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General Recommendations on Immunization Recommendations of the Advisory Committee on Immunization Practices (ACIP)



INSIDE: Continuing Education Examination

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION**

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CONTENTS

Introduction	1
Timing and Spacing of Immunobiologics	2
Contraindications and Precautions	9
Vaccine Administration	14
Storage and Handling of Immunobiologics	20
Altered Immunocompetence	24
Special Situations	29
Vaccination Records	36
Reporting Adverse Events after Vaccination	36
Vaccination Programs	38
Vaccine Information Sources	39
Acknowledgments	40
References	40
Abbreviations Used in This Publication	46
Definitions Used in This Report	46
Continuing Education Activity	CE-1

Disclosure of Relationship

CDC, our planners, and our presenters wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

This report will not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of the discussion of:

1. The nonsimultaneous administration of yellow fever vaccine and inactivated vaccines.
2. Progressive neurologic disorders are a precaution for the use of tetanus-reduced diphtheria acellular pertussis vaccine for adolescents and adults.
3. Contact allergy to latex is neither a contraindication nor a precaution to the use of meningococcal vaccine in the absence of an anaphylactic allergy.
4. Meningococcal conjugate vaccine should be administered intramuscularly, but if administered subcutaneously, repeating the dose is unnecessary.
5. Use of immune globulin, intravenous for postexposure prophylaxis or varicella.
6. Use of VariZIG for postexposure prophylaxis of varicella (unlicensed).

General Recommendations on Immunization

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

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Summary

This report is a revision of General Recommendations on Immunization and updates the 2002 statement by the Advisory Committee on Immunization Practices (ACIP) (CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices and the American Academy of Family Physicians. MMWR 2002;51[No. RR-2]). This report is intended to serve as a general reference on vaccines and immunization. The principal changes include 1) expansion of the discussion of vaccination spacing and timing; 2) an increased emphasis on the importance of injection technique/age/body mass in determining appropriate needle length; 3) expansion of the discussion of storage and handling of vaccines, with a table defining the appropriate storage temperature range for inactivated and live vaccines; 4) expansion of the discussion of altered immunocompetence, including new recommendations about use of live-attenuated vaccines with therapeutic monoclonal antibodies; and 5) minor changes to the recommendations about vaccination during pregnancy and vaccination of internationally adopted children, in accordance with new ACIP vaccine-specific recommendations for use of inactivated influenza vaccine and hepatitis B vaccine. The most recent ACIP recommendations for each specific vaccine should be consulted for comprehensive discussion. This report, ACIP recommendations for each vaccine, and other information about vaccination can be accessed at CDC's National Center for Immunization and Respiratory Diseases (proposed) (formerly known as the National Immunization Program) website at <http://www.cdc.gov/nip>.

Introduction

This report provides technical guidance about common vaccination concerns for clinicians and other health-care providers who administer vaccines to infants, children, adolescents, and adults. Vaccine recommendations are based on characteristics of the immunobiologic product, scientific knowledge about the principles of active and passive immunization, epidemiology and burden of diseases (i.e., morbidity, mortality, costs of treatment, and loss of productivity), vaccine safety considerations, cost analysis of preventive measures, published and unpublished studies, and expert opinion of public health officials and specialists in clinical and preventive medicine.

Benefits and risks are associated with using all immunobiologics (i.e., an antigenic substance or antibody-containing preparation). No vaccine is completely safe or effective. Benefits of vaccination include partial or complete protection against infection for the vaccinated person and overall benefits to society as a whole. Benefits include protection from symptomatic illness, improved quality of life and productivity, and prevention of death. Societal benefits include creation and maintenance of herd immunity against communicable diseases, prevention of disease outbreaks, and reduction in health-care–related costs. Vaccination risks range from common, minor, and local adverse effects to rare, severe, and life-threatening conditions. Therefore, recommendations for vaccination practices balance scientific evidence of benefits for each person and to society against the potential costs and risks for vaccination for the individual and programs.

Standards for child and adolescent vaccination practices and standards for adult vaccination practices (1,2) have been published to assist with implementing vaccination programs and maximizing their benefits. Any person or institution that provides vaccination services should adopt these standards to improve vaccination delivery and protect infants, children, adolescents, and adults from vaccine-preventable diseases.

