.  4 weeks if age 13 years or older. |  |  |  |

**NOTE: The above recommendations must be read along with the footnotes of this schedule.**

**Figure 9.1. cont’d**

**Footnotes — Recommended immunization schedule for persons aged 0 through 18 years—United States, 2016**

**9**

For further guidance on the use of the vaccines mentioned below, see: [**http://www.cdc.gov/vaccines/hcp/acip-recs/index.html.**](http://www.cdc.gov/vaccines/hcp/acip-recs/index.html)

For vaccine recommendations for persons 19 years of age and older, see the Adult Immunization Schedule [**www.cdc.gov/vaccines/schedules/hcp/adult.html**.](http://www.cdc.gov/vaccines/schedules/hcp/adult.html) **Additional information**

* For contraindications and precautions to use of a vaccine and for additional information regarding that vaccine, vaccination providers should consult the relevant ACIP statement available online at

[**http://www.cdc.gov/vaccines/hcp/acip-recs/index.html.**](http://www.cdc.gov/vaccines/hcp/acip-recs/index.html)

* For purposes of calculating intervals between doses, 4 weeks = 28 days. Intervals of 4 months or greater are determined by calendar months.
* Vaccine doses administered 4 days or less before the minimum interval are considered valid. Doses of any vaccine administered ≥5 days earlier than the minimum interval or minimum age should not be counted as valid doses and should be repeated as age-appropriate. The repeat dose should be spaced after the invalid dose by the recommended minimum interval. For further details, see *MMWR, General Recommendations on Immunization and Reports* / Vol. 60 / No. 2; Table 1. *Recommended and minimum ages and intervals between vaccine doses available* online at [**http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf**.](http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf)
* Information on travel vaccine requirements and recommendations is available at [**http://wwwnc.cdc.gov/travel/destinations/list**.](http://wwwnc.cdc.gov/travel/destinations/list)
* For vaccination of persons with primary and secondary immunodeficiencies, see Table 13, *“Vaccination of persons with primary and secondary immunodeficiencies,” in General Recommendations on Immunization* (ACIP), available at [**http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf**.;](http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf.%3B) and American Academy of Pediatrics. “Immunization in Special Clinical Circumstances,” in Kimberlin DW, Brady MT, Jackson MA, Long SS eds. *Red Book: 2015 report of the Committee on Infectious Diseases. 30th ed.* Elk Grove Village, IL: American Academy of Pediatrics.

1. **Hepatitis B (HepB) vaccine. (Minimum age: birth) Routine vaccination:**

**At birth:**

* + Administer monovalent HepB vaccine to all newborns before hospital discharge.
  + For infants born to hepatitis B surface antigen (HBsAg)-positive mothers, administer HepB vaccine and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth. These infants should be tested for HBsAg and antibody to HBsAg (anti-HBs) at age 9 through 18 months (preferably at the next well-child visit) or 1 to 2 months after completion of the HepB series if the series was delayed; CDC recently recommended testing occur at age 9 through 12 months; see [**http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6439a6.htm**.](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6439a6.htm)
  + If mother’s HBsAg status is unknown, within 12 hours of birth administer HepB vaccine regardless of birth weight. For infants weighing less than 2,000 grams, administer HBIG in addition to HepB vaccine within 12 hours of birth. Determine mother’s HBsAg status as soon as possible and, if mother is HBsAg-positive, also administer HBIG for infants weighing 2,000 grams or more as soon as possible, but no later than age 7 days.

**Doses following the birth dose:**

* + The second dose should be administered at age 1 or 2 months. Monovalent HepB vaccine should be used for doses administered before age 6 weeks.
  + Infants who did not receive a birth dose should receive 3 doses of a HepB-containing vaccine on a schedule of 0, 1 to 2 months, and 6 months starting as soon as feasible. See Figure 2.
  + Administer the second dose 1 to 2 months after the first dose (minimum interval of 4 weeks), administer the third dose at least 8 weeks after the second dose AND at least 16 weeks after the **first** dose. The final (third or fourth) dose in the HepB vaccine series should be administered **no earlier than age 24 weeks**.
  + Administration of a total of 4 doses of HepB vaccine is permitted when a combination vaccine containing HepB is administered after the birth dose.

**Catch-up vaccination:**

* + Unvaccinated persons should complete a 3-dose series.
  + A 2-dose series (doses separated by at least 4 months) of adult formulation Recombivax HB is licensed for use in children aged 11 through 15 years.
  + For other catch-up guidance, see Figure 2.

1. **Rotavirus (RV) vaccines. (Minimum age: 6 weeks for both RV1 [Rotarix] and RV5 [RotaTeq]) Routine vaccination:**

**Administer a series of RV vaccine to all infants as follows:**

1. If Rotarix is used, administer a 2-dose series at 2 and 4 months of age.
2. If RotaTeq is used, administer a 3-dose series at ages 2, 4, and 6 months.
3. If any dose in the series was RotaTeq or vaccine product is unknown for any dose in the series, a total of 3 doses of RV vaccine should be administered.

**Catch-up vaccination:**

* The maximum age for the first dose in the series is 14 weeks, 6 days; vaccination should not be initiated for infants aged 15 weeks, 0 days or older.
* The maximum age for the final dose in the series is 8 months, 0 days.
* For other catch-up guidance, see Figure 2.

1. **Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine. (Minimum age: 6 weeks. Exception: DTaP-IPV [Kinrix, Quadracel]: 4 years)**

**Routine vaccination:**

* + Administer a 5-dose series of DTaP vaccine at ages 2, 4, 6, 15 through 18 months, and 4 through 6 years. The fourth dose may be administered as early as age 12 months, provided at least 6 months have elapsed since the third dose.
  + Inadvertent administration of 4th DTaP dose early: If the fourth dose of DTaP was administered at least 4 months, but less than 6 months, after the third dose of DTaP, it need not be repeated.

**Catch-up vaccination:**

* + The fifth dose of DTaP vaccine is not necessary if the fourth dose was administered at age 4 years or older.
  + For other catch-up guidance, see Figure 2.

1. ***Haemophilus influenzae* type b (Hib) conjugate vaccine. (Minimum age: 6 weeks for PRP-T [ACTHIB, DTaP-IPV/Hib (Pentacel) and Hib-MenCY (MenHibrix)], PRP-OMP [PedvaxHIB or COMVAX], 12 months for PRP-T [Hiberix])**

**Routine vaccination:**

* + Administer a 2- or 3-dose Hib vaccine primary series and a booster dose (dose 3 or 4 depending on vaccine used in primary series) at age 12 through 15 months to complete a full Hib vaccine series.
  + The primary series with ActHIB, MenHibrix, or Pentacel consists of 3 doses and should be administered at 2, 4, and 6 months of age. The primary series with PedvaxHib or COMVAX consists of 2 doses and should be administered at 2 and 4 months of age; a dose at age 6 months is not indicated.
  + One booster dose (dose 3 or 4 depending on vaccine used in primary series) of any Hib vaccine should be administered at age 12 through 15 months. An exception is Hiberix vaccine. Hiberix should only be used for the booster (final) dose in children aged 12 months through 4 years who have received at least 1 prior dose of Hib-containing vaccine.
  + For recommendations on the use of MenHibrix in patients at increased risk for meningococcal disease, please refer to the meningococcal vaccine footnotes and also to *MMWR* February 28, 2014 / 63(RR01);1–13, available at [**http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf**.](http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf)

**Catch-up vaccination:**

* + If dose 1 was administered at ages 12 through 14 months, administer a second (final) dose at least 8 weeks after dose 1, regardless of Hib vaccine used in the primary series.
  + If both doses were PRP-OMP (PedvaxHIB or COMVAX), and were administered before the first birthday, the third (and final) dose should be administered at age 12 through 59 months and at least 8 weeks after the second dose.
  + If the first dose was administered at age 7 through 11 months, administer the second dose at least 4 weeks later and a third (and final) dose at age 12 through 15 months or 8 weeks after second dose, whichever is later.
  + If first dose is administered before the first birthday and second dose administered at younger than 15 months, a third (and final) dose should be administered 8 weeks later.
  + For unvaccinated children aged 15 months or older, administer only 1 dose.
  + For other catch-up guidance, see Figure 2. For catch-up guidance related to MenHibrix, please see the meningococcal vaccine footnotes and also *MMWR* February 28, 2014 / 63(RR01);1–13, available at [**http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf**.](http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf)

**Vaccination of persons with high-risk conditions:**

* + Children aged 12 through 59 months who are at increased risk for Hib disease, including chemotherapy recipients and those with anatomic or functional asplenia (including sickle cell disease), human immunodeficiency virus (HIV ) infection, immunoglobulin deficiency, or early component complement deficiency, who have received either no doses or only 1 dose of Hib vaccine before 12 months of age, should receive 2 additional doses of Hib vaccine 8 weeks apart; children who received 2 or more doses of Hib vaccine before 12 months of age should receive 1 additional dose.
  + For patients younger than 5 years of age undergoing chemotherapy or radiation treatment who received a Hib vaccine dose(s) within 14 days of starting therapy or during therapy, repeat the dose(s) at least 3 months following therapy completion.

1. ***Haemophilus influenzae* type b (Hib) conjugate vaccine. (cont’d)**
   * Recipients of hematopoietic stem cell transplant (HSCT) should be revaccinated with a 3-dose regimen of Hib vaccine starting 6 to 12 months after successful transplant, regardless of vaccination history; doses should be administered at least 4 weeks apart.
   * A single dose of any Hib-containing vaccine should be administered to unimmunized\* children and adolescents 15 months of age and older undergoing an elective splenectomy; if possible, vaccine should be administered at least 14 days before procedure.
   * Hib vaccine is not routinely recommended for patients 5 years or older. However, 1 dose of Hib vaccine should be administered to unimmunized\* persons aged 5 years or older who have anatomic or functional asplenia (including sickle cell disease) and unvaccinated persons 5 through 18 years of age with HIV infection.

*\* Patients who have not received a primary series and booster dose or at least 1 dose of Hib vaccine after 14 months of age are considered unimmunized.*

1. **Pneumococcal vaccines. (Minimum age: 6 weeks for PCV13, 2 years for PPSV23) Routine vaccination with PCV13:**
   * Administer a 4-dose series of PCV13 vaccine at ages 2, 4, and 6 months and at age 12 through 15 months.
   * For children aged 14 through 59 months who have received an age-appropriate series of 7-valent PCV (PCV7), administer a single supplemental dose of 13-valent PCV (PCV13).

**Catch-up vaccination with PCV13:**

* + Administer 1 dose of PCV13 to all healthy children aged 24 through 59 months who are not completely vaccinated for their age.
  + For other catch-up guidance, see Figure 2.

**Vaccination of persons with high-risk conditions with PCV13 and PPSV23:**

* + All recommended PCV13 doses should be administered prior to PPSV23 vaccination if possible.
  + For children 2 through 5 years of age with any of the following conditions: chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure); chronic lung disease (including asthma if treated with high-dose oral corticosteroid therapy); diabetes mellitus; cerebrospinal fluid leak; cochlear implant; sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; solid organ transplantation; or congenital immunodeficiency:
    1. Administer 1 dose of PCV13 if any incomplete schedule of 3 doses of PCV (PCV7 and/or PCV13) were received previously.
    2. Administer 2 doses of PCV13 at least 8 weeks apart if unvaccinated or any incomplete schedule of fewer than 3 doses of PCV (PCV7 and/or PCV13) were received previously.
    3. Administer 1 supplemental dose of PCV13 if 4 doses of PCV7 or other age-appropriate complete PCV7 series was received previously.
    4. The minimum interval between doses of PCV (PCV7 or PCV13) is 8 weeks.
    5. For children with no history of PPSV23 vaccination, administer PPSV23 at least 8 weeks after the most recent dose of PCV13.
  + For children aged 6 through 18 years who have cerebrospinal fluid leak; cochlear implant; sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; generalized malignancy; solid organ transplantation; or multiple myeloma:
    1. If neither PCV13 nor PPSV23 has been received previously, administer 1 dose of PCV13 now and 1 dose of PPSV23 at least 8 weeks later.
    2. If PCV13 has been received previously but PPSV23 has not, administer 1 dose of PPSV23 at least 8 weeks after the most recent dose of PCV13.
    3. If PPSV23 has been received but PCV13 has not, administer 1 dose of PCV13 at least 8 weeks after the most recent dose of PPSV23.
  + For children aged 6 through 18 years with chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure), chronic lung disease (including asthma if treated with

high-dose oral corticosteroid therapy), diabetes mellitus, alcoholism, or chronic liver disease, who have not received PPSV23, administer 1 dose of PPSV23. If PCV13 has been received previously, then PPSV23 should be administered at least 8 weeks after any prior PCV13 dose.

* + A single revaccination with PPSV23 should be administered 5 years after the first dose to children with sickle cell disease or other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; generalized malignancy; solid organ transplantation; or multiple myeloma.

1. **Inactivated poliovirus vaccine (IPV). (Minimum age: 6 weeks) Routine vaccination:**
   * Administer a 4-dose series of IPV at ages 2, 4, 6 through 18 months, and 4 through 6 years. The final dose in the series should be administered on or after the fourth birthday and at least 6 months after the previous dose.

**Catch-up vaccination:**

* + In the first 6 months of life, minimum age and minimum intervals are only recommended if the person is at risk of imminent exposure to circulating poliovirus (i.e., travel to a polio-endemic region or during an outbreak).
  + If 4 or more doses are administered before age 4 years, an additional dose should be administered at age 4 through 6 years and at least 6 months after the previous dose.
  + A fourth dose is not necessary if the third dose was administered at age 4 years or older and at least 6 months after the previous dose.
  + If both OPV and IPV were administered as part of a series, a total of 4 doses should be administered, regardless of the child’s current age. If only OPV were administered, and all doses were given prior to 4 years of age, one dose of IPV should be given at 4 years or older, at least 4 weeks after the last OPV dose.
  + IPV is not routinely recommended for U.S. residents aged 18 years or older.
  + For other catch-up guidance, see Figure 2.

