General Best Practice Guidelines for Immunization

Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP)

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1. Introduction

The Centers for Disease Control and Prevention (CDC) recommends routine vaccination to prevent 17 vaccine-preventable diseases that occur in infants, children, adolescents, or adults. This report provides information for clinicians and other health care providers about concerns that commonly arise when vaccinating persons of various ages. Providers and patients must navigate numerous issues, such as the timing of each dose, screening for contraindications and precautions, the number of vaccines to be administered, the educational needs of patients and parents, and interpreting and responding to adverse events. Vaccination providers help patients understand the substantial body of (occasionally conflicting) information about vaccination.

This vaccination best practice guidance is intended for clinicians and other health care providers who vaccinate patients in varied settings, including hospitals, provider offices, pharmacies, schools, community health centers, and public health clinics. The updated guidelines include 1) new information on simultaneous vaccination and febrile seizures; 2) enhancement of the definition of a "precaution" to include any condition that might

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confuse diagnostic accuracy; 3) confirmation that if a patient is not acutely moderately or severely ill, vaccination during hospitalization is a best practice; 4) more descriptive characterization of anaphylactic allergy; 5) incorporation of protocols for management of anaphylactic allergy; 6) allowances for alternate route (subcutaneous instead of intramuscular) for hepatitis A vaccination; 7) an age cutoff of 12 years through 17 years of age for validating a dose of intradermal influenza vaccine; 8) deletion of much of the content from storage and handling, including storage units, temperature monitoring, and expiration dates (because this content is now codified and continually updated in the CDC's Vaccine Storage and Handling Toolkit, available at www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html.); 9) incorporation of Infectious Diseases Society of America guidance on vaccination of persons with altered immunocompetence; 10) timing of intramuscular administration in patients with bleeding disorders; 11) updated data on vaccination record policy; 12) additional impacts of the Affordable Care Act (*1*,*2*) on adult vaccination; and 13) updated programmatic contact information on source material for vaccine information.

The guidance is organized in the following 10 documents: 1) Timing and Spacing of Immunobiologics; 2) Contraindications and Precautions; 3) Preventing and Managing Adverse Reactions; 4) Vaccine Administration; 5) Storage and Handling of Immunobiologics; 6) Altered Immunocompetence; 7) Special Situations; 8) Vaccination Records; 9) Vaccination Programs; and 10) Vaccine Information Sources. A glossary follows (see Appendix 1: Glossary).

This report will help vaccination providers to assess vaccine benefits and risks, use recommended administration practices, understand the most effective strategies for ensuring that vaccination coverage in the population remains high, and communicate the importance of vaccination to reduce the effects of vaccine-preventable disease. These best practice guidelines are intended for use in the United States; vaccine availability, use, and epidemiologic circumstances might differ in other countries and might warrant different guidance.

REFERENCES

1. The Patient Protection and Affordable Care Act, Pub. L. No. 111-148 (2010).
2. U.S. Department of Health and Human Services. Read the law: the Affordable Care Act, section by section. 2015; www.hhs.gov/healthcare/about-the-law/read-the-law/index.html. Accessed 9 March, 2017.

2. Methods

The Advisory Committee on Immunization Practices (ACIP) General Recommendations Work Group (GRWG) reviews the evidence for best practices regarding immunization and releases updated guidance every 3 to 5 years (see Appendix 2: Membership). Work group members are required to report conflicts of interests. Conflict of interest information for those individuals who must report is available upon request to the corresponding author. Relevant topics are those identified by ACIP as topics related to all vaccines, including timing and spacing of doses, vaccine administration, and vaccine storage and handling. New topics are added when ACIP decides previous ACIP good practice statements on general issues (such as combination vaccines, adolescent vaccination, or adult vaccination) should be revised and incorporated into the *General Best Practice Guidelines for Immunization*.

The best practice guidelines in this report update the previous ACIP *General Recommendations on Immunization* (*1*) and are based both on review and analysis of available scientific evidence and on expert opinion of the diverse group of health care providers and public health officials who are members of GRWG. This group includes professionals from academic medicine (pediatrics, family practice, and pharmacy); international (Canada), federal, and state public health professionals; and a member from the nongovernmental Immunization Action Coalition (see Appendix 2: Membership). This revision involved consensus-building based on new evidence from the published literature and opinion from subgroups of subject matter experts consulted on specific topics.

The process by which the guidelines were drafted varied for each document; each document is therefore discussed individually below. ACIP voted to accept the proposed guidance in October 2014; for additional information, see www.cdc.gov/vaccines/acip/meetings/meetings-info.html.

Timing and Spacing of Immunobiologics

GRWG met monthly beginning in January 2011, and formed a subgroup to focus on review of guidelines around administration of simultaneous vaccination and febrile seizures. Meetings were held in April, May, and June 2011 to discuss the evidence. Other issues related to timing and spacing of vaccinations were discussed between February 2012 and September 2014 over 7 meetings (in February 2012, June 2012, August 2012, November 2012, January 2013, January 2014, May 2014, and September 2014). The evidence supporting this document is based on expert opinion and arrived at by consensus. Presentations of the evidence were made to ACIP in June 2011, October 2011, and February 2013. Major changes include 1) guidance for simultaneous vaccination in the context of a risk for febrile seizures and 2) clarification of the use of the grace period between doses of the measles, mumps, rubella, and varicella vaccine (MMRV).

Contraindications and Precautions

GRWG met monthly and focused on revisions to the Contraindications and Precautions section beginning in January 2012, over 6 meetings (January 2012, February 2012, June 2012, August 2012, November, 2012, December 2012, and January 2013; see www.cdc.gov/vaccines/acip/meetings/meetings-info.html). The evidence supporting this document is based on a review of the published literature. Publications about vaccination during surgery, hospitalization, and anesthesia were obtained from the databases PubMed and MDConsult, searched from 1973 to 2014 using the MeSH (medical subject headings) terms “anesthesia” and “immunization”. The search and selection of studies was limited to English-language and human studies. The search and selection process yielded 20 publications, including review articles, observational studies, and letters to the editor. Presentations of proposed best practices were made to ACIP in February 2013 and a vote from ACIP affirming the language below was made in October 2014. Major changes include 1) enhancement of the definition of a “precaution” to include any condition that might confuse diagnostic accuracy and 2) guidance to vaccinate during a hospitalization if a patient is not acutely moderately or severely ill.

Preventing and Managing Adverse Reactions

GRWG met monthly and focused on revisions to the Preventing and Managing Adverse Reactions section beginning in April 2013, following revision to the document by the Allergy Subgroup. Selected members from this subgroup participated in the April 2013 main work group call. GRWG then met again in May 2013. The evidence supporting this document is based on expert opinion and arrived at by consensus. Presentations of proposed guidance were made to ACIP in June 2013, and a vote from ACIP affirming the language below was made in October 2014. Major changes included 1) more descriptive characterization of anaphylactic allergy and 2) incorporation of protocols for managing adverse reactions. ACIP voted to accept the proposed statement in October 2014.

Vaccine Administration

GRWG met monthly beginning in May 2013 to discuss Vaccine Administration and met for 4 additional meetings (July 2013, August 2013, December 2013 and September 2014). The evidence supporting this document is based on expert opinion and arrived at by consensus. Presentations of the proposed guidance were made to ACIP in October 2013, and a vote from ACIP affirming the language below was made in October 2014. Major changes from 2011 include 1) allowances for alternate administration route (subcutaneous instead of intramuscular) for hepatitis A vaccine and 2) an age cutoff of 12 years through 17 years of age for validating a dose of intradermal influenza vaccine if given in error. ACIP voted to accept the proposed statement in October 2014.

Storage and Handling of Immunobiologics

GRWG met in December 2013 to discuss Storage and Handling of Immunobiologics and met one additional time in January 2014. The evidence supporting this document is based on expert opinion and arrived at by consensus. A presentation of proposed language was made to ACIP in February 2014, and a vote from ACIP approving the language below was made in October 2014. Most of the 2011 language was removed because this content is now codified and continually updated in the CDC's Vaccine

Storage and Handling Toolkit, available at www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html. This content included Storage Units, Monitoring Storage Temperature, Vaccine Inventory, and Vaccine Transport.

Altered Immunocompetence

GRWG met twice in March and April 2014 to discuss best practices guidance for Altered Immunocompetence. This section incorporates general content from the Infectious Diseases Society of America (IDSA) policy statement *2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host* (*2*), to which CDC provided input in November 2011. The evidence supporting this document is based on expert opinion and arrived at by consensus. ACIP voted to accept this proposed statement in June 2015.

Special Situations

GRWG met in April 2012 and then in 4 follow-up meetings in May, August, and November 2012, and January 2013. A focal point of discussion involved best practices guidance for intramuscular administration of persons with increased bleeding risk. Subject matter experts from the National Center for Birth Defects and Developmental Disabilities (NCBDDD) were invited to a work group meeting, and revisions to the guidance involving the timing of intramuscular administration were made in collaboration with these subject matter experts, primarily to ensure that ACIP's best practices guidance does not conflict with NCBDDD recommendations regarding the timing of clotting factor deficiency replacement. The evidence supporting this document is based on expert opinion and arrived at by consensus.

GRWG presented the Special Situations section to ACIP in February 2013. ACIP voted to accept the proposed statement in June 2015.

Vaccination Records

GRWG met in August and September 2013, and presented the vaccination records language to ACIP in October 2013. The evidence supporting this document is based on expert opinion and arrived at by consensus. ACIP voted to accept this proposed best practices guidance in June 2015.

Vaccination Programs

GRWG met in April 2014. The major revision to this section is the addition of language related to Affordable Care Act (*3,4*) coverage of adult vaccination. The evidence supporting this document is based on expert opinion and arrived at by consensus. GRWG presented this section to ACIP in June 2014. ACIP voted to accept this proposed statement in June 2015.

Vaccination Information Sources

GRWG met in September 2014 and presented this section to ACIP. The evidence supporting this document is based on expert opinion and arrived at by consensus. ACIP voted to accept this proposed statement in June 2015.

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2. Rubin L, Levin M, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis*. 2014;58(3):e44-100. DOI: 10.1093/cid/cit684
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4. U.S. Department of Health and Human Services. Read the law: the Affordable Care Act, section by section. 2015; www.hhs.gov/healthcare/about-the-law/read-the-law/index.html. Accessed 9 March, 2017.

3. Timing and Spacing of Immunobiologics

Updates

Major changes to the best practice guidance for timing and spacing of immunobiologics include 1) guidance for simultaneous vaccination in the context of a risk for febrile seizures and 2) clarification of the use of the grace period between doses of MMRV.

General Principles for Vaccine Scheduling

Optimal response to a vaccine depends on multiple factors, including the type of vaccine, age of the recipient, and immune status of the recipient. Recommendations for the age at which vaccines are administered are influenced by age-specific risks for disease, age-specific risks for complications, age-specific responses to vaccination, and potential interference with the immune response by passively transferred maternal antibodies. Vaccines are generally recommended for members of the youngest age group at risk for experiencing the disease for which vaccine efficacy and safety have been demonstrated.

Tetanus and diphtheria toxoids require booster doses to maintain protective antibody concentrations (*1*). Unconjugated polysaccharide vaccines do not induce T-cell memory, and additional doses (although they elicit the same or a lower antibody concentration) might increase the duration of protection. Conjugation with a protein carrier improves the effectiveness of polysaccharide vaccines by inducing T-lymphocyte–dependent immunologic function (*2*). Many vaccines that stimulate both cell-mediated immunity and neutralizing antibodies (e.g., live, attenuated virus vaccines) can usually induce prolonged immunity, even if antibody titers decline over time (*3*). Subsequent exposure to such viruses usually results in a rapid anamnestic antibody response without viremia.

Approximately 90%-95% of recipients of a single dose of certain live vaccines administered by injection at the recommended age (i.e., measles, rubella, and yellow fever vaccines) develop protective antibodies, generally within 14 days of the dose. For varicella and mumps vaccines, 80%-85% of vaccinees are protected after a single dose. However, because a limited proportion (5%-20%) of measles, mumps, and rubella

(MMR) or varicella vaccinees fail to respond to 1 dose, a second dose is recommended to provide another opportunity to develop immunity (*4*). Of those who do not respond to the first dose of the measles component of MMR or varicella vaccine, 97%-99% respond to a second dose (*5*,*6*).

The *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Immunization Schedule* are revised annually. Physicians and other health care providers should ensure that they are following the most up-to-date schedules, which are available from CDC at www.cdc.gov/vaccines/schedules/hcp/index.html.

Spacing of Multiple Doses of the Same Antigen

Vaccination providers should adhere to recommended vaccination schedules (Table 3-1). Administration at recommended ages and in accordance with recommended intervals between doses of multidose antigens provides optimal protection.

Administration of doses of a multidose vaccine using intervals that are shorter than recommended might be necessary in certain circumstances, such as impending international travel or when a person is behind schedule on vaccinations but needs rapid protection. In these situations, an accelerated schedule can be implemented using intervals between doses that are shorter than intervals recommended for routine vaccination (*7*). The accelerated or minimum intervals and ages for scheduling catch-up vaccinations are available at www.cdc.gov/vaccines/schedules/hcp/index.html. Vaccine doses should not be administered at intervals less than these minimum intervals or at an age that is younger than the minimum age.*[(a)]

Before administering a vaccine dose, providers might need to verify that all previous doses were administered after the minimum age and in accordance with minimum intervals (Table 3-1). In clinical practice, vaccine doses occasionally are administered at intervals less than the minimum interval or at ages younger than the minimum age. Doses administered too close together or at too young an age can lead to a suboptimal immune response. However, administering a dose a few days earlier than the minimum interval or age is unlikely to have a substantially negative effect on the immune response to that dose. Known as the "grace period", vaccine doses administered ≤4 days before

the minimum interval or age are considered valid; however, local or state mandates might supersede this 4-day guideline (*7*).[b] (Day 1 is the day before the day that marks the minimum age or minimum interval for a vaccine.) The scenario most applicable to the grace period is a visit to a provider several days prior to the date indicated by the minimum interval, such as for a mild illness. Follow-up is unlikely soon after or even for a longer period of time following this mild illness visit; this therefore raises the question of whether vaccines be administered during the mild illness visit to avoid missed opportunities to vaccinate. Because of the unique schedule for rabies vaccine, the 4-day guideline does not apply to this vaccine (*8*). Doses of any vaccine administered ≥5 days earlier than the minimum interval or 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 (Table 3-1). For example, if the first and second doses of *Haemophilus influenzae* type b (Hib) were administered only 14 days apart, the second dose would be invalid and need to be repeated because the minimum interval from dose 1 to dose 2 is 4 weeks. The repeat dose should be administered ≥4 weeks after the invalid dose (in this case, the second) (*7*). The repeat dose is counted as the valid second dose. If the first and second doses of hepatitis A vaccine were administered less than 6 months apart, the second dose is invalid and should be repeated 6 months after the invalid second dose (*7*). However, if this repeat dose (the third dose) is administered anytime 6 months or more after the first dose, the series can be considered complete.

If the first dose in a series is given ≥5 days before the recommended minimum age, the dose should be repeated on or after the date when the child reaches at least the minimum age (*7*). If the vaccine is a live vaccine, ensuring that a minimum interval of 28 days has elapsed from the invalid dose is recommended (*7*). For example, if the first dose of varicella vaccine were inadvertently administered at age 10 months, the repeat dose would be administered no earlier than the child's first birthday (the minimum age for the first dose). If the first dose of varicella vaccine were administered at age 11 months and 2 weeks, the repeat dose should be administered no earlier than 4 weeks thereafter, which would occur after the first birthday.

Certain vaccines (e.g., adult tetanus and diphtheria toxoids [Td], pediatric diphtheria and tetanus toxoids [DT], tetanus toxoid) produce increased rates of local or systemic reactions in certain recipients when administered more frequently than recommended (*9*,*10*). Careful record keeping, maintenance of patient histories, use of immunization information systems (IISs), and adherence to recommended schedules can decrease the incidence of such reactions without adversely affecting immunity.

Simultaneous Administration

Simultaneous administration of vaccines is defined as administering more than one vaccine on the same clinic day, at different anatomic sites, and not combined in the same syringe. Experimental evidence and extensive clinical experience provide the scientific basis for administering vaccines simultaneously (*11*). Simultaneously administering all vaccines for which a person is eligible at the time of a visit increases the probability that a child, adolescent, or adult will be vaccinated fully by the appropriate age (*12*). A study conducted during a measles outbreak demonstrated that approximately one-third of measles cases among unvaccinated but vaccine-eligible preschool children might have been prevented if MMR had been administered at the same visit when another vaccine was administered (*13*). Simultaneous administration also is critical when preparing for foreign travel in the near future and when a health care provider is uncertain that a patient will return for additional doses of vaccine.

With some exceptions, simultaneously administering the most widely used live and inactivated vaccines has produced seroconversion rates and rates for adverse reactions similar to those observed when the vaccines are administered separately (*11*, *14-16)*. Routine administration of all age-appropriate doses of vaccines simultaneously is recommended for children for whom no specific contraindications exist at the time of the visit (*7*). MMR and varicella vaccine can be administered simultaneously (*7*). Live, attenuated influenza vaccine (LAIV) does not interfere with the immune response to MMR or varicella vaccines administered at the same visit (*17*). No data exist about the immunogenicity of oral Ty21a typhoid vaccine when administered concurrently or within 30 days of live-virus vaccines. In the absence of such data, if typhoid vaccination is warranted, administration should not be delayed because of recent administration of

live, attenuated virus vaccines (*18*). Simultaneous administration of pneumococcal polysaccharide vaccine (PPSV) and inactivated influenza vaccine elicits a satisfactory antibody response without increasing the incidence or severity of adverse reactions (*19*). Simultaneous administration of PPSV23 and inactivated influenza vaccine is recommended for all persons for whom both vaccines are indicated. Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) and inactivated influenza vaccine (IIV) can be administered simultaneously (*20*). Hepatitis B vaccine administered with yellow fever vaccine is as safe and immunogenic as when these vaccines are administered separately (*21*). Measles and yellow fever vaccines have been administered safely at the same visit and without reduction of immunogenicity of either component (*22*,*23*).

During the 2010-2011 influenza season, surveillance systems detected safety signals for febrile seizures in young children following IIV and PCV13 vaccines (*24*). CDC studied the health care visit records of more than 200,000 vaccinated children ages 6 months through 59 months through the Vaccine Safety Datalink Project during the 2010-2011 influenza season. The analyses found that febrile seizures following IIV and PCV13 vaccines given to this age group were rare, but did occur at higher than expected rates. The risk for febrile seizures peaked in children age 16 months and were more common when the 2 vaccines were given during the same health care visit. In this group, about one additional febrile seizure occurred among every 2,200 children vaccinated. After assessing benefits and risks, ACIP continues to recommend IIV and PCV13 be given concomitantly if both are recommended (*24*,*25*).

There are 2 exceptions to the recommendation that vaccines should be administered simultaneously. In persons with anatomic or functional asplenia, quadrivalent meningococcal conjugate vaccine (MCV4)-D (MenACWY-D, Menactra) and pneumococcal conjugate vaccine (PCV)13 (PCV13, Prevnar 13) should not be administered simultaneously (*26*). This is based on immunogenicity studies that showed reduced antibody concentrations for 3 serotypes of pneumococcus (subtypes 4, 6B, and 18C) when PCV7 was administered simultaneously with MenACWY-D. For persons with anatomic or functional asplenia, PCV13 should be administered first and MenACWY-D 4 weeks later.

In patients recommended to receive both PCV13 and PPSV23, the 2 vaccines should not be administered simultaneously (*27*). PCV13 should be administered first. If PPSV23 has been administered first, PCV13 should be administered no earlier than 8 weeks later in children 6-18 years, and one year later in adults 19 years and older. Immunogenicity studies evaluating responses to PCV13 and PPSV23 administered in series showed a better immune response when PCV13 was administered first. An evaluation of immune response after a second pneumococcal vaccination administered 1 year after the initial study doses showed that subjects who received PPSV23 as the initial study dose had lower antibody responses after subsequent administration of PCV13 than those who had received PCV13 as the initial dose followed by a dose of PPSV23, regardless of the level of the initial response to PPSV23 (*28*,*29*).

Depending on which vaccines are administered during the first year of life, a child might receive up to 9 injections at the 12- through 15-month visit (MMR, varicella, Hib, PCV13, pediatric diphtheria and tetanus toxoids and acellular pertussis [DTaP], inactivated poliovirus [IPV], hepatitis A, hepatitis B [HepB], and influenza vaccines). Although there is no exact limit on the number of injections, with a little flexibility, a provider can ensure that the primary series doses are given without administering too many injections at each visit. To reduce the number of injections at the 12- through 15-month visit, the hepatitis B series and 3 doses of IPV (*30*) can be administered before the child's first birthday.

There are many other examples of ways the vaccination schedule provides flexibility. The majority of children aged 1 year who have received 2 Hib vaccine doses (polyribosylribitol phosphate-meningococcal outer membrane protein [PRP-OMP]) or 3 Hib vaccine doses (PRP-tetanus [PRP-T]) and 3 previous doses of DTaP and PCV13 have protection against Hib, diphtheria, pertussis, tetanus, and pneumococcus, which lasts throughout infancy (*2*,*31*). The third (PRP-OMP) or fourth (PRP-T) dose of the Hib series and the fourth doses of DTaP and PCV13 are critical in boosting antibody titer and ensuring continued protection (*2*,*32-34*). The fourth dose of DTaP is recommended at age 15-18 months but may be administered as early as age 12 months if 6 months have elapsed since the third dose and if there is concern that the child might not return by age 18 months (*32*). For infants at low risk for infection with hepatitis B virus (i.e., mother

tested negative for hepatitis B surface antigen [HBsAg] at the time of delivery and is not in a high risk group), the hepatitis B series can be completed at any time for children aged 6-18 months (*35*). The minimum age for administration of combination vaccines is the oldest minimum age for any of the individual components; the minimum interval between doses is equal to the greatest minimum interval of any of the individual components. Recommended spacing of doses should be maintained (Table 3-1).

Combination Vaccines

Combination vaccines merge equivalent component vaccines into single products to prevent more than one disease or to protect against multiple strains of infectious agents causing the same disease. Licensed combination vaccines can be used whenever any components of the combination are indicated and its other components are not contraindicated and if licensed by the Food and Drug Administration (FDA) for that dose in the series. Use of combination vaccines can reduce the number of injections patients receive and alleviate concern associated with the number of injections (*30*,*36*,*37*). Studies have demonstrated that parents and providers might be uncomfortable with multiple injections during single visits (*38-40*). Potential advantages of combination vaccines include 1) improved vaccine coverage rates (*41*), 2) timely vaccination coverage for children who are behind in the schedule (*42-43*), 3) reduced shipping and stocking costs, 4) reduced costs for extra health care visits necessitated by deferral of vaccination, and 5) facilitation of additional new vaccines into vaccination programs.

Potential disadvantages of combination vaccines include the following: 1) adverse events that might occur more frequently after administration of a combination vaccine compared with administration of separate antigens at the same visit, such as fever that occurs with the combination MMRV vaccine and combination DTaP-HepB-IPV vaccine (*44*,*45*); 2) confusion and uncertainty about selection of vaccine combinations and schedules for subsequent doses, especially when vaccinations are given by multiple providers who might be using different products; 3) reduced pathogen coverage if the combination product covers fewer types of one particular vaccine-preventable disease-causing agent (*46*); 4) extra doses of certain antigens in the combination product (e.g., a

provider who administers 4 doses of DTaP-HepB-IPV vaccine will give an extra dose of hepatitis B component); and 5) a shorter shelf-life than the individual component vaccines. The economic impact of the use of combination vaccines is unclear because combination products have the potential for either increased or decreased costs compared with single-antigen component vaccines. The price of a combination vaccine might exceed the total price of separate vaccines containing the same antigens. However, combination vaccines might represent a better overall economic value if the direct and indirect costs of extra injections, delayed or missed vaccinations, and additional handling and storage are taken into consideration (*47*).

Licensed Combination Vaccines

In this report, a combination vaccine is defined as a product containing components that can be divided equally into independently available routine vaccines. A dash (-) between vaccine products indicates that products are supplied in their final form by the manufacturer and do not require mixing or reconstitution by the user. A slash (/) indicates that the products must be mixed or reconstituted by the user. Seven combination vaccines for which separate antigens or antigen combinations exist have been licensed by FDA since 1996 in the United States (Table 3-2) (*48-54*). In the future, combination vaccines might include increasing numbers of components in different arrays to protect against these and other diseases. (The status of licensure and recommendations for new vaccines is available at https://redbook.solutions.aap.org/.) The use of a combination vaccine generally is preferred over separate injections of the equivalent component vaccines (*55*). Considerations should include provider assessment,[c] patient preference, and the potential for adverse events. An exception is the first dose of MMRV. Unless the parent or caregiver expresses a preference for MMRV vaccine, MMR and varicella vaccine should be administered for the first dose for children aged 12-47 months (see Contraindications and Precautions) (*44*).

Situations might arise in which one component of a combination vaccine is specifically preferred to another component in that same vaccine. Future research considerations for newly licensed combination vaccines should focus on safety of doses that are not needed because a patient is already vaccinated against the agents, whether the

combination vaccine will improve the timeliness of vaccination, and potential reduced costs from disease prevention resulting from timely vaccination.

Combination Vaccines and FDA Licensure

Only combination vaccines licensed by FDA should be used (*55*). Vaccination providers should not combine separate vaccines into the same syringe to administer together unless mixing is indicated for the patient's age and is explicitly specified on the FDA-approved product label inserts. Only 2 combination vaccines, (DTaP-IPV/Hib vaccine, marketed as Pentacel, and Hib-MenCY, marketed as MenHibrix) contain separate antigen components for which FDA approves mixing by the user. The safety, immunogenicity, and effectiveness of unlicensed combinations are unknown.

Interchangeability of Formulations

FDA generally licenses a combination vaccine based on studies demonstrating that the product's immunogenicity (or efficacy) and safety are comparable or equivalent to monovalent or combination products licensed previously (*37*). FDA licensure also generally indicates that a combination vaccine may be used interchangeably with monovalent formulations and other combination products with similar component antigens produced by the same manufacturer to continue the vaccination series. For example, DTaP, DTaP-IPV/Hib, DTaP-HepB-IPV, and future DTaP vaccines that contain similar acellular pertussis antigens from the same manufacturer may be used interchangeably if licensed and indicated for the patient's age (*34*).

Interchangeability of Combination Vaccines from Different Manufacturers

Licensure of a vaccine by FDA does not necessarily indicate that the vaccine is interchangeable with products from other manufacturers. Such data are ascertained and interpreted more readily for diseases with known correlates of protective immunity (e.g., specific serologic markers). For diseases without such surrogate laboratory markers, prelicensure field vaccine efficacy (phase III) trials or postlicensure surveillance generally are required to determine protection (*56*). ACIP prefers that doses of vaccine in a series come from the same manufacturer; however, if this is not possible

or if the manufacturer of doses given previously is unknown, providers should administer the vaccine that they have available.

Vaccine Supply

Although vaccination providers should stock sufficient quantities of combination and monovalent vaccines needed to vaccinate children, adolescents, and adults against all diseases for which vaccines are recommended (*30*,*37*), all available types or brand-name products need not be stocked. Potential advantages of stocking a limited number of vaccines include 1) reducing confusion and potential errors when staff members must handle redundant products and formulations, 2) minimizing waste when less commonly used products expire, 3) decreasing cold storage capacity requirements, and 4) minimizing administrative costs related to accounting, purchasing, and handling. The National Pediatric Vaccine Stockpile exists to offset supply challenges (*57*).