The material in this report was prepared for publication by the National Center for Immunization and Respiratory Diseases, Anne Schuchat, MD, Director; and the Immunization Services Division, Lance E. Rodewald, MD, Director.

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To maximize the benefits of vaccination, this report provides general information about immunobiologics and provides practical guidelines about vaccine administration and technique. To minimize risk from vaccine administration, this report delineates situations that warrant precautions or contraindications to using a vaccine. These recommendations are intended for use in the United States because vaccine availability and use and epidemiologic circumstances differ in other countries. Individual circumstances might warrant deviations from these recommendations.

The relative balance of benefits and risks can change as diseases are controlled or eradicated. For example, because wild poliovirus transmission has been interrupted in the United States since 1979, the only indigenous cases of paralytic poliomyelitis reported since that time have been caused by live oral poliovirus vaccine (OPV) (3). In 1999, to eliminate the risk for vaccine-associated paralytic poliomyelitis (VAPP), exclusive use of inactivated poliovirus vaccine (IPV) was recommended for routine vaccination in the United States. However, because of superior ability to induce intestinal immunity and to prevent spread among close contacts, OPV remains the vaccine of choice for areas where wild poliovirus is still present (4). Until worldwide eradication of poliovirus is accomplished, continued vaccination of the U.S. population against poliovirus will be necessary.

Timing and Spacing of Immunobiologics

General Principles for Vaccine Scheduling

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

Certain products, including inactivated vaccines, toxoids, recombinant subunit, and polysaccharide conjugate vaccines, require administering 2 or more doses for development of an adequate and persisting antibody response. Tetanus and diphtheria toxoids require periodic reinforcement or booster doses to maintain protective antibody concentrations. Unconjugated polysaccharide vaccines do not induce T-cell memory, and booster doses are not expected to produce substantially in-

creased protection. Conjugation with a protein carrier improves the effectiveness of polysaccharide vaccines by inducing T-cell-dependent immunologic function. Vaccines that stimulate both cell-mediated immunity and neutralizing antibodies (e.g., live-attenuated virus vaccines) usually can induce prolonged immunity, even if antibody titers decline over time (5). Subsequent exposure to infection usually does not lead to viremia but to a rapid anamnestic antibody response.

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) have protective antibody (generally within 2 weeks of the dose). For varicella and mumps vaccines, 80%–85% of vaccinees are protected after a single dose. However, because a limited proportion of recipients (5%–15%) of measles-mumps-rubella (MMR) or varicella vaccine fail to respond to 1 dose, a second dose is recommended to provide another opportunity to develop immunity (6). The majority of persons who fail to respond to the first dose of MMR or varicella vaccine respond to a second dose (7,8).

The Recommended Childhood and Adolescent Immunization Schedule 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's National Center for Immunization and Respiratory Diseases (proposed) website (<http://www.cdc.gov/nip>).

Spacing of Multiple Doses of the Same Antigen

Vaccination providers should adhere as closely as possible to recommended vaccination schedules. Recommended ages and intervals between doses of multidose antigens provide optimal protection or have the best evidence of efficacy. Recommended vaccines and recommended intervals between doses are provided in this report (Table 1).

In certain circumstances, administering doses of a multidose vaccine at shorter than the recommended intervals might be necessary. This can occur when a person is behind schedule and needs to be brought up-to-date as quickly as possible or when international travel is impending. In these situations, an accelerated schedule can be implemented that uses intervals between doses shorter than those recommended for routine vaccination. Although the effectiveness of all accelerated schedules has not been evaluated in clinical trials, ACIP believes that when accelerated intervals are used, the immune response is acceptable and will lead to adequate protection. The accelerated or minimum intervals and ages that can be used for scheduling catch-up vaccinations are provided in this report (Table 1). Vaccine doses should not be administered at

TABLE 1. Recommended and minimum ages and intervals between vaccine doses of routinely recommended vaccines*