1. **Influenza vaccines. (Minimum age: 6 months for inactivated influenza vaccine [IIV], 2 years for live, attenuated influenza vaccine [LAIV])**

**Routine vaccination:**

* + Administer influenza vaccine annually to all children beginning at age 6 months. For most healthy, nonpregnant persons aged 2 through 49 years, either LAIV or IIV may be used. However, LAIV should NOT be administered to some persons, including 1) persons who have experienced severe allergic reactions to LAIV, any of its components, or to a previous dose of any other influenza vaccine; 2) children 2 through 17 years receiving aspirin or aspirin-containing products; 3) persons who are allergic to eggs; 4) pregnant women; 5) immunosuppressed persons; 6) children 2 through 4 years of age with asthma or who had wheezing in the past 12 months; or 7) persons who have taken influenza antiviral medications in the previous 48 hours. For all other contraindications and precautions to use of LAIV, see *MMWR* August 7, 2015 / 64(30):818–25 available at [**http://www.cdc.gov/mmwr/pdf/wk/mm6430.pdf.**](http://www.cdc.gov/mmwr/pdf/wk/mm6430.pdf)

**Figure 9.1. cont’d** *Continued*

1. **Influenza vaccines. (cont’d)**

**For children aged 6 months through 8 years:**

* + For the 2015–16 season, administer 2 doses (separated by at least 4 weeks) to children who are receiving influenza vaccine for the first time. Some children in this age group who have been vaccinated previously will also need 2 doses. For additional guidance, follow dosing guidelines in the 2015–16 ACIP influenza vaccine recommendations, *MMWR* August 7, 2015 / 64(30):818–25, available at [http://www.cdc.gov/mmwr/pdf/wk/mm6430.pdf.](http://www.cdc.gov/mmwr/pdf/wk/mm6430.pdf)
  + For the 2016–17 season, follow dosing guidelines in the 2016 ACIP influenza vaccine recommendations.

**For persons aged 9 years and older:**

* + Administer 1 dose.

1. **Measles, mumps, and rubella (MMR) vaccine. (Minimum age: 12 months for routine vaccination) Routine vaccination:**
   * Administer a 2-dose series of MMR vaccine at ages 12 through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 4 weeks have elapsed since the first dose.
   * Administer 1 dose of MMR vaccine to infants aged 6 through 11 months before departure from the United States for international travel. These children should be revaccinated with 2 doses of MMR vaccine, the first at age 12 through 15 months (12 months if the child remains in an area where disease risk is high), and the second dose at least 4 weeks later.
   * Administer 2 doses of MMR vaccine to children aged 12 months and older before departure from the United States for international travel. The first dose should be administered on or after age 12 months and the second dose at least 4 weeks later.

**Catch-up vaccination:**

* + Ensure that all school-aged children and adolescents have had 2 doses of MMR vaccine; the minimum interval between the 2 doses is 4 weeks.

1. **Varicella (VAR) vaccine. (Minimum age: 12 months) Routine vaccination:**
   * Administer a 2-dose series of VAR vaccine at ages 12 through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 3 months have elapsed since the first dose. If the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid.

**Catch-up vaccination:**

* + Ensure that all persons aged 7 through 18 years without evidence of immunity (see *MMWR* 2007 / 56 [No. RR-4], available at [**http://www.cdc.gov/mmwr/pdf/rr/rr5604.pdf**](http://www.cdc.gov/mmwr/pdf/rr/rr5604.pdf)) have 2 doses of varicella vaccine. For children aged 7 through 12 years, the recommended minimum interval between doses is 3 months (if the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid); for persons aged 13 years and older, the minimum interval between doses is 4 weeks.

1. **Hepatitis A (HepA) vaccine. (Minimum age: 12 months) Routine vaccination:**
   * Initiate the 2-dose HepA vaccine series at 12 through 23 months; separate the 2 doses by 6 to 18 months.
   * Children who have received 1 dose of HepA vaccine before age 24 months should receive a second dose 6 to 18 months after the first dose.
   * For any person aged 2 years and older who has not already received the HepA vaccine series, 2 doses of HepA vaccine separated by 6 to 18 months may be administered if immunity against hepatitis A virus infection is desired.

**Catch-up vaccination:**

* + The minimum interval between the 2 doses is 6 months.

**Special populations:**

* + Administer 2 doses of HepA vaccine at least 6 months apart to previously unvaccinated persons who live in areas where vaccination programs target older children, or who are at increased risk for infection. This includes persons traveling to or working in countries that have high or intermediate endemicity of infection; men having sex with men; users of injection and non-injection illicit drugs; persons who work with HAV-infected primates or with HAV in a research laboratory; persons with clotting-factor disorders; persons with chronic liver disease; and persons who anticipate close personal contact (e.g., household or regular babysitting) with an international adoptee during the first 60 days after arrival in the United States from a country with high or intermediate endemicity. The first dose should be administered as soon as the adoption is planned, ideally 2 or more weeks before the arrival of the adoptee.

1. **Meningococcal vaccines. (Minimum age: 6 weeks for Hib-MenCY [MenHibrix], 9 months for MenACWY-D [Menactra], 2 months for MenACWY-CRM [Menveo], 10 years for serogroup B meningococcal [MenB] vaccines: MenB-4C [Bexsero] and MenB-FHbp [Trumenba]) Routine vaccination:**
   * Administer a single dose of Menactra or Menveo vaccine at age 11 through 12 years, with a booster dose at age 16 years.
   * Adolescents aged 11 through 18 years with human immunodeficiency virus (HIV) infection should receive a 2-dose primary series of Menactra or Menveo with at least 8 weeks between doses.
   * For children aged 2 months through 18 years with high-risk conditions, see below.

**Catch-up vaccination:**

* + Administer Menactra or Menveo vaccine at age 13 through 18 years if not previously vaccinated.
  + If the first dose is administered at age 13 through 15 years, a booster dose should be administered at age 16 through 18 years with a minimum interval of at least 8 weeks between doses.
  + If the first dose is administered at age 16 years or older, a booster dose is not needed.
  + For other catch-up guidance, see Figure 2.

**Clinical discretion:**

* + Young adults aged 16 through 23 years (preferred age range is 16 through 18 years) may be vaccinated with either a 2-dose series of Bexsero or a 3-dose series of Trumenba vaccine to provide short-term protection against most strains of serogroup B meningococcal disease. The two MenB vaccines are not interchangeable; the same vaccine product must be used for all doses.

**Vaccination of persons with high-risk conditions and other persons at increased risk of disease:**

**Children with anatomic or functional asplenia (including sickle cell disease): Meningococcal conjugate ACWY vaccines:**

* + 1. Menveo
       - *Children who initiate vaccination at 8 weeks:* Administer doses at 2, 4, 6, and 12 months of age.
       - *Unvaccinated children who initiate vaccination at 7 through 23 months:* Administer 2 doses, with the second dose at least 12 weeks after the first dose AND after the first birthday.
       - *Children 24 months and older who have not received a complete series*: Administer 2 primary doses at least 8 weeks apart.
    2. MenHibrix
       - *Children who initiate vaccination at 6 weeks:* Administer doses at 2, 4, 6, and 12 through 15 months of age.
       - If the first dose of MenHibrix is given at or after 12 months of age, a total of 2 doses should be given at least 8 weeks apart to ensure protection against serogroups C and Y meningococcal disease.

1. **Meningococcal vaccines. (cont’d)**
   * 1. Menactra
        + *Children 24 months and older who have not received a complete series:* Administer 2 primary doses at least 8 weeks apart. If Menactra is administered to a child with asplenia (including sickle cell disease), do not administer Menactra until 2 years of age and at least 4 weeks after the completion of all PCV13 doses.

**Meningococcal B vaccines:**

1. Bexsero or Trumenba

*o Persons 10 years or older who have not received a complete series.* Administer a 2-dose series of Bexsero, at least 1 month apart. Or a 3-dose series of Trumenba, with the second dose at least 2 months after the first and the third dose at least 6 months after the first. The two MenB vaccines are not interchangeable; the same vaccine product must be used for all doses.

**Children with persistent complement component deficiency (includes persons with inherited or chronic deficiencies in C3, C5-9, properidin, factor D, factor H, or taking eculizumab (Soliriis® ):**

**Meningococcal conjugate ACWY vaccines:**

1. Menveo
   * *Children who initiate vaccination at 8 weeks:* Administer doses at 2, 4, 6, and 12 months of age.
   * *Unvaccinated children who initiate vaccination at 7 through 23 months:* Administer 2 doses, with the second dose at least 12 weeks after the first dose AND after the first birthday.
   * *Children 24 months and older who have not received a complete series*: Administer 2 primary doses at least 8 weeks apart.
2. MenHibrix
   * *Children who initiate vaccination 6 weeks:* Administer doses at 2, 4, 6, and 12 through 15 months of age.
   * If the first dose of MenHibrix is given at or after 12 months of age, a total of 2 doses should be given at least 8 weeks apart to ensure protection against serogroups C and Y meningococcal disease.
3. Menactra
   * *Children 9 through 23 months*: Administer 2 primary doses at least 12 weeks apart.
   * *Children 24 months and older who have not received a complete series*: Administer 2 primary doses at least 8 weeks apart.

**Meningococcal B vaccines:**

1. Bexsero or Trumenba

*o Persons 10 years or older who have not received a complete series*. Administer a 2-dose series of Bexsero, at least 1 month apart. Or a 3-dose series of Trumenba, with the second dose at least 2 months after the first and the third dose at least 6 months after the first. The two MenB vaccines are not interchangeable; the same vaccine product must be used for all doses.

**For children who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic, including countries in the African meningitis belt or the Hajj**

* administer an age-appropriate formulation and series of Menactra or Menveo for protection against serogroups A and W meningococcal disease. Prior receipt of MenHibrix is not sufficient for children traveling to the meningitis belt or the Hajj because it does not contain serogroups A or W.

**For children at risk during a community outbreak attributable to a vaccine serogroup**

* administer or complete an age- and formulation-appropriate series of MenHibrix, Menactra, or Menveo, Bexsero or Trumenba.

For booster doses among persons with high-risk conditions, refer to *MMWR* 2013 / 62(RR02);1–22, available at [**http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6202a1.htm**.](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6202a1.htm)

For other catch-up recommendations for these persons, and complete information on use of meningococcal vaccines, including guidance related to vaccination of persons at increased risk of infection, see *MMWR* March 22, 2013 / 62(RR02);1–22, and *MMWR* October 23, 2015 / 64(41); 1171–1176 available at [**http://www.cdc.gov/mmwr/pdf/rr/rr6202.pdf,**](http://www.cdc.gov/mmwr/pdf/rr/rr6202.pdf) **and** [**http://www.cdc.gov/mmwr/pdf/wk/mm6441.pdf.**](http://www.cdc.gov/mmwr/pdf/wk/mm6441.pdf)

1. **Tetanus and diphtheria toxoids and acellular pertussis (Tdap) vaccine. (Minimum age: 10 years for both Boostrix and Adacel)**

**Routine vaccination:**

* + Administer 1 dose of Tdap vaccine to all adolescents aged 11 through 12 years.
  + Tdap may be administered regardless of the interval since the last tetanus and diphtheria toxoid- containing vaccine.
  + Administer 1 dose of Tdap vaccine to pregnant adolescents during each pregnancy (preferred during 27 through 36 weeks gestation) regardless of time since prior Td or Tdap vaccination.

**Catch-up vaccination:**

* + Persons aged 7 years and older who are not fully immunized with DTaP vaccine should receive Tdap vaccine as 1 (preferably the first) dose in the catch-up series; if additional doses are needed, use Td vaccine. For children 7 through 10 years who receive a dose of Tdap as part of the

catch-up series, an adolescent Tdap vaccine dose at age 11 through 12 years should NOT be administered. Td should be administered instead 10 years after the Tdap dose.

* + Persons aged 11 through 18 years who have not received Tdap vaccine should receive a dose followed by tetanus and diphtheria toxoids (Td) booster doses every 10 years thereafter.
  + Inadvertent doses of DTaP vaccine:
    - If administered inadvertently to a child aged 7 through 10 years may count as part of the catch-up series. This dose may count as the adolescent Tdap dose, or the child can later receive a Tdap booster dose at age 11 through 12 years.
    - If administered inadvertently to an adolescent aged 11 through 18 years, the dose should be counted as the adolescent Tdap booster.
  + For other catch-up guidance, see Figure 2.

1. **Human papillomavirus (HPV) vaccines. (Minimum age: 9 years for 2vHPV [Cervarix], 4vHPV [Gardasil] and 9vHPV [Gardasil 9])**

**Routine vaccination:**

* + Administer a 3-dose series of HPV vaccine on a schedule of 0, 1–2, and 6 months to all adolescents aged 11 through 12 years. 9vHPV, 4vHPV or 2vHPV may be used for females, and only 9vHPV or 4vHPV may be used for males.
  + The vaccine series may be started at age 9 years.
  + Administer the second dose 1 to 2 months after the first dose (minimum interval of 4 weeks); administer the third dose 16 weeks after the second dose (minimum interval of 12 weeks) and 24 weeks after the first dose.
  + Administer HPV vaccine beginning at age 9 years to children and youth with any history of sexual abuse or assault who have not initiated or completed the 3-dose series.

**Catch-up vaccination:**

* + Administer the vaccine series to females (2vHPV or 4vHPV or 9vHPV) and males (4vHPV or 9vHPV) at age 13 through 18 years if not previously vaccinated.
  + Use recommended routine dosing intervals (see Routine vaccination above) for vaccine series catch-up.