Extra Doses of Vaccine Antigens

Administering extra antigens contained in a combination vaccine should be avoided in most situations (*55*). Using combination vaccines containing certain antigens not indicated at the time of administration to a patient might be justified when 1) the extra antigen is not contraindicated, 2) products that contain only the needed antigens are not readily available, and 3) potential benefits to the patient outweigh the potential risk for adverse events associated with the extra antigens. An extra dose of many live-virus vaccines and Hib or hepatitis B vaccine has not been found to be harmful (*58*,*59*). However, the risk for an adverse event might increase when extra doses are administered at an earlier time than the recommended interval for certain vaccines (e.g., tetanus toxoid vaccines and PPSV) (*19*,*32*,*60*).

A vaccination provider might not have vaccines available that contain only the antigens needed as indicated by a child's vaccination history. Alternatively, although the indicated vaccines might be available, the provider might prefer to use a combination vaccine to reduce the required number of injections. In such cases, the benefits and risks of administering the combination vaccine with an unneeded antigen should be carefully considered and discussed with the patient or parent.

When inactivated (i.e., killed) or subunit vaccines (which are often adsorbed to aluminum-salt adjuvants) are administered, the reactogenicity of the vaccine must be considered in balancing the benefits and risks of extra doses (*55*). Because clinical experience suggests low reactogenicity, an extra dose of Hib or hepatitis B vaccine may be administered as part of a combination vaccine to complete a vaccination series for another component of the combination. Administration of extra doses of tetanus toxoid vaccines earlier than the recommended intervals can increase the risk for severe local reactions (*20*,*33*). Examples of such vaccines include DTaP, DT (for children), and Td (for adolescents and adults). Extra doses of tetanus-toxoid–containing vaccines might be appropriate for certain patients, including for children who previously received DT or Td vaccine and need protection from pertussis (in DTaP or Tdap) or for immigrants with uncertain vaccination histories.

Conjugate Vaccine Carrier Proteins

Protein conjugates used in Hib conjugate vaccines produced in the United States include tetanus toxoid (in PRP-T) which is also used as a component of DTaP and Tdap vaccines (*61*). Simultaneous or sequential vaccination with Hib and these tetanus-toxoid containing vaccines is recommended when both are indicated (*55*). MCV4 and PCV13 both contain diphtheria-toxoid conjugates. There has been concern about simultaneous administration of vaccines containing like conjugates. One brand of MCV4, MenACWY-D (Menactra), demonstrates reduced immunogenicity of the antibody response to Streptococcal pneumonia strains when administered simultaneously with PCV13 compared with separate administration. It is recommended to space these vaccines by 28 days in a person with anatomic asplenia (*46*). Simultaneous or sequential vaccination of MCV4-CRM (Menveo), PCV13, and Tdap (*33*,*61*), all of which contain diphtheria toxoid, is not associated with reduced immunogenicity or increase in local adverse events.

Nonsimultaneous Administration

There is no evidence that inactivated vaccines interfere with the immune response to other inactivated vaccines or to live vaccines. Any inactivated vaccine can be administered either simultaneously or at any time before or after a different inactivated

vaccine or live vaccine (Table 3-3). The 2 exceptions, as mentioned above, are a 4-week interval between PCV13 and MenACWY-D in a person with anatomic asplenia and the separation of doses between PCV13 and PPSV23 (6-12 months recommended for non-high risk, 8 week minimum) if PCV13 is given first, 8 weeks in children 6-18 years, and 1 year minimum in adults 19 years and older if PPSV23 is given first (*26*).

Limited data are available regarding interference between live vaccines used in the United States. The immune response to one live-virus vaccine might be impaired if administered within 28 days (i.e., 4 weeks) of another live-virus vaccine (*62*,*63*). In a study conducted in 2 U.S. health maintenance organizations, the risk for varicella vaccine failure (i.e., varicella disease in a vaccinated person) among persons who received varicella vaccine within 28 days of MMR vaccination was threefold higher than among persons who received varicella vaccine >28 days after MMR vaccination (*64*). Another study determined that the response to yellow fever vaccine is not affected by monovalent measles vaccine administered 1-27 days earlier (*22*). The effect of nonsimultaneous administration of rubella, mumps, varicella, and yellow fever vaccines is unknown.

Two or more injectable or nasally administered live vaccines not administered on the same day should be separated by at least 4 weeks (Table 3-3), to minimize the potential risk for interference. If 2 such vaccines are separated by <4 weeks, the second vaccine administered should not be counted and the dose should be repeated at least 4 weeks later. On the day a live injectable or intranasal vaccine will be administered, providers should ensure that no live injectable or intranasal vaccine was given in the previous 28 days.

The 4-day grace period discussed earlier, which may be used to shorten the minimum interval between doses of the same vaccine, should not be applied to this 4-week interval between 2 different live vaccines (*55*). Confusion about this prohibition may arise when 2 live vaccines whose intervals are identical are administered simultaneously. For example, if MMR and varicella vaccines are administered on the same day, the second dose of each vaccine could come due 4 weeks later (depending on the patient's age). If either vaccine had been given alone at both time points, the 4-day grace period could be applied to the second dose. But in this situation the live vaccine rule prevents the grace

period from being applied to the second dose of either vaccine, because Varicella-2, if administered earlier than 4 weeks, could potentially be affected by MMR1, and likewise MMR2 could be affected by Varicella-1. Note that this prohibition also applies if the combination MMRV is used rather than individual MMR and varicella vaccines.

The oral vaccines Ty21a typhoid vaccine and rotavirus can be administered simultaneously with or at any interval before or after other live vaccines (injectable or intranasal) if indicated (*65*).

Spacing of Vaccines and Antibody-Containing Products

Live Vaccines

Ty21a typhoid, yellow fever, LAIV, zoster, and rotavirus vaccines may be administered at any time before, concurrent with, or after administration of any antibody-containing preparation such as immune globulin, hyperimmune globulin, or intravenous immune globulin (IGIV) (*66*). Blood (e.g., whole blood, packed red blood cells, and plasma) and other antibody-containing blood products (e.g., immune globulin, hyperimmune globulin, and IGIV) can inhibit the immune response to measles and rubella vaccines for ≥3 months. The effect of blood and immune globulin preparations on the response to mumps and varicella vaccines is unknown; however, commercial immune globulin preparations contain antibodies to these viruses. Blood products available in the United States are unlikely to contain a substantial amount of antibody to yellow fever virus. The length of time that interference with injectable live-virus vaccine (other than yellow fever) can persist after the antibody-containing product is a function of the amount of antigen-specific antibody contained in the product (*67-69*). Therefore, after an antibody-containing product is received, live vaccines (other than Ty21a typhoid, yellow fever, LAIV, zoster, and rotavirus vaccines) should be delayed until the passive antibody has degraded (Table 3-4). If a dose of injectable live-virus vaccine (other than yellow fever and zoster) is administered after an antibody-containing product but at an interval shorter than recommended in this report, the vaccine dose should be repeated unless serologic testing is feasible and indicates a response to the vaccine. The repeat dose or serologic testing should be performed after the interval indicated for the antibody-containing product (Table 3-5).

Although passively acquired antibodies can interfere with the response to rubella vaccine, the low dose of anti-Rho(D) globulin or any other blood product administered to postpartum women have not been demonstrated to reduce the response to the RA27/3 strain rubella vaccine (*70*). Congenital rubella syndrome and congenital varicella are conditions with considerable morbidity and represent a true risk in future pregnancies. Because of the importance of rubella and varicella immunity among women of child-bearing age (*4*,*71*), the postpartum vaccination of women without evidence of immunity to rubella or varicella with MMR, varicella, or MMRV vaccines should not be delayed because of receipt of anti-Rho(D) globulin or any other blood product during the last trimester of pregnancy or at delivery. Any reduction in immunity caused by anti-Rho(D) globulin or other blood products is outweighed by the opportunity to generate immunity. These women should be vaccinated immediately after giving birth and, if possible, tested ≥3 months later to ensure immunity to rubella and, if appropriate, to measles (*2*). Measles and rubella serologies have a low false-positive rate and are therefore acceptable for use in this limited postpartum context.

Interference might occur if administration of an antibody-containing product becomes necessary after administration of MMR or varicella vaccines. Usually, vaccine virus replication and stimulation of immunity occurs 1-2 weeks after vaccination. If the interval between administration of any of these vaccines and subsequent administration of an antibody-containing product is <14 days, vaccination should be repeated after the recommended interval (Tables 3-4 and 3-5) unless serologic testing indicates a protective antibody response (*7*).

A humanized mouse monoclonal antibody product (palivizumab) is available as prophylaxis for serious lower respiratory tract disease from respiratory syncytial virus among infants and young children. This product contains only antibody to respiratory syncytial virus and does not interfere with the immune response to licensed live or inactivated vaccines.

Inactivated Vaccines

Antibody-containing products interact less with inactivated, recombinant subunit, and polysaccharide vaccines and toxoids than with live vaccines (*72*). Therefore, administering inactivated vaccines and toxoids either simultaneously with or at any interval before or after receipt of an antibody-containing product should not substantially impair development of a protective antibody response (Table 3-4). The vaccine or toxoid and antibody preparation should be administered at different sites using the standard recommended dose.

Interchangeability of Single-Component Vaccines from Different Manufacturers

Certain vaccines that provide protection from the same diseases are available from different manufacturers, and these vaccines usually are not identical in antigen content or in amount or method of formulation. Manufacturers use different production processes, and their products might contain different concentrations of antigen per dose or a different stabilizer or preservative.

Available data indicate that infants who receive sequential doses of different Hib conjugate, hepatitis B, and hepatitis A vaccines produce a satisfactory antibody response after a complete primary series (*73*-*76*). All brands of Hib conjugate, hepatitis B,[(d)] hepatitis A, rotavirus,[(e)] and quadrivalent meningococcal conjugate vaccines are interchangeable within their respective series. If different brands of a particular vaccine require a different number of doses for series completion (e.g., Hib and rotavirus vaccines) and a provider mixes brands in the primary series, the higher number of doses is recommended for series completion (e.g., doses of either rotavirus or Hib vaccine). For Hib vaccines, any monovalent or combination conjugate vaccine is acceptable for the booster dose of the series, if only one product was used for the primary series (*55*).

Limited data are available about the safety, immunogenicity, and efficacy of using acellular pertussis (i.e., DTaP) vaccines from different manufacturers for successive doses of the pertussis series. Data from one study indicate that for the first 3 doses of the DTaP series, 1-2 doses of Tripedia (Sanofi Pasteur) followed by Infanrix

(GlaxoSmithKline) for the remaining dose (or doses) is comparable to 3 doses of Tripedia with regard to immunogenicity, as measured by antibodies to diphtheria, tetanus, and pertussis toxoids, and filamentous hemagglutinin (*77*). However, in the absence of a clear serologic correlate of protection for pertussis, the relevance of these immunogenicity data for protection against pertussis is unknown. When feasible, the same brand of DTaP vaccine should be used for all doses of the vaccination series (*55*). If vaccination providers do not know or have available the type of DTaP vaccine previously administered to a child, any DTaP vaccine may be used to continue or complete the series (*55*). For a child who needs 2 doses of influenza vaccine (IIV or LAIV), it is preferable to use the same type of vaccine for both doses. However, if the child is eligible for either IIV or LAIV, and the type of vaccine used for the first dose is not available, either vaccine can be used for the second dose (*55*). In a postlicensure study, meningococcal conjugate vaccines from different manufacturers were evaluated for successive doses of meningococcal conjugate vaccine. Persistence of antibodies were studied in recipients of MCV4-CRM after previous receipt of either MCV4-CRM or MenACWY-D. The percentage of persons with protective titers were the same for all serogroups. No data exist on the use of MenACWY-D after MCV4-CRM. Health care providers should use every opportunity to provide a dose when indicated, regardless of the vaccine brand used for the previous dose or doses. For vaccines in general, vaccination should not be deferred because the brand used for previous doses is not available or is unknown (*30*,*78*).

Lapsed Vaccination Schedule

Vaccination providers should administer vaccines as close to the recommended intervals as possible. However, intervals between doses that are longer than recommended typically do not reduce final antibody concentrations, although protection might not be attained until the recommended number of doses has been administered. With some exceptions (e.g. oral typhoid vaccine) an interruption in the vaccination schedule does not require restarting the entire series of a vaccine or toxoid or addition of extra doses (*7*).

Unknown or Uncertain Vaccination Status

Vaccination providers frequently encounter persons who do not have adequate documentation of vaccinations. With the exception of influenza vaccine and PPSV23, providers should only accept written, dated records as evidence of vaccination; self-reported doses of influenza vaccine and PPSV23 are acceptable (*60*,*79*). The rationale for acceptance for influenza vaccine is that the time period of recall is one year or less, making it very likely that correct recall will occur. The rationale for acceptance for PPSV23 is high frequency of vaccination leads to an increased rate of local reactions due to the reactogenicity of this vaccine. Although vaccinations should not be postponed if records cannot be found, an attempt to locate missing records should be made by contacting previous health care providers, reviewing state or local IISs, and searching for a personally held record. If records cannot be located within a reasonable time, these persons should be considered susceptible and started on the age-appropriate vaccination schedule. Serologic testing for immunity is an alternative to vaccination for certain antigens (e.g., measles, rubella, hepatitis A, and tetanus). However, commercial serologic testing might not always be sufficiently sensitive or standardized for detection of vaccine-induced immunity (with the exception of hepatitis B vaccination at 1-2 months after the final dose), and research laboratory testing might not be readily available.

[a] During measles outbreaks, if cases are occurring among infants aged <12 months, measles vaccination of infants as young as 6 months can be used as an outbreak control measure. However, doses administered at ages <12 months should not be counted as part of the series (*80*).

[b] In certain situations, local or state requirements might mandate that doses of selected vaccines be administered on or after specific ages. For example, a school entry requirement might not accept a dose of MMR or varicella vaccine administered before the child's first birthday. ACIP recommends that physicians and other health care providers comply with local or state vaccination requirements when scheduling and administering vaccines.

[c] Provider assessment should include number of injections, vaccine availability, likelihood of improved coverage, likelihood of patient return, and storage and cost considerations.

[d] The exception is the 2-dose hepatitis B vaccination series for adolescents aged 11-15 years. Only Recombivax HB (Merck Vaccine Division) should be used in the schedule. Engerix-B (GlaxoSmithKline) is not approved by FDA for this schedule.

[e] Based on expert opinion.

TABLE 3-1. Recommended and minimum ages and intervals between vaccine doses[a],[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**
DTaP-1[e]	2 months	6 weeks	8 weeks	4 weeks
DTaP-2	4 months	10 weeks	8 weeks	4 weeks
DTaP-3	6 months	14 weeks	6-12 months[f]	6 months[f]
DTaP-4	15-18 months	15 months[f]	3 years	6 months
DTaP-5[g]	4-6 years	4 years	—	—
HepA-1[e]	12-23 months	12 months	6-18 months	6 months
HepA-2	≥18 months	18 months	—	—
HepB-1	Birth	Birth	4 weeks-4 months	4 weeks
HepB-2	1-2 months	4 weeks	8 weeks-17 months	8 weeks
HepB-3[h]	6-18 months	24 weeks	—	—
Hib-1[(i)]	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3[j]	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	—	—
HPV-1[k]	11-12 years	9 years	8 weeks	4 weeks
HPV-2	11-12 years (+2 months)	9 years (+4 weeks)	4 months	12 weeks[k]
HPV-3[k], [l]	11-12 years (+6 months)	9 years (+5 months)	—	—
Influenza, inactivated[m]	≥6 months	6 months[n]	4 weeks	4 weeks
IPV-1[e]	2 months	6 weeks	8 weeks	4 weeks
IPV-2	4 months	10 weeks	8 weeks-14 months	4 weeks

IPV-3	6-18 months	14 weeks	3-5 years	6 months
IPV-4[o]	4-6 years	4 years	—	—
MenACWY-1[p]	11-12 years	6 weeks[q]	4-5 years	8 weeks
MenACWY-2	16 years	11 years (+8 weeks)[r]	—	—
MMR-1[s]	12-15 months	12 months	3-5 years	4 weeks
MMR-2[s]	4-6 years	13 months	—	—
MPSV4-1[p]	—	2 years	5 years	5 years
MPSV4-2	—	7 years	—	—
PCV13-1[i]	2 months	6 weeks	8 weeks	4 weeks
PCV13-2	4 months	10 weeks	8 weeks	4 weeks
PCV13-3	6 months	14 weeks	6 months	8 weeks
PCV13-4	12-15 months	12 months	—	—
PPSV-1	—	2 years	5 years	3 years
PPSV-2[m]	—	7 years	—	—
Rotavirus-1[u]	2 months	6 weeks	8 weeks	4 weeks
Rotavirus-2	4 months	10 weeks	8 weeks	4 weeks
Rotavirus-3[u]	6 months	14 weeks	—	—
RZV - 1	≥50 years	50 years	2-6 months	4 weeks
RZV - 2	≥50 years (+ 2-6 months)	50 years + 4 weeks	—	—
Td	11-12 years	7 years	10 years	5 years
Tdap[v]	≥11 years	7 years	—	—
Varicella-1	12-15 months	12 months	3-5 years	12 weeks[w]
Varicella-2	4-6 years	15 months[x]	—	—
ZVL[y]	≥60 years	60 years	—	—

Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis; HepA = hepatitis A; HepB = hepatitis B; Hib = Haemophilus influenzae type b; HPV = human papillomavirus; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; PRP-OMP = polyribosylribitol phosphate-meningococcal outer membrane protein conjugate; RZV = recombinant zoster vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; ZVL = zoster vaccine live.

(a) Combination 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. The minimum interval between doses is equal to the greatest interval of any of the individual components.

(b) Information on travel vaccines, including typhoid, Japanese encephalitis, and yellow fever, is available at https://wwwnc.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://emergency.cdc.gov/bioterrorism/.

(c) "Months" refers to calendar months.

(d) Within a number range, a hyphen (-) should be read as "through."

(e) Combination vaccines containing the hepatitis B component are available (see Table 3-2). These vaccines should not be administered to infants aged <6 weeks because of the other vaccine components (i.e., Hib, DTaP, HepA, and IPV).

(f) The 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 prospectively, but can be added retrospectively.

(g) If a fourth dose of DTaP is given on or after the fourth birthday, a fifth dose is not needed

(h) HepB-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.

(i) For Hib and PCV13, children receiving the first dose of vaccine at age ≥7 months require fewer doses to complete the series.

(j) If PRP-OMP (Pedvax-Hib, Merck Vaccine Division) was administered at ages 2 and 4 months, a dose at age 6 months is not necessary. The final dose has a minimum age of 12 months.

(k) Quadrivalent and nine-valent HPV vaccines are approved for males and females aged 9-26 years. The 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 5 months between the first and third dose. Dose 3 need not be repeated if it is administered at least 5 months 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.

(l) A two-dose schedule of HPV vaccine is recommended for most persons beginning the series between 9 through 14 years of age. See HPV vaccine-specific recommendations for details.
https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6549a5.pdf

(m) One dose of influenza vaccine per season is recommended for most persons. To determine which children younger than 9 years should receive 2 doses in a single season, please see influenza vaccine-specific recommendations (*81*).

(n) The minimum age for inactivated influenza vaccine varies by vaccine manufacturer. See package insert for vaccine-specific minimum ages.

(o) A fourth dose is not needed if the third dose was administered at ≥4 years and at least 6 months after the previous dose.

(p) Revaccination with meningococcal vaccine is recommended for previously vaccinated persons who remain at high risk for meningococcal disease (*46*).

(q) MenACWY-D (Menactra) can be given as young as 9 months for high-risk persons. MenACWY-CRM (Menveo) can be given as young as 2 months for high-risk persons. Hib-MenCY can be given as young as 6 weeks for high-risk persons. Hib-MenCY is given as a 4-dose series at 2 months, 4 months, 6 months and 12-18 months.

[r] For routine non-high risk adolescent vaccination, the minimum age for the booster dose is 16 years.

[s] Combination MMRV vaccine can be used for children aged 12 months-12 years. See text for details.

[t] A second dose of PPSV23 5 years after the first dose is recommended for persons aged ≤65 years at highest risk for serious pneumococcal infection and those who are likely to have a rapid decline in pneumococcal antibody concentration (*60*).

[u] The 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 aged ≥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. If 2 doses of Rotarix (GlaxoSmithKline) are administered as age appropriate, a third dose is not necessary.

[v] Only 1 dose of Tdap is recommended. 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.

[w] A special grace period of 2 months, based on expert opinion, can be applied to the minimum interval of 3 months, when evaluating records retrospectively, which results in an acceptable minimum interval of 4 weeks. An additional 4 days should not be added on to this grace period.

[x] A special grace period of 2 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.

[y] Zoster vaccine live is recommended as a single dose for persons aged ≥60 years.

TABLE 3-2. FDA-licensed combination vaccines[a]

Vaccine[b]	Trade name (year licensed)	Age range	Routinely recommended ages
HepA-HepB	Twinrix (2001)	≥18 years	Three doses on a schedule of 0, 1, and 6 months
DTaP-HepB-IPV	Pediarix (2002)	6 weeks-6 years	Three-dose series at 2, 4, and 6 months of age
MMRV	ProQuad (2005)	12 months-12 years	Two doses, the first at 12-15 months, the second at 4-6 years
DTaP-IPV	Kinrix (2008)	4-6 years	Fifth dose of DTaP and fourth dose of IPV
DTaP-IPV/Hib	Pentacel (2008)	6 weeks-4 years	Four-dose schedule at 2, 4, 6, and 15-18 months of age
Hib-MenCY	MenHibrix (2012)	6 weeks-18 months	Four-dose schedule at 2, 4, 6, and 12-15 months of age[c]
DTaP-IPV	Quadracel (2015)	4-6 years	Fifth dose of DTaP and fourth or fifth dose of IPV

Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; FDA = Food and Drug Administration; HepA = hepatitis A; HepB = hepatitis B; Hib = Haemophilus influenzae type b; IPV = inactivated poliovirus; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

Source: (*82*).

[a] Although MMR, DTaP, DT, Td, and Tdap are combination vaccines, they are not included on this list because they are not available in the United States as single-antigen products.

[b] In descriptions of combination vaccines, dash (-) indicates products in which the active components are supplied in their final (combined) form by the manufacturer; slash (/) indicates products in which active components must be mixed by the user.

[c] Hib-MenCY can be used for routine dosing of Hib vaccine but is recommended only for meningococcal vaccination in persons at high-risk of meningococcal disease.

TABLE 3-3. Guidelines for spacing of live and inactivated antigens	
Antigen combination	**Recommended minimum interval between doses**
Two or more inactivated[a],[b]	May be administered simultaneously or at any interval between doses
Inactivated and live[c]	May be administered simultaneously or at any interval between doses
Two or more live injectable[c]	28 days minimum interval, if not administered simultaneously

Source: (*82*).

[a] Certain experts suggest a 28-day interval between tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine and tetravalent meningococcal conjugate vaccine if they are not administered simultaneously.

[b] In persons with functional or anatomic asplenia, MCV-D and PCV13 should not be administered simultaneously and should be spaced by 4 weeks. Likewise for persons with immunosuppressive high-risk conditions indicated for PCV13 and PPSV23, PCV13 should be administered first, and PPSV23 should be administered no earlier than 8 weeks later. For persons 65 years old or older indicated for PCV13 and PPSV23, PCV13 should be administered first and PPSV23 should be administered 6-12 months later.

[c] The live oral vaccines Ty21a typhoid vaccine and rotavirus vaccine may be administered simultaneously with or at any interval before or after inactivated or live injectable vaccines.

TABLE 3-4. Guidelines for administering antibody-containing products[a] and vaccines

Type of administration	Products administered		Recommended minimum interval between doses
Simultaneous (during the same clinic day)	Antibody-containing products and inactivated antigen		Can be administered simultaneously at different anatomic sites or at any time interval between doses
	Antibody-containing products and live antigen		Should not be administered simultaneously.[b] 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 3-5)
Nonsimultaneous	**Administered first**	**Administered second**	
	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 antigens	Dose related[b],[c]

	MMR vaccine, varicella vaccine, and combined measles, mumps, rubella, varicella vaccine antigens	Antibody-containing products	2 weeks[b]

[a] Blood products containing substantial amounts of immune globulin include intramuscular, subcutaneous, and intravenous immune globulin, specific hyperimmune globulin (e.g., hepatitis B immune globulin, tetanus immune globulin, varicella zoster immune globulin, and rabies immune globulin), whole blood, packed red blood cells, plasma, and platelet products.

[b] Yellow 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.

[c] The 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 3-5).

TABLE 3-5. Recommended intervals between administration of antibody-containing products and measles- or varicella-containing vaccine, by product and indication for vaccination		
Product/Indication	**Dose (mg IgG/kg) and route[a]**	**Recommended interval before measles- or varicella-containing vaccine[b] administration (months)**
Blood transfusion		
RBCs, washed	10 mL/kg, negligible IgG/kg IV	None
RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	3
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 Immune Globulin Intravenous (Human)	1.0 mL/kg (50 mg IgG/kg) IV	6
Cytomegalovirus 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 month stay	0.02 mL/kg (3.3 mg IgG/kg) IM	3
International travel, ≥3 month 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 deficiencies[d]	300-400 mg/kg IV[d]	8
Immune thrombocytopenic purpura treatment	400 mg/kg IV	8
Postexposure varicella prophylaxis	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])[e]	15 mg/kg IM	None
Rabies IG	20 IU/kg (22 mg IgG/kg) IM	4
Tetanus IG	250 units (10 mg IgG/kg) IM	3
Varicella IG	125 units/10 kg (60-200 mg IgG/kg) IM, maximum 625 units	5

Abbreviations: HIV = human immunodeficiency virus; IG = immune globulin; IgG = immune globulin G; IGIV = intravenous immune globulin; mg IgG/kg = milligrams of immune globulin G per kilogram of body weight; IM = intramuscular; IV = intravenous; RBCs = red blood cells.

[a] This 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.

[b] Does not include zoster vaccine. Zoster vaccine may be given with antibody-containing blood products.

[c] Assumes a serum IgG concentration of 16 mg/mL.

[d] Measles vaccination is recommended for children with mild or moderate immunosuppression from HIV infection, and varicella vaccination may be considered for children with mild or moderate immunosuppression from HIV infection, but both are contraindicated for persons with severe immunosuppression from HIV or any other immunosuppressive disorder.

[e] Contains antibody only to respiratory syncytial virus.

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4. Contraindications and Precautions

Updates

Major changes to the best practice guidance in this section include 1) enhancement of the definition of a "precaution" to include any condition that might confuse diagnostic accuracy and 2) recommendation to vaccinate during a hospitalization if a patient is not acutely moderately or severely ill.

General Principles

Contraindications (conditions in a recipient that increases the risk for a serious adverse reaction) and precautions to vaccination are conditions under which vaccines should not be administered. Because the majority of contraindications and precautions are temporary, vaccinations often can be administered later when the condition leading to a contraindication or precaution no longer exists. A vaccine should not be administered when a contraindication is present; for example, MMR vaccine should not be administered to severely immunocompromised persons (*1*). However, certain conditions are commonly misperceived as contraindications (i.e., are not valid reasons to defer vaccination).

National standards for pediatric vaccination practices have been established and include descriptions of valid contraindications and precautions to vaccination (*2*). Persons who administer vaccines should screen patients for contraindications and precautions to the vaccine before each dose of vaccine is administered (Table 4-1). Screening is facilitated by consistent use of screening questionnaires, which are available from certain state vaccination programs and other sources (e.g., the Immunization Action Coalition, http://www.immunize.org).

Severely immunocompromised persons generally should not receive live vaccines (*3*). Because of the theoretical risk to the fetus, women known to be pregnant generally should not receive live, attenuated virus vaccines (*4*). Persons who experienced

encephalopathy within 7 days after administration of a previous dose of pertussis-containing vaccine not attributable to another identifiable cause should not receive additional doses of a vaccine that contains pertussis (*4*,*5*). Severe Combined Immunodeficiency (SCID) disease and a history of intussusception are both contraindications to the receipt of rotavirus vaccines (*6*).