Vaccine and dose no.	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
Hepatitis B (HepB)-1 [†]	Birth	Birth	1–4 months	4 weeks
HepB-2	1–2 months	4 weeks	2–17 months	8 weeks
HepB-3 [§]	6–18 months	24 weeks	—	—
Diphtheria-tetanus-acellular pertussis (DTaP)-1 [†]	2 months	6 weeks	2 months	4 weeks
DTaP-2	4 months	10 weeks	2 months	4 weeks
DTaP-3	6 months	14 weeks	6–12 months [¶]	6 months ^{¶**}
DTaP-4	15–18 months	12 months	3 years	6 months [¶]
DTaP-5	4–6 years	4 years	—	—
<i>Haemophilus influenzae</i> type b (Hib)-1 ^{†,††}	2 months	6 weeks	2 months	4 weeks
Hib-2	4 months	10 weeks	2 months	4 weeks
Hib-3 ^{§§}	6 months	14 weeks	6–9 months [¶]	8 weeks
Hib-4	12–15 months	12 months	—	—
Inactivated poliovirus (IPV)-1 [†]	2 months	6 weeks	2 months	4 weeks
IPV-2	4 months	10 weeks	2–14 months	4 weeks
IPV-3	6–18 months	14 weeks	3–5 years	4 weeks
IPV-4	4–6 years	18 weeks	—	—
Pneumococcal conjugate (PCV)-1 ^{††}	2 months	6 weeks	2 months	4 weeks
PCV-2	4 months	10 weeks	2 months	4 weeks
PCV-3	6 months	14 weeks	6 months	8 weeks
PCV-4	12–15 months	12 months	—	—
Measles-mumps-rubella (MMR)-1 ^{¶¶}	12–15 months	12 months	3–5 years	4 weeks
MMR-2 ^{¶¶}	4–6 years	13 months	—	—
Varicella (Var)-1 ^{¶¶}	12–15 months	12 months	3–5 years	12 weeks ^{***}
Var-2 ^{¶¶}	4–6 years	15 months	—	—
Hepatitis A (HepA)-1 [†]	12–23 months	12 months	6–18 months [¶]	6 months [¶]
HepA-2	18–41 months	18 months	—	—
Influenza inactivated ^{†††}	6–59 months	6 months ^{§§§}	1 month	4 weeks
Influenza live attenuated ^{†††}	—	5 years	6–10 weeks	6 weeks
Meningococcal conjugate [†]	11–12 years	11 years	—	—
Meningococcal polysaccharide (MPSV)-1	—	2 years	5 years ^{§§§}	5 years ^{¶¶¶}
MPSV-2 ^{****}	—	7 years	—	—
Tetanus-diphtheria	11–12 years	7 years	10 years	5 years
Tetanus-diphtheria acellular pertussis (Tdap) ^{††††}	≥11 years	10 years	—	—
Pneumococcal polysaccharide (PPV)-1	—	2 years	5 years	5 years
PPV-2 ^{§§§§}	—	7 years	—	—
Human papillomavirus (HPV)-1 ^{¶¶¶¶}	11–12 years	9 years	2 months	4 weeks
HPV-2	11–12 years (+2 months)	109 months	4 months	12 weeks
HPV-3	11–12 years (+6 months)	112 months	—	—
Rotavirus (RV)-1 ^{*****}	2 months	6 weeks	2 months	4 weeks
RV-2	4 months	10 weeks	2 months	4 weeks
RV-3	6 months	14 weeks	—	—
Zoster ^{†††††}	60 years	60 years	—	—

* Combination vaccines are available. Use of licensed combination vaccines is preferred over separate injections of their equivalent component vaccines (Source: CDC. Combination vaccines for childhood immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP). MMWR 1999;48[No. RR-5]). 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.

TABLE 1. (Continued) Recommended and minimum ages and intervals between vaccine doses of routinely recommended vaccines*