**Figure 9.1. cont’d**

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| **TABLE 9.2** Recommended and Minimum Ages and Intervals Between Vaccine Dosesa,b,c,d | | | | |
| **Vaccine and Dose Number** | **Recommended Age for This Dose** | **Minimum Age for This Dose** | **Recommended Interval to Next Dose** | **Minimum Interval to Next Dose** |
| Diphtheria and tetanus toxoids and acellular pertussis (DTaP)-1e | 2 mo | 6 wk | 8 wk | 4 wk |
| DTaP-2 | 4 mo | 10 wk | 8 wk | 4 wk |
| DTaP-3 | 6 mo | 14 wk | 6–12 mof | 6 mof |
| DTaP-4 | 15–18 mo | 15 mo | 3 y | 6 moe |
| DTaP-5 | 4–6 y | 4 y | — | — |
| *Haemophilus influenzae* type b (Hib)-1e,g | 2 mo | 6 wk | 8 wk | 4 wk |
| Hib-2 | 4 mo | 10 wk | 8 wk | 4 wk |
| Hib-3h | 6 mo | 14 wk | 6–9 mo | 8 wk |
| Hib-4 | 12–15 mo | 12 mo | — | — |
| Hepatitis A (HepA)-1e | 12–23 mo | 12 mo | 6–18 mo | 6 mo |
| HepA-2 | ≥ 18 mo | 18 mo | — | — |
| Hepatitis B (HepB)-1 | Birth | Birth | 4 wk–4 mo | 4 wk |
| HepB-2 | 1–2 mo | 4 wk | 8 wk–17 mo | 8 wk |
| HepB-3i | 6–18 mo | 24 wk | — | — |
| Herpes zosterj | ≥ 60 y | 60 y | — | — |
| Human papillomavirus (HPV)-1k | 11–12 y | 9 y | 8 wk | 4 wk |
| HPV-2 | 11–12 y (+2 mo) | 9 y (+4 wk) | 4 mo | 12 wkr(l) |
| HPV-3l | 11–12 y (+6 mo) | 9 y (+24 wk) | — | — |
| Inactivated poliovirus (IPV)-1e | 2 mo | 6 wk | 8 wk | 4 wk |
| IPV-2 | 4 mo | 10 wk | 8wk–14 mo | 4 wk |
| IPV-3 | 6–18 mo | 14 wk | 3–5 y | 6 mo |
| IPV-4m | 4–6 y | 4 y | — | — |
| Influenza, inactivatedn | ≥ 6 mo | 6 moo | 4 wk | 4 wk |
| Live, attenuated influenza vaccine (LAIV, intranasal)n | 2–49 y | 2 y | 4 wk | 4 wk |
| Measles, mumps, and rubella (MMR)-1p | 12–15 mo | 12 mo | 3–5 y | 4 wk |
| MMR-2p | 4–6 y | 13 mo | — | — |
| Pneumococcal conjugate vaccine (PCV)-1g | 2 mo | 6 wk | 8 wk | 4 wk |
| PCV-2 | 4 mo | 10 wk | 8 wk | 4 wk |
| PCV-3 | 6 mo | 14 wk | 6 mo | 8 wk |
| PCV-4 | 12–15 mo | 12 mo | — | — |
| Pneumococcal polysaccharide vaccine (PPSV)-1 | — | 2 y | 5 y | 3 y |
| PPSV-2q | — | 7 y | — | — |
| Quadrivalent meningococcal conjugate vaccine (MCV4)-1r | 11–12 y | 6 wks | 4–5 y | 8 wk |
| MCV4–2 | 16 y | 11 y (+8 wk) | — | — |
| Quadrivalent meningococcal polysaccharide vaccine (MPSV4)r | — | 2 y | 5 y | 5 y |
| MPSV4–2 | — | 7 y | — | — |
| Rotavirus-1t | 2 mo | 6 wk | 8 wk | 4 wk |
| Rotavirus-2 | 4 mo | 10 wk | 8 wk | 4 wk |
| Rotavirus-3u | 6 mo | 14 wk | — | — |
| Tetanus and diphtheria toxoids (Td) | 11–12 y | 7 y | 10 y | 5 y |

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*Continued on following page*

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| --- | --- | --- | --- | --- |
| **TABLE 9.2** Recommended and Minimum Ages and Intervals Between Vaccine Dosesa,b,c,d *(Continued)* | | | | |
| **Vaccine and Dose Number** | **Recommended Age for This Dose** | **Minimum Age for This Dose** | **Recommended Interval to Next Dose** | **Minimum Interval to Next Dose** |
| Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap)v | ≥11 y | 7 y | — | — |
| Varicella-1p | 12–15 mo | 12 mo | 3–5 y | 12 wkw |
| Varicella-2p | 4–6 y | 15 mox | — | — |
| aCombination vaccines are available. Use of licensed combination vaccines is generally preferred to separate injections of their equivalent component vaccines. When administering combination vaccines, the minimum age for administration is the oldest age for any of the individual components (exception: the minimum age for the first dose of MenHibrix is 6 weeks); the minimum interval between doses is equal to the greatest interval of any of the individual components.  bInformation on travel vaccines, including typhoid, Japanese encephalitis, and yellow fever, is available at <http://www.cdc.gov/travel>. Information on other vaccines that are licensed in the United States but not distributed, including anthrax and smallpox, is available at [http://www.bt.cdc.gov](http://www.bt.cdc.gov/).  cIn the recommended interval and the minimum interval columns, “months” refers to calendar months.  dWithin a number range, a dash refers to “through.”  eCombination vaccines containing the HepB component are available (see [Table 9.1](#_bookmark0)). These vaccines should not be administered to infants <6 weeks because of the other components (i.e., Hib, DTaP, HepA, and IPV).  fThe minimum recommended interval between DTaP-3 and DTaP-4 is 6 months. However, DTaP-4 need not be repeated if administered at least 4 months after DTaP-3. This is a special grace period of 2 months which can be used if evaluating records retrospectively. An additional 4 days should not be added to this grace period.  gFor Hib and PCV, children receiving the first dose of vaccine at age ≥7 months require fewer doses to complete the series.  hIf polyribosylribitol phosphate-meningococcal outer membrane protein conjugate (PRP-OMP; Pedvax-Hib, Merck Vaccine Division) was administered at ages 2 and 4 months, a dose at age 6 months is not necessary.  iHepB-3 should be administered at least 8 weeks after HepB-2 and at least 16 weeks after HepB-1 and should not be administered before age 24 weeks.  jHerpes zoster vaccine is recommended as a single dose for persons aged ≥60 years.  kBivalent HPV vaccine is approved for females age 9–25 years. Quadrivalent HPV vaccine is approved for males and females age 9–26 years. Nine-valent HPV vaccine is approved for females age 9–26 years, and males age 9–15 years.  lThe minimum age for HPV-3 is based on the baseline minimum age for the first dose (i.e., 9 years) and the minimum interval of 24 weeks between the first and third dose. Dose 3 need not be repeated if it is administered at least 16 weeks after the first dose and the intervals between dose 1 and dose 2, and dose 2 and dose 3, are maintained at 4 weeks and 12 weeks, respectively.  mA fourth dose is not needed if the third dose was administered at ≥4 years and at least 6 months after the previous dose.  nOne dose of influenza vaccine per season is recommended for most persons. Please see influenza vaccine specific chapter to determine which children age <9 years should receive two doses in a single season.  oThe minimum age for inactivated influenza vaccine varies by vaccine manufacturer. See package insert for vaccine-specific minimum ages.  pCombination MMRV vaccine can be used for children ages 12 months to 12 years.  qA second dose of PPSV 5 years after the first dose is recommended for persons age ≤65 years who are at highest risk for serious pneumococcal infection and for persons likely to have a rapid decline in pneumococcal antibody concentration. (Source: CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices [ACIP]. *MMWR Recomm Rep.* 1997;46[RR-8]:1–24).  rRevaccination with meningococcal conjugate vaccine is recommended for previously vaccinated persons who remain at high risk for meningococcal disease. (Source: CDC. Updated recommendations from the Advisory Committee on Immunization Practices (ACIP) for revaccination of persons at prolonged increased risk for meningococcal disease. *MMWR Morb Mortal Wkly Rep*. 2009;58:1042–1043).  sMenACWY-D (Menactra) can be given as young as 9 months of age for high-risk persons, MenACWY-CRM (Menveo) can be given as young as 2 months of age for high-risk persons. Hib-MenCY can be given as young as 6 weeks of age for high-risk persons. Hib-MenCY is a four-dose series at ages 2 months, 4 months, 6 months, and 12 to 18 months.  tThe first dose of rotavirus must be administered at age 6 weeks through 14 weeks and 6 days. The vaccine series should not be started for infants age ≥15 weeks, 0 days. Rotavirus should not be administered to children older than 8 months, 0 days of age regardless of the number of doses received between 6 weeks and 8 months, 0 days of age.  uIf two doses of Rotarix (GlaxoSmithKline) are administered as age appropriate, a third dose is not necessary.  vOnly one dose of Tdap is recommended for nonpregnant persons. Subsequent doses should be given as Td. For management of a tetanus-prone wound in persons who have received a primary series of tetanus-toxoid–containing vaccine, the minimum interval after a previous dose of any tetanus-containing vaccine is 5 years.  wThe minimum interval from varicella-1 to varicella-2 for persons beginning the series at age ≥13 years is 4 weeks. For persons younger than 13 years, a special grace period of 2 months can be applied to the minimum interval, so the minimum interval would also be 4 weeks for this age cohort. However, an additional 4 days should not be added to this grace period for this age cohort.  xA special grace period of 3 months, based on expert opinion, can be applied to the minimum age of 15 months when evaluating records retrospectively, which results in an acceptable minimum age of 13 months. An additional 4 days should not be added on to this grace period. | | | | |

schedules has not been evaluated in clinical trials, immune responses with accelerated intervals are likely to induce ade- quate protection.5 [Table 9.2](#_bookmark3) lists accelerated, or minimum, intervals and ages that can be used for scheduling catchup vaccinations.

Administration of doses of a vaccine at intervals less than the minimum intervals or earlier than the minimum age (see [Table 9.2](#_bookmark3)) may result in a reduced immune response with diminished vaccine efficacy and should be avoided.2,5 Multiple doses of some live vaccines are recommended to stimulate an

immune response to different types of the same virus, such as poliovirus types 1, 2, and 3, or to induce immunity in persons who failed to mount an immune response to an earlier dose of vaccine, such as measles.53,67 These multiple doses consti- tute a primary vaccination series and are not booster doses.

## Spacing of Different Vaccines

[Table 9.2](#_bookmark3) includes guidelines for spacing administration of different vaccines.5 Inactivated vaccines are not known

to interfere with the immune response to other inactivated vaccines or to live vaccines (see below for exceptions). An inactivated vaccine can be administered simultaneously or at any time before or after a different inactivated vaccine or live vaccine.

The possibility that two doses of the same or different live virus vaccines administered within too short an interval may inhibit the immunologic response to the second dose is based on evidence from animal and human studies. Petralli and colleagues68,69 reported that the immune response to smallpox vaccination was affected by prior administration of live attenu- ated measles vaccine. Interferon produced in response to the initial dose of measles virus vaccine has been postulated to inhibit replication of vaccinia virus in the subsequent vaccine dose. In a study in two U.S. health maintenance organizations, persons who received varicella vaccine less than 30 days after MMR vaccination had an increased risk of varicella vaccine failure (i.e., varicella disease in a vaccinated person) of 2.5- fold compared with persons who received varicella vaccine before or 30 days or more after MMR.70 In contrast, Stefano and colleagues71 determined that the response to yellow fever vaccine is not affected by monovalent measles vaccine admin- istered 1 to 27 days earlier. In general, live virus vaccines administered orally do not interfere with live virus vaccines administered parenterally or orally, although a reduction in the seroconversion rate following the first dose of monovalent rotavirus vaccine has been reported when this dose is admin- istered concurrently with OPV.72 The effect of nasally admin- istered vaccine on the response to other live vaccines not administered at the same visit is not known.