A precaution is a condition in a recipient that might increase the risk for a serious adverse reaction, might cause diagnostic confusion, or might compromise the ability of the vaccine to produce immunity (e.g., administering measles vaccine to a person with passive immunity to measles from a blood transfusion administered up to 7 months prior) (*7*). A person might experience a more severe reaction to the vaccine than would have otherwise been expected; however, the risk for this happening is less than the risk expected with a contraindication. In general, vaccinations should be deferred when a precaution is present. However, a vaccination might be indicated in the presence of a precaution if the benefit of protection from the vaccine outweighs the risk for an adverse reaction.

The presence of a moderate or severe acute illness with or without a fever is a precaution to administration of all vaccines (Table 4-1). The decision to administer or delay vaccination because of a current or recent acute illness depends on the severity of symptoms and etiology of the condition. The safety and efficacy of vaccinating persons who have mild illnesses have been documented (*8*-*11*). Vaccination should be deferred for persons with a moderate or severe acute illness. This precaution avoids causing diagnostic confusion between manifestations of the underlying illness and possible adverse effects of vaccination or superimposing adverse effects of the vaccine on the underlying illness. After they are screened for contraindications, persons with moderate or severe acute illness should be vaccinated as soon as the acute illness has improved. Studies indicate that failure to vaccinate children with minor illnesses can impede vaccination efforts (*12*–*14*). Among persons whose compliance with medical care cannot be ensured, use of every opportunity to administer appropriate vaccines is critical.

Hospitalization should be used as an opportunity to provide recommended vaccinations. Health care facilities are held to standards of offering influenza vaccine for hospitalized patients, so providers are incentivized to vaccinate these patients at some point during hospitalization (*15)*. Likewise, patients admitted for elective procedures will not be acutely ill during all times during their hospitalization. Most studies that have explored the effect of surgery or anesthesia on the immune system were observational, included only infants and children, and were small and indirect, in that they did not look at the immune effect on the response to vaccination specifically (*16-35*). They do not provide convincing evidence that recent anesthesia or surgery significantly affect response to vaccines. Current, recent, or upcoming anesthesia/surgery/hospitalization is not a contraindication to vaccination (*16-35*). Efforts should be made to ensure vaccine administration during the hospitalization or at discharge. For patients who are deemed moderately or severely ill throughout the hospitalization, vaccination should occur at the earliest opportunity (i.e., during immediate post-hospitalization follow-up care, including home or office visits) when patients' clinical symptoms have improved.

A personal or family history of seizures is a precaution for MMRV vaccination; this is because a recent study found an increased risk for febrile seizures in children 12-23 months who receive MMRV compared with MMR and varicella vaccine (*36*).

Clinicians or other health care providers might misperceive certain conditions or circumstances as valid contraindications or precautions to vaccination when they actually do not preclude vaccination (*2*) (Table 4-2). These misperceptions result in missed opportunities to administer recommended vaccines (*37*).

Routine physical examinations and procedures (e.g., measuring temperatures) are not prerequisites for vaccinating persons who appear to be healthy. The provider should ask the parent or guardian if the child is ill. If the child has a moderate or severe illness, the vaccination should be postponed.

TABLE 4-1. Contraindications and precautions[a] to commonly used vaccines			
Vaccine	**Citation**	**Contraindications**	**Precautions**
DT, Td	(*4*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	GBS <6 weeks 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 years have elapsed since the last tetanus-toxoid-containing vaccine Moderate or severe acute illness with or without fever
DTaP	(*38*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures), not attributable to another identifiable cause, within 7 days of administration of previous dose of DTP or DTaP	Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy; defer DTaP until neurologic status clarified and stabilized Temperature of ≥105°F (≥40.5°C) within 48 hours after vaccination with a previous dose of DTP or DTaP Collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours after receiving a previous dose of DTP/DTaP Seizure ≤3 days after receiving a previous dose of DTP/DTaP Persistent, inconsolable crying lasting ≥3 hours within 48 hours after receiving a previous dose of DTP/DTaP GBS <6 weeks 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 years have elapsed

			since the last tetanus-toxoid–containing vaccine Moderate or severe acute illness with or without fever
Hepatitis A	(*39*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
Hepatitis B	(*40*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Hypersensitivity to yeast	Moderate or severe acute illness with or without fever
Hib	(*41*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Age <6 weeks	Moderate or severe acute illness with or without fever
HPV	(*42*)	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
IIV	(*43*)	Severe allergic reaction (e.g., anaphylaxis) after previous dose of influenza vaccine or to vaccine component.	GBS <6 weeks after a previous dose of influenza vaccine Moderate or severe acute illness with or without fever Egg allergy other than hives, e.g., angioedema, respiratory distress, lightheadedness, recurrent emesis; or required epinephrine or another emergency medical intervention (IIV may be administered in an inpatient or outpatient medical setting and under the supervision of a health care provider who is able to recognize and manage severe allergic conditions).

IPV	(*44*)	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
LAIV[(b)]	(*43*)	Severe allergic reaction (e.g., anaphylaxis) after a vaccine component, including egg protein Concomitant use of aspirin or aspirin-containing medication in children and adolescents LAIV4 should not be administered to persons who have taken influenza antiviral medications within the previous 48 hours.	GBS <6 weeks after a previous dose of influenza vaccine Asthma in persons aged 5 years old or older Medical conditions which might predispose to higher risk of complications attributable to influenza[(c)] Moderate of severe acute illness with or without fever
MenACWY	(*45*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
MenB	(46,47)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
MMR[(d),(e)]	(*1*)	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, long-term	Recent (≤11 months) receipt of antibody-containing blood product (specific interval depends on product) History of thrombocytopenia or thrombocytopenic purpura Need for tuberculin skin testing or interferon-gamma release assay (IGRA) testing[(h)] Moderate or severe acute illness with or without fever

		immunosuppressive therapy[f] or patients with HIV infection who are severely immunocompromised) Family history of altered immunocompetence[g]	
MPSV4	(*48*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
PCV13	(*49*)	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
PPSV23	(*50*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
RIV	(*43*)	Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine	GBS <6 weeks after a previous dose of influenza vaccine Moderate or severe acute illness with or without fever
Rotavirus	(*6*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component SCID History of intussusception	Altered immunocompetence other than SCID Chronic gastrointestinal disease[h] Spina bifida or bladder exstrophy[i] Moderate or severe acute illness with or without fever

Tdap	(*51*)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures), not attributable to another identifiable cause, within 7 days of administration of previous dose of DTP, DTaP, or Tdap	GBS <6 weeks 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 years have elapsed since the last tetanus-toxoid–containing vaccine Moderate or severe acute illness with or without fever
Varicella[(d),(e)]	(*52*)	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, long-term immunosuppressive therapy[(f)] or patients with HIV infection who are severely immunocompromised)[(e)] Pregnancy Family history of altered immunocompetence[(g)]	Recent (≤11 months) receipt of antibody-containing blood product (specific interval depends on product) Moderate or severe acute illness with or without fever Receipt of specific antiviral drugs (acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination (avoid use of these antiviral drugs for 14 days after vaccination)

Zoster	(*53*)	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, long-term immunosuppressive therapy[f] or patients with HIV infection who are severely immunocompromised)[e] Pregnancy	Moderate or severe acute illness with or without fever Receipt of specific antiviral drugs (acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination (avoid use of these antiviral drugs for 14 days after vaccination)

Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; DTP = diphtheria toxoid, tetanus toxoid, and pertussis; GBS = Guillain-Barré syndrome; Hib = *Haemophilus influenzae* type b; HIV = human immunodeficiency virus; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; SCID = severe combined immunodeficiency; RIV=recombinant influenza vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

[a] Events 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.

[b] In addition, ACIP recommends LAIV not be used for pregnant women, immunosuppressed persons, persons with egg allergy, and children aged 2-4 years who have asthma or who have had a wheezing episode noted in the medical record within the past 12 months, or for whom parents report that a health care provider stated that they had wheezing or asthma within the last 12 months. LAIV should not be administered to persons who have taken influenza antiviral medications within the previous 48 hours. Persons who care for severely immunosuppressed persons who require a protective environment should not receive LAIV, or should avoid contact with such persons for 7 days after receipt.

[c] **Source:** (*52*).

[d] HIV-infected children may receive varicella vaccine if CD4+ T-lymphocyte count is ≥15% and should receive MMR vaccine if they are aged ≥12 months and do not have evidence of current severe immunosuppression (i.e., individuals aged ≤5 years must have CD4+T lymphocyte [CD4] percentages ≥15% for ≥6 months; and individuals aged >5 years must have CD4+percentages ≥15% and CD4+≥200 lymphocytes/mm^3 for ≥6 months) or other current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those older than age 5 years, the assessment of severe immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged ≤5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥6 months above age-specific CD4+count criteria: CD4+count >750 lymphocytes/mm^3 while aged ≤12 months and CD4+count ≥500 lymphocytes/mm^3 while aged 1 through 5 years. **Sources:** (*1,50*).

[e] MMR 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.

[f] A substantially 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.

[g] family history of congenital or hereditary immunodeficiency in first-degree relatives (e.g., parents and siblings), unless the immune competence of the potential vaccine recipient has been substantiated clinically or verified by a laboratory.

[h] If 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 or IGRA 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 or IGRA, do so with the understanding that reactivity might be reduced by the vaccine.

[i] For details, see (*55*).

TABLE 4-2. Conditions incorrectly perceived as contraindications to vaccination (i.e., vaccines may be given under these conditions)	
Vaccine	**Conditions commonly misperceived as contraindications**
General for all vaccines, including DTaP, pediatric DT, adult Td, adolescent-adult Tdap, IPV, MMR, Hib, hepatitis A, hepatitis B, varicella, rotavirus, PCV13, IIV, LAIV, PPSV23, MenACWY, MPSV4, HPV, 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 therapy[(a)] 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 GBS[(c)]
DTaP	Fever of <105°F (<40.5°C), fussiness or mild drowsiness after a previous dose of 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)
Hepatitis B	Pregnancy Autoimmune disease (e.g., systemic lupus erythematosus or rheumatoid arthritis)
HPV	Immunosuppression Previous equivocal or abnormal Papanicolaou test Known HPV infection Breastfeeding History of genital warts
IIV	Nonsevere (e.g., contact) allergy to latex, thimerosal, or egg Concurrent administration of Coumadin (generic: warfarin) or aminophylline
IPV	Previous receipt of ≥1 dose of oral polio vaccine

LAIV	Health care providers that 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)
MMR[(d),(e)]	Positive tuberculin skin test Simultaneous tuberculin skin or interferon-gamma release assay (IGRA) testing[(f)] Breastfeeding Pregnancy of recipient's mother or other close or household contact Recipient is female of child-bearing age Immunodeficient family member or household contact Asymptomatic or mildly symptomatic HIV infection Allergy to eggs
PPSV23	History of invasive pneumococcal disease or pneumonia
Rotavirus	Prematurity Immunosuppressed household contacts Pregnant household contacts
Tdap	History of fever of ≥105°F (≥40.5°C) for <48 hours after vaccination with a previous dose of DTP or DTaP History of collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours 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 hours within 48 hours after receiving a previous dose of DTP/DTaP History of extensive limb swelling after DTP/DTaP/Td that is not an Arthus-type reaction History of stable neurologic disorder History of brachial neuritis Latex allergy that is not anaphylactic Breastfeeding Immunosuppression
Varicella	Pregnancy of recipient's mother or other close or household contact Immunodeficient family member or household contact[(g)] Asymptomatic or mildly symptomatic HIV infection Humoral immunodeficiency (e.g., agammaglobulinemia)

Zoster	Therapy with low-dose methotrexate (≤0.4 mg/kg/week), azathioprine (≤3.0 mg/kg/day), or 6-mercaptopurine (≤1.5 mg/kg/day) for treatment of rheumatoid arthritis, psoriasis, polymyositis, sarcoidosis, inflammatory bowel disease, or other conditions Health care 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

Abbreviations: DT = diphtheria and tetanus toxoids; DTP = diphtheria toxoid, tetanus toxoid, and pertussis; DTaP = diphtheria and tetanus toxoids and acellular pertussis; GBS = Guillain-Barré syndrome; HBsAg = hepatitis B surface antigen; Hib = *Haemophilus influenzae* type b; HIV = human immunodeficiency virus; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

(a) Antibacterial drugs might interfere with Ty21a oral typhoid vaccine, and certain antiviral drugs might interfere with varicella-containing vaccines and LAIV4.

(b) Hepatitis B vaccination should be deferred for infants weighing <2,000 g if the mother is documented to be HBsAg negative. Vaccination should commence at chronological age 1 month or at hospital discharge. For infants born to HBsAg-positive women, hepatitis B immune globulin and hepatitis B vaccine should be administered within 12 hours after birth, regardless of weight.

(c) An exception is Guillain-Barré syndrome within 6 weeks of a dose of influenza vaccine or tetanus-toxoid–containing vaccine, which are precautions for influenza vaccines and tetanus-toxoid containing vaccines, respectively.

(d) MMR 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.

(e) HIV-infected children should receive immune globulin after exposure to measles. HIV-infected children can receive varicella and measles vaccine if CD4+ T-lymphocyte count is >15%. (*54*).

(f) Measles vaccination might suppress tuberculin reactivity temporarily. Measles-containing vaccine can be administered on the same day as tuberculin skin or IGRA 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 or IGRA, do so with the understanding that reactivity might be reduced by the vaccine.

(g) If a vaccinee experiences a presumed vaccine-related rash 7-25 days after vaccination, the person should avoid direct contact with immunocompromised persons for the duration of the rash.

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5. Preventing and Managing Adverse Reactions

Updates

Major changes to the best practice guidance include 1) more descriptive characterization of anaphylactic allergy and 2) incorporation of protocols for managing adverse reactions.

Benefit and Risk Communication

Parents, guardians, legal representatives, and adolescent and adult patients should be informed about the benefits of and risks from vaccines in language that is culturally sensitive and at an appropriate educational level. Opportunity for questions should be provided before each vaccination. Discussion of the benefits of and risks from vaccination is sound medical practice and is required by law.

The National Childhood Vaccine Injury Act of 1986 (*1)* requires that vaccine information materials be developed for each vaccine covered by the Act (uscode.house.gov). These materials, known as vaccine information statements (VISs), must be provided by all public and private vaccination providers each time a vaccine is administered. Copies of VISs are available from state health authorities responsible for vaccination and from CDC (www.cdc.gov/vaccines/hcp/vis/index.html). Translations of VISs into languages other than English are available from certain state vaccination programs and from the Immunization Action Coalition website (http://www.immunize.org). The act does not require that a signature be obtained; however, documentation of consent might be recommended or required by certain state or local health authorities or school authorities.

Some parents or patients question the need for or safety of vaccinations and want to discuss the risks from and benefits of certain vaccines. Some refuse certain vaccines or reject all vaccinations for personal or religious reasons. Having a basic understanding of

how patients and parents of patients view vaccine risk and developing effective approaches to address vaccine safety concerns are imperative for vaccination providers.

Each person understands and reacts to vaccine information on the basis of different factors, including previous experience, education, personal values, method of data presentation, perceptions of the risk for disease and perceived ability to control these risks, and risk tolerance. In some circumstances, decisions about vaccination are based on inaccurate information about risk provided by the media and certain websites. Websites and other sources of vaccine information may be inaccurate or incomplete. Health care providers can be a pivotal source of science-based credible information by discussing with parents and patients the risks from and benefits of vaccines, which helps patients make informed decisions.

When a parent or patient initiates a discussion about a perceived vaccine adverse reaction, the health care provider should discuss the specific concerns and provide factual information, using appropriate language. Effective, empathetic vaccine risk communication is essential in responding to misinformation and concerns, with health care providers recognizing that risk assessment and decision-making can be difficult and confusing. Certain vaccines might be acceptable to a parent who is resistant to other vaccines. This partial acceptance can be used to facilitate additional communication. Their concerns can be addressed using the VIS and offering other resource materials (e.g., vaccination information from CDC: www.cdc.gov/vaccines/hcp/vis/index.html).

The American Academy of Pediatrics (AAP) does not recommend that providers exclude from their practice patients whose parents or guardians question or refuse vaccination. However, an effective public health strategy is to identify common ground and discuss measures that need to be followed if the decision is to defer vaccination (*2*). Health care providers should reinforce key points about each vaccine, including safety, and emphasize risks for disease among unvaccinated children.

Parents should be advised of state laws regarding entry to schools or child-care facilities, which might require that unvaccinated children be excluded from the facility during outbreaks (www.cdc.gov/vaccines/imz-managers/coverage/schoolvaxview/requirements/index.html). These discussions should be documented in the patient's medical record, including the refusal to receive certain vaccines (i.e., informed refusal). When a vaccine is refused when first offered the provider should take the opportunity to offer the vaccine again at the next visit.

Preventing Adverse Reactions

Vaccines are intended to produce active immunity to specific antigens. An adverse reaction is an undesirable side effect that occurs after a vaccination. Vaccine adverse reactions are classified as 1) local, 2) systemic, or 3) allergic (additional information is available at https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm. Local reactions (e.g., redness) are usually the least severe and most frequent. Systemic reactions (e.g., fever) occur less frequently than local reactions, and severe allergic reactions (e.g., anaphylaxis) are the least frequent reactions. Severe adverse reactions are rare (*3*).

Some of the systemic reactions may be complicated by the onset of syncope. 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) began detecting a trend of increasing syncope reports that coincided with the licensure of 3 vaccines for adolescents: human papillomavirus (HPV), MenACWY, and Tdap (*4*). Of particular concern among adolescents has been the risk for serious secondary injuries, including skull fracture and cerebral hemorrhage. Of 463 VAERS reports of syncope during January 1, 2005, to July 31, 2007, a total of 41 listed syncope with secondary injury with information on the timing after vaccination, and the majority of these syncope reports (76%) occurred among adolescents.

Among all age groups, 80% of reported syncope episodes occur within 15 minutes of vaccine administration (additional information is available at www.cdc.gov/vaccinesafety/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 (*4*). If syncope develops, patients should be observed until the symptoms resolve.

Although allergic reactions are a common concern for vaccine providers, these reactions are uncommon and anaphylaxis following vaccines is rare, occurring at a rate of approximately one per million doses for many vaccines (*5*). Epinephrine and equipment for managing an airway should be available for immediate use (*6*). The best practice to prevent allergic reactions is to identify individuals at increased risk by obtaining a history of allergy to previous vaccinations and vaccine components that might indicate an underlying hypersensitivity. Acute allergic reactions following vaccinations might be caused by the vaccine antigen, residual animal protein, antimicrobial agents, preservatives, stabilizers, or other vaccine components (*7*). Components of each vaccine are listed in the respective package insert. An extensive list of vaccine components and their use, as well as the vaccines that contain each component, has been published (*8*) and also is available from CDC (www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf). Additional information and tables of potential allergens in different vaccines are available at (www.vaccinesafety.edu/components-Allergens.htm). The allergens identified in the history can be cross-checked against the allergens identified in package inserts.

Managing Acute Vaccine Reactions

Vaccine providers should be familiar with identifying immediate-type allergic reactions, including anaphylaxis, and be competent in treating these events at the time of vaccine administration. Providers should also have a plan in place to contact emergency medical services immediately in the event of a severe acute vaccine reaction.

Allergic reactions can include: local or generalized urticaria (hives) or angioedema; respiratory compromise due to wheezing or swelling of the throat; hypotension; and shock. Immediate-immunoglobulin E (IgE)–mediated (type 1) immune reactions, such as anaphylaxis, usually occur within minutes of parenteral administration and involve specific IgE interactions with discrete antigens (*9*,*10*). Rapid recognition and initiation of treatment are required to prevent possible progression to respiratory failure or cardiovascular collapse. It is important to note that urticaria may not be present in all cases of anaphylaxis. For respiratory or cardiovascular symptoms, or other signs or symptoms of anaphylaxis, immediate intramuscular epinephrine is the treatment of choice (*11*,*12*). Additional doses of epinephrine as well as other drugs also might be indicated (Tables 5-1 and 5-2) (*12*). If hypotension is present, the patient should be placed in a recumbent position with the legs elevated. Maintenance of the airway, oxygen administration, and intravenous normal saline might be necessary. After the patient is stabilized, arrangements should be made for immediate transfer to an emergency facility for additional evaluation and treatment. Because anaphylaxis may recur after patients begin to recover, monitoring in a medical facility for several hours is advised, even after complete resolution of symptoms and signs. Additional information on management of patients with anaphylaxis has been published (*9*).

Persons Who Have Had an Allergic Reaction Following a Previous Immunization

For an individual patient who has experienced an immediate reaction to immunization, it is important to identify the type of reaction that occurred, obtain a history of prior allergic reactions, and try to identify the particular agent responsible. An algorithm

approach to these patients has been published *(13*) and additional advice is available for allergists on the evaluation of these adverse events (*10*). In general, a history of a severe allergic reaction to a vaccine should be considered a contraindication to additional doses of the same vaccine (*13*). Referral of the individual to an allergist for evaluation is usually indicated to possibly determine the component responsible, before making decisions regarding administration of the additional doses of the same vaccine or other vaccines that have the same components. Patients who have not had a severe allergic reaction following a vaccine, but who have a history of possible allergy to a vaccine component can often be vaccinated safely after careful evaluation (*6*).

Influenza Vaccination of Persons with a History of Egg Allergy

Severe allergic and anaphylactic reactions can occur in response to a number of influenza vaccine components, but such reactions are rare (*6*). All but the recombinant inactivated influenza vaccine may have come into contact with egg protein. The use of influenza vaccines for persons with a history of egg allergy has been reviewed recently by ACIP (*14*). VAERS data mining did not identify a higher than expected proportion of serious allergic events after influenza vaccination during the 2011-2012 season, relative to all other reported vaccines and adverse events in the database. Persons with a history of egg allergy should receive recombinant inactivated vaccine (if 18 years or older), or IIV.

Other measures, such as dividing and administering the vaccine by a 2-step approach and skin testing with vaccine, are not recommended (*10*).

All vaccines should be administered in settings in which personnel and equipment for rapid recognition and treatment of anaphylaxis are available. ACIP recommends that all vaccination providers be certified in cardiopulmonary resuscitation (CPR), have an office emergency plan, and ensure that all staff are familiar with the plan (*6*). Some persons who report allergy to egg might not be egg-allergic. Those who are able to eat lightly cooked egg (e.g., scrambled egg) without reaction are unlikely to be allergic.

Egg-allergic persons might tolerate egg in baked products (e.g., bread or cake). Tolerance to egg-containing foods does not exclude the possibility of egg allergy (*15*). Egg allergy can be confirmed by a consistent medical history of adverse reactions to eggs and egg-containing foods, plus skin and/or blood testing for IgE antibodies to egg proteins.

A previous severe allergic reaction to influenza vaccine, regardless of the component suspected to be responsible for the reaction, is a contraindication to future receipt of the vaccine (*14*).

Yellow Fever Vaccination of Persons with a History of Egg Allergy

Yellow fever vaccine contains egg protein. There have been insufficient studies to determine which patients with egg allergy may be able to receive yellow fever vaccine, but there are reports of patients with true egg allergy safely receiving yellow fever vaccine after evaluation by specialists with expertise in the management of allergic reactions (*16*,*17*). According to the manufacturer, persons who are able to eat eggs or egg products may receive the vaccine (*18*). However, potential hypersensitivity reactions might occur in persons with a history of minor reactions to eggs. For egg-sensitive persons, a scratch test or intradermal test can be performed before administering the vaccine to check for reactivity. If a person has a severe egg-sensitivity or has a positive skin test to the vaccine, but the vaccination is recommended because of their travel destination-specific risk, desensitization can be performed under direct supervision of a physician experienced in the management of anaphylaxis. The desensitization procedure is detailed in the product insert (see yellow fever recommendations at www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm094074.htm).

Vaccines with MMR or Varicella Components and Persons with a History of Egg Allergy

Varicella vaccine is grown in human diploid cell cultures and can safely be administered to persons with a severe allergy to eggs or egg proteins (*19*). Measles and mumps vaccine viruses are grown in chick embryo fibroblast tissue culture. However, persons with a severe egg allergy can receive measles- or mumps-containing vaccines in the usual manner because the content of these proteins is extremely low (*20*). The rare severe allergic reactions after measles- or mumps-containing vaccines or varicella are thought to be caused by other components of the vaccine (e.g., gelatin) (*21-24*). MMR, MMRV, varicella and other vaccines contain hydrolyzed gelatin as a stabilizer.

Vaccines and Persons with a History of Allergy to Substances Other than Eggs

Persons who have had an anaphylactic reaction to gelatin or gelatin-containing products should be evaluated by an allergist prior to receiving gelatin-containing vaccines (*6*).

Certain vaccines contain trace amounts of antimicrobial agents or other preservatives (e.g., neomycin or thimerosal), although allergies to these are rare. No licensed vaccine contains penicillin or penicillin derivatives.

Most often, neomycin hypersensitivity manifests as contact dermatitis, a delayed-type (cell-mediated) immune response rather than immediate-hypersensitivity (IgE-mediated allergy)–type response (*25,26*). A history of delayed-type reactions to neomycin is not a contraindication for administration of neomycin-containing vaccines. There has only been 1 reported case of immediate hypersensitivity reaction following a neomycin-containing vaccine (*27*). Persons who have had anaphylactic reactions to neomycin should be evaluated by an allergist prior to receiving vaccines containing neomycin (*6*).

Thimerosal, an organic mercurial compound in use since the 1930s, is added to certain immunobiologics as a preservative. Since mid-2001, vaccines routinely recommended for infants younger than 6 months of age have been manufactured without thimerosal as a preservative (*14*). Live, attenuated vaccines have never contained thimerosal. Thimerosal-free formulations of inactivated influenza vaccine are available. Inactivated influenza vaccine also is available in formulations with only trace amounts of thimerosal, which remains as a manufacturing residual but is not added at the higher concentration that would be necessary for it to function as a preservative. Thimerosal at a preservative concentration is present in certain other vaccines that can be administered to children (e.g., Td and DT). Information about the thimerosal content of vaccines is available from FDA at http://www.fda.gov/cber/vaccine/thimerosal.htm.

Reactions to thimerosal have been described as local delayed-type hypersensitivity reactions with only rare reports of immediate reactions (*28-31).* Thimerosal elicits positive delayed-type hypersensitivity patch tests in 1%-18% of persons tested; however, these tests have no relevance to acute allergic reactions that might occur within minutes or hours after immunization (*32,33*). The majority of persons do not experience reactions to thimerosal administered as a component of vaccines even when patch or intradermal tests for thimerosal indicate hypersensitivity (*31)*. A local or delayed-type hypersensitivity reaction to thimerosal is not a contraindication to receipt of a vaccine that contains thimerosal (*34*).

Latex is sap from the rubber tree. Latex contains naturally occurring plant proteins that can be responsible for immediate-type allergic reactions. Latex is processed to form either natural rubber latex products such as gloves or dry, natural rubber products such as syringe plunger tips and vial stoppers. Synthetic rubber is also used in gloves, syringe plungers, and vial stoppers but does not contain the latex proteins linked to immediate-type allergic reactions. Natural rubber latex or dry, natural rubber used in vaccine packaging generally is noted in the manufacturers' package inserts.

Immediate-type allergic reactions due to latex allergy have been described after vaccination, but such reactions are rare (*35*).

If a person reports a severe anaphylactic allergy to latex, vaccines supplied in vials or syringes that contain natural rubber latex should be avoided if possible (*6*). If not, if the decision is made to vaccinate, providers should be prepared to treat immediate allergic reactions due to latex, including anaphylaxis. The most common type of latex hypersensitivity is a delayed-type (type 4, cell-mediated) allergic contact dermatitis (*36*). For patients with a history of contact allergy to latex, vaccines supplied in vials or syringes that contain dry natural rubber or natural rubber latex may be administered.