Vaccine and dose no.	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
†	Combination vaccines containing the Hepatitis B component are available (HepB-Hib, DTaP-HepB-IPV, and HepA-HepB). These vaccines should not be administered to infants aged <6 weeks because of the other components (i.e., Hib, DTaP, HepA, and IPV).			
§	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.			
¶	Calendar months.			
**	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.			
††	For Hib and PCV, children receiving the first dose of vaccine at age ≥7 months require fewer doses to complete the series (CDC. Recommended childhood and adolescent immunization schedule—United States, 2006. MMWR 2005; 54 [Nos. 51 & 52]:Q1-Q4).			
§§	If PRP-OMP (Pedvax-Hib®, Merck Vaccine Division) was administered at age 2 and 4 months, a dose at age 6 months is not required.			
¶¶	Combination measles-mumps-rubella-varicella (MMRV) vaccine can be used for children aged 12 months–12 years.			
***	The minimum interval from VAR-1 to VAR-2 for persons beginning the series at age ≥13 years is 4 weeks.			
†††	Two doses of influenza vaccine are recommended for children aged <9 years who are receiving the vaccine for the first time. Children aged <9 years who have previously received influenza vaccine, and persons aged ≥9 years require only 1 dose per influenza season.			
§§§	The minimum age for inactivated influenza vaccine varies by vaccine manufacturer. Only Fluzone (manufactured by sanofi pasteur) is approved for children aged 6–35 months. The minimum age for Fluvirin (manufactured by Novartis) is 4 years. For Fluarix and FluLevel (manufactured by GlaxoSmithKline), the minimum age is 18 years.			
¶¶¶	Certain experts recommend a second dose of MPSV 3 years after the first dose for persons at increased risk for meningococcal disease.			
****	A second dose of meningococcal vaccine is recommended for persons previously vaccinated with MPSV who remain at high risk for meningococcal disease. MCV4 is preferred when revaccinating persons aged 11–55 years, but a second dose of MPSV is acceptable. (Source: CDC. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2005;54[No. RR-7]).			
††††	Only 1 dose of Tdap is recommended. Subsequent doses should be administered as Td. If vaccination to prevent tetanus and/or diphtheria disease is required for children aged 7–9 years, Td should be administered (minimum age for Td is 7 years). For one brand of Tdap, the minimum age is 11 years. The preferred interval between Tdap and a previous dose of Td is 5 years. In persons who have received a primary series of tetanus-toxoid-containing vaccine, for management of a tetanus-prone wound, the minimum interval after a previous dose of any tetanus-containing vaccine is 5 years.			
§§§§	A second dose of PPV is recommended for persons at highest risk for serious pneumococcal infection and those who are likely to have a rapid decline in pneumococcal antibody concentration. Revaccination 3 years after the previous dose can be considered for children at highest risk for severe pneumococcal infection who would be aged <10 years of age at the time of revaccination. (Source: CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1997;46[No. RR-8]).			
¶¶¶¶	HPV is approved only for females aged 9–26 years.			
*****	The first dose of RV must be administered at age 6–12 weeks. The vaccine series should not be started at age ≥13 weeks. RV should not be administered to children aged ≥33 weeks regardless of the number of doses received at age 6–32 weeks.			
†††††	Herpes zoster vaccine is approved as a single dose for persons who are aged ≥60 years with a history of varicella.			

intervals less than these minimum intervals or earlier than the minimum age.*

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 limited number of days earlier than the minimum interval or age is unlikely to have a substantially negative effect on the immune response to that dose. Therefore, ACIP recommends that vaccine doses administered 4 or fewer days before the minimum interval or age be counted as valid.† However, because of its unique sched-

*During measles outbreaks, if cases are occurring among infants aged <12 months, measles vaccination of infants as young as 6 months can be undertaken as an outbreak control measure. However, doses administered at ages <12 months should not be counted as part of the series (Source: CDC. Measles, mumps, and rubella vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1998;47[No. RR-8]).

†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.

ule, this recommendation does not apply to the rabies vaccine (9). Doses administered 5 or more days earlier than the minimum interval or age of any vaccine 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 1). For example, if *Haemophilus influenzae* type b (Hib) doses one and two were administered only 2 weeks apart, because the minimum interval from dose one to dose two is 4 weeks, dose two is invalid and should be repeated. The repeat dose should be administered 4 or more weeks after the invalid (second) dose. The repeat dose would be counted as the second valid dose. Doses administered 5 or more days before the minimum age should be repeated on or after the child reaches the minimum age and 4 or more weeks after the invalid dose. For example, if the first dose of varicella vaccine were administered at age 10 months, the repeat dose would be administered no earlier than the child's first birthday. If the first dose of varicella vaccine were administered at age 11 months and 2 weeks, the repeat dose could be administered 2 weeks after the first birthday.