To minimize the potential risk for interference, parenterally

or nasally administered live virus vaccines not administered on the same day should be administered 4 weeks or more apart whenever possible. If parenterally or nasally adminis- tered live virus vaccines are separated by less than 4 weeks, the live virus vaccine given second should be readministered 4 or more weeks after the previous dose.5 Yellow fever vaccine can be administered at any time after single-antigen measles vaccine (single-antigen measles vaccine is not currently avail- able in the United States). Oral and parenteral live virus vac- cines can be administered simultaneously or at any interval before or after each other, if indicated.5

# SIMULTANEOUS ADMINISTRATION OF DIFFERENT VACCINES

Simultaneous administration of all indicated vaccines is an essential component of childhood vaccination programs.2,5 Simultaneous administration of different vaccines is particu- larly important when return of the recipient for further vaccination is uncertain, imminent exposure to several vaccine- preventable diseases is expected, or a vaccinee is preparing for international travel on short notice. The Strategic Advisory Group of Experts (SAGE) of the World Health Organization supports multiple vaccine injections in a single visit, and encourages this practice based on the benefits they confer.73

Unless specifically licensed for injection in the same syringe, different vaccines administered simultaneously should be injected separately and at different anatomic sites. If both upper and lower limbs must be used for simultaneous admin- istration of different vaccines, the anterolateral thigh is often chosen for intramuscular injections and the triceps region for subcutaneous injections. If more than one injection must be administered in a single limb of an infant or young child, the thigh usually is preferred because of its large muscle mass. The distance separating two injections in the same limb should be sufficient (e.g., 1 inch or more) to minimize the

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| **TABLE 9.3** Guidelines for Spacing of Live and Inactivated Antigens | |
| **Antigen Combination** | **Recommended Minimum Interval Between Doses** |
| Two or more inactivateda,b | Can be administered simultaneously or at any interval between doses |
| Inactivated and live | Can be administered simultaneously or at any interval between doses |
| Two or more live intranasal or injectablec | 4-wk minimum interval if not administered simultaneously |
| aThe American Academy of Pediatrics suggests a 1-month interval between tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis vaccine and tetravalent meningococcal conjugate vaccine if these vaccines are not administered on the same day.75  bIn persons with functional or anatomic asplenia, MenACWY-D (Menactra) and PCV13 should not be administered simultaneously and should be spaced by 4 weeks. Likewise, for persons with immunosuppressive high-risk conditions for invasive pneumococcal disease, if both PCV13 and PPSV23 are indicated, PCV13 should be administered first and PPSV23 should be administered 8 weeks later. For persons with immunocompetent high-risk conditions for invasive pneumococcal disease and healthy persons aged ≥65 years indicated for both PCV13 and PPSV23, PCV13 should be administered first, and PPSV23 should be administered 1 year later.  cLive oral vaccines (e.g., Ty21a typhoid vaccine and rotavirus vaccine) can be administered on the same day or at any interval before or after inactivated or live injectable vaccines. | |

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chance of overlapping local reactions.5,13,14 In general, different vaccines, including live virus products, can be administered simultaneously without reducing their safety and effectiveness ([Table 9.3](#_bookmark25)).74 Studies of cortisol concentration and behavioral responses to vaccination indicate that responses are similar in infants who receive two injections during one visit and infants who receive a single injection, suggesting that a second injec- tion does not increase stress.76,77

Increased severity or incidence of adverse reactions has not been observed after simultaneous administration of the most widely used vaccines.5 Similarly, simultaneous administration of vaccines generally does not cause immunologic interfer- ence, with two exceptions. Pneumococcal conjugate vaccine and Menactra brand meningococcal conjugate vaccine should not be administered simultaneously in children with func- tional or anatomic asplenia, because Menactra interferes with the immune response to the seven-valent pneumococcal con- jugate vaccine (and presumably PCV13 as well). Children with functional or anatomic asplenia are at high risk for pneumo- coccal infection. All doses of pneumococcal conjugate vaccine should be administered first and then a dose of Menactra should be administered 4 weeks after the last dose of pneu- mococcal conjugate vaccine. Interference is not known to occur with other brands of meningococcal conjugate vaccine and pneumococcal conjugate vaccine. Pneumococcal polysac- charide vaccine may interfere with the immune response to pneumococcal conjugate vaccines. If both doses are indicated, they should not be administered simultaneously. For persons with immunosuppressive high-risk conditions indicated for both PCV13 and PPSV23, PCV13 should be administered first, with PPSV23 administered 8 weeks later. For persons with immunocompetent high-risk conditions for invasive pneumo- coccal disease or for healthy persons aged 65 years or older indicated for both PCV13 and PPSV23, PCV13 should be administered first, with PPSV23 administered 1 year later. Pneumococcal conjugate vaccine should be administered first, followed by pneumococcal polysaccharide vaccine at least 8 weeks later.74,77,78

# INTERFERENCE BY IMMUNOGLOBULINS

Passively acquired antibodies can interfere with the immune response to certain vaccines, both live and inactivated, and to toxoids. The result can be the absence of seroconversion or a blunting of the immune response with lower final antibody concentrations in the vaccinee. This potential for interference underlies the recommendation that hepatitis B vaccine and hepatitis B immunoglobulin be administered at separate sites when administered simultaneously. Passively acquired anti- body does not affect the immune response to all vaccines.

## Interference With Live Virus Vaccines

To elicit an adequate immune response, live vaccine virus must replicate in the recipient. The probable mechanism by which passively acquired immunoglobulin blunts the immune response is neutralization of vaccine virus, resulting in inhibi- tion of viral replication and insufficient antigenic mass.79 For example, persisting transplacentally acquired maternal measles antibodies inhibit the response to live measles vaccine in infants for as long as 12 months and perhaps longer.80,81 The age to which inhibition persists has been correlated with con- centrations of maternal or cord blood antibodies.82–84 Rubella vaccine virus may be less susceptible than measles vaccine virus to these transplacentally acquired maternal antibod- ies.83,85 The effect of blood and immunoglobulin preparations on the response to mumps and varicella vaccines is unknown, but commercial immunoglobulin preparations contain anti- bodies to these viruses. The effect of blood and immuno- globulin preparations on the response to live rotavirus and influenza vaccines is unknown.

Intramuscular or intravenous administration of

immunoglobulin–containing preparations (e.g., immuno- globulin, hyperimmunoglobulins, intravenous immunoglob- ulin, and blood) before or simultaneously with certain vaccines also can affect the immune response to live virus vac- cines. When partially attenuated Edmonston B measles vaccine, which is no longer available in the United States, was administered concurrently with measles immunoglobulin in an effort to reduce the incidence of adverse events associated with this vaccine, the rate of seroconversion was not affected but the geometric mean titer of serum measles antibody was diminished.86 In a study of an investigational bacterial poly- saccharide immunoglobulin (BPIG), children had a reduced immune response to live measles vaccine for as long as 5 months after receipt of BPIG.87 The measles antibody serocon- version rate and geometric mean titer were lower among chil- dren who received BPIG compared with children who received placebo. Blunting of the immune response to live rubella vaccine also occurred after receipt of BPIG but was less marked and of shorter duration.

Although passively acquired antibodies can interfere with

the response to rubella vaccine, the low dose of anti-Rh(D) globulin administered to postpartum women has not been demonstrated to inhibit the immune response to RA27/3 strain rubella vaccine.88 Parenterally administered immuno- globulin preparations also do not seem to adversely affect the immune response to yellow fever vaccine.89 Although high concentrations of passively acquired antibodies may reduce the serum antibody response to live poliovirus vaccine, they have little effect on replication of vaccine virus and develop- ment of gastrointestinal tract immunity.55,89–91 Data are insuf- ficient to determine the extent to which passively acquired antibodies interfere with the immune response to other live viral or bacterial vaccines, such as varicella, mumps, LAIV, zoster, and typhoid (Ty21a strain). A humanized mouse

monoclonal antibody product (palivizumab) is available for prevention of respiratory syncytial virus infection among infants and young children. This product contains only anti- body to respiratory syncytial virus; hence, it will not interfere with immune response to live vaccines.92

## Interference With Inactivated and Component Vaccines

Interference with current inactivated and component vaccines is less marked than with live vaccines and requires exposure to large doses of passively acquired antibodies.93 The mecha- nism by which passively acquired antibodies interfere with the immunologic response to inactivated and toxoid vaccines is not clear. Moderate doses of parenterally administered immu- noglobulins have not inhibited development of a protective immune response to DTP, tetanus toxoid, and Hib conjugate vaccines.94,95 Although the concurrent administration of inac- tivated hepatitis A vaccine and immunoglobulin can result in lower serum antibody concentrations than if vaccine alone is administered, seroconversion rates have not been dimin- ished.96,97 Infants with high concentrations of passively acquired maternal antibody to hepatitis A virus had lower serum antibody concentrations after receipt of hepatitis A vaccine but had seroconversion rates similar to those of vaccinated infants without maternal antibodies.98 Similarly, seroconversion rates to inactivated polio vaccine given on a 2-, 4-, and 6-month schedule were lower among infants who had high maternal antibody levels for all three poliovirus types.99

# RECOMMENDATIONS FOR SPACING ADMINISTRATION OF VACCINES AND IMMUNOGLOBULINS

Interference of immunoglobulins with the immune response to vaccines is dose-related and more likely to occur and to persist for a longer period after receipt of larger doses of immunoglobulins.87,100 The recommended interval between administration of immunoglobulin preparations and vaccines is based on whether evidence suggests interference between immunoglobulin and the vaccine, the dose of the immuno- globulin administered, and the expected half-life of immuno- globulin G. [Tables 9.4](#_bookmark28) and [9.5](#_bookmark32) list the recommended intervals between administration of immunoglobulin preparations and various live and killed vaccines.

In the United States, inactivated and component (subunit) vaccines may be administered simultaneously with or at any time before or after receipt of an immunoglobulin prepara- tion.2,5 The vaccine and immunoglobulin preparation should be administered at different sites, and the standard recom- mended doses of the corresponding vaccines should be given. Supplemental doses are not indicated.

Recommendations for administration of live virus vaccines vary on the basis of the aforementioned considerations. After receipt of an immunoglobulin preparation or other blood product, measles vaccine should be deferred during the inter- vals listed in [Table 9.5](#_bookmark32).5,91,101 Human blood and immuno- globulin preparations also contain rubella, mumps, and varicella antibodies. High doses of passively acquired antibod- ies can inhibit the immune response to live rubella vaccine for as long as 3 months.87,102 The effect of immunoglobulin prepa- rations on the response to live mumps and live varicella vac- cines has not been defined. To reduce the possibility of interference, postponement of administration of rubella,

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| **TABLE 9.4** Guidelines for Administering Antibody-Containing Productsa and Vaccines | | |
| **Simultaneous Administration (During Same Clinic Day)** | | |
| **Products** | **Recommended Minimum Interval Between Doses** | |
| Antibody-containing products and inactivated antigenb | Can be administered simultaneously at different anatomic sites or at any interval between doses | |
| Antibody-containing products and live antigen | Should not be administered simultaneously.c If simultaneous administration of measles-containing vaccine or varicella vaccine is unavoidable, administer at different sites and revaccinate or test for seroconversion after the recommended interval (see [Table 9.5](#_bookmark32)) | |
| **Nonsimultaneous Administration** |  |  |
| **Products** |  |  |
| **Administer First** | **Administer Second** | **Recommended Minimum Interval Between Doses** |
| Antibody-containing products | Inactivated antigen | No interval necessary |
| Inactivated antigen | Antibody-containing products | No interval necessary |
| Antibody-containing products | Measles, mumps, rubella vaccine, varicella vaccine, and combined measles, mumps, rubella, varicella vaccine | Depends on dose of antibody receivedc,d |
| Measles, mumps, rubella, varicella vaccine, and combined measles, mumps, rubella, varicella vaccine antigens | Antibody-containing products | 2 wkc |
| aBlood products containing substantial amounts of immunoglobulin include intramuscular and intravenous immunoglobulin, specific hyperimmunoglobulin (e.g., hepatitis B immunoglobulin, tetanus immunoglobulin, varicella zoster immunoglobulin, and rabies immunoglobulin), whole blood, packed red blood cells, plasma, and platelet products. Pneumococcal polysaccharide and pneumococcal conjugate vaccines should be separated by at least 8 weeks in high-risk immunosuppressed persons and by 1 year in healthy or immunocompetent high-risk persons. In persons with asplenia, pneumococcal conjugate vaccine and Menactra brand meningococcal conjugate vaccine should not be given simultaneously. The series of PCV13 should be administered first, with Menactra administered 4 weeks after the final dose of PCV13.  bHepatitis B immunoglobulin (HBIg) and hepatitis B vaccine need to be administered at separate sites.  cYellow fever vaccine, rotavirus vaccine, oral Ty21a typhoid vaccine, live attenuated influenza vaccine, and zoster vaccine are exceptions to these recommendations. These live attenuated vaccines can be administered at any time before or after or simultaneously with an antibody-containing product.  dThe duration of interference of antibody-containing products with the immune response to the measles component of measles-containing vaccine, and possibly varicella vaccine, is dose-related (see [Table 9.5](#_bookmark32)). | | |

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mumps, and varicella vaccines for the intervals indicated in [Table 9.5](#_bookmark32) is prudent.5

Immunoglobulin preparations administered too soon after vaccination with MMR or varicella vaccines can interfere with the immune response. If administration of an immunoglobu- lin preparation becomes necessary less than 2 weeks after receipt of MMR, its component vaccines, or varicella vaccine, readministration of the vaccine is recommended after the appropriate interval listed in [Tables 9.4](#_bookmark28) and [9.5](#_bookmark32), unless sero- logic testing indicates an antibody response.5,53 For example, if whole blood is administered less than 14 days after receipt of varicella vaccine, the vaccine should be readministered at least 6 months after the whole blood unless serologic testing indicates an adequate immune response to the initial dose of varicella vaccine.

Although data are not available on the effect of passive antibody on the response to rotavirus vaccine, the ACIP rec- ommends that live rotavirus vaccine may be administered at any time before, concurrent with, or after administration of any blood product, including antibody-containing products.27 Because the immune responses to OPV, zoster, and yellow fever vaccines have not been demonstrated to be adversely affected by immunoglobulin preparations, these vaccines can be administered at any time in relation to receipt of immuno- globulin preparations.89 Live oral typhoid (Ty21a) vaccine also is recommended for administration irrespective of the receipt of immunoglobulin preparations.5,103 LAIV can be adminis- tered at any time before or after receipt of an antibody- containing blood product.5

# INTERCHANGEABILITY OF VACCINES FROM DIFFERENT MANUFACTURERS

Combination and monovalent vaccines against the same dis- eases with similar antigens and produced by the same manu- facturer are considered interchangeable in most situations.2,5 However, supporting data on the safety, immunogenicity, and efficacy of using comparable vaccines from different manufacturers for different doses of a vaccination series fre- quently are limited or unavailable. When the same vaccine cannot be used to complete an immunization series, similar vaccines produced by different manufacturers or produced by the same manufacturer in different countries generally have been considered acceptable to complete the immunization series provided each vaccine is given according to licensed recommendations.