Reporting Adverse Events After Vaccination

Modern vaccines are safe and effective; however, adverse events have been reported after administration of all vaccines (*3*). More complete information about adverse reactions to a specific vaccine is available in the package insert for each vaccine and from CDC at https://www.cdc.gov/vaccines/vac-gen/side-effects.htm. An adverse event is an untoward event that occurs after a vaccination that might be caused by the vaccine product or vaccination process. These events range from common, minor, local reactions to rare, severe, allergic reactions (e.g., anaphylaxis). Reporting to VAERS helps establish trends, identify clusters of adverse events, or generate hypotheses. However, establishing evidence for cause and effect on the basis of case reports and case series alone is usually not possible, because health problems that have a temporal association with vaccination do not necessarily indicate causality.

Many adverse events require more detailed epidemiologic studies to compare the incidence of the event among vaccinees with the incidence among unvaccinated persons. Potential causal associations between reported adverse events after vaccination can be assessed through epidemiologic or clinical studies.

The National Childhood Vaccine Injury Act of 1986 (*1)* requires health care personnel and vaccine manufacturers to report to VAERS specific adverse events that occur after vaccination. The reporting requirements are different for manufacturers and health care personnel. Manufacturers are required to report all adverse events that occur after vaccination to VAERS, whereas health care providers are required to report events that

appear in the reportable events table on the VAERS website at https://vaers.hhs.gov/docs/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf.

In addition to the mandated reporting of events listed on the reportable events table, health care personnel should report to VAERS all events listed in product inserts as contraindications, as well as all clinically significant adverse events, even if they are uncertain that the adverse event is related causally to vaccination (*6*). Persons other than health care personnel also can report adverse events to VAERS.

General information on VAERS is available at https://vaers.hhs.gov/index.html. Specific information for healthcare providers is available at https://vaers.hhs.gov/resources/infoproviders.html. Reporting to VAERS is fully electronic and can be done using an online reporting tool or a writable PDF; instructions are available at https://vaers.hhs.gov/reportevent.html. Further assistance on VAERS reporting is available through email at info@VAERS.org and the VAERS toll free number 1-800-822-7967.

National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program, established by the National Childhood Vaccine Injury Act of 1986 (*1*), is a no-fault system in which persons thought to have experienced an injury or to have died as a result of administration of a covered vaccine can seek compensation. The program became operational on October 1, 1988, and is intended as an alternative to civil litigation under the traditional tort system in that negligence need not be proven. Claims arising from covered vaccines must first be adjudicated through the program before civil litigation can be pursued.

The program relies on the Vaccine Injury Table, which lists the vaccines covered by the program and the injuries (including death), disabilities, illnesses, and conditions for which compensation might be awarded. The table defines the time during which the first

symptom or substantial aggravation of an injury must appear after vaccination to be eligible. Successful claimants receive a legal presumption of causation if a condition listed in the table is proven, thus avoiding the need to prove actual causation in an individual case. Claimants also can prevail for conditions not listed in the reportable events table if they prove causation for covered vaccines. Additional information is available from the Health Resources and Services Administration (HRSA at www.hrsa.gov/vaccine-compensation/index.html or by telephone at 800-338-2382). Persons who would like to file a claim for vaccine injury should contact the U.S. Court of Federal Claims (717 Madison Place, N.W., Washington, DC 20005; telephone: 202-357-6400).

TABLE 5-1: Rapid overview: Emergent management of anaphylaxis in infants and children[a]	
Diagnosis is made clinically:	The most common signs and symptoms are cutaneous (eg, sudden onset of generalized urticaria, angioedema, flushing, pruritus). However, 10 to 20% of patients have no skin findings.
	Danger signs: Rapid progression of symptoms, evidence of respiratory distress (e.g., stridor, wheezing, dyspnea, increased work of breathing, retractions, persistent cough, cyanosis), signs of poor perfusion, abdominal pain, vomiting, dysrhythmia, hypotension, collapse.
Acute management:	The first and most important therapy in anaphylaxis is epinephrine. There are NO absolute contraindications to epinephrine in the setting of anaphylaxis.
	Airway: Immediate intubation if evidence of impending airway obstruction from angioedema. Delay may lead to complete obstruction. Intubation can be difficult and should be performed by the most experienced clinician available. Cricothyrotomy may be necessary.
	IM epinephrine (1 mg/mL preparation): Epinephrine 0.01 mg/kg should be injected intramuscularly in the midouter thigh. For large children (>50 kg), the maximum is 0.5 mg per dose. If there is no response or the response is inadequate, the injection can be repeated in 5 to 15 minutes (or more frequently). If epinephrine is injected promptly IM, patients respond to one, two, or at most, three injections. If signs of poor perfusion are present or symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below).
	Place patient in recumbent position, if tolerated, and elevate lower extremities.
	Oxygen: Give 8 to 10 L/minute via facemask or up to 100% oxygen, as needed.
	Normal saline rapid bolus: Treat poor perfusion with rapid infusion of 20 mL/kg. Reevaluate and repeat fluid boluses (20 mL/kg), as needed. Massive fluid shifts with severe loss of intravascular volume can occur. Monitor urine output.
	Albuterol: For bronchospasm resistant to IM epinephrine, give albuterol 0.15 mg/kg (minimum dose: 2.5 mg) in 3 mL saline inhaled via nebulizer. Repeat, as needed.
	H1 antihistamine: Consider giving diphenhydramine 1 mg/kg (max 40 mg) IV.
	H2 antihistamine: Consider giving ranitidine 1 mg/kg (max 50 mg) IV.
	Glucocorticoid: Consider giving methylprednisolone 1 mg/kg (max 125 mg) IV.
	Monitoring: Continuous noninvasive hemodynamic monitoring and pulse oximetry monitoring should be performed. Urine output should be monitored in patients receiving IV fluid resuscitation for severe hypotension or shock.
Treatment of refractory symptoms:	Epinephrine infusion:[b] In patients with inadequate response to IM epinephrine and IV saline, give epinephrine continuous infusion at 0.1 to 1 mcg/kg/minute, titrated to effect.
	Vasopressors:[b] Patients may require large amounts of IV crystalloid to maintain blood pressure. Some patients may require a second vasopressor (in addition to epinephrine). All vasopressors should be given by infusion pump, with the doses titrated continuously according

	to blood pressure and cardiac rate/function monitored continuously and oxygenation monitored by pulse oximetry
IM: intramuscular; IV: intravenous.	
[a] A child is defined as a prepubertal patient weighing less than 40 kg. [b] All patients receiving an infusion of epinephrine and/or another vasopressor require continuous noninvasive monitoring of blood pressure, heart rate and function, and oxygen saturation. We suggest that pediatric centers provide instructions for preparation of standard concentrations and also provide charts for established infusion rate for epinephrine and other vasopressors in infants and children.	

Table 5-2: Rapid overview: Emergency management of anaphylaxis in adults	
Diagnosis is made clinically:	The most common signs and symptoms are cutaneous (e.g., sudden onset of generalized urticaria, angioedema, flushing, pruritus). However, 10 to 20% of patients have no skin findings.
	Danger signs: Rapid progression of symptoms, respiratory distress (e.g., stridor, wheezing, dyspnea, increased work of breathing, persistent cough, cyanosis), vomiting, abdominal pain, hypotension, dysrhythmia, chest pain, collapse.
Acute management:	The first and most important treatment in anaphylaxis is epinephrine. There are NO absolute contraindications to epinephrine in the setting of anaphylaxis.
	Airway: Immediate intubation if evidence of impending airway obstruction from angioedema. Delay may lead to complete obstruction. Intubation can be difficult and should be performed by the most experienced clinician available. Cricothyrotomy may be necessary.
Promptly and simultaneously, give:	IM epinephrine (1 mg/mL preparation): Give epinephrine 0.3 to 0.5 mg intramuscularly, preferably in the midouter thigh. Can repeat every 5 to 15 minutes (or more frequently), as needed. If epinephrine is injected promptly IM, most patients respond to one, two, or at most, three doses. If symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below).
	Place patient in recumbent position, if tolerated, and elevate lower extremities.
	Oxygen: Give 8 to 10 L/minute via facemask or up to 100% oxygen, as needed.
	Normal saline rapid bolus: Treat hypotension with rapid infusion of 1 to 2 liters IV. Repeat, as needed. Massive fluid shifts with severe loss of intravascular volume can occur.
	Albuterol (salbutamol): For bronchospasm resistant to IM epinephrine, give 2.5 to 5 mg in 3 mL saline via nebulizer. Repeat, as needed.
Adjunctive therapies:	H1 antihistamine:[a] Consider giving diphenhydramine 25 to 50 mg IV (for relief of urticaria and itching only).
	H2 antihistamine:[a] Consider giving ranitidine 50 mg IV.
	Glucocorticoid:[a] Consider giving methylprednisolone 125 mg IV.
	Monitoring: Continuous noninvasive hemodynamic monitoring and pulse oximetry monitoring should be performed. Urine output should be monitored in patients receiving IV fluid resuscitation for severe hypotension or shock.
Treatment of refractory symptoms:	Epinephrine infusion[b],: For patients with inadequate response to IM epinephrine and IV saline, give

	epinephrine continuous infusion, beginning at 0.1 mcg/kg/minute by infusion pump[c] . Titrate the dose continuously according to blood pressure, cardiac rate and function, and oxygenation.
	Vasopressors[b]: Some patients may require a second vasopressor (in addition to epinephrine). All vasopressors should be given by infusion pump, with the doses titrated continuously according to blood pressure and cardiac rate/function and oxygenation monitored by pulse oximetry.
	Glucagon: Patients on beta blockers may not respond to epinephrine and can be given glucagon 1 to 5 mg IV over 5 minutes, followed by infusion of 5 to 15 mcg/minute. Rapid administration of glucagon can cause vomiting.
Instructions on how to prepare and administer epinephrine for IV continuous infusions are available as separate tables in UpToDate.	
IM: intramuscular; IV: intravenous.	
[a] These medications should not be used as initial or sole treatment. [b] All patients receiving an infusion of epinephrine and another vasopressor require continuous noninvasive monitoring of blood pressure, heart rate and function, and oxygen saturation. [c] For example, the initial infusion rate for a 70 kg patient would be 7 mcg/minute. This is consistent with the recommended range for non–weight-based dosing for adults, which is 2 to 10 mcg/minute. Non–weight-based dosing can be used if the patient's weight is not known and cannot be estimated.	

Source: (*37*).

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6. Vaccine Administration

Updates

Major changes to the best practice guidance include 1) allowances for alternate administration route (subcutaneous instead of intramuscular) for hepatitis A vaccine and 2) an age cutoff of 12 years through 17 years of age for validating a dose of intradermal influenza vaccine if given in error.

Infection Control and Sterile Technique

General Precautions

Persons administering vaccinations should follow appropriate precautions to minimize risk for disease exposure and spread. Hands should be cleansed with an alcohol-based waterless antiseptic hand rub or washed with soap and water before preparing vaccines for administration and between each patient contact (*1*). Occupational Safety and Health Administration (OSHA) regulations do not require gloves to be worn when administering vaccinations, unless persons administering vaccinations have open lesions on their hands or are likely to come into contact with a patient's body fluids (*2*). If worn, gloves should be changed between patients.

Vaccine Administration: Preparation and Timely Disposal

Vaccines should be drawn up in a designated clean medication area that is not adjacent to areas where potentially contaminated items are placed. Multi-dose vials to be used for more than one patient should not be kept or accessed in the immediate patient treatment area. This is to prevent inadvertent contamination of the vial through direct or indirect contact with potentially contaminated surfaces or equipment that could then lead to infections in subsequent patients (*3*).

Different vaccines should never be mixed in the same syringe unless specifically licensed for such use (*4*). Single-dose vials and manufacturer-filled syringes are designed for single-dose administration and should be discarded if vaccine has been withdrawn or reconstituted and subsequently not used within the time frame specified by the manufacturer. Syringes that are prefilled by the manufacturer and activated (i.e., syringe cap removed or needle attached) but unused should be discarded at the end of the clinic day. For inactivated vaccines manufacturers, typically recommend use within the same day that a vaccine is withdrawn or reconstituted. When in doubt about the appropriate handling of a vaccine, vaccination providers should contact that vaccine's manufacturer.

ACIP discourages the routine practice of providers' prefilling syringes for several reasons. Because the majority of vaccines have a similar appearance after being drawn into a syringe, prefilling might result in administration errors. Because unused prefilled syringes also typically must be discarded if not used within the same day that they are filled, vaccine wastage might occur. The FDA does not license administration syringes for vaccine storage.

In certain circumstances in which a single vaccine type is being used (e.g., in preparation for a community influenza vaccination campaign), filling a small number (10 or fewer) of syringes may be considered (*5*). The doses should be administered as soon as possible after filling, by the same person who filled the syringes. Unused syringes that are prefilled by the manufacturer and activated (i.e., syringe cap removed or needle attached) should be discarded at the end of the clinic day.

Safe Use of Needles and Syringes

Needles and syringes used for vaccine injections must be sterile and disposable. A separate needle and syringe should be used for each injection. Changing needles between drawing vaccine from a vial and injecting it into a recipient is not necessary unless the needle has been damaged or contaminated (*6*).

Bloodborne diseases (e.g., hepatitis B, hepatitis C, human immunodeficiency virus [HIV]) are occupational hazards for clinicians and other health care providers. The Needlestick Safety and Prevention Act (*2*) was enacted in 2000 to reduce the incidence of needlestick injury and the consequent risk for bloodborne diseases acquired from patients. The act directed OSHA to strengthen its existing bloodborne pathogen standards. The revised standards became effective in 2001 (*2*). These federal regulations require the use of engineering and work practice controls to eliminate or minimize employee exposure to bloodborne pathogens (see www.osha.gov/SLTC/bloodbornepathogens/standards.html). Engineering controls means controls (e.g., sharps disposal containers, self-sheathing needles, 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 (see www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10051). Needle-shielding or needle-free devices that might satisfy the occupational safety regulations for administering injectable vaccines are available in the United States (*7-8*). The regulations also require maintenance of records documenting injuries caused by needles and other medical sharp objects and that nonmanagerial employees be involved in the evaluation and selection of safety-engineered devices before they are procured. Additional information about implementation and enforcement of these regulations is available from OSHA.

To prevent inadvertent needlestick injury or reuse, safety mechanisms should be deployed after use and needles and syringes should be discarded immediately in labeled, puncture-proof containers located in the same room where the vaccine is administered (*5*). Used needles should never be recapped.

Route of Administration

Injectable Route

Routes of administration are recommended by the manufacturer for each immunobiologic (Table 6-1). With the exceptions of bacille Calmette-Guérin (BCG) vaccine and smallpox vaccine (administered intraepidermally), injectable vaccines are administered by the intramuscular, subcutaneous, or intradermal route. Deviation from the recommended route of administration might reduce vaccine efficacy (*9*, *10*) or increase the risk for local adverse reactions (*11-13*).

The method of administration of injectable vaccines is determined, in part, by the inclusion of adjuvants in some vaccines. An adjuvant is a vaccine component distinct from the antigen that enhances the immune response to the antigen, but might also increase risk of adverse reactions. To decrease risk of local adverse events, inactivated vaccines containing an adjuvant should be injected into a muscle. Administering a vaccine containing an adjuvant either subcutaneously or intradermally can cause local irritation, induration, skin discoloration, inflammation, and granuloma formation.

Intramuscular Injections

Needle Length

Injectable immunobiologics should be administered where local, neural, vascular, or tissue injury is unlikely. Use of longer needles has been associated with less redness or swelling than occurs with shorter needles because of injection into deeper muscle mass (*11*). Appropriate needle length depends on age and body mass. Injection technique is the most important parameter to ensure efficient intramuscular vaccine delivery.

For all intramuscular injections, the needle should be long enough to reach the muscle mass and prevent vaccine from seeping into subcutaneous tissue, but not so long as to involve underlying nerves, blood vessels, or bone (*10*,*14-16*). Vaccinators should be

familiar with the anatomy of the area into which they are injecting vaccine. Intramuscular injections are administered at a 90-degree angle to the skin, preferably into the anterolateral aspect of the thigh or the deltoid muscle of the upper arm, depending on the age of the patient (Table 6-2).

The needle gauge for intramuscular injection is 22-25 gauge. A decision on needle length and site of injection must be made for each person on the basis of the size of the muscle, the thickness of adipose tissue at the injection site, the volume of the material to be administered, injection technique, and the depth below the muscle surface into which the material is to be injected (Figure 1). Some experts allow intramuscular injection with a ⅝-inch needle but ONLY if the skin is stretched flat (*16*). If the subcutaneous and muscle tissue are bunched to minimize the chance of striking bone (*14*), a 1-inch needle or larger is required to ensure intramuscular administration. Aspiration before injection of vaccines or toxoids (i.e., pulling back on the syringe plunger after needle insertion but before injection) is not necessary because no large blood vessels are present at the recommended injection sites, and a process that includes aspiration might be more painful for infants (*17*).

Infants (Aged <12 Months)

For the majority of infants, the anterolateral aspect of the thigh is the recommended site for injection because it provides comparatively larger muscle mass than the deltoid (Figure 2) (*18*). In certain circumstances (e.g., physical obstruction to other sites and no reasonable indication to defer doses), the gluteal muscle can be used. If the gluteal muscle must be used, care should be taken to define the anatomic landmarks.[a] For the majority of infants, a 1-inch needle is sufficient to penetrate the thigh muscle.

Toddlers (Aged 12 Months-2 Years)

For toddlers, the anterolateral thigh muscle is preferred, and when this site is used, the needle should be at least 1 inch long. The deltoid muscle can be used if the muscle mass is adequate. If 2 vaccines are to be administered in a single limb, they should be spaced an inch apart (*4,19*).

Children (Aged 3-10 Years)

The deltoid muscle is preferred for children aged 3-10 years (*18*); the needle length for deltoid site injections can range from ⅝ to 1 inch on the basis of technique. The anterolateral thigh can also be used (*20*). In this case the needle length should be 1 inch to 1.25 inches. Knowledge of body mass can be useful for estimating the appropriate needle length (*21*).

Young Adolescents (Aged 11-18 years)

The deltoid muscle is preferred for adolescents 11-18 years of age. The anterolateral thigh can also be used. For injection into the anterolateral thigh, most adolescents will require a 1-1.5-inch needle to ensure intramuscular administration (*21*).

Adults (Aged ≥19 Years)

For adults, the deltoid muscle is recommended for routine intramuscular vaccinations (*18*) (Figure 3). The anterolateral thigh also can be used. For adults a measurement of body mass/weight is allowable prior to vaccination, understanding that resources to measure body mass/weight are not available in all clinical settings. For men and women who weigh <130 lbs (<60 kg), a ⅝-inch needle is sufficient to ensure intramuscular injection in the deltoid muscle if the injection is made at a 90-degree angle and the tissue is not bunched. For men and women who weigh 130-152 lbs (60-70 kg), a 1-inch needle is sufficient. For women who weigh 152-200 lbs (70-90 kg) and men who weigh 152-260 lbs (70-118 kg), a 1- to 1.5-inch needle is recommended. For women who weigh >200 lbs (>90 kg) or men who weigh >260 lbs (>118 kg), a 1.5-inch needle is recommended (Table 6-2) (*15*).

Subcutaneous Injections

Subcutaneous injections are administered at a 45-degree angle, usually into the thigh for infants aged <12 months and in the upper-outer triceps area of persons aged ≥12 months. Subcutaneous injections may be administered into the upper-outer triceps area of an infant if necessary. A ⅝-inch, 23- to 25-gauge needle should be inserted into the subcutaneous tissue (Figures 4 and 5) (*4*).

Intradermal Injections

One brand of injectable influenza vaccine is licensed to be administered intradermally. It is packaged as a pre-filled 3/50-inch microneedle injector system and approved for persons 18-64 years of age. The approved site is the skin over the deltoid muscle.

Intradermal influenza vaccine injection of someone 12-17 years of age can be counted as a valid dose on the presumption that their skin thickness is similar to someone 18-64 years of age. A dose of intradermal vaccine given to someone younger than 12 years of age or older than 64 years of age should not be counted as valid (personal communication with manufacturer).

Oral Route

Rotavirus, adenovirus, cholera vaccine, and oral typhoid vaccines are the only vaccines administered orally in the United States. Oral typhoid capsules should be administered as directed by the manufacturer. The capsules should not be opened or mixed with any other substance. Rotavirus vaccines are licensed for infants. There are 2 brands of rotavirus vaccine, and they have different types of applicators. Providers should consult package inserts for details. A dose of rotavirus vaccine need not be repeated if the vaccine is spit up or vomited. The infant should receive the remaining recommended doses of rotavirus vaccine following the routine schedule (*5*).

Intranasal Route

LAIV is approved for healthy nonpregnant persons aged 2-49 years and is the only vaccine administered by the intranasal route. The administration 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 administration. 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 (*5*).

Severely immunosuppressed persons (i.e., those who require care in a protected environment, e.g., bone marrow transplant patients, patients with severe combined immunodeficiency disease) should not administer LAIV. It would be uncommon for persons with these conditions to be in a role administering vaccines. Other persons at increased 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 aged ≥50 years (*22*).

Multiple Injections

If multiple vaccines are administered at a single visit, administer each preparation at a different anatomic site (*23*). The location of all injection sites with the corresponding vaccine injected should be documented in each patient's medical record. Health care practices should consider using a vaccination site map so that all persons administering vaccines routinely use a particular anatomic site for each particular vaccine.

For infants and younger children, if more than 2 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 (separate anatomic sites [i.e. ≥1 inch] if possible) so that any local reactions can be differentiated (*8,24*). For older children and adults, the deltoid muscle can be used for more than one intramuscular injection. If a vaccine and an immune globulin preparation are administered simultaneously (e.g., Td/Tdap and

tetanus immune globulin [TIG], hepatitis B and hepatitis B immunoglobulin [HBIG]), separate limbs should be used for each injection (*25*,*26*).

Jet Injections

Jet injectors are needle-free devices that pressurize liquid medication, forcing it through a nozzle orifice into a narrow stream capable of penetrating skin to deliver a drug or vaccine into intradermal, subcutaneous, or intramuscular tissues (*27*,*28*). Immune responses generated by jet injectors against both attenuated and inactivated viral and bacterial antigens are usually equivalent to, and occasionally greater than, immune responses induced by needle injection. However, local reactions or injuries (e.g., skin laceration, transient neuropathy, hematoma) are sometimes more frequent on delivery of vaccine by jet injectors compared with needle injection, depending on the inherent irritability of the vaccine and operator technique (*28*).

Multiple use jet injectors using the same nozzle for consecutive injections without intervening sterilization were used in mass vaccination campaigns from the 1950s through the 1990s (*28*); however, these were found to be unsafe because of the possibility of bloodborne pathogen transmission (*29-32*) and should not be used. A new generation of jet injectors with disposable cartridges and syringes has been developed since the 1990s. With a new, sterile dose chamber and nozzle for each patient and correct use, these devices do not have the same safety concerns as multiple-use nozzle jet injectors. Several of the newer devices have been approved by FDA for sale in the United States (*28*) and for use with individual vaccines. Jet injectors prevent needlestick injuries to health care providers (*2*) and can overcome improper, unsterile reuse and other drawbacks of needles and syringes in developing countries (*7*,*33*,*34*).

Methods for Alleviating Discomfort and Pain Associated with Vaccination

Comfort measures, such as distraction (e.g., playing music or pretending to blow away the pain), cooling of the injection site(s), topical analgesia, ingestion of sweet liquids, breastfeeding, swaddling, and slow, lateral swaying can help infants or children cope with the discomfort associated with vaccination (*35-37*). Pretreatment (30-60 minutes before injection) with a 5% topical lidocaine-prilocaine emulsion might decrease the pain of vaccination by causing superficial anesthesia (*38*,*39*). Evidence indicates that this cream does not interfere with the immune response to MMR (*40*). Topical lidocaine-prilocaine emulsion should not be used on infants aged <12 months who are receiving treatment with methemoglobin-inducing agents (e.g., acetaminophen, amyl nitrate, nitroprusside, dapsone) because of the possible development of methemoglobinemia (*41*). Use of a topical refrigerant (vapocoolant) spray immediately before vaccination can reduce the short-term pain associated with injections and can be as effective as lidocaine-prilocaine cream (*42*). Evidence does not support use of antipyretics before or at the time of vaccination; however, they can be used for the treatment of fever and local discomfort that might occur following vaccination. Studies of children with previous febrile seizures have not demonstrated antipyretics to be effective in the prevention of febrile seizures (*43*).

Clinical Implications of Nonstandard Vaccination Practices

Best practice guidance for route, site, and dosage of immunobiologics is derived from data from clinical trials, practical experience, normal periodicity of health care visits, and theoretical considerations. ACIP discourages variations from the recommended route, site, volume, or number of doses of any vaccine.

Variation from the recommended route and site can result in inadequate protection. In adults (but not in infants) (*44*), the immunogenicity of hepatitis B is substantially lower when the gluteal rather than the deltoid site is used for administration (*6*). Hepatitis B administered intradermally might result in a lower seroconversion rate and final titer of

hepatitis B surface antibody than when administered by the deltoid intramuscular route (*45*,*46*). Hepatitis B administered by any route other than intramuscular, or in adults at any site other than the deltoid or anterolateral thigh, should not be counted as valid and should be repeated (*6*). Similarly, doses of rabies vaccine administered in the gluteal site should not be counted as valid doses and should be repeated (*47*). Hepatitis A vaccine and meningococcal conjugate vaccine do not need to be repeated if administered by the subcutaneous route (*48*-*49*). However, for DTaP, Hib, and PCV13, there is no evidence related to immunogenicity of these 3 vaccines given subcutaneously. Providers should address circumstances in which dose(s) of these vaccines have been administered subcutaneously on a case-by-case basis. Inactivated influenza vaccine is immunogenic when administered in a lower-than-standard dose by the intradermal route to healthy adult volunteers. Intradermal injection produced antibody responses similar to intramuscular injection in vaccinees aged 18-60 years (*50*). However, the immunogenicity for persons aged ≥65 years is inadequate, and varying the recommended route and dose either with the intradermal product licensed through 64 years of age or with other influenza vaccines is not recommended (*19*).

Live, attenuated injectable vaccines (e.g., MMR, varicella, yellow fever) and certain inactivated vaccines (e.g., meningococcal polysaccharide) are recommended by the manufacturers to be administered by subcutaneous injection. PPSV23and IPV are recommended by the manufacturer to be administered by the subcutaneous or intramuscular route. Response to vaccines recommended by the subcutaneous route is unlikely to be affected if the vaccines are administered by the intramuscular rather than subcutaneous route. Repeating doses of vaccine administered by the intramuscular route when recommended to be by the subcutaneous route is not necessary (*6*).

Administering volumes smaller than recommended (e.g., inappropriately divided doses) might result in inadequate protection. Using reduced doses administered at multiple vaccination visits that equal a full dose or using smaller divided doses is not recommended (*4*). Any vaccination using less than the standard dose should not be counted, and the person should be revaccinated according to age unless serologic testing indicates that an adequate response has developed. However, if 2 half-volume

formulations of vaccine have already been administered on the same clinic day to a patient recommended for the full volume formulation, these 2 doses can count as one full dose. If less than a full recommended dose of a vaccine is administered because of syringe, applicator, or needle leakage, the dose should be repeated (*5*). Using larger-than-recommended dosages can be hazardous because of excessive local or systemic concentrations of antigens or other vaccine constituents.

[a] If the gluteal muscle is chosen, injection should be administered lateral and superior to a line between the posterior superior iliac spine and the greater trochanter or in the ventrogluteal site, the center of a triangle bounded by the anterior superior iliac spine, the tubercle of the iliac crest, and the upper border of the greater trochanter.