Certain vaccines produce increased rates of local or systemic reactions in certain recipients when administered too frequently (e.g., adult tetanus-diphtheria toxoid [Td]; pedi-

atric diphtheria-tetanus toxoid [DT]; tetanus toxoid; and tetanus, reduced diphtheria acellular pertussis vaccine for adolescents and adults) (10,11). Such reactions might result from formation of antigen-antibody complexes. Optimal record keeping, maintaining patient histories, and adhering to recommended schedules can decrease the incidence of such reactions without adversely affecting immunity.

Simultaneous Administration

Experimental evidence and extensive clinical experience provide the scientific basis for administering vaccines simultaneously (i.e., during the same office visit, not combined in the same syringe). Simultaneously administering all vaccines for which a person is eligible is critical, including for childhood vaccination programs, because simultaneous administration increases the probability that a child will be vaccinated fully at the appropriate age (1). A study conducted during a measles outbreak demonstrated that approximately one third of measles cases among unvaccinated but vaccine-eligible preschool children could have been prevented if MMR had been administered at the same visit when another vaccine was administered (12). Simultaneous administration also is critical when preparing for foreign travel and/or if uncertainty exists that a person will return for further doses of vaccine.

Simultaneously administering the most widely used live and inactivated vaccines have produced seroconversion rates and rates for adverse reactions similar to those observed when the vaccines are administered separately (13–16). Routinely administering all age-appropriate doses of vaccines simultaneously is recommended for children for whom no specific contraindications exist at the time of the visit. Administering combined MMR (or measles-mumps-rubella-varicella [MMRV] vaccine) yields safety and immunogenicity results similar to administering individual measles, mumps, and rubella vaccines at different sites. Therefore, no medical basis exists for administering these vaccines separately for routine vaccination instead of the preferred MMR combined vaccine (6). Administering separate antigens would result in a delay in protection for the deferred components. Response to MMR and varicella vaccines administered on the same day is identical to vaccines administered a month apart (17), and administration of MMRV combined vaccine is similar to administration of MMR and varicella vaccines on the same day (18). No evidence exists that oral rotavirus vaccine (RV) interferes with live vaccines administered by injection or intranasally (e.g., MMR and live-attenuated influenza vaccine [LAIV]). RV can be administered simultaneously or at any interval before or after injectable or intranasal live vaccines (19). No data exist about the immunogenicity of oral Ty21a

typhoid vaccine when administered concurrently or within 30 days of other live virus vaccines. In the absence of such data, if typhoid vaccination is warranted, administration should not be delayed because of administration of live-attenuated virus vaccines (20).

Simultaneously administering pneumococcal polysaccharide vaccine (PPV) and inactivated influenza vaccine elicits a satisfactory antibody response without increasing the incidence or severity of adverse reactions (21). Simultaneously administering PPV and inactivated influenza vaccine is recommended for all persons for whom both vaccines are indicated.

Hepatitis B vaccine (HepB) administered with yellow fever vaccine is as safe and immunogenic as when these vaccines are administered separately (22). Measles and yellow fever vaccines have been administered safely at the same visit and without reduction of immunogenicity of each of the components (23,24).

Depending on vaccines administered in the first year of life, children aged 12–15 months might receive up to nine injections during a single visit (MMR, varicella, Hib, pneumococcal conjugate, diphtheria and tetanus toxoids and acellular pertussis [DTaP], IPV, hepatitis A, HepB, and influenza [seasonal] vaccines). To reduce the number of injections at the 12–15-month visit, the IPV and HepB series can be expedited and completed before the child's first birthday. MMRV can be administered as soon as possible on or after the first birthday and the fourth dose of DTaP administered at age 15 months. The majority of children aged 1 year who have received 2 (polyribosylribitol phosphate-meningococcal outer membrane protein [PRP-OMP]) or 3 (PRP-tetanus [PRP-T], diphtheria CRM197 [CRM, cross-reactive material] protein conjugate [HbOC]) previous doses of Hib vaccine and 3 previous doses of DTaP and pneumococcal conjugate vaccine (PCV) have had protection (25,26). The third (PRP-OMP) or fourth (PRP-T, HbOC) dose of the Hib series, and the fourth doses of DTaP and PCV are critical in boosting antibody titer and ensuring continued protection (26–29). However, the booster dose of the pneumococcal conjugate series can be deferred until age 15–18 months for children who are likely to return for future visits. The fourth dose of DTaP is recommended at age 15–18 months but can be administered as early as age 12 months under certain circumstances (27). For infants at low risk for infection with hepatitis B virus (i.e., the mother tested negative for hepatitis B surface antigen [HBsAg] at the time of delivery), the HepB series can be completed at any time for children aged 6–18 months. With use of certain HepB combination vaccines (i.e., combination Hib-HepB vaccine), the minimum age of administration of the final dose is 12 months because of the minimum age requirement for the last dose of the Hib series (30). Recommended spacing of doses should be maintained (Table 1).