Some diseases have serologic correlates of immunity that can be used to evaluate vaccine interchangeability. For example, in studies in which one or more doses of hepatitis B vaccine produced by one manufacturer were followed by doses from another manufacturer, the immune response was comparable to that resulting from use of a single vaccine type.104–106 Whereas Hib conjugate vaccines differ in antigen composi- tion, interchangeability of different products has been vali- dated on the basis of the accepted serologic correlate of immunity against Hib invasive disease.107–109

Determination of vaccine interchangeability is more diffi- cult for diseases without serologic correlates of immunity. When feasible, acellular pertussis vaccine from the same

|  |  |  |
| --- | --- | --- |
| **TABLE 9.5** Recommended Intervals Between Administration of Antibody-Containing Products and Measles- or Varicella-Containing Vaccine, By-product and Indication for Vaccination | | |
| **Product/Indication** | **Dose (Including Milligrams of Immunoglobulin G/kg of Body Weight) and Routea** | **Recommended Interval Before Measles- or Varicella-Containing Vaccineb Administration (Mo)** |
| Blood transfusion | | |
| Red blood cells (RBCs), washed | 10 mL/kg (negligible) IV | None |
| RBCs, adenine-saline added | 10 mL/kg (10 mg IgG/kg) IV | 3 |
| Packed RBCs (hematocrit 65%)c | 10 mL/kg (60 mg IgG/kg) IV | 6 |
| Whole blood (hematocrit 35%–50%)c | 10 mL/kg (80–100 mg IgG/kg) IV | 6 |
| Plasma/platelet products | 10 mL/kg (160 mg IgG/kg) IV | 7 |
| Botulinum immunoglobulin intravenous (human) | 1.5 mL/kg (75 mg IgG/kg) IV | 6 |
| Cytomegalovirus intravenous immunoglobulin (IgIV) | 150 mg/kg maximum | 6 |
| Hepatitis A Ig | | |
| Contact prophylaxis | 0.02 mL/kg (3.3 mg IgG/kg) IM | 3 |
| International travel, <3 mo stay | 0.02 mL/kg (3.3 mg IgG/kg) IM | 3 |
| International travel, ≥3 mo stay | 0.06 mL/kg (10 mg IgG/kg) IM | 3 |
| Hepatitis B Ig | 0.06 mL/kg (10 mg IgG/kg) IM | 3 |
| IGIV | | |
| Replacement therapy for immune deficienciesd | 300–400 mg/kg IVd | 8 |
| Immune thrombocytopenic purpura treatment | 400 mg/kg IV | 8 |
| Postexposure varicella prophylaxise | 400 mg/kg IV | 8 |
| Postexposure measles prophylaxis for immunocompromised contacts | 400 mg/kg IV | 8 |
| Immune thrombocytopenic purpura treatment | 1000 mg/kg IV | 10 |
| Kawasaki disease | 2 g/kg IV | 11 |
| Measles prophylaxis Ig, standard (i.e., nonimmunocompromised contact) | 0.50 mL/kg (80 mg IgG/kg) IM | 6 |
| Monoclonal antibody to respiratory syncytial virus F protein (e.g., Synagis [MedImmune])f | 15 mg/kg IM | None |
| Rabies Ig | 20 IU/kg (22 mg IgG/kg) IM | 4 |
| Tetanus Ig | 250 U (10 mg IgG/kg) IM | 3 |
| Varicella Ig (VariZIG) | 125 U/10 kg (60–200 mg IgG/kg) IM, maximum 625 U | 5 |
| aThis table is not intended for determining the correct indications and dosages for using antibody-containing products. Unvaccinated persons might not be protected fully 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.  bDoes not include zoster vaccine. Zoster vaccine may be given with antibody-containing blood products.  cAssumes a serum IgG concentration of 16 mg/mL.  dMeasles vaccination is recommended for children with mild immunosuppression from HIV infection, and varicella vaccination may be considered for children with mild immunosuppression, but both are contraindicated for persons with severe immunosuppression from HIV or any other immunosuppressive disorder.  eLicensed VariZIG, similar to licensed varicella-zoster immunoglobulin (VZIG), is a purified human Ig preparation made from plasma containing high levels of antivaricella antibodies (IgG).  fContains antibody only to respiratory syncytial virus. | | |

manufacturer is preferred for the entire primary vaccination series.58 In the absence of a correlate for *Bordetella pertussis* infection, interchangeability of acellular pertussis vaccines is difficult to assess. Available data from one study indicate that, for the first three doses of the DTaP series, one or two doses of Tripedia (manufactured by Aventis Pasteur) followed by Infan- rix (manufactured by GlaxoSmithKline) for the remaining

doses(s) is comparable to three doses of Tripedia with regard to immunogenicity, as measured by antibodies to diphtheria, tetanus, and pertussis toxoids and filamentous hemaggluti- nin.110 However, in the absence of a clear serologic correlate of protection for pertussis, the relevance of these immunogenic- ity data for protection against pertussis is unknown. Any DTaP vaccine can be used to complete the DTaP series if the

product(s) administered for earlier doses are unknown or unavailable.5,58,111

# HYPERSENSITIVITY TO VACCINE COMPONENTS

## Types of Reactions

Hypersensitivity reactions after vaccination can be local or systemic and can vary in severity from mild discomfort at the site of vaccination to severe anaphylaxis. Onset can be imme- diate or delayed. Serious allergic reactions are rare. Whether a specific hypersensitivity reaction is caused by a vaccine com- ponent or an unrelated environmental allergen can be difficult to determine. However, symptoms occurring immediately after vaccination that are suggestive of an anaphylactic reac- tion generally contraindicate further administration of that vaccine to the recipient.2,5

Urticaria and anaphylactic reactions have been reported after administration of DTP, DT (diphtheria and tetanus toxoids–pediatric), Td (diphtheria and tetanus toxoids–adult), and tetanus toxoid.112–114 A severe allergic reaction (e.g., ana- phylaxis) to a previous dose of vaccine or to a vaccine com- ponent is a contraindication to the respective vaccine. Although immunoglobulin E–type antibodies to tetanus and diphtheria antigens have been identified in some patients with these symptoms, transient urticaria-like rashes are not a contraindi- cation to subsequent vaccination because they are unlikely to be anaphylactic unless they appear within minutes after vaccination.114–116 A serum sickness–type reaction caused by circulating complexes of vaccine antigen and previously acquired antibody is the probable cause of these reactions, and subsequent vaccination at a 10-year interval is unlikely to result in the necessary ratio of antigen-to-antibody concentra- tion to form immune complexes.114,117

Tetanus toxoid is contraindicated in persons who experi-

enced an immediate anaphylactic reaction to tetanus toxoid– containing vaccine, unless the person can be desensitized to the toxoid.2 Because of the importance of tetanus immuniza- tion and the uncertainty about which vaccine component might be the cause of the reaction, the patient may be referred to an allergist for evaluation and possible desensitiza- tion.114,118,119 On occasion, a history of an allergic reaction to tetanus vaccine may refer to a reaction to tetanus antitoxin of equine origin given for tetanus prophylaxis before human- derived tetanus immunoglobulin became available in the 1960s. Before use of tetanus toxoid is discontinued because of an alleged episode of anaphylaxis, skin testing and possible desensitization should be considered.118,120

Urticaria also has been reported following pneumococcal conjugate, MMR, varicella, and smallpox vaccines.121–124

Immediate or delayed onset of generalized urticaria and angioedema that can progress to respiratory distress and hypo- tension has been reported after receipt of inactivated mouse brain-derived Japanese encephalitis vaccine.125–127 The patho- genesis of these reactions is not known. Mouse brain–derived Japanese encephalitis vaccine is no longer available in the United States. A vero cell–derived Japanese encephalitis vaccine is available in the United States for people 2 years of age and older.128,129

# VACCINE COMPONENTS CAUSING HYPERSENSITIVITY

## Proteins

Egg protein is a constituent of vaccines prepared with use of embryonated chicken eggs, such as influenza and yellow

fever vaccines. On rare occasions, these vaccines can induce anaphylaxis or other immediate hypersensitivity reactions, and these reactions are sometimes attributed to egg protein antigen.2,5,130–132 As a result, yellow fever vaccine generally is contraindicated in persons with a history of anaphylac- tic reactions to egg ingestion unless desensitization has been successfully completed. For example, persons needing yellow fever vaccine who have a history of systemic anaphylaxis- like symptoms after egg ingestion can be skin tested with yellow fever vaccine before vaccination and desensitized if necessary.130

While a history of anaphylaxis following influenza vaccine is a contraindication to further doses of influenza vaccine, evidence does not support allergy to egg as a cause of anaphy- laxis following influenza vaccine. A history of allergy to eggs is not a contraindication to vaccination with influenza vaccine; however, influenza vaccination should only occur under the supervision of a provider who is able to recognize and manage severe allergic conditions. Measles and mumps vaccines are produced in chick embryo fibroblast cell culture. Persons with hypersensitivity to eggs are at low risk for anaphylactic reac- tions to these vaccines, and skin testing with vaccine is not predictive of allergic reaction after immunization.2,133–135 Neither skin testing nor administration of gradually increasing doses of vaccine is required when these vaccines are adminis- tered to persons who are allergic to eggs.2,5,53,101,133

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Live virus vaccines, such as measles, mumps, rubella, yellow

fever, and varicella, contain gelatin as a stabilizer. Persons with a history of allergy to gelatin have experienced, on rare occa- sions, an anaphylactic reaction after vaccination with such a vaccine.121,124,134–136 Skin testing of persons with a history of systemic anaphylaxis-like symptoms after gelatin ingestion may be useful to identify persons at risk for severe hypersen- sitivity reactions to vaccination. A regimen for administering particular vaccines to persons with anaphylaxis to compo- nents contained in those vaccines has been published.137 Because gelatin used as a vaccine stabilizer may be of porcine origin, whereas ingested food gelatin may be of bovine origin, absence of a history of allergy to gelatin-containing foods does not eliminate the possibility of a gelatin-mediated reaction to vaccine.

Approximately 6% of persons who receive a booster dose of human diploid rabies vaccine have a serum sickness– type illness.138,139 This reaction is thought to be caused by sensitization to human albumin that has been altered chemi- cally by a virus-inactivating agent used in the production of the vaccine.2,140

Anaphylaxis following recombinant hepatitis B vaccines rarely has been reported and usually is attributed to hypersen- sitivity to residual yeast protein in the vaccine.141

## Latex

Latex is liquid sap from the commercial rubber tree. Latex contains naturally occurring impurities (e.g., plant proteins and peptides), which are believed to be responsible for allergic reactions. Latex is processed to form natural rubber latex and dry natural rubber. Natural rubber latex and dry natural rubber might contain the same plant impurities as latex but in lesser amounts. Natural rubber latex is used to produce medical gloves, catheters, and other products, whereas dry natural rubber is used in syringe plungers, vial stoppers, and injection ports on intravascular tubing. Synthetic rubber and synthetic latex also are used in medical gloves, syringe plungers, and vial stoppers, but they do not contain natural rubber or natural latex or the impurities linked to allergic reactions.

The most common type of latex sensitivity is contact-type (type IV) allergy, usually as a result of prolonged contact with

natural rubber latex–containing gloves.142 Although injection procedure–associated latex allergies among patients with dia- betes mellitus have been described,143–145 allergic reactions, including anaphylaxis, after vaccination procedures are rare. Only one report of an allergic reaction after administering hepatitis B vaccine in a patient with known severe allergy (anaphylaxis) to latex has been published.146

If a person reports a severe (anaphylactic) allergy to latex, vaccines supplied in vials or syringes that contain natural rubber should not be administered, unless the benefit of vac- cination outweighs the risk of an allergic reaction to the vaccine. For latex allergies other than anaphylactic allergies, such as a history of contact allergy to latex gloves, vaccines supplied in vials or syringes that contain natural rubber latex or dry natural rubber can be administered.5

## Antimicrobial Agents

Live virus vaccines may contain trace amounts of one or more antimicrobial agents, such as neomycin, streptomycin, and polymyxin B. Vaccine contents are listed in each manu- facturer’s product label for each vaccine. The most common allergic response to neomycin is a delayed-type (cell-mediated) local contact dermatitis consisting of an erythematous, pruritic papule that occurs 48 to 96 hours after vaccine administra- tion.2,5,147 Such delayed-type reactions are not contraindica- tions for vaccination.2,5,147,148 However, persons who have experienced an anaphylactic reaction to neomycin or to another vaccine constituent should not receive vaccines containing that antimicrobial agent.2,5,149,150 No vaccines licensed in the United States contain penicillin or penicillin derivatives.

## Thimerosal

Thimerosal is an organic mercurial compound in use since the 1930s and added to certain immunobiologic products as a preservative. A joint statement issued by the U.S. Public Health Service and the AAP in 1999151 established the goal of remov- ing thimerosal as soon as possible from vaccines routinely recommended for infants. Although no evidence exists of any harm caused by low concentrations of thimerosal in vaccines and the risk was only theoretical,152 this goal was established as a precautionary measure.

Since mid-2001, vaccines produced in the United States that are recommended routinely for infants younger than 6 months of age have been manufactured without thimerosal as a pre- servative and contain no thimerosal or only trace amounts. Thimerosal as a preservative is present in certain other vaccines. Examples are tetanus toxoid, Td, DT, certain formulations of influenza vaccine, and meningococcal polysaccharide vaccine in multidose vials.153 Formulations of influenza vaccine with a reduced concentration of thimerosal or no thimerosal as a preservative are available in the United States.153

Receiving thimerosal-containing vaccines has been postu- lated to lead to induction of allergy in some persons.154,155 However, there is limited scientific evidence for this assertion. Hypersensitivity to thimerosal usually consists of local delayed-type hypersensitivity reactions.156–158 Thimerosal elicits positive delayed-type hypersensitivity patch tests in 1% to 18% of persons tested, but these tests have limited or no clinical relevance.159,160 Most patients do not experience reac- tions to thimerosal administered as a component of vaccines, even when patch or intradermal tests for thimerosal indicate hypersensitivity.156,160 A localized or delayed-type hypersensi- tivity reaction to thimerosal is not a contraindication to receipt of a vaccine that contains thimerosal.2,5

# MANAGEMENT OF ACUTE VACCINE ADVERSE REACTIONS

Although rare after vaccination, the immediate onset and life- threatening nature of an anaphylactic reaction require that personnel and facilities providing vaccination be capable of providing initial care for suspected anaphylaxis. Epinephrine and equipment for maintaining an airway should be available for immediate use.