TABLE 6-1. Dose and route of administration for selected vaccines		
Vaccine	**Dose**	**Route**
DTaP, DT, Td, Tdap	0.5 mL	IM
DTaP-HepB-IPV	0.5 mL	IM
DTaP/Hib	0.5 mL	IM
DTaP-IPV/Hib	0.5 mL	IM
DTaP-IPV	0.5 mL	IM
Hib	0.5 mL	IM
Hib-MenCY	0.5 mL	IM
HepA	≤18 years: 0.5 mL ≥19 years: 1.0 mL	IM
HepB	≤19 years: 0.5 mL[a] ≥20 years: 1.0 mL	IM
HepA-HepB	≥18 years: 1.0 mL	IM
LAIV	0.2 mL divided dose between nares	Intranasal spray
IIV	6-35 months: 0.25 mL or 0.5 mL ≥3 years: 0.5 mL 18-64 years: 0.1 mL	IM ID
MMR	0.5 mL	Subcut
MMRV	0.5 mL	Subcut
MenACWY	0.5 mL	IM
MPSV4	0.5 mL	Subcut
PCV13	0.5 mL	IM
PPSV23	0.5 mL	IM or Subcut
HPV	0.5 mL	IM
IPV	0.5 mL	IM or Subcut

Rotavirus (RV1 or RV5)	(1.0 mL or 2.0 mL)	Oral
Varicella	0.5 mL	Subcut
Herpes zoster	0.65 mL	Subcut

Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; HepA = hepatitis A; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IM = intramuscular; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MenCY = bivalent meningococcal conjugate vaccine component; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; RV1 = live, attenuated monovalent rotavirus vaccine; RV5 = live, reassortment pentavalent rotavirus vaccine; Subcut = subcutaneous; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

Source: Adapted from Immunization Action Coalition: http://www.immunize.org.

[a] Persons aged 11-15 years may be administered Recombivax HB (Merck), 1.0 mL (adult formulation) on a 2-dose schedule.

TABLE 6-2. Needle length and injection site of IM injections for children aged ≤18 years (by age) and adults aged ≥19 years (by sex and weight)		
Age group	**Needle length**	**Injection site**
Children (birth-18 years)		
Neonates[a]	5/8 inch (16 mm)[b]	Anterolateral thigh
Infants, 1-12 months	1 inch (25 mm)	Anterolateral thigh
Toddlers, 1-2 years	1-1.25 inch (25-32 mm)	Anterolateral thigh[c]
	5/8[b]-1 inch (16-25 mm)	Deltoid muscle of arm
Children, 3-10 years	5/8[b]-1 inch (16-25 mm)	Deltoid muscle of arm[c]
	1-1.25 inches (25-32 mm)	Anterolateral thigh
Children, 11-18 years	5/8[b]-1 inch (16-25 mm)	Deltoid muscle of arm[c]
	1-1.5 inches (25-38 mm)	Anterolateral thigh
Adults (≥19 years)		
Men and women, <60 kg (130 lbs)	1 inch (25 mm) [d]	Deltoid muscle of arm
Men and women, 60-70 kg (130-152 lbs)	1 inch (25 mm)	
Men, 70-118 kg (152-260 lbs)	1-1.5 inches (25-38 mm)	
Women, 70-90 kg (152-200 lbs)		
Men, >118 kg (260 lbs)	1.5 inches (38 mm)	
Women, >90 kg (200 lbs)		

Abbreviation: IM = intramuscular.

Source: (*14*).

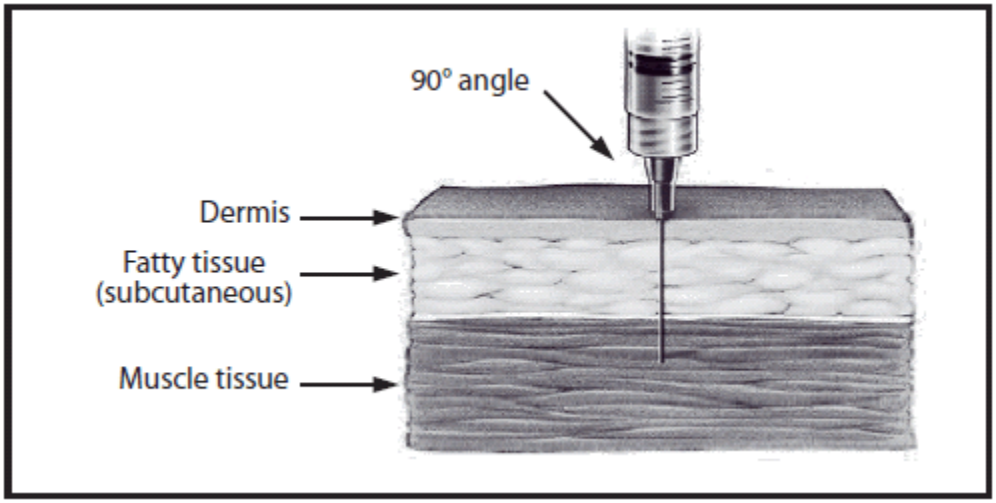
(a) First 28 days of life.

(b) If skin is stretched tightly and subcutaneous tissues are not bunched.

(c) Preferred site.

(d) Some experts recommend a 5/8-inch needle for men and women who weigh <60 kg, if used, skin must be stretched tightly (do not bunch subcutaneous tissue)

Figure 1. Intramuscular needle insertion



Source: Adapted from California Immunization Branch.

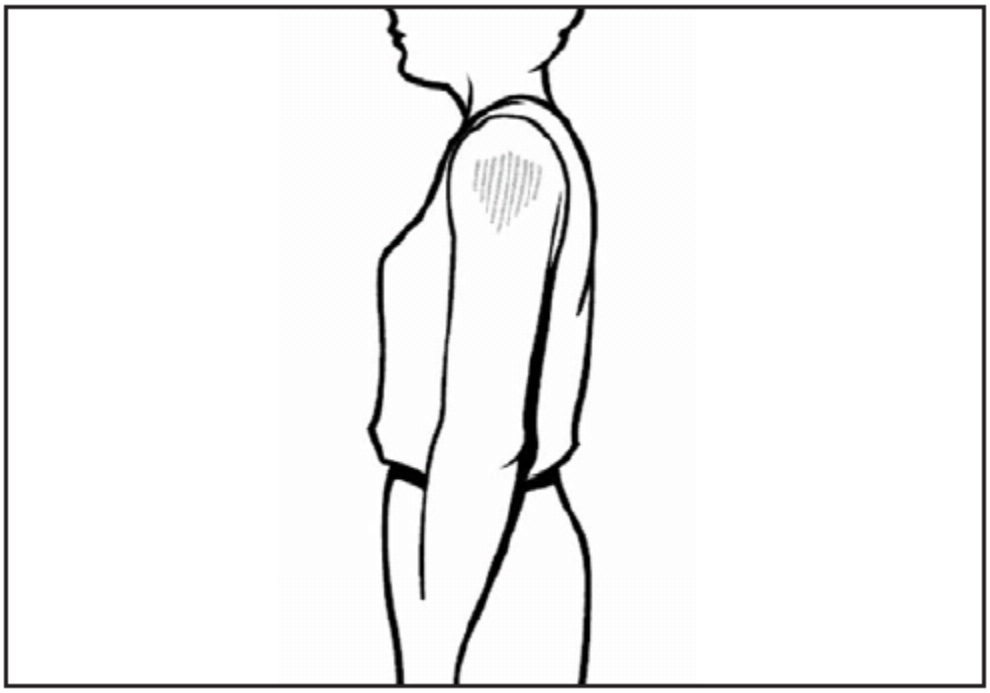
Alternate Text: This drawing shows intramuscular needle insertion into a cross-section of skin. The needle is inserted at a 90-degree angle and penetrates the dermis, fatty tissue (subcutaneous), and muscle tissue.

Figure 2. Intramuscular/subcutaneous site of administration: anterolateral thigh

Source: Adapted from Minnesota Department of Health.

Alternate Text: This drawing shows a mother holding an infant. The anterolateral aspect of the infant's thigh is shaded, showing the proper site for intramuscular/subcutaneous vaccine administration.

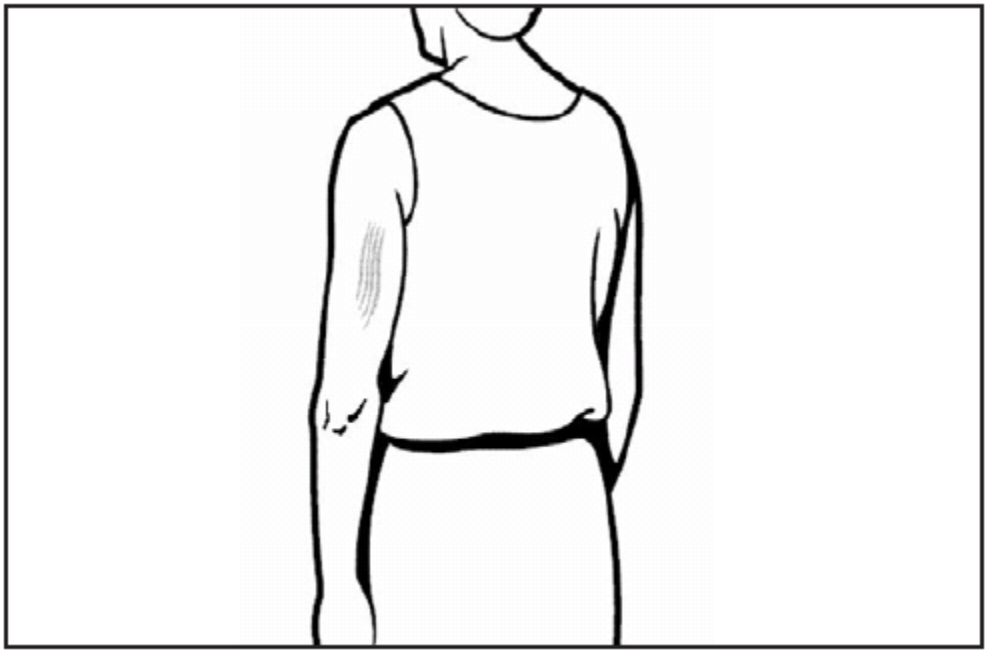
Figure 3. Intramuscular site of administration: deltoid



Source: Adapted from Minnesota Department of Health.

Alternate Text: This line drawing is a side view of an adult. The deltoid muscle of the arm is shaded, showing the proper site for intramuscular vaccine administration.

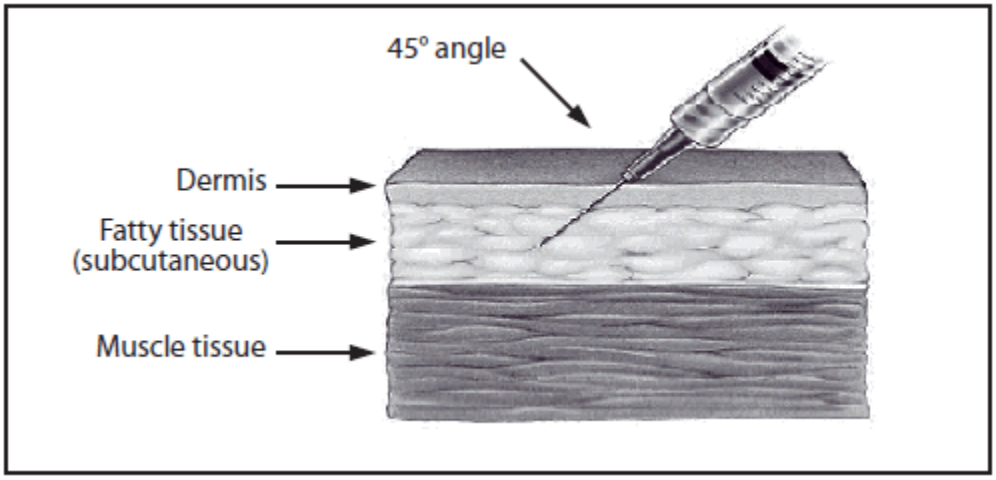
Figure 4. Subcutaneous site of administration: triceps



Source: Adapted from the Minnesota Department of Health.

Alternate Text: This line drawing is a rear/dorsal view of an adult. The triceps muscle of the arm is shaded, showing the proper site for subcutaneous vaccine administration.

Figure 5. Subcutaneous needle insertion



Source: Adapted from California Immunization Branch.

Alternate Text: This drawing shows subcutaneous needle insertion into a cross-section of skin. The needle is inserted at a 45-degree angle and penetrates the dermis and fatty tissue (subcutaneous) but not the muscle tissue.

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7. Storage and Handling of Immunobiologics

Updates

Most of the 2011 language was removed because this content is now codified and continually updated in the CDC's Vaccine Storage and Handling Toolkit, available at www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html. This content included Storage Units, Monitoring Storage Temperature, Vaccine Inventory, and Vaccine Transport.

General Principles

Failure to adhere to recommended specifications for storage and handling of immunobiologics can reduce or destroy their potency, resulting in inadequate or no immune response in the recipient (www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html). Recommendations in the product package inserts, including methods for reconstitution of the vaccine, should be followed carefully. Maintenance of vaccine quality is the shared responsibility of all handlers of vaccines from the time a vaccine is manufactured until administration. All vaccines should be inspected on delivery and monitored during storage to ensure that the recommended storage temperatures are maintained. Vaccines should continue to be stored at recommended temperatures immediately upon receipt until use. Inadequate vaccine storage also can result in significant costs to replace vaccine inventory (www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html).

Storage Temperature

Vaccines licensed for refrigerator storage should be stored at 36°F-46°F (2°C-8°C). Liquid vaccines containing an aluminum adjuvant permanently lose potency when exposed to freezing temperatures. Inactivated vaccines that are stored in a liquid state (i.e., non-lyophilized [freeze-dried]) but that do not contain aluminum adjuvants should also generally be kept at refrigerator temperature, although whether or not they lose

potency when frozen is not known. Inactivated lyophilized vaccines generally do not need to be frozen, but lyophilized varicella-containing vaccines that are recommended to be stored frozen lose potency when exposed to higher temperatures because the viruses degrade more quickly at storage temperatures that are warmer than recommended (Table 7-1). These varicella-containing vaccines also can be prone to losses in sterility if kept too cold, due to increased gas permeability of the rubber vaccine vial (observed with use of dry ice at temperatures below -58°F or -50°C [personal communication, manufacturer]).

Response to Out-of-Range Temperature Reading

An out-of-range temperature reading should prompt immediate action. A plan should be developed ahead of time to address various types of emergencies that might require removal of vaccine from the original storage unit. Transfer of vaccines to a predesignated alternative emergency storage site might be necessary if a temperature problem cannot be resolved immediately (e.g., plugging in an unplugged unit or closing a door that has been left open). It is critical to avoid freezing vaccine during transport (improperly packing vaccine with ice can damage vaccines). Vaccine should be marked "do not use" and moved to the alternate site after verifying that the alternate unit is at the proper temperature. Determinations of vaccine viability in practice include consideration of both time and magnitude of temperature excursions and should be made in consultation with state/local public health departments or the vaccine manufacturer, as one or both of these groups may have additional information based on a broad international perspective. Damage to the immunogenicity of a vaccine exposed to temperatures outside of the recommended range might not be apparent visually. As a general rule, vaccines that have been stored at inappropriate temperatures should not be administered unless public health authorities or the manufacturer determine it is safe and effective to do so. If such vaccines already have been administered, vaccine exposed to inappropriate temperatures that is inadvertently administered should generally be repeated. Clinicians should consult promptly with state or local health departments in these situations. Consultation with CDC is available when necessary.

TABLE 7-1. Vaccine storage temperature recommendations		
Nonlyophilized, aluminum-adjuvanted vaccines		
Vaccines	**Vaccine storage temperature**	**Diluent storage temperature**
Diphtheria-tetanus-containing vaccines (DT, Td) or pertussis-containing vaccines (DTaP, Tdap)	2°C-8°C (36°F-46°F) Do not freeze	No diluent[a]
HepA and HepB	2°C-8°C (36°F-46°F) Do not freeze	No diluent
MenB[b]	2°C-8°C (36°F-46°F) Do not freeze	No diluent
PCV13	2°C-8°C (36°F-46°F) Do not freeze	No diluent
HPV[b]	2°C-8°C (36°F-46°F) Do not freeze	No diluent
Nonlyophilized, nonaluminum-adjuvanted vaccines		
Vaccines	**Vaccine storage temperature**	**Diluent storage temperature**
PRP-OMP Hib	2°C-8°C (36°F-46°F)	No diluent
IPV[b]	2°C-8°C (36°F-46°F)	No diluent
MenACWY[b],[c]	2°C-8°C (36°F-46°F)	No diluent
PPSV	2°C-8°C (36°F-46°F)	No diluent
IIV[b]	2°C-8°C (36°F-46°F)	No diluent
RZV[b]	2°C-8°C (36°F-46°F) Do not freeze	2°C-8°C (36°F-46°F) Do not freeze

Lyophilized (non-varicella) vaccines		
Vaccines	**Vaccine storage temperature**	**Diluent storage temperature**
PRP-T Hib[b]	2°C-8°C (36°F-46°F) [d]	2°C-8°C (36°F-46°F) Do not freeze
MMR[b]	2°C-8°C (36°F-46°F) [d]	(2°C-25°C) 35°F-77°F Can be refrigerated or stored at room temperature
Varicella-containing vaccines		
Vaccines	**Vaccine storage temperature**	**Diluent storage temperature**
MMRV[b]	-58°F-5°F (-50°C to -15°C)	35°F-77°F (2°C-25°C) Can be refrigerated or stored at room temperature
Varicella[b]	-58°F-5°F (-50°C to -15°C)	35°F-77°F (2°C-25°C) Can be refrigerated or stored at room temperature
Herpes zoster[b]	-58°F-5°F (-50°C to -15°C)	35°F-77°F (2°C-25°C) Can be refrigerated or stored at room temperature
Noninjectable vaccines		
Vaccines	**Vaccine storage temperature**	**Diluent storage temperature**
RV5 vaccine[b]	2°C-8°C (36°F-46°F) Do not freeze	No diluent
RV1 vaccine[b]	2°C-8°C (36°F-46°F) Do not freeze	The diluent may be stored at a controlled room temperature 20°C-25°C (68°F-77°F). Do not freeze
LAIV[b]	2°C-8°C (36°F-46°F)	No diluent

Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; HepA = hepatitis A; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MenB = Serogroup B meningococcal vaccine; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; MPSV4 = quadrivalent

meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; PRP-OMP = polyribosylribitol phosphate-meningococcal outer membrane protein conjugate; PRP-T = polyribosylribitol phosphate polysaccharide conjugated to a tetanus toxoid; PRP-T Hib = polyribosylphosphate tetanus-toxoid conjugate Hib vaccine; PRP-T Hib-MenCY = polyribosylphosphate-tetanus-toxoid Hib vaccine with a bivalent Meningococcal vaccine; RV = rotavirus; RV1 = live, attenuated monovalent rotavirus vaccine; RV5 = live, reassortment pentavalent rotavirus vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

Sources: (*1,2*).

(a) DTaP-Daptacel is sometimes used as a diluent for ActHib.

(b) Protect from light.

(c) There are 2 meningococcal conjugate vaccines; Menactra is nonlyophilized, and Menveo is lyophilized. Both powder and diluent should be stored at 35°F-46°F.

(d) The lyophilized pellet may be stored at freezer temperature; the reconstituted vaccine should be stored at refrigerator temperature.

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8. Altered Immunocompetence

Updates

This section incorporates general content from the Infectious Diseases Society of America policy statement, *2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host* (*1*), to which CDC provided input in November 2011. The evidence supporting this guidance is based on expert opinion and arrived at by consensus.

General Principles

Altered immunocompetence, a term often used synonymously with immunosuppression, immunodeficiency, and immunocompromise, can be classified as primary or secondary. Primary immunodeficiencies generally are inherited and include conditions defined by an inherent absence or quantitative deficiency of cellular, humoral, or both components that provide immunity. Examples include congenital immunodeficiency diseases such as X-linked agammaglobulinemia, SCID, and chronic granulomatous disease. Secondary immunodeficiency is acquired and is defined by loss or qualitative deficiency in cellular or humoral immune components that occurs as a result of a disease process or its therapy. Examples of secondary immunodeficiency include HIV infection, hematopoietic malignancies, treatment with radiation, and treatment with immunosuppressive drugs. The degree to which immunosuppressive drugs cause clinically significant immunodeficiency generally is dose related and varies by drug. Primary and secondary immunodeficiencies might include a combination of deficits in both cellular and humoral immunity. Certain conditions like asplenia and chronic renal disease also can cause altered immunocompetence.

Determination of altered immunocompetence is important to the vaccine provider because incidence or severity of some vaccine-preventable diseases is higher in persons with altered immunocompetence; therefore, certain vaccines (e.g., inactivated influenza vaccine, pneumococcal vaccines) are recommended specifically for persons with these

diseases (*2*,*3*). Administration of live vaccines might need to be deferred until immune function has improved. This is primarily a safety concern, because persons who have altered immunocompetence and receive live vaccines might be at increased risk for an adverse reaction because of uninhibited growth of the attenuated live virus or bacteria. Vaccines might be less effective during the period of altered immunocompetence. Inactivated vaccines might best be deferred during a period of altered immunocompetence; in this circumstance, the concern is with effectiveness and not safety. Additionally, if an inactivated vaccine is administered during the period of altered immunocompetence, it might need to be repeated after immune function has improved.

The degree of altered immunocompetence in a patient should be determined by a physician. The challenge for clinicians and other health care providers is assessing the safety and effectiveness of vaccines for conditions associated with primary or secondary immunodeficiency, especially when new therapeutic modalities are being used and information about the safety and effectiveness of vaccines has not been characterized fully in persons receiving these drugs (Table 8-1). Laboratory studies can be useful for assessing the effects of a disease or drug on the immune system. Tests useful to assess humoral immunity include immunoglobulin (and immunoglobulin subset) levels and specific antibody levels (e.g., tetanus and diphtheria). Tests that demonstrate the status of cellular immunity include lymphocyte numbers (i.e., a complete blood count with differential), a test that delineates concentrations and proportions of lymphocyte subsets (i.e., B and T lymphocytes, CD4+ B lymphocytes versus CD8+ T lymphocytes), and tests that measure T-cell proliferation or function in response to specific or nonspecific stimuli (e.g., lymphocyte proliferation assays) (*4*,*5*). The ability to characterize a drug or disease condition as affecting cellular or humoral immunity is only the first step; using this information to draw inferences about whether particular vaccines are indicated or whether caution is advised with use of live or inactivated vaccines is more complicated and might require consultation with an infectious diseases or immunology specialist.

Altered Immunocompetence as an Indication to Receive a Vaccine Outside of Routinely Recommended Age Groups

This section describes situations in which vaccines are recommended outside of the routine-age-based recommendation because the risk for vaccine-preventable disease is increased due to altered immunocompetence. Persons with altered immunocompetence generally are recommended to receive polysaccharide-based vaccines (PCV13, PPSV23, and Hib), on the basis of increased risk for disease if the vaccine is withheld. For certain specific categories of altered immunocompetence, patients are also recommended to receive polysaccharide based vaccines (MenACWY, Hib-MenCY, and MPSV4).

Pneumococcal Vaccines

Two types of vaccine against invasive pneumococcal disease are available in the United States: PCV13 and PPSV23. PCV13 is recommended routinely for all children beginning at age 2 months through age 59 months and for adults aged 65 years or older. PCV13 is also recommended for children, adolescents, and adults with conditions that place them at high risk for invasive disease from *Streptococcus pneumoniae*. PCV13 is recommended for persons aged 6-64 years who have not previously received PCV13 and have congenital immunodeficiency disorders (including B- or T-lymphocyte deficiency, complement deficiencies, and phagocytic disorders), anatomic or functional asplenia (including sickle cell disease and other hemoglobinopathies), HIV infection, cochlear implant, cerebrospinal fluid leak, chronic renal failure, nephrotic syndrome, iatrogenic immunosuppression, or other immunocompromising conditions.

PPSV23 is licensed for use in persons aged ≥2 years and recommended routinely for adults aged 65 years and older. PPSV23 is also recommended for persons age 2 through 64 years with congenital immunodeficiency disorders, anatomical and functional asplenia, HIV infection, cochlear implant, cerebrospinal fluid leak, and iatrogenic immunosuppression. Complete recommendations on use of PCV13 and PPSV23 are available in the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Immunization Schedule* (*2*,*6*).

Meningococcal Vaccines

Three types of meningococcal vaccines are licensed in the United States: meningococcal conjugate (MenACWY and Hib-MenCY), meningococcal polysaccharide (MPSV4), and serogroup B meningococcal (MenB) vaccines. Persons with functional or anatomic asplenia (including sickle cell disease) and persistent complement component deficiency (including persons taking eculizumab [Soliris]) (*7*) are at increased risk for meningococcal disease and should receive both MenACWY and MenB vaccines. For children 2 months through 23 months of age, an age-appropriate series of meningococcal conjugate vaccine should be administered. If MenACWY-D (Menactra) is administered to a child with asplenia, it should be after 2 years of age and at least 4 weeks after the completion of all PCV13 doses. A 2-dose primary series of either MenACWY-CRM (Menveo) or MenACWY-D (Menactra) should be administered to persons 2 years of age or older with asplenia or complement deficiency. Following the primary series of vaccine, a 3-year interval to the next dose is recommended for persons who received their previous dose at younger than 7 years. A 5-year interval is recommended for persons who received their previous dose at age 7 years or older. Although MPSV4 is the only meningococcal vaccine licensed for persons older than 55 years of age, adults 56 years and older with asplenia or complement deficiency should be vaccinated with MenACWY-CRM or MenACWY-D rather than MPSV4 (*8*). Meningococcal serogroup B vaccines are licensed for persons 10-25 years of age and are recommended for persons 10 years of age or older for persons with high-risk conditions like functional or anatomic asplenia or persistent complement component deficiency. There are presently no recommendations for booster doses of either MenB vaccine (*9,10*). Complete recommendations for use of meningococcal vaccines are available in the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Schedule* (*2,6*).

Hib Vaccines

Hib conjugate vaccines are available in single or combined antigen preparations. Hib vaccine is recommended routinely for all children through age 59 months. Children 12 through 59 months who are at high risk for invasive Hib disease (i.e., recipients of chemotherapy or radiation for malignant neoplasms, recipients of hematopoietic cell transplant, or those with functional or anatomic asplenia, HIV infection, immunoglobulin deficiency, or early complement component deficiency) and who are unvaccinated or received only one dose of Hib disease before 12 months of age should receive 2 additional doses of Hib vaccine; those who received 2 or more doses of Hib before 12 months of age should receive one additional dose. A child younger than 5 years of age receiving chemotherapy or radiation therapy should have Hib doses repeated if the doses were received during therapy or within 14 days of starting therapy; repeat doses should be started at least 3 months after completion of therapy. Recipients of hematopoietic cell transplants should be revaccinated with 3 doses of Hib vaccine, starting 6-12 months after successful transplant, regardless of vaccination history or age. Children 5-18 years of age with HIV who are unimmunized[(a)] should receive a dose of Hib vaccine; Hib vaccination is not recommended in HIV-infected adults. Unimmunized[(a)] asplenic patients older than 59 months of age or adults should receive a dose of Hib vaccine. Anyone 15 months of age or older who is undergoing a splenectomy and is unimmunized[(a)] should receive a dose of Hib vaccine (*11*). Complete recommendations for use of Hib vaccine are available in the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Immunization Schedule* (*2,6*).