Use of combination vaccines can reduce the number of injections required at an office visit. 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 licensed combination vaccines is preferred to separate injection of their equivalent component vaccines to reduce the number of injections and missed opportunities to protect through vaccination (31). Only combination vaccines licensed by FDA should be used. Individual vaccines should never be mixed in the same syringe unless they are approved specifically for mixing by FDA. Only one vaccine (DTaP and PRP-T Hib vaccine, marketed as TriHIBit[®] [manufactured by sanofi pasteur]) is licensed by FDA for mixing in the same syringe. This vaccine should not be used for primary vaccination in infants aged 2, 4, and 6 months, but it can be used as the last dose of the Hib vaccine series on or after age 12 months.

Nonsimultaneous Administration

No evidence exists that inactivated vaccines interfere with the immune response to other inactivated vaccines or to live vaccines. An inactivated vaccine can be administered either simultaneously or at any time before or after a different inactivated vaccine or live vaccine (Table 2).

Data are limited about interference between live vaccines. The immune response to one live-virus vaccine might be impaired if administered within 30 days of another live-virus vaccine (32,33). In a study conducted in two U.S. health maintenance organizations, persons who received varicella vaccine <30 days after MMR vaccination had an increased risk for varicella vaccine failure (i.e., varicella disease in a vaccinated person) of 2.5-fold compared with persons who re-

TABLE 2. Guidelines for spacing of live and inactivated antigens

Antigen combination	Recommended minimum interval between doses
Two or more inactivated*	Can be administered simultaneously or at any interval between doses
Inactivated and live	Can be administered simultaneously or at any interval between doses
Two or more live intranasal or injectable†	4-week minimum interval, if not administered simultaneously

* Certain experts suggest a 1-month interval between tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis vaccine and quadrivalent meningococcal conjugate vaccine if they are not administered simultaneously.

† Live oral vaccines (e.g., Ty21a typhoid vaccine and rotavirus vaccine) can be administered simultaneously or at any interval before or after inactivated or live injectable vaccines.

Source: American Academy of Pediatrics. Pertussis. In: Pickering LK, Baker, CJ, Long SS, McMillan J, eds., Red Book: 2006 Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics.

ceived varicella vaccine before or >30 days after MMR (34). In comparison, another study determined that the response to yellow fever vaccine is not affected by monovalent measles vaccine administered 1–27 days earlier (23). The effect of nonsimultaneously administering rubella, mumps, varicella, and yellow fever vaccines is unknown.

To minimize the potential risk for interference, injectable or nasally administered live vaccines not administered on the same day should be administered >4 weeks apart whenever possible (Table 2). If injectable or nasally administered live vaccines are separated by <4 weeks, the vaccine-administered second should not be counted as a valid dose and should be repeated. The repeat dose should be administered >4 weeks after the last invalid dose. Yellow fever vaccine can be administered at any time after single-antigen measles vaccine. Oral vaccines (Ty21a typhoid vaccine and RV) can be administered simultaneously or at any interval before or after other live vaccines (injectable or intranasal) if indicated.