Anaphylaxis usually begins within several minutes of administration of vaccine. Rapid recognition and initiation of treatment are required to prevent possible progression to car- diovascular collapse. If flushing, facial edema, urticaria, itching, swelling of the mouth or throat, wheezing, difficulty breathing, or other signs of anaphylaxis occur, the patient should be placed in a recumbent position with the legs ele- vated. It is important to note that urticaria might not be present in all cases of anaphylaxis. Aqueous epinephrine (1 : 1000) should be administered intramuscularly and can be repeated within 5 to 15 minutes.161 A dose of diphenhy- dramine hydrochloride may shorten the reaction, but it will have little immediate effect. Maintenance of an airway and oxygen administration may be necessary. Arrangements should be made for immediate transfer to an emergency facil- ity for further evaluation and treatment. All patients should be observed for 4 to 24 hours after onset of symptoms.161

Syncope (vasovagal or vasodepressor reaction) can occur

after vaccination and is most common among adolescents and young adults. In 2005, the Vaccine Adverse Event Reporting System (VAERS) detected a trend of increasing syncope reports that coincided with licensure of three vaccines for adolescents: HPV, quadrivalent meningococcal vaccine (MCV4), and Tdap.162 Of particular concern among adolescents has been the risk for serious secondary injuries, including skull fracture and cerebral hemorrhage after a fall and subsequent head injury. Of 463 VAERS reports of syncope between January 1, 2005 and July 31, 2007, 41 listed syncope with secondary injury with information on the timing after vaccination, and most of these syncope reports (76%) occurred among adoles- cents. Among all age groups, 80% of reported syncope epi- sodes occur within 15 minutes of vaccine administration (additional information is available at [http://www.cdc.gov/](http://www.cdc.gov/concerns/fainting.html) [concerns/fainting.html](http://www.cdc.gov/concerns/fainting.html)). Providers should take appropriate measures to prevent injuries if a patient becomes weak or dizzy or loses consciousness. Adolescents and adults should be seated or lying down during vaccination. Vaccine providers, particularly when vaccinating adolescents, should consider observing patients (with patients seated or lying down) for 15 minutes after vaccination to decrease the risk for injury should they faint.162 If syncope develops, patients should be observed until the symptoms resolve.

# SPECIAL CONSIDERATIONS

## Vaccination of Preterm Infants

The immune response to vaccination is a function of postnatal rather than gestational age.163–165 Transplacentally acquired maternal antibody is present in lower concentrations and, thus, persists for a shorter interval in preterm infants than in gestationally mature infants.164,166–168 Because preterm infants have less transplacentally acquired maternal antibody, inhibi- tion of the immune response in preterm infants may be less than that in full-term infants.164,169

In most cases, infants born prematurely, regardless of birth weight, should be vaccinated at the same chronological age and according to the same schedule and precautions as full- term infants and children.5 Birth weight and size are not factors in deciding whether to postpone routine vaccination

of a clinically stable preterm infant,170–174 except for hepatitis B vaccine. The full recommended dose of each vaccine should be used. Divided or reduced doses are not recommended.175

Decreased seroconversion rates might occur among certain preterm infants with birth weights of less than 2000 g after administration of hepatitis B vaccine at birth.176 However, by chronological age 1 month, all preterm infants, regardless of initial birth weight or gestational age, are likely to respond as adequately as older and larger infants.177–180 Infants weighing less than 2000 g born to hepatitis B surface antigen (HBsAg)- negative mothers should receive the first dose of the hepatitis B vaccine series at chronological age 1 month or hospital discharge, if hospital discharge occurs when the infant is younger than 1 month of age. Low-birth-weight infants born to HBsAg-positive mothers should receive hepatitis B vaccine within 12 hours after birth. The initial vaccine dose should not be counted toward completion of the hepatitis B series, and three additional doses of hepatitis B vaccine should be administered, beginning when the infant is 1 to 2 months of age. For mothers with unknown HBsAg status, hepatitis B vaccine is recommended within 12 hours of birth, regardless of low-birth-weight status.

In addition to hepatitis B vaccines, hepatitis B immuno-

globulin (HBIG) is recommended for infants whose mothers are HBsAg-positive or unknown. If the mother is HBsAg- positive, HBIG should be given within 12 hours of birth. If the mother is HBsAg-unknown, providers should first attempt to determine the mother’s status. However, if the infant’s birth weight is less than 2000 g, HBIG should be given within 12 hours of birth. If the infant’s birth weight is 2000 g or greater, providers need to continue determining the mothers’ status but should administer a dose of HBIG as soon as possible but before 7 days passes unless the mother is found to be HBsAg-negative.

Several studies suggest that the incidence of adverse events after vaccination of preterm infants is the same as or lower than that of full-term infants vaccinated at the same chrono- logical age.168,181,182 A temporal association between receipt of DTP and HibTITER Hib vaccine and a transient increase or recurrence of apnea in premature infants has been reported, although the significance of this finding is unclear.183 Neither of these vaccines is currently available in the United States.

A preterm infant who is still hospitalized at 2 months of age can receive the vaccines routinely scheduled at that age. However, in countries in which OPV is used, IPV may be con- sidered for hospitalized infants. Because poliovirus vaccine strains are excreted after receipt of OPV, IPV will decrease the risk of transmission of vaccine viruses in the hospital.67,184 ACIP supports rotavirus vaccination of preterm infants accord- ing to the same schedule and precautions as full-term infants and under the following conditions: the infant’s chronological age meets the age requirements for rotavirus vaccine (e.g., 6 weeks through 14 weeks and 6 days of age for dose 1), the infant is clinically stable, and the vaccine is administered at the time of discharge from the neonatal intensive care unit (NICU) or nursery or after discharge from the NICU or nursery. Although the lower level of maternal antibody to rotavirus in very preterm infants theoretically could increase the risk for adverse reactions from rotavirus vaccine, ACIP believes the benefits of vaccinating an infant when age-eligible, clinically stable, and no longer in the hospital outweigh the theoretic risks.27

# BREASTFEEDING AND IMMUNIZATION

Neither inactivated nor live virus vaccines administered to a lactating mother or infant who is breastfeeding have adverse consequences.2,5 Because inactivated and component vaccines do not multiply in the body, they pose no special risk for

lactating women or their infants. Lactating women also may safely receive live virus vaccines, such as MMR, LAIV, OPV, and varicella without interruption of their breastfeeding sched- ule.5,53,184,185 Although vaccines that contain attenuated live viruses or bacteria replicate in the vaccine recipient, most live vaccine strains are not known to be secreted in human milk. An exception is rubella vaccine virus, which has been detected in human milk and recovered from the nasopharynx and throat of some breastfed infants after maternal immuniza- tion.186,187 In one study, transient seroconversion to rubella virus without evidence of clinical disease was noted in 25% of the breastfed infants.186 Breastfed infants who acquired rubella vaccine virus and rubella-specific antibodies from human milk have a normal immune response to rubella vaccine administered at 15 to 18 months of age.188

Breastfeeding of infants does not adversely affect their

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development of a protective immune response and is not a contraindication for any routinely administered vaccine.2,5 Live oral rotavirus vaccines are less immunogenic and effica- cious among children in developing countries compared with middle income and industrialized countries. Higher titers of rotavirus immunoglobulin A and neutralizing activity in human milk consumed by infants at the time of immuniza- tion has been proposed as a cause of this reduced immuno- genicity.189 However, a clinical trial found no difference in the proportion of infants who seroconverted to rotavirus vaccine between those who were either breastfeed or not breastfeeding during the 30 minutes prior to and after each vaccine dose was administered.190 Yellow fever vaccine should be avoided in breastfeeding women. Two cases (one confirmed, one proba- ble) of yellow fever vaccine–associated acute neurotropic disease (YEL-AND) have been detected in infants whose mothers were vaccinated but were not vaccinated themselves. In both infants, vaccine virus was recovered from the cerebro- spinal fluid (CSF) of the infant, but the exact mode of trans- mission was not precisely determined because vaccine was not recovered from human milk. However, when nursing mothers cannot avoid or postpone travel to areas endemic for yellow fever in which risk of acquisition is high, they should be vac- cinated.191 Compared with infants who are formula fed, breastfed infants may have an enhanced immune response to certain oral and parenteral vaccines, such as conjugate Hib vaccine, OPV, and DT.192–194 However, the significance of such an effect is unclear.

# VACCINATION DURING PREGNANCY

Risk for a developing fetus from vaccination of the mother during pregnancy primarily is theoretical. No evidence exists of risk from vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids.195,196 Live vaccines pose a theoretical risk to the fetus. Benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high, when infection would pose a risk to the mother or fetus, and when the vaccine is unlikely to cause harm.

Recommendations for vaccination during pregnancy can be found in the annual U.S. adult immunization schedule.64 Pregnant women who are not immunized or only partially immunized against tetanus should complete the primary series.197 The number of doses needed to complete the primary series should be administered. One of these doses should be Tdap. Tdap is optimally administered at 27 to 36 weeks’ gesta- tion. Women for whom the vaccine is indicated but who have not completed the recommended three-dose series during pregnancy should receive follow-up after delivery to ensure the series is completed. Use of pertussis vaccine in pregnant women may lead to transfer of higher levels of pertussis anti- body across the placenta to the fetus and results in protection

from pertussis in the first few months of life when the disease is most severe.198 Therefore, a dose of Tdap is recommended for pregnant women during every pregnancy, preferably during 27 to 36 weeks of gestation.59

Women in the second and third trimesters of pregnancy are at increased risk for hospitalization from influenza. Therefore, routine influenza vaccination is recommended for all women who will be pregnant (in any trimester) during influenza season, usually November through March in the United States.28 Influenza vaccination of a pregnant woman also reduces the risk of medically-attended respiratory tract illness in the newborn.199

IPV can be administered to pregnant women who are at risk for exposure to wild-type poliovirus infection.75,200 Preg- nancy is not a contraindication to hepatitis B vaccine. Current vaccines contain noninfectious HBsAg and should cause no risk to the fetus.201 Hepatitis A, pneumococcal polysaccharide, meningococcal conjugate, and meningococcal polysaccharide vaccines should be considered for women at increased risk for those infections.202–206

Pregnant women who must travel to areas where the risk for yellow fever is high should receive yellow fever vaccine because the limited theoretical risk from vaccination is sub- stantially outweighed by the risk for yellow fever infection.203,207 Pregnancy is a contraindication for smallpox (vaccinia), measles, mumps, rubella, and varicella-containing vaccines. Smallpox (vaccinia) vaccine is the only vaccine known to cause harm to a fetus when administered to a pregnant woman. In addition to the vaccinee herself, smallpox (vac- cinia) vaccine should not be administered to a household contact of a pregnant woman. However, in a postevent setting, or smallpox emergency, pregnancy or having a household contact who is pregnant would not be considered contraindi- cations, because of a different risk/benefit consideration. Although of theoretical concern, no cases of congenital rubella or varicella syndrome or abnormalities attributable to fetal infection have been observed among infants born to suscep- tible women who received rubella or varicella vaccines during pregnancy.53,208 Because of the importance of protecting women of childbearing age against rubella and varicella, rea- sonable practices in any vaccination program include asking women if they are pregnant or might become pregnant in the next 4 weeks, not vaccinating women who state that they are pregnant, explaining the theoretical risk for the fetus if MMR or varicella vaccine were administered to a women who is pregnant, and counseling women who are vaccinated not to become pregnant during the 4 weeks after MMR or varicella vaccination.53,208,209

Routine pregnancy testing of women of childbearing age

before administering a live virus vaccine is not recommended.53 If vaccination of an unknowingly pregnant woman occurs or if she becomes pregnant within 4 weeks after MMR or varicella vaccination, she should be counseled about the theoretical basis of concern for the fetus; however, MMR or varicella vac- cination during pregnancy should not be regarded as a reason to terminate pregnancy.185,209

All pregnant women should be evaluated for immunity to rubella and varicella and should be tested for the presence of HBsAg in every pregnancy.53,185,201,210 Women susceptible to rubella and varicella should be vaccinated immediately after delivery or after the termination of the pregnancy. A woman found to be HBsAg-positive should be followed carefully to ensure that the infant receives HBIG and begins the hepatitis B vaccine series no later than 12 hours after birth and com- pletes the recommended hepatitis B vaccine series on sched- ule.201 No known risk exists for the fetus from passive immunization of pregnant women with immunoglobulin preparations.

# VACCINATION OF HOUSEHOLD CONTACTS

Administration of live and inactivated vaccines to household members does not present a known hazard to pregnant women. Although transmission of varicella vaccine virus from a 12-month-old infant to his pregnant mother has been reported, no virus was detected in fetal tissue after an elective abortion.211 Pregnancy of a household contact is not a contra- indication to administration of varicella vaccine or any other vaccine in the childhood immunization schedule to a house- hold member.185,212

# VACCINES RECEIVED OUTSIDE THE UNITED STATES

The ability of a clinician to determine that a person is pro- tected on the basis of country of origin and the person’s records alone is limited. Vaccines administered outside the United States generally can be accepted as valid if the schedule was similar to that recommended in the United States (i.e., minimum ages and intervals; see [Table 9.2](#_bookmark3)). Only written documentation should be accepted as evidence of previous vaccination. Written records are more likely to predict protec- tion if the vaccines, dates of administration, intervals between doses, and the person’s age at the time of vaccination are comparable to U.S. recommendations.5 Although vaccines with inadequate potency have been produced in other coun- tries,213,214 most vaccines used worldwide are produced with adequate quality control standards and are potent.