Vaccination of Contacts of Persons with Altered Immunocompetence

Household contacts and other close contacts of persons with altered immunocompetence should receive all age- and exposure-appropriate vaccines, with the exception of smallpox vaccine (*12*,*13*). Receipt of vaccines will prevent the vaccine-preventable disease, so there can be no potential transmission to the contact with altered immunocompetence. The live MMR, varicella, and rotavirus vaccines should be administered to susceptible household contacts and other close contacts of immunocompromised patients when indicated. Zoster vaccine can be administered when indicated. MMR vaccine viruses are not transmitted to contacts, and transmission of varicella-zoster virus vaccine strain is rare (*14*,*15*). No specific precautions are needed unless the varicella vaccine recipient has a rash after vaccination, in which case direct contact with susceptible household contacts with altered immunocompetence should be avoided until the rash resolves (*14*,*15*). All members of the household should wash their hands after changing the diaper of an infant who received rotavirus vaccine. This minimizes rotavirus transmission, as shedding may occur up to one month after the last dose (*16*,*17*). Household and other close contacts of persons with altered immunocompetence should receive annual influenza vaccination. Introduction of low levels of vaccine viruses into the environment likely is unavoidable when administering LAIV. LAIV vaccine viruses are cold-adapted, so they can replicate in the nose and generate an immune response without entering the lungs (i.e., they are temperature sensitive and replicate poorly at core body temperatures). No instances have been reported of illness caused by attenuated vaccine virus infections among health care providers or immunocompromised patients. LAIV may be administered to healthy household and other close contacts of persons with altered immunocompetence unless the person with altered immunocompetence is in a protective environment, typically defined as a specialized patient-care area with a positive airflow relative to the corridor, high-efficiency particulate air filtration, and frequent air changes (*3*). No preference exists for inactivated influenza vaccine use by health care workers or other persons who have close contact with persons with lesser degrees of immunosuppression (e.g.,

persons with diabetes, persons with asthma taking high-dose corticosteroids, or persons infected with HIV), and no preference exists for inactivated influenza vaccine use by health care workers or other healthy persons aged 5-49 years in close contact with all other groups at high risk.

Inactivated Vaccines: Safety

All inactivated vaccines can be administered safely to persons with altered immunocompetence, whether the vaccine is a killed whole-organism or a recombinant, subunit, split-virus, toxoid, polysaccharide, or polysaccharide protein-conjugate vaccine.

Inactivated Vaccines: Effectiveness

Except for inactivated influenza vaccine, vaccination during chemotherapy or radiation therapy should be avoided if possible because antibody response might be suboptimal. Patients vaccinated within a 14-day period before starting immunosuppressive therapy or while receiving immunosuppressive therapy should be considered unimmunized and should be revaccinated at least 3 months after therapy is discontinued if immune competence has been restored. Patients who have quantitative B-cell deficiencies and are receiving immunoglobulin therapy should not receive either inactivated or live vaccines while receiving the immunoglobulin therapy because of concerns about effectiveness of the vaccines. Patients on chemotherapy with anti-B cell antibodies (e.g., rituximab) should wait at least 6 months after therapy before being vaccinated with inactivated vaccines. Some experts recommended longer than 6 months for some anti-B cell antibodies. For other forms of altered immunocompetence, if inactivated vaccines are indicated, the usual schedules are recommended. However, the effectiveness of such vaccinations might be suboptimal (*1*).

Live, Attenuated Viral and Bacterial Vaccines: Effectiveness

The same rationale regarding effectiveness that exists with inactivated vaccines also exists with live vaccines.

Live, Attenuated Viral and Bacterial Vaccines: Safety

Severe complications have followed vaccination with certain live, attenuated viral and live, attenuated bacterial vaccines among persons with altered immunocompetence (*18-26*). Persons with most forms of altered immunocompetence should not receive live vaccines (MMR, varicella, MMRV, LAIV, zoster, yellow fever, Ty21a oral typhoid, BCG, smallpox, and rotavirus). However, exceptions exist, and are discussed in this section.

Patients with any defect in phagocytic function (e.g., chronic granulomatous disease, leukocyte adhesion deficiency, myeloperoxidase deficiency, Chediak-Higashi syndrome) should NOT receive live bacterial vaccines. Patients with a specific type of defect in phagocytic function—chronic granulomatous disease—should receive otherwise indicated live attenuated viral vaccines in addition to inactivated vaccines but should NOT receive live bacterial vaccines. Patients with defects in phagocytic function that are undefined or known to be accompanied by defects in T-cell and natural killer cell function (e.g., leukocyte adhesion deficiency, myeloperoxidase deficiency, Chediak-Higashi syndrome) should NOT receive live attenuated viral or bacterial vaccines. These conditions include specific deficits in T-cell and natural killer cell function, reducing the response to live viral vaccine antigens to an extent not seen in chronic granulomatous disease (*1*). Children with deficiencies in complement should receive otherwise indicated live, attenuated viral and live, attenuated bacterial vaccines. Children with asplenia should not receive LAIV, but can receive other indicated live, attenuated viral and live, attenuated bacterial vaccines.

Persons with severe cell-mediated immunodeficiency should not receive live, attenuated viral or bacterial vaccines. Patients with defects of the interferon-gamma/interleukin-12 axis should not receive live bacterial vaccines. Patients with deficiencies of interferon-gamma or interferon-alpha should not receive live viral or live bacterial vaccine. These defects involve a deficiency in cytokine production which affects the immune response to a wide scope of antigens, both bacterial and viral (*1*). Two factors support vaccination of HIV-exposed or HIV-infected infants with rotavirus vaccines: 1) the HIV diagnosis might not be established in infants born to HIV-infected mothers before the age of the first rotavirus vaccine dose (only 1.5%-3% of HIV-exposed infants in the United States will be determined to be HIV-infected), and 2) the vaccine strains of rotavirus are considerably attenuated. Patients taking exogenous interferon as therapy should not receive live bacterial or live viral vaccines.

Children with HIV infection are at increased risk for complications from varicella and herpes zoster infection compared with immunocompetent children (*27*,*28*). Limited data among HIV-infected children younger than 8 years (specifically, those individuals with CDC class N, A, or B with age-specific CD4+ T-lymphocyte percentages of ≥15%) indicate that single-component varicella vaccine is immunogenic, effective, and safe (*14*,*28*). Data on use of varicella vaccine in HIV-infected adolescents and adults are lacking. However, on the basis of expert opinion, the safety of varicella vaccine in HIV-infected persons older than 8 years with comparable levels of immune function (CD4+T-lymphocyte count greater than 200 cells/mm^3) is likely to be similar to that of children aged younger than 8 years (*14*). Varicella vaccine should be considered for persons who meet these criteria. Eligible HIV-infected persons 12 months of age or older should receive 2 doses of single-component varicella vaccine with a 3-month interval between doses (*14*,*28*). Doses separated by <3 months are invalid for persons with HIV infection. MMRV vaccine should not be administered to any HIV-infected person.

Persons with HIV infection are at increased risk for severe complications if infected with measles. No severe or unusual adverse events have been reported after measles vaccination among HIV-infected persons who did not have evidence of severe

immunosuppression (*29-32*). Two doses of MMR vaccine are recommended for all HIV-infected individuals aged ≥12 months who do not have evidence of current severe immunosuppression (i.e., individuals aged ≤5 years must have CD4+T lymphocyte [CD4+] percentages ≥15% for ≥6 months, and individuals aged >5 years must have CD4+percentages ≥15% and CD4+≥200 lymphocytes/mm^3 for ≥6 months) and do not have current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those >5 years, the assessment of severe immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged ≤5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥6 months above age-specific CD4+count criteria: CD4+count >750 lymphocytes/mm^3 while aged ≤12 months and CD4+count ≥500 lymphocytes/mm^3 while aged 1 through 5 years (*33*). Similarly, repeat doses of MMR vaccination are recommended for individuals with perinatal HIV infection who were vaccinated prior to establishment of effective combination antiretroviral therapy (cART). They should receive 2 appropriately spaced doses of MMR vaccine once effective cART has been established (individuals aged ≤5 years must have CD4+percentages ≥15% for ≥6 months; individuals aged >5 years must have CD4+percentages ≥15% and CD4+≥200 lymphocytes/mm^3 for ≥6 months) unless they have other acceptable current evidence of measles, rubella, and mumps immunity.

HIV-infected persons who are receiving regular doses of IGIV are unlikely to respond to varicella vaccine or MMR vaccine because of the continued presence of passively acquired antibody. However, because of the potential benefit, MMR and varicella vaccines should be considered approximately 14 days before the next scheduled dose of IGIV (if not otherwise contraindicated), although an optimal immune response might not occur depending on the presence of neutralizing antibodies against the vaccine virus. Vaccination should be repeated (if not otherwise contraindicated) after the recommended interval (see Table 3-5 in the Timing and Spacing of Immunobiologics of this document). In most cases, this is after the therapy has been discontinued.

Patients with leukemia, lymphoma, or other malignancies whose disease is in remission, who have restored immunocompetence, and whose chemotherapy has been discontinued for at least 3 months can receive live-virus vaccines. Persons with impaired humoral immunity (e.g., hypogammaglobulinemia or dysgammaglobulinemia) may be vaccinated with varicella vaccine (*14*). However, most persons with these disorders also receive periodic doses of IGIV. Appropriate spacing should be maintained between administration of IGIV and varicella vaccine in an attempt to prevent an inadequate response to vaccination caused by the presence of neutralizing antibodies from the IGIV.

Zoster incidence is higher in persons with altered immunocompetence (*34*). Adults with most types of altered immunocompetence are expected to maintain residual immunity to varicella-zoster virus because of chronic latent infection that protects against primary varicella but provides incomplete protection against zoster. Zoster vaccine is contraindicated in persons with primary or acquired immunodeficiency (e.g., lymphoma, leukemia, tumors involving bone marrow, and patients receiving chemotherapy) and some HIV infected patients (*34*). Zoster vaccine may be administered to certain persons age 60 or older with altered immunocompetence, such as persons receiving low dosages of immunosuppressive medications, those with isolated B-cell deficiencies (i.e., impaired humoral immunity), or those with HIV infection who have CD4+ T-lymphocyte counts >200 cells/mm^3.

Recipients of Hematopoietic Cell Transplants

A hematopoietic cell transplant (HCT) results in immunosuppression because of the hematopoietic ablative therapy administered before the transplant, drugs used to prevent or treat graft-versus-host disease, and, in some cases, from the underlying disease process necessitating transplantation (*35-37*). HCT involves ablation of the bone marrow followed by reimplantation of the person's own stem cells or stem cells from a donor. Antibody titers to vaccine-preventable diseases (e.g., tetanus, poliovirus, measles, mumps, rubella, and encapsulated bacteria) decrease 1-4 years after autologous or allogeneic HCT if the recipient is not revaccinated. HCT recipients of all ages are at increased risk for certain vaccine-preventable diseases, including diseases caused by

encapsulated bacteria (i.e., pneumococcal, meningococcal, and Hib infections). As a result, HCT recipients who received vaccines prior to their HCT should be revaccinated routinely after HCT, regardless of the source of the transplanted stem cells (*35-37*). Vaccination or revaccination doses of pneumococcal vaccines, DTaP vaccine, Hib vaccine, hepatitis A vaccine, hepatitis B vaccine, meningococcal vaccines, IPV, inactivated influenza vaccines, and human papillomavirus (HPV) vaccines (for individuals aged 9-26 years) are recommended after HCT (*1,35*). Varicella, zoster, and MMR vaccines may be administered after HCT if 24 months have passed since HCT, the patient does NOT have graft-vs-host disease, and is considered immunocompetent. Yellow fever vaccine, rabies vaccine, tick-borne encephalitis vaccine, and Japanese encephalitis vaccine are not routinely administered vaccines, so their use post-HCT will be driven by a disease-specific risk such as exposure or travel. If someone has received yellow fever vaccine prior to an HCT, another dose should be administered post-HCT (*38*). BCG, LAIV, typhoid vaccine, and rotavirus vaccine are not recommended after HCT. Most inactivated vaccines should be initiated 6 months after the HCT (*37*). Inactivated influenza vaccine should be administered beginning at least 6 months after HCT and annually thereafter for the life of the patient. A dose of inactivated influenza vaccine can be given as early as 4 months after HCT, but a second dose should be considered in this situation (*37*). A second dose is recommended routinely for all children younger than 9 years receiving influenza vaccine for the first time. Sequential administration of 3 doses of pneumococcal conjugate vaccine is recommended, beginning 3-6 months after the transplant, followed by a dose of PPSV23 (*35*). Some sources state a 4-week interval between these doses as reasonable with the dose of PPSV23 being replaced by a dose of PCV13 in the context of graft-versus-host disease (*35*). Others sources support 3 doses of PCV13 at 8-week intervals, with a dose of PPSV23 recommended 8 weeks after the last dose of PCV13 and 12 months after the HCT (*1*). A 3-dose regimen of Hib vaccine should be administered beginning 6 months after transplant; at least 1 month should separate the doses (*37*). This series should be given regardless of whether or not vaccine doses were administered prior to the HCT. The revaccination schedule for pertussis-containing vaccines includes 3 doses of DTaP for patients <7 years (*14*). For patients ≥7 years, providers have 3 options for

revaccination: 1) 3 doses of DTaP; 2) one dose of Tdap and 2 doses of DT; or 3) one dose of Tdap and 2 doses of Td (*16*).

Providers need to make a clinical judgment whether they will follow the revaccination schedule described above, even if doses were not administered prior to the HCT. There are specific recommendations for Hib and pertussis-containing vaccines. Use of the 3-dose Hib schedule following HCT is supported for both patients that received Hib prior to HCT and those who did not receive Hib prior to HCT (*6*,*11*). For children >6 years who did not receive previous doses of pertussis-containing vaccine prior to the HCT, the preferred schedule following HCT is a dose of Tdap followed by 2 doses of Td (personal communication, subject matter experts). This is identical to one of the alternative regimens for revaccination doses, described above.

Conditions or Drugs that Might Cause Immunodeficiencies

Asplenia and use of corticosteroids or certain drugs have the potential to be immunosuppressive and are presumed to cause some degree of altered immunocompetence.

Anatomic or Functional Asplenia

Persons with anatomic asplenia (e.g., surgical removal or congenital absence of the spleen) or functional asplenia (as occurs in persons with sickle cell disease) are at increased risk for infection by encapsulated bacteria, especially *S. pneumoniae* (pneumococcus), *N. meningitidis* (meningococcus), and Hib (*7*,*8*,*39*). Children should receive an age-appropriate series of PCV13. Unvaccinated children 2-5 years should receive 2 doses of PCV13. Children ≥6 years should receive a dose of PCV13 if they have not previously received a dose of PCV13. Persons aged ≥2 years should receive 2 doses of PPSV23 separated by 5 years, beginning 8 or more weeks after completing all recommended doses of PCV13 (*6*,*7*,*40*,*41*). In circumstances where both PCV13 and PPSV23 are indicated, doses of PCV13 should be administered first followed by PPSV23 8 weeks after the last dose of PCV13.

Meningococcal conjugate (MenACWY) and serogroup B (MenB) vaccines are recommended for persons with anatomic or functional asplenia (including sickle cell disease). For children 2-23 months of age, a series of MenACWY-CRM (Menveo) or Hib-MenCY (MenHibrix) should be administered. For persons ≥2 years of age, a 2-dose primary series of either MenACWY-CRM or MenACWY-D (Menactra) should be administered. If a person with functional or anatomic asplenia is catching up on pneumococcal conjugate vaccine (PCV13), and the provider only carries MenACWY-D, indicated doses of PCV13 should be completed first and MenACWY-D should be given 4 weeks after the PCV13 series is completed. Following the primary series of vaccine, a 3-year interval to the next dose is recommended for asplenic children who received their last previous dose at age younger than 7 years. A 5-year interval for asplenic persons is recommended for persons who received their last previous dose at age 7 years or older. Meningococcal B (MenB) vaccine should be administered as either a 2-dose series of MenB-4C (Bexsero) or a 3-dose series of MenB-FHbp (Trumenba). The same vaccine product must be used for all doses. Based on available data and expert opinion, MenB-4C or MenB-FHbp may be administered concomitantly with MenACWY vaccines, but at a different anatomic site, if feasible. There are presently no recommendations for booster doses of either MenB vaccine.

Hib vaccine is recommended routinely for all children through age 59 months. Children 12-59 months with functional or anatomic asplenia and who are unvaccinated or who received only one dose of Hib disease before 12 months of age should receive 2 doses of Hib vaccine; those who received 2 or more doses of Hib before 12 months of age should receive one additional dose. Unimmunized[(a)] asplenic patients older than 59 months of age should receive one dose of Hib vaccine. Anyone ≥15 months of age who is undergoing a splenectomy and is unimmunized[(a)] should receive one dose of Hib vaccine.

Pneumococcal, meningococcal, and Hib vaccinations should be administered at least 14 days before elective splenectomy, if possible. If the vaccinations are not administered before surgery, they should be administered after the procedure as soon as the patient's condition is stable.

Corticosteroids

The amount of systemically absorbed corticosteroids and the duration of administration needed to suppress the immune system of an otherwise immunocompetent person are not well defined. Although the immunosuppressive effects of steroid treatment vary, the majority of clinicians consider a dose equivalent to either ≥2 mg/kg of body weight or ≥20 mg/day of prednisone or equivalent for persons who weigh >10 kg when administered for ≥14 consecutive days as sufficiently immunosuppressive to raise concern about the safety of vaccination with live-virus vaccines (*37*). This dosage is referred to as "high-dose corticosteroids". Corticosteroids used in greater than physiologic doses also can reduce the immune response to vaccines. Vaccination providers should defer live-virus vaccination for at least 1 month after discontinuation of high-dose systemically absorbed corticosteroid therapy administered for ≥14 days. Following vaccination, the decision needs to be made when to restart immunosuppressive therapy. There are no specific recommendations about when to restart immunosuppressive medicines. However, when initiating immunosuppressive therapy, providers should wait 4 weeks after a live vaccine and 2 weeks after an inactivated vaccine. However, if patients require therapy for chronic inflammatory conditions, this therapy should not be delayed because of past administration of vaccines (*1*).

Corticosteroid therapy usually is not a contraindication to administering live-virus vaccine when administration is 1) short term (i.e., <14 days); 2) a low to moderate dose (i.e., <20 mg of prednisone or equivalent per day or <2mg/kg body weight per day for a young child); 3) long-term, alternate-day treatment with short-acting preparations; 4) maintenance physiologic doses (replacement therapy); or 5) topical (skin or eyes), inhaled, or by intra-articular, bursal, or tendon injection (*37*). No evidence of an increased risk for more severe reactions to live, attenuated viral vaccines has been reported among persons receiving corticosteroid therapy by aerosol, and such therapy is not a reason to delay vaccination.

Other Immunosuppressive Drugs

When feasible, clinicians should administer all indicated vaccines before initiation of chemotherapy, before treatment with other immunosuppressive drugs, and before radiation or splenectomy. Persons receiving chemotherapy or radiation for leukemia and other hematopoietic malignancies, or for solid tumors, should be assumed to have altered immunocompetence. Live, attenuated vaccines should not be administered for at least 3 months after such immunosuppressive therapy. Inactivated vaccines administered during chemotherapy should be readministered after immune competence is regained. Children vaccinated before receiving chemotherapy for leukemia, lymphoma, other malignancies, or radiation generally are thought to retain immune memory after treatment, although revaccination with the common childhood vaccines after chemotherapy for acute lymphoblastic leukemia might be indicated (*42*). In general, revaccination of a person after chemotherapy or radiation therapy is considered unnecessary if the previous vaccination occurred before therapy and not during therapy, with the exception of recipients of HCT, who should be revaccinated as recommended previously. Determination of the level of immune memory and the need for revaccination should be made by the treating physician.

Certain immunosuppressive medications are administered to prevent solid organ transplant rejection. Live vaccines should be withheld for 2 months following discontinuation of anti-rejection therapies in patients with a solid organ transplant. Zoster vaccine should be withheld one month following discontinuation of anti-rejection therapies (*34*).

Other immunosuppressive medications include human immune mediators like interleukins and colony-stimulating factors, immune modulators, and medicines like tumor necrosis factor-alpha inhibitors and anti-B cell antibodies. Inactivated and live vaccines should be administered 2 or more weeks before initiating such therapies. Live vaccines should be withheld 3 months following such therapies, and both inactivated and live vaccines should be withheld at least 6 months following therapy with anti-B cell antibodies. Some experts recommend longer than 6 months following anti-B cell

antibodies. Anti-B cell antibodies suppress antibody-producing cells for a prolonged duration, hence the longer interval recommended before administering vaccines (*17*). Zoster vaccine is an exception and should be withheld 1 month following anti-B cell antibodies.

[a] 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.

TABLE 8-1. Vaccination of persons with primary and secondary immunodeficiencies				
Primary	Specific immunodeficiency	Contraindicated vaccines[a]	Risk-specific recommended vaccines[a]	Effectiveness and comments
B-lymphocyte (humoral)	Severe antibody deficiencies (e.g., X-linked agammaglobulinemia and common variable immunodeficiency)	OPV[b] Smallpox[c] LAIV BCG Ty21a (live typhoid) Yellow fever MMR MMRV	Pneumococcal Hib (children 12-59 months of age)[d]	The effectiveness of any vaccine is uncertain if it depends only on the humoral response (e.g., PPSV23or MPSV4) IGIV interferes with the immune response to measles vaccine and possibly varicella vaccine
	Less severe antibody deficiencies (e.g., selective IgA deficiency and IgG subclass deficiency)	OPV[b] BCG Yellow fever[e] Other live vaccines appear to be safe	Pneumococcal Hib (children 12-59 months of age)[d]	All vaccines likely effective; immune response might be attenuated
T-lymphocyte (cell-mediated and humoral)	Complete defects (e.g., SCID disease, complete DiGeorge syndrome)	All live vaccines[f],[g],[h]	Pneumococcal Hib (children 12-59 months of age)[d]	Vaccines likely to be effective

	Partial defects (e.g., most patients with DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia)	All live vaccines[(f),(g),(h)]	Pneumococcal Meningococcal Hib (children 12-59 months of age)[(d)]	Effectiveness of any vaccine depends on degree of immune suppression
	Interferon-gamma/ Interleukin 12 axis deficiencies	All live bacterial vaccines (All live vaccines contraindicated in Interferon-gamma or interferon-alpha deficiencies)	None	
Complement	Persistent complement, properdin, or factor B deficiency;	None	Pneumococcal Meningococcal Hib (children 12-59 months of age)[(d)]	All routine vaccines likely effective
	Taking eculizumab (Soliris)	None	Meningococcal	
Phagocytic function	Chronic granulomatous disease	Live bacterial vaccines[(f)]	None	Live viral vaccines likely safe and effective

	Phagocytic deficiencies that are undefined or accompanied by defects in T-cell and NK cell dysfunction (such as a Chediak-Higashi syndrome, Leukocyte Adhesion Deficiency [LAD], and myeloperoxidase deficiency)	MMR MMRV Varicella OPV[(b)] Smallpox BCG LAIV Ty21a Yellow Fever and bacterial vaccines[(f)],[(g)]	Pneumococcal	All inactivated vaccines safe and likely effective
Secondary	HIV/AIDS	OPV[(b)] Smallpox BCG LAIV MMRV Withhold MMR, varicella, and zoster in severely immunocompromised persons Yellow fever vaccine might have a contraindication or a precaution depending on clinical parameters of immune function[(i)]	Pneumococcal Hib[(d)], [(j)] HepB	MMR and Varicella vaccine in those with mild immunosuppression, rotavirus, and all inactivated vaccines, including inactivated influenza as per routine vaccination schedule, might be effective[(k)]
	Generalized malignant neoplasm, transplantation, immunosuppres	Live viral and bacterial, depending on immune status[(f)],[(g)],[(l)]	Pneumococcal Hib[(m)]	Effectiveness of any vaccine depends on degree of

	sive or radiation therapy			immune suppression
	Asplenia	LAIV	Pneumococcal Meningococcal Hib[(d),(n)]	All routine vaccines likely effective
	Chronic renal disease	LAIV	Pneumococcal HepB[(o)]	All routine vaccines likely effective

Abbreviations: AIDS = acquired immunodeficiency syndrome; BCG = bacille Calmette-Guérin; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; HIV = human immunodeficiency virus; IG = immunoglobulin; IGIV = immune globulin intravenous; IgA = immune globulin A; IgG = immune globulin G; LAIV = live, attenuated influenza vaccine; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; OPV = oral poliovirus vaccine (live); PPSV23= pneumococcal polysaccharide vaccine; SCID = severe combined immunodeficiency; Ty21a = live oral typhoid vaccine.

Source: (*43*).

(a) Other vaccines that are universally or routinely recommended should be given if not contraindicated. An exception is patients with B-cell deficiencies receiving immunoglobulins, who should not receive either live or inactivated vaccines, due to safety (live vaccines) and efficacy (live and inactivated vaccines) concerns.
(b) OPV is no longer available in the United States.

(c) This table refers to contraindications for nonemergency vaccination (i.e., the ACIP recommendations); emergency response recommendations are addressed in the clinical guidance for smallpox vaccine use in an emergency.

(d) Children 12-59 months: if unimmunized or received zero or only 1 dose, and that dose was administered before 12 months of age, should receive 2 Hib doses, 8 weeks apart; if received 2 or more doses before age 12 months, and none after 12 months, should receive 1 Hib dose 8 weeks after the last dose; if completed a primary series and received a booster dose at age 12 months or older, no additional Hib doses are recommended.

(e) There are no data to support IgA deficiency as a contraindication for yellow fever vaccine.

(f) Live bacterial vaccines: BCG, adenovirus, and oral Ty21a *Salmonella Typhi* vaccine.

(g) Live viral vaccines: MMR, MMRV, OPV, LAIV, yellow fever, zoster, rotavirus, varicella, and vaccinia (smallpox). Nonemergency smallpox vaccination is not recommended for children younger than 18 years or the general public.

(h) Regarding T-lymphocyte immunodeficiency as a contraindication for rotavirus vaccine, data exist only for SCID.

(i) Symptomatic HIV infection or CD4+ T-lymphocyte count of <200/mm^3 or <15% of total lymphocytes for children aged <6 years is a contraindication to yellow fever vaccine administration. Asymptomatic HIV infection with CD4+ T-lymphocyte count of 200-499/mm^3 for persons aged ≥6 years or 15%-24% of total lymphocytes for children aged <6 years is a precaution for yellow fever vaccine administration. Details of yellow fever vaccine recommendations are available from CDC (*44*)

(j) Patients 5-18 years of age who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age.

(k) HIV-infected children should be considered for varicella vaccine if CD4+ T-lymphocyte count is ≥15% and should receive MMR vaccine if they are aged ≥12 months and do not have 1) evidence of current severe immunosuppression (i.e., individuals aged ≤5 years must have CD4+T lymphocyte [CD4] percentages ≥15% for ≥6 months; and individuals aged >5 years must have CD4+percentages ≥15% and CD4+≥200 lymphocytes/mm^3 for ≥6 months) and 2) other current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those older than age 5 years, the assessment of severe

immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged ≤5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥6 months above age-specific CD4+count criteria: CD4+count >750 lymphocytes/mm^3 while aged ≤12 months and CD4+count ≥500 lymphocytes/mm^3 while aged 1 through 5 years (*33*).

(l) Withholding inactivated vaccines also is recommended with some forms of immunosuppressive therapy, like anti-CD20 antibodies, induction or consolidation chemotherapy, or patients with major antibody deficiencies receiving immunoglobulins. Inactivated influenza vaccine is an exception, but consideration should be given to repeating doses of any inactivated vaccine administered during these therapies.

(m) Persons younger than 60 months undergoing chemotherapy or radiation therapy who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age; HCT patients of any ages, regardless of Hib vaccine history.

(n) Persons older than 59 months who are asplenic and persons 15 months or older who are undergoing elective splenectomy who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age.

(o) Indicated based on the risk from dialysis-based bloodborne transmission.

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9. Special Situations

Updates

Major revisions to this section of the best practices guidance include the timing of intramuscular administration and the timing of clotting factor deficiency replacement.

Concurrent Administration of Antimicrobial Agents and Vaccines

With a few exceptions, use of an antimicrobial agent does not interfere with the effectiveness of vaccination. Antibacterial agents have no effect on inactivated, recombinant subunit, or polysaccharide vaccines or toxoids. They also have no effect on response to live, attenuated vaccines, except live oral Ty21a typhoid and BCG vaccines. Ty21a typhoid vaccine should not be administered to persons receiving antimicrobial agents until 72 hours after the last dose of antimicrobial (*1*). If feasible, to avoid a possible reduction in vaccine effectiveness, antibacterial drugs should not be started or resumed until 1 week after the last dose of Ty21a. Antimicrobial or immunosuppressive agents may interfere with the immune response to BCG and should only be used under medical supervision (for additional information, see http://www.merck.com/product/usa/pi_circulars/b/bcg/bcg_pi.pdf).

Antiviral drugs used for treatment or prophylaxis of influenza virus infections have no effect on the response to inactivated influenza vaccine (*2*). However, live, attenuated influenza vaccine should not be administered until 48 hours after cessation of therapy with antiviral influenza drugs. If feasible, to avoid possible reduction in vaccine effectiveness, antiviral medication should not be administered for 14 days after LAIV administration (*2*). If influenza antiviral medications are administered within 2 weeks after receipt of LAIV, the LAIV dose should be repeated 48 or more hours after the last dose of antiviral medication. Alternatively, persons receiving antiviral drugs within the period 2 days before to 14 days after vaccination with LAIV may be revaccinated with another approved vaccine formulation (e.g., IIV or recombinant influenza vaccine). Antiviral drugs active against herpesviruses (e.g., acyclovir or valacyclovir) might reduce

the efficacy of vaccines containing live, attenuated varicella zoster virus (i.e., Varivax, ProQuad, and Zostavax) (*3*,*4*). These drugs should be discontinued at least 24 hours before administration, if possible. If clinically appropriate, delay use or resumption of antiviral therapy for 14 days after vaccination. No data exist to suggest that commonly used antiviral drugs have an effect on rotavirus vaccine or MMR.

Administration of Live Vaccines and Tuberculin Skin Tests (TSTs) and Interferon-gamma Release Assays (IGRAs)

Measles illness, severe acute or chronic infections, HIV infection, and malnutrition can create a relatively anergic state during which the TST might have a false-negative reaction (*5*-*7*). Although live, attenuated measles vaccine theoretically can suppress TST reactivity, the degree of suppression is likely less than that occurring from acute infection from wild-type measles virus. Screening children for tuberculosis exposure is accomplished by medical history rather than TST testing; universal TST screening of all children is no longer recommended, though TST screening is sometimes indicated (e.g., for persons at increased risk for tuberculosis exposure based on medical history, or for employees for occupational health reasons).

In a general screening situation, a TST may be administered simultaneously with live vaccines, or should be deferred for 28 days after vaccination. The TST and measles-containing vaccine can be administered at the same visit (this is the preferred option). Simultaneously administering the TST and measles-containing vaccine does not interfere with reading the TST result at 48-72 hours and ensures that the person has received measles vaccine. If the measles-containing vaccine has been administered recently, TST screening should be delayed for at least 4 weeks after vaccination. A delay in performing the TST removes the concern of any theoretical transient suppression of TST reactivity. Some providers choose to perform TST screening and then delay the vaccine until the patient returns to have the TST read. This option is the least favored because it delays receipt of the measles-containing vaccine and risks having neither the TST nor vaccination completed if the patient does not return.

Because of similar concerns about smallpox vaccine and TST suppression, a TST should not be performed until 4 weeks after smallpox vaccination (*8*).No data exist regarding the potential degree of TST suppression that might be associated with other live, attenuated virus vaccines (e.g., varicella or yellow fever). However, in the absence of data, following guidelines for measles-containing vaccine when scheduling TST screening and administering other live, attenuated virus vaccines is prudent. If the opportunity to vaccinate might be missed, vaccination should not be delayed only because of these theoretical considerations. TST can be repeated 4 weeks after vaccination if it is negative and concern for TB infection persists.

Interferon gamma release assays (IGRAs), such as the QuantiFERON-TB Gold In-Tube test and the T-Spot TB test, are blood-test alternatives to the TST for detecting *Mycobacterium tuberculosis* infection. The IGRA requires only a single visit to complete and may be less effected by previous BCG vaccination (*9*). The same timing guidelines that apply to the interval between a live vaccine and TST apply to IGRA (i.e., 28 days between live vaccine and IGRA if they do not occur on the same day), because IGRA (like TST) might be suppressed through immunologic mechanisms. The potential for a previous TST to cause boosting of future TST results should be considered in adults who have a negative initial TST (*9*). Two-step testing, in which TST is repeated in a short time frame (e.g., 1 to 3 weeks) after an initial negative TST, can illicit boosting and identify persons whose immune response may have waned with time since infection or BCG vaccination. For people undergoing serial screening for infection, for instance health care personnel who are tested yearly, differentiation of positive tests due boosting versus new infection is important (9). The 2-step test, in which the test is given twice in a short time frame, reduces the chance of these false negatives, which are important to identify among adults who may have had or plan to have repeat testing anyway—for example, health care personnel who are tested yearly (*9*). Because this test consists of 2 TSTs separated by an interval of 1-3 weeks, there is a greater window of time during which live vaccine replication could suppress reactivity. If a live vaccine is administered, the first dose of a 2-step TST should be delayed for 4 weeks, and if additional doses of live vaccines are indicated thereafter, they should be delayed until the second TST is measured.

TST or IGRA reactivity in the absence of active tuberculosis is not a contraindication to administration of any vaccine, including live, attenuated virus vaccines.

Note that TST screening of an asymptomatic individual is clinically different than testing a person suspected to have active tuberculosis. If a person is suspected to have active tuberculosis, MMR vaccine is typically not administered. Active tuberculosis should be considered severe acute illness, and moderate or severe acute illness is a precaution for vaccination.

Although no studies have reported on the effects of MMR vaccine on persons with active untreated tuberculosis, a theoretical basis exists for concern that measles vaccine might exacerbate active tuberculosis (*10*). As a result, before administering MMR to persons with untreated active tuberculosis, initiating antituberculosis therapy is advisable (*10*). Considering whether concurrent immunosuppression (e.g., immunosuppression caused by HIV infection) is present before administering live, attenuated vaccines also is necessary, because immunosuppression is a contraindication to MMR vaccine.

Vaccination of Preterm Infants

In the majority of cases, preterm infants (infants born before 37 weeks' gestation), regardless of birth weight, should be vaccinated at the same chronological age and according to the same schedule and using the same precautions as for full-term infants and children. Birth weight and size are not factors in deciding whether to vaccinate a clinically stable preterm infant (*11-15*), except for hepatitis B vaccination. The full recommended dose of each vaccine should be used. Divided or reduced doses are not recommended.

Decreased seroconversion rates might occur among certain preterm infants (i.e., those with low birth weights [<2,000 g]) after administration of hepatitis B vaccine at birth (*16*). However, by the chronological age of 1 month, all preterm infants, regardless of initial birth weight, are likely to respond as adequately as larger infants (*17-19*). Infants weighing <2,000 g born to 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 one month of age. Preterm low-birth-weight–infants born to HBsAg-positive mothers should receive immunoprophylaxis with hepatitis B vaccine within 12 hours after birth. The initial vaccine dose should not be counted toward completion of the hepatitis B series, and 3 additional doses of hepatitis B vaccine should be administered, beginning when the infant is aged 1 month. 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 Immunoglobulin (HBIG) is recommended for infants whose mothers are HBsAg positive or unknown. If the mother is HBsAg positive, HBIG must be given within 12 hours of birth. If the mother's HBsAg status is unknown, providers should first attempt to determine the mother's status. Regardless, if the infant is preterm or low birth weight, HBIG must be given within 12 hours of birth. If the infant is neither preterm nor low birth weight, providers have up to 7 days from birth to determine if the mother is HBsAg negative; because the protective efficacy of HBIG declines the longer that administration is delayed, if results are unlikely to be known by day 7 of life, HBIG should be given no later than day 7 if not earlier. If the mother is determined to be HBsAg positive, HBIG should be administered as soon as possible (*20*).

If a child aged at least 6 weeks has been in the hospital since birth, deferral of rotavirus vaccine is recommended until the time of discharge. If an infant were to be vaccinated with rotavirus vaccine while still needing care in the NICU or nursery, at least a theoretic risk exists for vaccine virus being transmitted to infants in the same unit who are acutely ill and to preterm infants who are not age-eligible for vaccine (*21*). The rotavirus vaccine series should not be initiated for infants aged ≥15 weeks, 0 days.

Breastfeeding and Vaccination

With 2 exceptions, neither inactivated nor live-virus vaccines administered to a lactating woman affect the safety of breastfeeding for women or their infants. Although live viruses in vaccines can replicate in the mother, the majority of live viruses in vaccines

have been demonstrated not to be excreted in human milk. Varicella vaccine virus has not been found in human milk (*22*). Although rubella vaccine virus has been excreted in human milk, the virus usually does not infect the infant. If infection does occur, it is well tolerated because the virus is attenuated (*23*). Inactivated, recombinant, subunit, polysaccharide, and conjugate vaccines, as well as toxoids, pose no risk for mothers who are breastfeeding or for their infants. Breastfeeding is a contraindication for smallpox vaccination of the mother because of the theoretical risk for contact transmission from mother to infant. Yellow fever vaccine should be avoided in breastfeeding women, because 2 cases (one confirmed, one probable) 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 cerebrospinal fluid of the infant, but the exact mode of transmission was not precisely determined because vaccine virus was not recovered from breast milk (*24*). However, when nursing mothers cannot avoid or postpone travel to areas endemic for yellow fever in which risk for acquisition is high, these women should be vaccinated.

Limited data indicate that breastfeeding can enhance the response to certain vaccine antigens (*25*). There are no data to suggest that passive transfer of antibodies in human milk can affect the efficacy of live-virus vaccines. Breastfed infants should be vaccinated according to the recommended schedule (*26-28*).

Vaccination During Pregnancy

No evidence exists of risk to the fetus from vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids (*29,30*). In spite of the lack of evidence of risk, HPV vaccine, an inactivated vaccine, is not recommended during pregnancy. Live vaccines administered to a pregnant woman pose a theoretical risk to the fetus; therefore, live, attenuated virus and live bacterial vaccines generally are contraindicated during pregnancy. Women should avoid conception for 4 weeks after vaccination with live vaccines. However, 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 are developed using ACIP's *Guiding Principles for Development of ACIP Recommendations for Vaccination During Pregnancy and Breastfeeding* (*31*).

Women who are pregnant should receive a dose of Tdap for the prevention of infant pertussis whether or not they have previously received Tdap. Vaccination of the mother generates antibodies that pass transplacentally to the fetus (*32*). Vaccination in the third trimester optimizes the duration of this antibody protection until after birth. Additionally, preventing pertussis in the mother reduces the risk that the infant is exposed to pertussis after birth (*33*). Health care personnel should administer Tdap during pregnancy, preferably during the third trimester. If Tdap is not administered during pregnancy to women who have never received it, it should be administered immediately postpartum. Pregnant women who are not vaccinated or are only partially vaccinated against tetanus should complete the primary series (*34*). Women for whom Td is indicated but who did not complete the recommended 3-dose series during pregnancy should receive follow-up after delivery to ensure the series is completed. One dose of the tetanus vaccine series should be Tdap, if Tdap has not already been received.

Pregnant and postpartum women are at higher risk for severe illness and complications from influenza than women who are not pregnant (*2*,*35*). Pregnant women have protective levels of anti-influenza antibodies after vaccination (*36*,*37*). Passive transfer of anti-influenza antibodies that might provide protection from vaccinated women to neonates has been reported (*36*,*38*-*41*). Routine vaccination with inactivated influenza vaccine is recommended for all women who are or will be pregnant (in any trimester) during influenza season.

IPV can be administered to pregnant women who are at risk for exposure to wild-type poliovirus. This includes travelers to areas or countries where polio is epidemic or endemic; members of communities or specific population groups with disease caused by wild polioviruses; laboratory workers who handle specimens that might contain polioviruses; health care personnel who have close contact with patients who might be excreting wild polioviruses; and unvaccinated persons whose children will be receiving

oral poliovirus vaccine (*42*). Hepatitis A, pneumococcal polysaccharide, meningococcal conjugate, and meningococcal polysaccharide vaccines should be considered for women at increased risk for those infections (*43-45*). Pregnant women who must travel to areas where there is a risk for acquiring yellow fever should receive yellow fever vaccine, because the limited theoretical risk from vaccination is outweighed substantially by the risk for yellow fever infection (*24,46*). Hepatitis B vaccine is not contraindicated in pregnancy and should be given to a pregnant woman for whom it is indicated (*20,47*).

Pregnancy is a contraindication for smallpox (vaccinia) vaccine and measles-, mumps-, rubella-, and varicella-containing vaccines. Smallpox vaccine is the only vaccine known to harm a fetus when administered to a pregnant woman. In addition, smallpox vaccine should not be administered to a household contact of a pregnant woman (*8*). Women who are pregnant should not have close contact with anyone who has recently (within the last 28 days) received the smallpox vaccine. Data from studies of children born to mothers inadvertently vaccinated with rubella vaccine during pregnancy demonstrate rubella antibody in unvaccinated infants. This could represent passive transfer of maternal antibody or a fetal antibody response to vaccine virus infection in the fetus. No cases of congenital rubella or varicella syndrome or abnormalities attributable to fetal infection have been observed among infants born to susceptible women who inadvertently received rubella or varicella vaccines during pregnancy (*48-50*). Because of the importance of protecting women of childbearing age against rubella and varicella, reasonable 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 or plan to become pregnant within that interval; explaining the theoretical risk for the fetus if MMR, varicella, or MMRV vaccine were administered to a woman who is pregnant; and counseling women who are vaccinated not to become pregnant during the 4 weeks after MMR, varicella, or MMRV vaccination (*10,48-51*). MMRV is an unlikely option for a pregnant woman because the vaccine is only licensed through 12 years of age. Routine pregnancy testing of women of childbearing age before administering a live-virus vaccine is not recommended (*3,10*). If a pregnant woman is inadvertently vaccinated or 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 vaccination during pregnancy should not be considered a reason to terminate pregnancy (*3*,*10*,*50*).

Persons who receive MMR vaccine do not transmit the vaccine viruses to contacts (*10*). Transmission of varicella vaccine virus to contacts is exceedingly rare (*3*). MMR and varicella vaccines should be administered when indicated to children and other household contacts of pregnant women (*10*). Infants living in households with pregnant women should be vaccinated with rotavirus vaccine according to the same schedule as infants in households without pregnant women.

Pregnant women should be evaluated for evidence of immunity to rubella and varicella and be tested for the presence of HBsAg during every pregnancy (*10*,*20*,*52*). Women without evidence of immunity to rubella and varicella should be vaccinated immediately after delivery. A second dose of varicella vaccine should be administered 4-8 weeks later. A woman found to be HBsAg positive should be followed-up carefully to ensure that the infant receives HBIG and begins the hepatitis B vaccine series no later than 12 hours after birth and that the infant completes the recommended hepatitis B vaccine series on schedule (*20*). No known risk exists for the fetus from passive immunization of pregnant women with immune globulin preparations.

Persons Vaccinated Outside the United States

Clinicians have a limited ability to determine whether persons are protected on the basis of their country of origin and their vaccination records alone. Vaccines administered outside the United States generally can be accepted as valid if the schedule (i.e., minimum ages and intervals) is similar to that recommended in the United States. With the exception of influenza vaccine, only written documentation should be accepted as evidence of previous vaccination. Written records are more likely to predict protection if the vaccines, dates of administration, intervals between doses, and age at the time of vaccination are comparable to U.S. recommendations. Although vaccines with inadequate potency have been produced in other countries (*53*,*54*), the majority of

vaccines used worldwide are produced with adequate quality control standards and are potent.

Persons vaccinated outside of the United States can enter the country through a number of different mechanisms. Those seeking to immigrate to the United States may be vaccinated under the authority of a civil surgeon or a panel physician. Some enter the United States as refugees and are vaccinated under the authority of the Office of Refugee Resettlement, part of the Administration for Children and Families, in the Department of Health and Human Services.

Adopted children's birth countries often have vaccination schedules that differ from the recommended childhood vaccination schedule in the United States. Differences in the U.S. schedule and those used in other countries include the vaccines administered, the recommended ages of administration, and the number and timing of doses.

Data are inconclusive regarding the extent to which an internationally adopted child's vaccination record reflects the child's protection. A child's record might indicate administration of MMR vaccine when only single-antigen measles vaccine was administered. A study of children adopted from orphanages in the People's Republic of China, Russia, and countries in Eastern Europe determined that 67% of children with documentation of >3 doses of DTP before adoption had nonprotective titers to these antigens (*54*). In contrast, children adopted from these countries who received vaccination in the community (not only from orphanages) and had documentation of ≥1 doses of DTP exhibited protective titers 67% of the time (*54*). However, antibody testing was performed by using a hemagglutination assay, which tends to underestimate protection and cannot directly be compared with antibody concentration (*55*). Data are likely to remain limited for areas other than the People's Republic of China, Russia, and Eastern Europe. Health care providers should ensure that household contacts of international adoptees are vaccinated adequately, particularly for measles, hepatitis A, and hepatitis B (*56*).

Health care providers may use one of multiple approaches if the immunogenicity of vaccines or the completeness of series administered to persons outside the United States is in question. Repeating the vaccinations is an acceptable option that usually is safe and prevents the need to obtain and interpret serologic tests. If avoiding unnecessary injections is desired, judicious use of serologic testing might help determine which vaccinations are needed. For some vaccines, the most readily available serologic tests cannot document protection against infection. This best practices document provides guidance on possible approaches to evaluation and revaccination for each vaccine recommended in the United States (Table 9-1).

DTaP Vaccine

Vaccination providers can revaccinate children younger than 7 years of age with DTaP vaccine without regard to recorded doses; however, data indicate increased rates of local adverse reactions after the fourth and fifth doses of DTaP (*57*). If a revaccination approach is adopted and a severe local reaction occurs, serologic testing for specific IgG antibody to tetanus and diphtheria toxins can be measured before administering additional doses. Protective concentration[(a)] indicates that additional doses are unnecessary and subsequent vaccination should occur as age appropriate. No established serologic correlates exist for protection against pertussis.

For a child whose record indicates receipt of ≥3 doses of DTP or DTaP, serologic testing for specific IgG antibody to both diphtheria and tetanus toxin before additional doses is a reasonable approach. If a protective concentration is present, recorded doses are considered valid, and the vaccination series should be completed as age appropriate. An indeterminate antibody concentration might indicate immunologic memory but waning antibody; serologic testing can be repeated after a booster dose if vaccination providers or parents want to avoid revaccination with a complete series.

Alternately, for a child whose records indicate receipt of ≥3 doses, a single booster dose can be administered followed by serologic testing after 1 month for specific IgG antibody to both diphtheria and tetanus toxins. If the child has a protective concentration, the

recorded doses are considered valid, and the vaccination series should be completed as age appropriate. Children with an indeterminate concentration after a booster dose should be revaccinated with a complete series.

Hepatitis A Vaccine

Children aged 12-23 months without documentation of hepatitis A vaccination or serologic evidence of immunity should be vaccinated on arrival in the United States (*45*). Persons who have received 1 dose should receive the second dose if 6-18 months have passed since the first dose was administered.

Hepatitis B Vaccine

Persons not known to be vaccinated for hepatitis B should receive an age-appropriate series of hepatitis B vaccine. A person whose records indicate receipt of ≥3 doses of vaccine is considered protected, and additional doses are not needed if ≥1 dose was administered at age ≥24 weeks. Persons who received their last hepatitis B vaccine dose at an age <24 weeks should receive an additional dose at age ≥24 weeks. People who have received <3 doses of vaccine should complete the series at the recommended intervals and ages.

All foreign-born persons and immigrants, refugees, and internationally adopted children born in Asia, the Pacific Islands, Africa, and other regions of high or intermediate hepatitis B endemicity should be tested for HBsAg, regardless of vaccination status (*58*). Those determined to be HBsAg positive should be monitored for development of liver disease. Household members of HBsAg-positive children or adults should be vaccinated if they are not already immune.

Hib Vaccine

Interpretation of a serologic test to verify whether children who were vaccinated >2 months previously are protected against Hib bacteria can be difficult. Because the number of vaccinations needed for protection decreases with age and because adverse

events are rare (*59*), age-appropriate vaccination should be provided. Hib vaccination is not recommended routinely for persons aged ≥5 years (*59*).

Meningococcal Vaccine

Quadrivalent meningococcal conjugate vaccines are not routinely used in other countries in adolescents (the United Kingdom is the exception). Unless patients have documented receipt they should be considered unvaccinated and receive the age-appropriate doses.

MMR Vaccine

The simplest approach to resolving concerns about MMR vaccination is to revaccinate with 1 or 2 doses of MMR vaccine, depending on age. Serious adverse events after MMR vaccinations are rare (*10*). No evidence indicates that administering MMR vaccine increases the risk for adverse reactions among persons who are already immune to measles, mumps, or rubella as a result of previous vaccination or natural disease. Doses of measles-containing vaccine administered before the first birthday should not be counted as part of the series (*10*). Alternatively, serologic testing for IgG antibody to vaccine viruses indicated on the vaccination record can be considered. Serologic testing is widely available for measles and rubella IgG antibody. A person whose record indicates receipt of monovalent measles or measles-rubella vaccine on or after the first birthday and who has protective antibody against measles and rubella should receive 1 or 2 doses of MMR or MMRV as age appropriate to ensure protection against mumps and varicella (and rubella if measles vaccine alone had been administered). If a person whose record indicates receipt of MMR at age ≥12 months has a protective concentration of antibody to measles, no additional vaccination is needed unless a second dose is required for school entry.

Pneumococcal Vaccines

Many industrialized countries now routinely use pneumococcal vaccines. Although recommendations for pneumococcal polysaccharide vaccine also exist in many countries, the pneumococcal conjugate vaccine might not be routinely administered. PCV13 and PPSV23 should be administered according to age-appropriate vaccination schedules or as indicated by the presence of underlying medical conditions (*43,60*).

Poliovirus Vaccine

The simplest approach to vaccinating with poliovirus vaccine is to revaccinate persons aged <18 years with IPV according to the U.S. schedule. Adverse events after IPV are rare (*42*). Children appropriately vaccinated with 3 doses of OPV in economically developing countries might have suboptimal seroconversion, including to type 3 poliovirus (*42*).

Rotavirus Vaccine

Rotavirus vaccination should not be initiated for infants aged ≥15 weeks, 0 days. Infants who began the rotavirus vaccine series outside the United States but who did not complete the series and who are still aged ≤8 months, 0 days, should follow the routine schedule and receive doses to complete the series. If the brand of a previously administered dose is live, reassortment pentavalent rotavirus vaccine or is unknown, a total of 3 doses of rotavirus vaccine should be documented for series completion. All doses should be administered by age 8 months, 0 days.

Td and Tdap Vaccines

Children aged ≥7 years who are not considered fully vaccinated for pertussis should receive Tdap vaccine. “Fully vaccinated” means at least 5 doses of DTaP before the seventh birthday or at least 4 doses of DTaP before the seventh birthday if the fourth dose is given after the fourth birthday. One dose of Tdap is recommended after the

seventh birthday. If additional doses of vaccine are needed, Td should be administered as age appropriate.

Varicella Vaccine

Varicella vaccine is not available in most countries. A person who lacks evidence of varicella immunity should be vaccinated as age appropriate (*3*,*59*).

Zoster Vaccine

In the United States, zoster vaccination is recommended for all persons aged ≥60 years who have no contraindications, including persons who report a previous episode of zoster or who have chronic medical conditions. For persons who do not have documentation of receipt of zoster vaccine, the vaccine should be offered at the patient's first clinical encounter with the health care provider. The vaccine is administered as a single 0.65-mL subcutaneous dose. Zoster vaccination is not indicated to treat acute zoster, to prevent persons with acute zoster from developing postherpetic neuralgia, or to treat ongoing postherpetic neuralgia. Patients do not need to be asked about their history of varicella or to have serologic testing conducted to determine zoster immunity prior to administration of zoster vaccine.

Vaccinating Persons with Increased Bleeding Risk

Providers often avoid giving intramuscular injections or choose alternative routes for persons with bleeding disorders because of the risk for hematoma formation after injections. In one study, hepatitis B vaccine was administered intramuscularly to 153 persons with hemophilia. The vaccination was administered with a 23-gauge or smaller caliber needle, followed by application of steady pressure to the site for 1-2 minutes. The vaccinations resulted in a low (4%) bruising rate, and no patients required factor supplementation (*61*). Whether antigens that produce more local reactions (e.g., pertussis) would produce an equally low rate of bruising is unknown.

When hepatitis B or any other intramuscularly administered vaccine is indicated for a patient with a bleeding disorder, the vaccine should be administered intramuscularly if a physician familiar with the patient's bleeding risk determines that the vaccine can be administered by this route with reasonable safety. If the patient receives antihemophilia or similar therapy, intramuscularly administered vaccinations can be scheduled shortly after such therapy is administered. A fine-gauge needle (23-gauge or smaller caliber) should be used for the vaccination, followed by firm pressure on the site, without rubbing, for at least 2 minutes. The patient or family should be given information on the risk for hematoma from the injection. Patients receiving anticoagulation therapy presumably have the same bleeding risk as patients with clotting factor disorders and should follow the same guidelines for intramuscular administration. If possible, vaccination could be scheduled prior to the use of these medications, so that the patients' risk of bleeding is not increased by their therapeutic action.

[a] Enzyme immunoassay tests are available. Physicians should contact the laboratory performing the test for interpretive standards and limitations. Protective concentrations for antibody to diphtheria and tetanus toxins are defined as >0.1 IU/mL.

TABLE 9-1. Approaches to evaluation and vaccination of persons vaccinated outside the United States who have no (or questionable) vaccination records		
Vaccine	**Recommended approach**	**Alternative approach[a]**
DTaP	Revaccination with DTaP, with serologic testing for specific IgG antibody to tetanus and diphtheria toxins in the event of a severe local reaction	Persons whose records indicate receipt of ≥3 doses: serologic testing for specific IgG antibody to diphtheria and tetanus toxins before administering additional doses (see text), or administer a single booster dose of DTaP, followed by serological testing after 1 month for specific IgG antibody to diphtheria and tetanus toxins with revaccination as appropriate (see text)
HepA	Age-appropriate revaccination	Serologic testing for IgG antibodies to hepatitis A
HepB	Age-appropriate revaccination and serologic testing for HBsAg[b]	—
Hib	Age-appropriate revaccination	—
HPV	Age-appropriate revaccination	—
Meningococcal conjugate (MenACWY)	Age-appropriate revaccination	—
MMR	Revaccination with MMR	Serologic testing for IgG antibodies to measles, mumps, and rubella
Pneumococcal conjugate (or in some cases, both PCV13 and PPSV23)	Age-appropriate revaccination	—

Poliovirus	Revaccination with inactivated poliovirus vaccine	—
Rotavirus	Age-appropriate revaccination	—
Tdap	Age-appropriate revaccination of persons who are candidates for Tdap vaccine	—
Varicella	Age-appropriate revaccination of persons who lack evidence of varicella immunity	—
Zoster	Age-appropriate revaccination	—

Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis; HBsAg = hepatitis B surface antigen; HepA = hepatitis A; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; HPV = human papillomavirus; IgG = immune globulin G; MMR = measles, mumps, and rubella; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

[a] There is a recommended approach for all vaccines and an alternative approach for some vaccines.

[b] In rare instances, hepatitis B vaccine can give a false-positive HBsAg result up to 18 days after vaccination; therefore, blood should be drawn to test for HBsAg before vaccinating (*20*).