The number of American families adopting children from outside the United States has increased substantially in recent years.215 Adopted children’s birth countries often have immu- nization schedules that differ from the recommended child- hood immunization schedule in the United States. Differences between schedules used in other countries include the vac- cines administered, the recommended ages of administration, and the number and timing of doses (see Chapters 74 to 76). The ACIP has published guidelines for assessing and vaccinat- ing international adoptees.5 Children adopted in the United States from other countries should receive vaccines according to U.S.-recommended schedules.

Data are inconclusive regarding the extent to which an internationally adopted child’s immunization record reflects the child’s protection. A child’s record might indicate admin- istration of MMR vaccine when only single-antigen measles vaccine was administered. A study of children adopted from the People’s Republic of China, Russia, and Eastern Europe determined that only 39% (range: 17%–88% by country) of children with documentation of more than three doses of DTP before adoption had protective serologic concentrations of diphtheria and tetanus antitoxin.216 This finding raised ques- tions about whether the vaccines received were potent or whether the immunization records purporting to show receipt of at least three doses were an accurate reflection of the true number of doses actually received. However, antibody testing was performed by a hemagglutination assay, which may underestimate protection and cannot directly be compared with antitoxin concentration measured by other tests.217 A second study measured antibody to diphtheria and tetanus toxins among 51 children who had records of having received two or more doses of DTP. Most of the children were from Russia, Eastern Europe, and Asian countries, and 78% had received all vaccine doses in an orphanage; 94% had evidence of protection against diphtheria (enzyme immunoassay [EIA]

>0.1 IU/mL). A total of 84% had protection against tetanus

(EIA >0.5 IU/mL). Among children without protective tetanus antitoxin concentrations, all except one had records of three

or more doses of vaccine, and most nonprotective concentra- tions were categorized as indeterminate (EIA 0.05–0.49 IU/ mL).218 Reasons for the discrepant findings in these two studies probably relate to different laboratory methods; the study using a hemagglutination assay might have underestimated the number of children who were protected. Additional studies using standardized methods are needed.

If a question exists regarding whether vaccines adminis- tered outside the United States were immunogenic, several approaches may be considered. Repeating the vaccinations as age-appropriate is an acceptable option; this usually is safe and avoids the need to obtain and interpret serologic tests.5 If avoiding unnecessary injections is desired, judicious use of serologic testing can help determine which immunizations are needed, particularly for DTP/DTaP vaccine. Although no established serologic correlates exist for protection against per- tussis, diphtheria and tetanus antitoxin levels may be used as surrogates to assess whether doses listed on the immunization record actually were received or were potent.5

Increased rates of moderate to severe local adverse reac- tions after the fourth and fifth doses of DTP or DTaP have been reported.108 If a revaccination option is adopted and a severe local reaction occurs, serologic testing for specific immuno- globulin G antibody to tetanus and diphtheria toxins can be performed before administering additional doses. Protective concentrations indicate that further doses are unnecessary, and subsequent vaccination should occur as age-appropriate. Instead of revaccinating a child with DTaP when there is a question about the validity of a record that indicates receipt of three or more doses of DTP or DTaP, serologic testing for specific immunoglobulin G antibody to diphtheria *and* tetanus toxin can be obtained. If a protective concentration is present, recorded doses can be considered valid, and the vaccination series should be completed as age-appropriate. Indeterminate antibody concentration might indicate immunologic memory but waning antibody. Serologic testing can be repeated after a booster dose if the vaccination provider wants to avoid revac-

cination with a complete series.5

Children 7 years of age or older who are not considered fully vaccinated for pertussis should receive one dose of Tdap vaccine. “Fully vaccinated” means at least five doses of DTaP before the seventh birthday or at least four doses of DTaP before the seventh birthday if the fourth dose is given after the fourth birthday.

Serologic testing for HBsAg is recommended for all inter- national adoptees born in Asia, the Pacific Islands, Africa, and other regions of high or intermediate endemicity.218 Children determined to be HBsAg-positive should be monitored for development of liver disease.201 Household members of HBsAg-positive children should be vaccinated. A child whose records indicate receipt of three or more doses of vaccine can be considered protected, and additional doses are not needed if at least one dose was administered at or after 6 months of age. Children who received their last hepatitis B vaccine dose when younger than 6 months of age should receive an addi- tional dose at 6 months of age or older.5 Children who have received fewer than three doses should complete the series at the recommended intervals and ages (see [Table 9.2](#_bookmark3)).

The simplest approach to vaccinating a child with uncer- tain polio vaccine records is to revaccinate with IPV according to the U.S. Schedule. Adverse events after IPV are rare.

# VACCINATION OF PERSONS WITH A PERSONAL OR FAMILY HISTORY OF SEIZURES

Infants and young children with a personal history of seizures or a parent or sibling with a history of seizures are at increased

risk for seizures after receipt of whole-cell pertussis, MMR (or monovalent measles) vaccine, or MMRV vaccine.53,219–221 In most cases, these seizures are brief, self-limited, and associated with fever. Studies have not established a causal association between these seizures and residual seizure disorders or per- manent neurologic sequelae.222,223 Acellular pertussis vaccines are associated less often with fever than are whole-cell pertus- sis vaccines; whole-cell DTP is no longer available in the United States.

Because neurologic disorders such as epilepsy and degen- erative disorders marked by loss of developmental milestones often become manifest during infancy, pertussis vaccination may coincide with onset or recognition of such disorders and cause confusion about the etiologic role of the vaccine. For infants with a personal history of a seizure, delaying pertussis vaccination is recommended until a progressive neurologic disorder is excluded or the cause of the seizure has been estab- lished.57,58 Because measles vaccine is administered at an age when a child’s neurologic status is likely to already have been established, deferring measles immunization of a child with a personal history of a seizure is not recommended.53,184

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Pertussis and measles vaccinations are not contraindicated in persons with a family history of seizures. Even though children with a parent or sibling who has had a seizure are themselves at increased risk for a seizure, the benefits of administering pertussis and measles vaccine to children with a family history of seizures substantially outweigh the small risks because the seizures are usually febrile in origin, gener- ally have a benign outcome, and are not likely to be confused with manifestations of a previously unrecognized neurologic disorder.53,58,184,222,224 In June 2009, after consideration of the postlicensure data and other evidence, ACIP adopted recom- mendations regarding use of MMRV vaccine for the first and second doses and identified a personal or family (i.e., sibling or parent) history of seizure as a precaution for use of MMRV vaccine. For the first dose of measles, mumps, rubella, and varicella vaccines at age 12 to 47 months, either MMR vaccine and varicella vaccine or MMRV vaccine may be used. Providers who are considering administering MMRV vaccine should discuss the benefits and risks of both vaccination options with the parents or caregivers. Unless the parent or caregiver expresses a preference for MMRV vaccine, CDC recommends that MMR vaccine and varicella vaccine should be adminis- tered for the first dose in this age group. For the second dose of measles, mumps, rubella, and varicella vaccines at any age (15 months to 12 years) and for the first dose at age 48 months or older, use of MMRV vaccine generally is preferred over separate injections of its equivalent component vaccines (i.e., MMR vaccine and varicella vaccine). This recommenda- tion is consistent with ACIP’s 2009 provisional general recom- mendations regarding use of combination vaccines which state that use of a combination vaccine generally is preferred over its equivalent component vaccines.5

# VACCINATION DURING ACUTE ILLNESS

The decision to administer or delay vaccination because of an intercurrent or recent acute illness depends on evaluation of the etiology of the disease and the severity of symptoms.2,5 Mild illness, febrile (temperature ≥38°C) or afebrile, is not a contraindication to vaccination. Although one study reported a lower rate of seroconversion to the measles but not to the rubella or mumps components of MMR vaccine in children with evidence of a recent or current upper respiratory tract infection compared with children without this history,223 a difference in seroconversion to measles vaccine in healthy children compared with children who are ill has not been found in other studies.81,225–228

Acute minor illnesses, such as upper respiratory tract infec- tion, diarrhea, and acute otitis media, are common during infancy and childhood.229 Postponing vaccination in children with minor febrile or afebrile illness constitutes a missed opportunity to protect a child from disease, can contribute to outbreaks of vaccine-preventable disease, and can significantly impede efforts to immunize infants and young children on schedule.230–233 Every opportunity should be used to provide indicated vaccines and to avoid missed opportunities in persons who may not return for medical care and administra- tion of recommended vaccines.2,5,234,235 The potential benefit of preventing disease by timely vaccination far outweighs any small possible risk of vaccine failure.

Vaccination usually is deferred in persons who have moder- ate or severe illness. A person with signs or symptoms of moderate or severe illness at the scheduled time of vaccination should be requested to return as soon as the illness improves so that vaccines can be administered at the recommended ages. Waiting until after a person has recovered from the acute phase of a moderate or severe illness avoids superimposing a reaction to vaccination on the underlying illness or mistakenly attribut- ing a manifestation of the underlying illness to the vaccine.2,5

# CONTRAINDICATIONS TO AND PRECAUTIONS REGARDING VACCINATION

Vaccine contraindications and precautions are described in the manufacturer’s product labeling and in the recommendations for the use of vaccines developed by national advisory

committees such as the ACIP and the Committee on Infectious Diseases of the AAP. In the United States, the content of the product label is regulated by the Food and Drug Administra- tion on the basis of specific studies required of the manufac- turer to prove the safety and efficacy of a specific product. Most recommendations of vaccine advisory committees are the same as those in the product label. However, differences some- times exist because of advisory committees’ assessments of the risks and benefits of a given recommendation, their goal to make immunization as practical as possible, and their respon- sibility to develop recommendations for the use of vaccines in circumstances in which specific safety and efficacy data may be limited but for which physicians, nurses, and public health officials need guidance. For example, the manufacturer’s product label recommends that women vaccinated with live varicella virus vaccine avoid becoming pregnant for 3 months, whereas the ACIP and AAP advise waiting only 1 month.1,185,236 Similarly, the AAP and ACIP advise that pregnancy should not be considered a contraindication to hepatitis B vaccination, whereas the manufacturer’s product label states that hepatitis B vaccine should only be given to pregnant women if clearly indicated.1,201,237,238

A contraindication indicates that a vaccine should not be administered. In contrast, a precaution specifies a situation in which vaccine may be administered if the benefit of vaccina- tion to the individual patient is judged to outweigh the risk.5 Contraindications and precautions may be generic and apply to all vaccines, or they may be specific to one or more vaccines ([Table 9.6](#_bookmark39)). The following two guidelines apply to all vaccines:

(a) An anaphylactic reaction to a vaccine or vaccine constituent

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| **TABLE 9.6** Contraindications and Precautionsa to Commonly Used Vaccines | | |
| **Vaccine** | **Contraindications** | **Precautions** |
| Diphtheria and tetanus toxoids and acellular pertussis (DTaP) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component  Encephalopathy (e.g., coma, decreased level of consciousness, or prolonged seizures), not attributable to another identifiable cause, within 7 days of administration of previous dose of diphtheria toxoid, tetanus toxoid, and pertussis (DTP) or DTaP | Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy; defer DTaP until neurologic status clarified and stabilized  Temperature of ≥40.5°C within 48 h after vaccination with a previous dose of DTP or DTaP  Collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 h after receiving a previous dose of DTP/DTaP  Seizure ≤3 days after receiving a previous dose of DTP/ DTaP  Persistent, inconsolable crying lasting ≥3 h within 48 h after receiving a previous dose of DTP/DTaP  Guillain-Barré syndrome (GBS) <6 wk after previous dose of tetanus toxoid–containing vaccine  History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid–containing or tetanus toxoid–containing vaccine; defer vaccination until at least 10 y have elapsed since the last tetanus toxoid– containing vaccine  Moderate or severe acute illness with or without fever |
| Diphtheria and tetanus toxoids (DT), tetanus and diphtheria toxoids (Td) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component | GBS < 6 wk after previous dose of tetanus toxoid– containing vaccine  History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid–containing or tetanus toxoid–containing vaccine; defer vaccination until at least 10 y have elapsed since the last tetanus-toxoid– containing vaccine  Moderate or severe acute illness with or without fever |
| *Haemophilus influenzae* type b (Hib) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component  Age <6 wk | Moderate or severe acute illness with or without fever |
| Hepatitis A | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component | Moderate or severe acute illness with or without fever |