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10. Vaccination Records

Records of Health Care Providers

Appropriate and timely vaccination documentation helps ensure not only that persons in need of recommended vaccine doses receive them but also that adequately vaccinated patients do not receive excess doses. Curtailing the number of excess doses administered to patients controls costs incurred by patients, providers, insurers, vaccination programs, and other stakeholders. In addition, avoidance of excess doses of vaccines should decrease the number of adverse reactions to vaccines. Health care providers who administer vaccines covered by the National Vaccine Injury Compensation Program (VICP) are required under the National Childhood Vaccine Injury Act (*1*) to ensure that the permanent medical record of the recipient (or a permanent office log or file) indicates the date the vaccine was administered, the vaccine manufacturer, the vaccine lot number, and the name, address, and title of the person administering the vaccine. This Act applies to any vaccine for which there is a routine recommendation for childhood vaccination, even if many or most doses of the vaccine are administered to adults (e.g., influenza vaccine). In addition, the provider is required to record the edition date of the VIS distributed and the date those materials were provided. The Act considers a health care provider to be any licensed health care professional, organization, or institution, whether private or public (including federal, state, and local departments and agencies), under whose authority a specified vaccine is administered. This information should be kept for all vaccines, not just for those required by the Act. Providers and staff members also should systematically update patients' permanent medical records to reflect any documented episodes of adverse events after vaccination and any serologic test results related to vaccine-preventable diseases (e.g., those for rubella screening and anti-HBs).

Personal Records of Patients

Official childhood vaccination records have been adopted by every state and territory and the District of Columbia to encourage uniformity of records and to facilitate assessment of vaccination status by schools and child-care centers. The records also are key tools in vaccination education programs aimed at increasing parental and patient awareness of the need for vaccines. This record can exist in electronic file format or in hardcopy format. A permanent vaccination record should be established for each newborn infant and maintained by the parent or guardian. The parent or guardian should be educated about the importance of keeping the record up-to-date and instructed to keep the record indefinitely. These records should be distributed to new parents and/or guardians before discharge from the hospital or birthing center. Using vaccination records for adolescents and adults also is encouraged. Standardized adult vaccination records are available at www.immunize.org.

Immunization Information Systems (IISs)

IISs (formerly referred to as immunization registries) are confidential, population-based, computerized information systems that collect and consolidate vaccination data from multiple health care providers within a geographic area. IISs are a critical tool that can increase and sustain vaccination coverage by consolidating vaccination records from multiple providers, generating reminder and recall vaccination notices for each person, and providing official vaccination forms and vaccination coverage assessments (*2*). Providers should be aware of state and/or regional IISs and requirements for reporting.

Changing vaccination providers during the course of an individual's vaccination series is common in the United States. In addition to changes in providers, the vaccination records of persons who have changed vaccination providers often are unavailable or incomplete or might not have been entered into an IIS (*2*). Missing or inaccurate information regarding vaccines received previously might preclude accurate determination of which vaccines are indicated at the time of a visit, resulting in administration of extra doses.

A fully operational IIS also can prevent duplicate vaccinations, forecast when the next dose is due, limit missed appointments, allow recall for those who missed appointments, determine when vaccines need to be repeated (the technical IIS term for this is "evaluation"), reduce vaccine waste, and reduce staff time required to produce or locate vaccination records or certificates. Most IISs have additional capabilities, such as measurement of vaccination update and coverage, aid in tracking vaccine inventory and placing vaccine orders, recall of vaccine by lot number, maintenance of lifetime vaccination histories, and interoperability with other health information systems. The National Vaccine Advisory Committee recommends that vaccination providers participate in these systems when possible. Electronic health records should maintain interoperability with IISs as part of an effort to improve the quality of care, reduce health disparities, engage patients and families in their health, improve the coordination of care, improve population health, and ensure adequate privacy and security protection for personal health information (see www.cdc.gov/ehrmeaningfuluse/introduction.html)

One of the national Healthy People objectives for 2020 is 95% participation of children aged <6 years in a fully operational population-based IIS (objective 20.1) (*3*,*4*). Participating in an IIS means having two or more vaccinations recorded in the IIS. 2012 IIS data indicate that approximately 86% of children aged <6 years with two or more vaccinations were participating in IISs (*4*,*5*).

The National Vaccine Advisory Committee recommends that public health departments work toward including adults in all state IISs, reduce barriers to including adult vaccination records in IISs, and ensure that IISs meet new standards of EHR interoperability to track and maintain adult vaccination records (*6*).

Nationally, 57.8 million U.S. adults aged 19 years or older participated in an IIS in 2012 (*4*). This number reflects adults who may have had childhood vaccines entered during childhood and now have aged to adults. In 2013, 32% of U.S. adults had a record in the IIS and at least one vaccination administered during adulthood.

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11. Vaccination Programs

Updates

The major revision to this section is the addition of language related to Affordable Care Act (*1*) coverage of adult vaccination.

General Principles

Universal vaccination is a critical part of quality health care and should be accomplished through routine and catch-up vaccination provided in physicians' offices, public health clinics, and other appropriate settings. In the United States, vaccination is considered primarily the responsibility of individual health care providers and health care systems serving patients.

Certain programs and other efforts attempt to ensure all patients receive the full schedule of appropriate vaccinations by removing barriers posed by access to immunizations, cost, or other factors. Such efforts may include school-located clinics, school-based health centers, back-to-school immunization clinics, public health clinics for schoolchildren, periodic influenza vaccination clinics, public health nurse tracking of childhood immunizations, and government-sponsored financing of vaccines through the Vaccines for Children and Section 317 program (www.cdc.gov/vaccines/hcp/admin/vfc.html).

In the United States, vaccination programs have eliminated many vaccine-preventable diseases and markedly reduced the incidence of others (*2*). Because infants and young children were the principal recipients of most vaccines developed during the twentieth century (e.g., poliovirus vaccine), many persons in the United States might believe that vaccinations are solely for the young; however, vaccinations are recommended for persons of all ages (*3*,*4*). Improved vaccination coverage can result in additional reductions in the incidence of vaccine-preventable diseases that affect persons throughout the life span, and decrease associated morbidity and mortality.

Vaccination of Children and Adolescents

Physicians and other pediatric vaccination providers should adhere to the standards for child and adolescent vaccination practices (*5*). These standards are published by the National Vaccine Advisory Committee and define appropriate vaccination practices for both public and private sectors. The standards provide guidance on practices that eliminate barriers to vaccination, including eliminating unnecessary prerequisites for receiving vaccinations, eliminating missed opportunities to vaccinate, improving procedures to assess vaccination needs, enhancing knowledge about vaccinations among parents and providers, and improving management and reporting of adverse events. In addition, the standards address the importance of recall and reminder systems and using assessments to monitor clinic or office vaccination coverage levels. Health care providers should simultaneously administer as many vaccine doses as possible as indicated on the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* (*3*).

While rates of childhood vaccination are generally higher than rates of adult vaccination, for some doses coverage rates are still low, like the birth dose of hepatitis B vaccine. Community health care providers, as well as state and local public health vaccination programs, should coordinate with partners to identify and maximize outreach to populations at risk for undervaccination and vaccine-preventable diseases. For example, the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) is a categorical federal grant program administered by the U.S. Department of Agriculture through state health departments. The program provides supplemental foods, health care referrals, and nutrition education to low-income pregnant, breastfeeding, or postpartum women, as well as to infants and children aged <5 years. Between 8.5 and 8.9 million people participated in this program in 2013 (www.fns.usda.gov/pd/wicmain.htm). In collaboration, WIC and state vaccination programs assess regularly the vaccination coverage levels of WIC participants and develop new strategies and aggressive outreach procedures in sites with coverage levels <90%. Vaccination programs and private providers are encouraged to refer eligible

children to obtain WIC nutritional services, at www.fns.usda.gov/wic/immunization-screening-and-referral-wic (*6*).

Adolescent-Specific Issues

Vaccinations are recommended throughout life, including during adolescence. The age range for adolescence is defined as 11-21 years by many professional associations, including the American Academy of Pediatrics and the American Medical Association (*7,8*). Definitions of these age cutoffs differ depending on the source of the definition and the source's purpose for creating a definition. Vaccination of adolescents is critical for preventing diseases for which adolescents are at particularly high or increasing risk, such as meningococcal disease and human papillomavirus infection. Three vaccines recommended for adolescents have been licensed since 2005: MenACWY and Tdap were licensed in 2005, and HPV was licensed in 2006. A second dose of varicella vaccine is recommended for persons who received 1 dose of varicella vaccine after age 12 months. In addition, annual seasonal influenza vaccination is recommended for persons aged >6 months who have no contraindications. To ensure vaccine coverage, clinicians and other health care providers who treat adolescents must review vaccination history on every occasion that an adolescent has an office visit.

National goals for vaccination coverage for adolescents aged 13-15 years were included in *Healthy People 2020*, at www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases. Targets of 80% coverage were specified for one dose of Tdap, one dose of meningococcal conjugate vaccine, and 3 doses of HPV vaccine. Results of the published 2014 National Immunization Survey—Teen indicate that coverage rates for 13-17 years olds is 87.6% for one dose of Tdap and 79.3% for one dose of meningococcal vaccine. Coverage rates for 13-17 years olds for HPV vaccine are considerably lower—39.7% for females and 21.6% for males (*9,10*).

Ensuring adolescents receive routine and catch-up vaccination and achieving high levels of vaccination coverage present challenges. In general, adolescents do not visit health care providers frequently. Health care providers should promote annual preventive

visits (*11*), including one specifically for adolescents aged 11 and 12 years. The annual visits should be used as opportunities to provide routinely recommended vaccine doses, additional catch-up doses needed for lapsed vaccine series, vaccines recommended for high-risk groups, additional doses that might have been recently recommended, and other recommended health care services. Additional strategies include adolescent immunizations at community-based venues such as pharmacies and schools.

All vaccine doses should be administered according to ACIP vaccine-specific statements and with the most recent schedules for both routine and catch-up vaccination. Before leaving any visit for medical care, adolescents should be encouraged to schedule return visits for any additional vaccine doses needed. During visits that occur outside of influenza season, providers should discuss and recommend seasonal influenza vaccination and make explicit plans for vaccination, including timing and anticipated setting (e.g., health care provider's office, school, or pharmacy). Catch-up vaccination with multidose adolescent vaccines generally can occur according to the routine dosing schedule for these vaccines, although in some circumstances the clinician or health care provider might use minimum intervals for vaccine doses. These circumstances include an outbreak that increases risk for disease or the likelihood that doses will be missed in the future (e.g., because of transportation challenges). Because of lack of efficacy data for HPV vaccine administration using minimum intervals, providers are encouraged, when possible, to use routine dosing intervals for females aged 11-26 years and males aged 11-21 years who have not yet received 3 HPV vaccine doses as recommended (*3*,*4*).

One of the challenges of adolescent vaccination is ensuring that current, complete vaccination histories are available. Insurers, covered services, or reimbursement levels can change, and these changes might affect reimbursement for vaccine doses and vaccination services directly while also causing disruptions in an adolescent's access to vaccination providers or venues. In circumstances in which a vaccination record is unavailable, vaccination providers should attempt to obtain this information from various sources (e.g., parent, previous providers, or school records). More detail about how to obtain these records is available from CDC at www.cdc.gov/vaccines/hcp/admin/immuniz-records.html. With the exception of

influenza and pneumococcal polysaccharide vaccines, if documentation of a vaccine dose is not available, the adolescent should be considered unvaccinated for that dose. Regardless of the venue in which an adolescent receives a dose of vaccine, that vaccine dose should be documented in the patient's chart or in an office log, and the information should be entered into an IIS. The adolescent also should be provided with a record that documents the vaccination history.

Adult Vaccination

In 2013, the National Vaccine Advisory Committee published updated standards for adult vaccination (*12*). These standards are targeted to distinct groups involved in adult vaccination, including immunizing providers, non-immunizing providers, professional health care organizations, and public health departments. All health care providers, whether they provide immunizations or not, should incorporate immunization needs assessment into every clinical encounter, strongly recommend needed vaccine(s) and either administer vaccine(s) or refer patients to a provider who can immunize, stay up-to-date on, and educate patients about vaccine recommendations, implement systems to incorporate vaccine assessment into routine clinical care, and understand how to access immunization information systems (i.e., immunization registries) (*12*).

Vaccination rates in adults are considered suboptimal (*13*,*14*). New *Healthy People 2020* goals include specific subsets of adults, including institutionalized adults aged ≥18 years (for pneumococcal vaccines) and noninstitutionalized adults at high risk aged >18 years (for pneumococcal vaccines) (*9*).

The most substantial barrier to vaccination coverage is lack of knowledge about these vaccines among adult patients and adult providers. Other barriers are cost (incomplete Medicare coverage for recommended vaccines) (*15*) and the lack of financing mechanisms for newly licensed and recommended vaccines. Effective for private health insurance plans drafted or updated after September 2010, coverage for all immunizations that are included on the immunization schedule(s) must be covered

without deductibles or co-pays, when delivered by an in-network provider. For this reason, cost may present less of a barrier to adult vaccination as time passes.

A common challenge for health care providers is vaccinating adults with unknown vaccination records. In general (except for influenza and pneumococcal polysaccharide vaccines), adults should receive a vaccine dose if the dose is recommended and no record of previous administration exists. If an adult has a record of military service and does not have records available, providers can assume that the person has received all vaccines recommended by the military at the time of service entry. Serologic testing might be helpful in clarifying immune status if questions remain, because at different times and depending on military assignments, there might be inter-service and individual differences.

Evidence-based Interventions to Increase Vaccination Coverage

The independent, nonfederal Task Force on Community Preventive Services, whose membership is appointed by CDC, provides public health decision-makers with recommendations on population-based interventions to promote health and prevent disease, injury, disability, and premature death. The recommendations are based on systematic reviews of the scientific literature about effectiveness and cost-effectiveness of these interventions. In addition, the task force identifies critical information about the other effects of these interventions, the applicability to specific populations and settings, and the potential barriers to implementation. Additional information, including updates of published reviews, is available from *The Community Guide* at http://www.thecommunityguide.org.

Beginning in 1996, the task force systematically reviewed published evidence on the effectiveness and cost-effectiveness of population-based interventions to increase coverage of vaccines recommended for routine use among children, adolescents, and adults. A total of 197 articles were identified that evaluated a relevant intervention, met inclusion criteria, and were published during 1980-1997. Reviews of 17 specific

interventions were published in 1999 (*13*,*14*,*16*,*17*). Using the results of their review, the task force made recommendations about the use of these interventions (*15*). Several interventions were identified and recommended on the basis of published evidence. Follow-up reviews were published in 2000, and a review of interventions to improve the coverage of adults at high risk was conducted in 2005 (*15*,*17*). The interventions and the recommendations are summarized in this section of this report (Table 11-1). Interventions designated for adults younger than 65 years at high risk for influenza, invasive pneumococcal disease, and hepatitis B, include provider reminder systems or a menu of items (combinations of strategies) (Table 11-2). In 1997, the task force categorized vaccination requirements for child care, school, and college as a recommended strategy (*14*).

A 2008 update of the original task force systematic review of the evidence on the effectiveness of provider assessment and feedback for increasing coverage rates found that this strategy remains an effective intervention (*18*). This later update reviewed 19 new studies published during 1997-2007. The updated review supports the original task force recommendation for use of assessment and feedback based on strong evidence of effectiveness. The task force reviewed studies of assessment and feedback as a strategy that were conducted in a range of settings, including private practice, managed care, public health, community health settings, and academic centers. Studies have assessed the effectiveness of this intervention to improve coverage with MMR, DTP, DTaP, Hib, influenza, pneumococcal, and Td vaccines (*16*). The most updated information on this review is available at www.thecommunityguide.org/findings/vaccination-programs-provider-assessment-and-feedback. As recognized by the task force, routine assessment and feedback of vaccination rates obtained at the provider site is one of the most effective strategies for achieving high, sustainable vaccine coverage. Since 1995, all states receiving federal funds for vaccination programs have been required to conduct annual assessments of vaccination rates both in public health clinics and in private provider offices. Primarily to aid local and state health departments in their efforts to conduct assessments and assist providers, CDC has developed numerous software applications to measure vaccination rates in provider practices.

Other General Programmatic Issues

Programmatic challenges, evolving issues, and effective interventions related to adult and adolescent vaccination programs have been described by other advisory groups and expert groups. Additional evidence-based approaches are being developed for certain issues (e.g., settings for adolescent vaccination delivery) through ongoing research and evaluation. Among current programmatic challenges, vaccine financing is especially difficult because certain problems and solutions differ markedly from one state to another. Practitioners interested in beginning or continuing to provide vaccinations to patients are encouraged to consult with local and state public health vaccination programs to learn about publicly funded programs that might be available in their areas for patients who need vaccination but have insufficient health insurance coverage and no financial resources. If not already participating, providers who care for adolescents and children aged <19 years should enroll in the Vaccines for Children Program (www.cdc.gov/vaccines/hcp/admin/vfc.html). Through this program's provision of ACIP-recommended, federally purchased vaccines, participating providers are able to fully vaccinate eligible children whose parents might not otherwise be able to afford the vaccinations. Interested providers are encouraged to work with insurers, state and specialty-specific medical organizations, vaccine manufacturers, and other stakeholders to address financial barriers to achieving high vaccination coverage. With availability of safe and effective vaccines for 18 vaccine-preventable diseases, the capacity for realizing the potential benefits of these products in the United States depends on reaching children, adolescents, and adults through dedicated, knowledgeable vaccination providers and efficient, strong vaccination programs at local, state, and federal levels.

TABLE 11-1. Recommendations regarding interventions to improve coverage of vaccines recommended for routine use among children, adolescents, and adults	
Intervention	**Recommendation**
Increase community demand for vaccination	
Client reminder or recall systems	Recommended
Requirements for entry to schools, child- care facilities, and colleges	Recommended
Community education alone	Insufficient evidence
Community-based interventions implemented in combination	Recommended
Clinic-based education	Insufficient evidence
Patient or family incentives	Recommended
Patient or family monetary sanctions	Insufficient evidence
Client-held medical records	Insufficient evidence
Enhance access to vaccination services	
Reducing out-of-pocket costs	Recommended
Enhancing access through the U.S. Department of Agriculture's Women, Infants, and Children (WIC) program	Recommended
Home visits, outreach, and case management targeted to particularly hard-to-reach populations to increase vaccination rates	Recommended
Enhancing access at schools	Recommended
Expanding access in health care settings	Recommended as part of multicomponent interventions only
Enhancing access at organized child care centers	Recommended
Focus on providers	
Provider reminder or recall systems	Recommended

Provider assessment and feedback	Recommended
Standing orders	Recommended
Provider education alone	Insufficient evidence
Health care systems-based interventions integrated in combination	Recommended
Immunization information systems	Recommended
Source: www.thecommunityguide.org/topic/vaccination.	

TABLE 11-2. Strategies to improve influenza, pneumococcal polysaccharide, and hepatitis B vaccine coverage among high-risk adults younger than 65 years	
One or both of these interventions to improve access to vaccination services	1. Expanded access in health care settings 2. Reducing client out-of-pocket costs
PLUS: One or more of these provider or system based interventions	1. Standing orders 2. Provider reminder systems 3. Provider assessment or feedback
AND/OR: One or both of these interventions to increase client demand for vaccination services	1. Client reminder systems 2. Client education

Source (15)

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12. Vaccine Information Sources

In addition to these general recommendations, the following sources contain specific and updated vaccine information.

CDC-INFO Contact Center

The CDC-INFO contact center is supported by CDC and provides public health-related information, including vaccination information, for health care providers and the public, 24 hours a day, 7 days a week. To contact CDC-INFO online at any time, visit wwwn.cdc.gov/dcs/RequestForm.aspx. To contact CDC-INFO by telephone, call between 8 am to 8 pm Eastern Time Monday through Friday at [English and Spanish]: 800-232-4636; telephone [TTY]: 800-232-6348.

CDC's National Center for Immunization and Respiratory Diseases

CDC's National Center for Immunization and Respiratory Diseases website provides direct access to ACIP's best practices for vaccination guidance, vaccination schedules, automated child schedulers, an adult immunization scheduler, vaccine safety information, publications, provider education and training, and links to other vaccination-related websites (www.cdc.gov/vaccines/hcp/admin/immuniz-records.html).

Morbidity and Mortality Weekly Report (MMWR)

Some ACIP guidance regarding vaccine use, statements of vaccine policy as they are developed, and reports of specific disease activity are published by CDC in the *MMWR* series and can be found at www.cdc.gov/vaccines/hcp/acip-recs/index.html. Electronic subscriptions are free (www.cdc.gov/mmwr/mmwrsubscribe.html). Subscriptions to print versions also are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402-9235 (telephone: 202-512-1800).

American Academy of Family Physicians (AAFP)

Information from the professional organization of family physicians is available at www.aafp.org/home.html.

American Academy of Pediatrics (AAP)

Every 3 years, AAP issues the *Red Book: Report of the Committee on Infectious Diseases*, which contains a composite summary of AAP and ACIP recommendations concerning infectious diseases and vaccinations for infants, children, and adolescents (telephone: 888-227-1770; website: www.aap.org/en-us/Pages/Default.aspx).

American College of Physicians (ACP)

Produced by faculty of ACP's Quality Improvement Programs and members of the ACP Adult Immunization Advisory Board, the ACP Guide to Adult Immunization helps internists develop systematic processes for incorporating immunization in their day-to-day practice (see www.acponline.org/).

American Congress of Obstetricians and Gynecologists (ACOG)

The American Congress of Obstetricians and Gynecologists (ACOG), formerly the American College of Obstetricians and Gynecologists, is a professional association of physicians specializing in obstetrics and gynecology in the United States. Information about ACOG can be found at www.acog.org.

American Pharmacists Association (APhA)

Founded in 1852, APhA is the largest association of pharmacists in the United States, with more than 62,000 practicing pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians as members. Information about APhA educational activities can be found at www.pharmacist.com/immunization-center.

Group on Immunization Education of the Society of Teachers of Family Medicine

The Group on Immunization Education of the Society of Teachers of Family Medicine provides information for clinicians, including the free program Shots. Shots includes the childhood, adolescent, and adult schedules for iPhone, Palm, and Windows devices, as well as online versions (http://www.immunizationed.org/).

Immunization Action Coalition (IAC)

IAC provides child, teen, and adult immunization information for health care professionals and their patients at www.immunize.org. Free materials include CDC-reviewed technical pieces, patient handouts, VISs in multiple languages, and the weekly immunization news and information service "IAC Express," available at www.immunize.org/express. Information for the general public about vaccines and vaccine-preventable diseases is available at www.vaccineinformation.org.

Institute for Vaccine Safety

Located at the Johns Hopkins University School of Public Health, the Institute for Vaccine Safety provides information about vaccine safety concerns and objective and timely information to physicians and health care providers and parents. The Institute for Vaccine Safety also includes links to tables that include all vaccine components (www.vaccinesafety.edu).

State and Local Health Departments

State and local health departments provide technical advice through hotlines, e-mail, and websites, including printed information regarding vaccines and immunization schedules, posters, and other educational materials (see www.cdc.gov/vaccines/imz-managers/awardee-imz-websites.html and www.cdc.gov/mmwr/international/relres.html).

Vaccine Education Center

Located at the Children's Hospital of Philadelphia, the Vaccine Education Center provides patient and provider vaccine information (www.chop.edu/centers-programs/vaccine-education-center).

Appendix 1: Glossary

Adverse event. An untoward event that occurs after a vaccination that might be caused by the vaccine product or vaccination process. Adverse events include those that have the following characteristics: 1) vaccine induced (caused by the intrinsic characteristic of the vaccine preparation and the individual response of the vaccinee): these events would not have occurred without vaccination (e.g., vaccine-associated paralytic poliomyelitis); 2) vaccine potentiated: the events would have occurred anyway but were precipitated by the vaccination (e.g., first febrile seizure in a predisposed child); 3) programmatic error: the event was caused by technical errors in vaccine preparation, handling, or administration; and 4) coincidental: the event was associated temporally with vaccination by chance or caused by underlying illness. Special studies are needed to determine whether an adverse event is a reaction to the vaccine or the result of another cause. **Sources:** Chen RT. Special methodological issues in pharmacoepidemiology studies of vaccine safety. In: Strom BL, ed. *Pharmacoepidemiology*. 3rd ed. Sussex, England: John Wiley & Sons; 2000:707-732; and Fenichel GM, Lane DA, Livengood JR, Horwitz SJ, Menkes JH, Schwartz JF. Adverse events following immunization: assessing probability of causation. *Pediatr Neurol.* 1989;5:287--90.

Adverse reaction. An undesirable medical condition that has been demonstrated to be caused by a vaccine. Evidence for the causal relation is usually obtained through randomized clinical trials, controlled epidemiologic studies, isolation of the vaccine strain from the pathogenic site, or recurrence of the condition with repeated vaccination (i.e., rechallenge); synonyms include side effect and adverse effect.

Adjuvant. A vaccine component distinct from the antigen that enhances the immune response to the antigen.

Antitoxin. A solution of antibodies against a toxin. Antitoxin can be derived from either human (e.g., tetanus immune globulin) or animal (usually equine) sources (e.g.,

diphtheria and botulism antitoxin). Antitoxins are used to confer passive immunity and for treatment.

Hyperimmune globulin (specific). Special preparations obtained from blood plasma from donor pools preselected for a high antibody content against a specific antigen (e.g., hepatitis B immune globulin, varicella-zoster immune globulin, rabies immune globulin, tetanus immune globulin, vaccinia immune globulin, cytomegalovirus immune globulin, botulism immune globulin).

Immune globulin. A sterile solution containing antibodies, which are usually obtained from human blood. It is obtained by cold ethanol fractionation of large pools of blood plasma and contains 15%-18% protein. Intended for intramuscular administration, immune globulin is primarily indicated for routine maintenance of immunity among certain immunodeficient persons and for passive protection against measles and hepatitis A.

Immunobiologic. Antigenic substances (e.g., vaccines and toxoids) or antibody-containing preparations (e.g., globulins and antitoxins) from human or animal donors. These products are used for active or passive immunization or therapy. Examples of immunobiologics include antitoxin, immune globulin and hyperimmune globulin, monoclonal antibodies, toxoids, and vaccines.

Intravenous immune globulin. A product derived from blood plasma from a donor pool similar to the immune globulin pool, but prepared so that it is suitable for intravenous use. Intravenous immune globulin is used primarily for replacement therapy in primary antibody-deficiency disorders, for treatment of Kawasaki disease, immune thrombocytopenic purpura, hypogammaglobulinemia in chronic lymphocytic leukemia, and certain cases of human immunodeficiency virus infection (Table 3-5).

Monoclonal antibody. An antibody product prepared from a single lymphocyte clone, which contains only antibody against a single antigen.

Simultaneous. In the context of vaccine timing and spacing, occurring on the same clinic day, at different anatomic sites, and not combined in the same syringe.

Toxoid. A modified bacterial toxin that has been made nontoxic, but retains the ability to stimulate the formation of antibodies to the toxin.

Vaccination and immunization. The terms vaccine and vaccination are derived from *vacca*, the Latin term for cow. Vaccine was the term used by Edward Jenner to describe material used (i.e., cowpox virus) to produce immunity to smallpox. The term vaccination was used by Louis Pasteur in the 19th century to include the physical act of administering any vaccine or toxoid. Immunization is a more inclusive term, denoting the process of inducing or providing immunity by administering an immunobiologic. Immunization can be active or passive. Active immunization is the production of antibody or other immune responses through administration of a vaccine or toxoid. Passive immunization means the provision of temporary immunity by the administration of preformed antibodies. Although persons often use the terms vaccination and immunization interchangeably in reference to active immunization, the terms are not synonymous because the administration of an immunobiologic cannot be equated automatically with development of adequate immunity.

Vaccine. A suspension of live (usually attenuated) or inactivated microorganisms (e.g., bacteria or viruses) or fractions thereof administered to induce immunity and prevent infectious disease or its sequelae. Some vaccines contain highly defined antigens (e.g., the polysaccharide of *Haemophilus influenzae* type b or the surface antigen of hepatitis B); others have antigens that are complex or incompletely defined (e.g., *Bordetella pertussis* antigens or live, attenuated viruses).

Appendix 2: Membership

Advisory Committee on Immunization Practices

Membership List, October 2014

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