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| **TABLE 9.6** Contraindications and Precautionsa to Commonly Used Vaccines (*Continued)* | | |
| **Vaccine** | **Contraindications** | **Precautions** |
| Hepatitis B | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component; hypersensitivity to yeast | Infant weight <2000 gb  Moderate or severe acute illness with or without fever |
| Human papillomavirus vaccine (2vHPV, 4vHPV, 9vHPV) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component | Moderate or severe acute illness with or without fever; pregnancy |
| Inactivated influenza vaccine (IIV, RIV) | Severe allergic reaction (e.g., anaphylaxis) after previous dose of influenza vaccine | GBS <6 wk after a previous dose of influenza vaccine Moderate or severe acute illness with or without fever |
| Inactivated poliovirus (IPV) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component | Pregnancy  Moderate or severe acute illness with or without fever |
| Live attenuated influenza vaccine (LAIV) | Severe allergic reaction (e.g., anaphylaxis) after previous dose or to vaccine component, including egg protein  Persons aged <2 y or >49 y  Those with contraindications listed in the package insert: Children ages 2–17 y who are receiving aspirin or aspirin-containing products; persons who have experienced severe allergic reactions to the vaccine or any of its compounds, or to a previous dose of any influenza vaccine; pregnant women; immunosuppressed persons; persons with a history of egg allergy; children ages 2–4 y who have asthma or who have had a wheezing episode noted in the medical record within the past 12 mo, or for whom parents report that a health care provider stated that they had wheezing or asthma within the last 12 mo  Persons who have taken influenza antiviral medications within the previous 48 hc | GBS <6 wk after a previous dose of influenza vaccine The safety of LAIV in persons with underlying medical  conditions that might predispose them to complications after wild-type influenza infection (e.g., chronic pulmonary, cardiovascular [except isolated hypertension], renal, hepatic, neurologic, hematologic, or metabolic disorders [including diabetes mellitus]) has not been established. These conditions, in addition to asthma in persons age ≥5 y, should be considered precautions for the use of LAIV  Moderate or severe acute illness with or without fever |
| Measles, mumps, and rubella (MMR)d,e | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component  Pregnancy  Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapyf or patients with HIV infection who are severely immunocompromised)e | Recent (≤11 mo) receipt of antibody-containing blood product (specific interval depends on product)g  History of thrombocytopenia or thrombocytopenic purpura Need for tuberculin skin testingh or interferon gamma  release assay (IGRA) testing  Moderate or severe acute illness with or without fever |
| Pneumococcal conjugate vaccine (PCV13) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose of PCV13, or any diphtheria toxoid–containing vaccine or to a component of a vaccine (PCV13 or any diphtheria toxoid–containing vaccine) | Moderate or severe acute illness with or without fever |
| Pneumococcal polysaccharide vaccine (PPSV) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component | Moderate or severe acute illness with or without fever |
| Quadrivalent meningococcal conjugate vaccine (MCV4) and monovalent meningococcal b vaccine | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component | Moderate or severe acute illness with or without fever |
| Quadrivalent meningococcal polysaccharide vaccine (MPSV4) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component | Moderate or severe acute illness with or without fever |
| Rotavirus | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component  Severe combined immunodeficiency (SCID) History of intussusception | Altered immunocompetence other than SCID Chronic gastrointestinal diseasei  Spina bifida or bladder exstrophyi  Moderate or severe acute illness with or without fever |

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| **TABLE 9.6** Contraindications and Precautionsa to Commonly Used Vaccines (*Continued)* | | |
| **Vaccine** | **Contraindications** | **Precautions** |
| Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component  Encephalopathy (e.g., coma, decreased level of consciousness, or prolonged seizures), not attributable to another identifiable cause, within 7 days of administration of previous dose of DTP, DTaP, or Tdap | GBS <6 wk after a previous dose of tetanus toxoid– containing vaccine  Progressive or unstable neurological disorder, uncontrolled seizures, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized  History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria toxoid-containing or tetanus toxoid–containing vaccine; defer vaccination until at least 10 y have elapsed since the last tetanus toxoid– containing vaccinej  Moderate or severe acute illness with or without fever |
| Varicella | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component  Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapyf or patients with HIV infection who are severely immunocompromised)e  Pregnancy | Recent (≤11 mo) receipt of antibody-containing blood product (specific interval depends on product)k  Moderate or severe acute illness with or without fever |
| Zoster | Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component  Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapy or patients with HIV infection who are severely immunocompromisede,f  Pregnancy | Moderate or severe acute illness with or without fever |
| aEvents or conditions listed as precautions should be reviewed carefully. Benefits of and risks for administering a specific vaccine to a person under these circumstances should be considered. If the risk from the vaccine is believed to outweigh the benefit, the vaccine should not be administered. If the benefit of vaccination is believed to outweigh the risk, the vaccine should be administered. Whether and when to administer DTaP to children with proven or suspected underlying neurologic disorders should be decided on a case-by-case basis.  bHepatitis B vaccination should be deferred for infants weighing <2000 g if the mother is documented to be hepatitis B surface antigen (HBsAg)- negative at the time of the infant’s birth. Vaccination can commence at chronological age 1 month or at hospital discharge. For infants born to HBsAg-positive women, hepatitis B immunoglobulin and hepatitis B vaccine should be administered within 12 hours after birth, regardless of weight.  cSource: Fiore AE, Uyeki TM, Broder K, et al; Centers for Disease Control and Prevention (CDC). Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Recomm Rep*. 2010;59(RR-8):1–62.  dHIV-infected children may receive varicella and measles vaccine if CD4+ T-lymphocyte count is >15%. (Source: Adapted from American Academy of Pediatrics. Passive immunization. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015.  eMMR and varicella-containing vaccines can be administered on the same day. If not administered on the same day, these vaccines should be separated by at least 28 days.  fSubstantially immunosuppressive steroid dose is considered to be ≥2 weeks of daily receipt of 20 mg or 2 mg/kg body weight of prednisone or equivalent.  gSee [Table 9.5](#_bookmark32) for details.  hIf active tuberculosis is suspected, MMR should be delayed. Measles vaccination might suppress tuberculin reactivity temporarily. Measles- containing vaccine can be administered on the same day as tuberculin skin testing. If testing cannot be performed until after the day of MMR vaccination, the test should be postponed for ≥4 weeks after the vaccination. If an urgent need exists to skin test, do so with the understanding that reactivity might be reduced by the vaccine.  iFor details, see Cortese MM, Parashar UD; Centers for Disease Control and Prevention (CDC). Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2009;58(RR-2):1–25.  jWith the exception of pregnant woman who should be vaccinated during every pregnancy regardless of interval since last tetanus toxoid–containing dose.  kVaccine should be deferred for the appropriate interval if replacement immunoglobulin products are being administered (see [Table 9.5](#_bookmark32)). | | |

contraindicates further use of that vaccine or vaccines contain- ing that constituent (see “Vaccine Components Causing Hypersensitivity” above). (b) Moderate or severe acute illness, regardless of the absence or presence of fever, is a precaution to vaccination (see “Vaccination During Acute Illness” above).

Immunosuppression resulting from underlying disease or therapy is a contraindication for receipt of most live vac- cines.5,53,184 MMR vaccine is recommended for HIV-infected persons who are not severely immunosuppressed.172,209,217,239 Varicella vaccine can be considered for HIV-infected persons

not severely immunosuppressed.185 Rotavirus vaccine is con- traindicated in infants diagnosed with severe combined immu- nodeficiency (SCID).240,241 Corticosteroid therapy can suppress the immune system of an otherwise healthy person, although the minimal dose and duration of therapy necessary to cause immunosuppression are not well defined. Underlying disease, concurrent therapies, and the frequency and route of admin- istration of corticosteroids also can affect immunosuppres- sion. Steroid therapy does not usually contraindicate administration of live vaccines when given in low to moderate doses administered daily or on alternate days, physiologic

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| **TABLE 9.7** Conditions Commonly Misperceived as Contraindications to Vaccination | |
| **Vaccine** | **Conditions Commonly Misperceived as Contraindications (i.e., Vaccination May Be Administered Under These Conditions)** |
| General for all vaccines, including diphtheria and tetanus toxoids and acellular pertussis (DTaP), pediatric diphtheria and tetanus toxoids (DT), adult tetanus and diphtheria toxoids (Td), adolescent–adult tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap), inactivated poliovirus (IPV), measles, mumps, and rubella (MMR), *Haemophilus influenzae* type b (Hib), hepatitis A, hepatitis B, varicella, rotavirus, pneumococcal conjugate vaccine (PCV), trivalent inactivated influenza vaccine (IIV) live, attenuated influenza vaccine (LAIV), pneumococcal polysaccharide vaccine (PPSV 23), quadrivalent meningococcal conjugate vaccine (MCV4), quadrivalent meningococcal polysaccharide vaccine (MPSV4), serogroup B meningococcal human papillomavirus (HPV) vaccine, and herpes zoster | Mild acute illness with or without fever  Mild-to-moderate local reaction (i.e., swelling, redness, soreness); low-grade or moderate fever after previous dose  Lack of previous physical examination in well-appearing person Current antimicrobial therapya  Convalescent phase of illness  Preterm birth (hepatitis B vaccine is an exception in certain circumstances)b Recent exposure to an infectious disease  History of penicillin allergy, other nonvaccine allergies, relatives with allergies, or receiving allergen extract immunotherapy  History of Guillain-Barré syndromec |
| DTaP | Temperature of <40.5°C, fussiness, or mild drowsiness after a previous dose of diphtheria toxoid, tetanus toxoid, and pertussis (DTP)/DTaP  Family history of seizures  Family history of sudden infant death syndrome  Family history of an adverse event after DTP or DTaP administration  Stable neurologic conditions (e.g., cerebral palsy, well-controlled seizures, or developmental delay) |
| Tdap | History of temperature of ≥40.5°C for <48 h after vaccination with a previous dose of DTP or DTaP  History of collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 h after receiving a previous dose of DTP/DTaP  History of seizure <3 days after receiving a previous dose of DTP/DTaP  History of persistent, inconsolable crying lasting >3 h within 48 h after receiving a previous dose of DTP/DTaP  History of extensive limb swelling after DTP/DTaP/Td that is not an Arthus-type reaction  Stable neurologic disorder History of brachial neuritis  Latex allergy that is not anaphylactic Breastfeeding  Immunosuppression |
| IPV | Previous receipt of ≥1 dose of oral polio vaccine |
| MMRd,e | Positive tuberculin skin test Simultaneous tuberculin skin testingf Breastfeeding  Pregnancy of recipient’s mother or other close or household contact Recipient is female of childbearing age  Immunodeficient family member or household contact Asymptomatic or mildly symptomatic HIV infection Allergy to eggs |
| Hepatitis B | Pregnancy  Autoimmune disease (e.g., systemic lupus erythematosus or rheumatoid arthritis) |
| Varicella | Pregnancy of recipient’s mother or other close or household contact Immunodeficient family member or household contactg Asymptomatic or mildly symptomatic HIV infection  Humoral immunodeficiency (e.g., agammaglobulinemia) |
| Inactivated influenza vaccine (IIV) | Nonsevere (e.g., contact) allergy to latex, thimerosal, or egg Concurrent administration of Coumadin or aminophylline |
| LAIV | Healthcare providers who see patients with chronic diseases or altered immunocompetence (an exception is providers for severely immunocompromised patients requiring care in a protected environment)  Breastfeeding  Contacts of persons with chronic disease or altered immunocompetence (an exception is contacts of severely immunocompromised patients requiring care in a protected environment) |
| PPSV | History of invasive pneumococcal disease or pneumonia |
| HPV | Immunosuppression  Previous equivocal or abnormal Papanicolaou test Known HPV infection  Breastfeeding  History of genital warts |

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| **TABLE 9.7** Conditions Commonly Misperceived as Contraindications to Vaccination *(Continued)* | |
| **Vaccine** | **Conditions Commonly Misperceived as Contraindications (i.e., Vaccination May Be Administered Under These Conditions)** |
| Rotavirus | Prematurity  Immunosuppressed household contacts Pregnant household contacts |
| Zoster | Therapy with low-dose methotrexate (≤0.4 mg/kg per week), azathioprine  (≤3.0 mg/kg per day), or 6-mercaptopurine (≤1.5 mg/kg per day) for treatment of rheumatoid arthritis, psoriasis, polymyositis, sarcoidosis, inflammatory bowel disease, or other conditions  Healthcare providers of patients with chronic diseases or altered immunocompetence  Contacts of patients with chronic diseases or altered immunocompetence Unknown or uncertain history of varicella in a U.S.-born person |
| aAntibacterial drugs might interfere with Ty21a oral typhoid vaccine, and certain antiviral drugs might interfere with varicella-containing vaccines and LAIV.  bHepatitis B vaccination should be deferred for infants weighing <2000 g if the mother is documented to be hepatitis B surface antigen (HBsAg)-negative at the time of the infant’s birth. Vaccination can commence at chronological age 1 month or at hospital discharge. For infants born to HBsAg-positive women, hepatitis B immunoglobulin and hepatitis B vaccine should be administered within 12 hours after birth, regardless of weight.  cAn exception is Guillain-Barré syndrome within 6 weeks of a dose of influenza vaccine or tetanus-toxoid–containing vaccine, which are precautions for influenza vaccine and tetanus-toxoid–containing vaccines, respectively.  dMMR and varicella vaccines can be administered on the same day. If not administered on the same day, these vaccines should be separated by at least 28 days.  eHIV-infected children should receive immunoglobulin after exposure to measles. HIV-infected children can receive varicella and measles vaccine if CD4+ T-lymphocyte count is >15%. (Source: Modified from American Academy of Pediatrics. Passive immunization. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015.)  fMeasles vaccination might suppress tuberculin reactivity temporarily. Measles-containing vaccine can be administered on the same day as tuberculin skin testing. If testing cannot be performed until after the day of MMR vaccination, the test should be postponed for at least 4 weeks after the vaccination. If an urgent need exists to skin test, do so with the understanding that reactivity might be reduced by the vaccine.  gIf a vaccinee experiences a presumed vaccine-related rash 7 to 25 days after vaccination, the person should avoid direct contact with immunocompromised persons for the duration of the rash. | |

maintenance doses, or doses administered topically, by aerosol, or by local (e.g., intraarticular) injection.5,184 In most cases, persons receiving high doses of systemic corticosteroids (i.e.,

≥2 mg/kg per day or 20 mg/day of prednisone or its equiva- lent) for less than 14 days can receive live vaccines immediately after discontinuation of therapy.2,5 However, live vaccines usually are not administered to persons who have received high doses of systemic corticosteroids for 14 days or more until at least 1 month after cessation of steroid therapy.5,184

Live vaccines usually are contraindicated for pregnant women because of a theoretical risk to the fetus (see “Vaccina-

tion During Pregnancy” above). However, the small theoreti- cal risk from administration of a live vaccine to a pregnant woman is sometimes far outweighed by the risk of contracting a disease with serious consequences for mother and fetus (e.g., yellow fever vaccine).

Healthcare providers sometimes inappropriately consider a condition to be a contraindication or precaution to vaccina- tion.2,5 Withholding vaccine in such situations results in a missed opportunity to administer needed vaccine ([Table 9.7](#_bookmark51)).

References for this chapter are available at [ExpertConsult.com](http://www.ExpertConsult.com/).

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