Spacing of Vaccines and Antibody-Containing Products

Live Vaccines

Ty21a typhoid, yellow fever, and LAIV vaccines can be administered at any time before, concurrent with, or after administering any immune globulin, hyperimmune globulin, or intravenous immune globulin (IGIV). 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 or more months. The effect of blood and immune globulin preparations on the response to mumps and varicella vaccines is unknown, but 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 vaccine virus. The length of time that interference with injectable live vaccination (except yellow fever vaccine) can persist after the antibody-containing product is a function of the amount of antigen-specific antibody contained in the product (35–37). Therefore, after an antibody-containing product is received, live vaccines (except yellow fever vaccine, oral Ty21a typhoid vaccine, and LAIV) should be delayed until the passive antibody has degraded (Table 3). If a dose of injectable live-virus vaccine (except yellow fever vaccine) 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 vac-

TABLE 3. Guidelines for administering antibody-containing products* and vaccines

Simultaneous administration		
Combination		Recommended minimum interval between doses
Antibody-containing products and inactivated antigen		Can be administered simultaneously at different sites or at any time interval between doses.
Antibody-containing products and live antigen		Should not be administered simultaneously. [†] 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.
Nonsimultaneous administration		
Product administered		Recommended minimum interval between doses
First	Second	
Antibody-containing products	Inactivated antigen	Not applicable
Inactivated antigen	Antibody-containing products	Not applicable
Antibody-containing products	Live antigen	Dose-related ^{†,§,¶}
Live antigen	Antibody-containing products	2 weeks [†]

*Blood products containing substantial amounts of immunoglobulin include intramuscular 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 cells, plasma, and platelet products.

[†]Yellow fever, oral Ty21a typhoid vaccine, and live-attenuated influenza vaccine are exceptions to these recommendations. These live-attenuated vaccines can be administered at any time before, after, or simultaneously with an antibody-containing product without substantially decreasing the antibody response.

[§]Rotavirus vaccine (RV) should be deferred for 6 weeks after receipt of an antibody-containing product if possible. However, if the 6-week deferral would cause the first dose of RV to be scheduled for age ≥ 13 weeks, a shorter deferral interval should be used to ensure the first dose of RV is administered no later than age 13 weeks.

[¶]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.

cine. The repeat dose or serologic testing should be performed after the interval indicated for the antibody-containing product (Table 4).

Although passively acquired antibodies can interfere with the response to rubella vaccine, the low dose of anti-Rho(D) globulin administered to postpartum women has not been demonstrated to reduce the response to the RA27/3 strain rubella vaccine (38). Because of the importance of rubella and varicella immunity among childbearing-aged women (6,39), the postpartum vaccination of women without evidence of immunity to rubella or varicella with single-antigen rubella, MMR, varicella, or MMRV vaccine 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. These women should be vaccinated immediately after delivery and, if possible, tested 3 or more months later to ensure immunity to rubella and, if appropriate, to measles (6).

Interference can occur if administering an antibody-containing product becomes necessary after administering MMRV or its individual components. Usually, vaccine virus replication and stimulation of immunity will occur 1–2 weeks after vaccination. If the interval between administering 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 and 4), unless serologic testing indicates an antibody response. RV

should be deferred for 6 weeks after receipt of an antibody-containing product if possible. However, if the 6-week deferral would cause the first dose of RV to be scheduled for a child aged ≥ 13 weeks, a shorter deferral interval should be used to ensure the first dose of RV is administered no later than age 13 weeks (19).

A humanized mouse monoclonal antibody product (palivizumab) is available for prevention of respiratory syncytial virus infection among infants and young children. This product contains only antibody to respiratory syncytial virus and will not interfere with immune response to currently licensed live or inactivated vaccines.

Inactivated Vaccines

Antibody-containing products interact less with inactivated vaccines, toxoids, recombinant subunit, and polysaccharide vaccines than with live vaccines (40). 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). The vaccine or toxoid and antibody preparation should be administered at different sites by using the standard recommended dose. Increasing the vaccine dose volume or number of vaccinations is not indicated or recommended.

TABLE 4. Suggested intervals between administration of antibody-containing products for different indications and measles-containing vaccine and varicella-containing vaccine*

Product/indication	Dose, including mg immunoglobulin G (IgG)/kg body weight*	Recommended interval before measles or varicella-containing vaccine administration (months)
Respiratory syncytial virus immune globulin (IG) monoclonal antibody (Synagis™)†	15 mg/kg intramuscularly (IM)	None
Tetanus IG	250 units (10 mg IgG/kg) IM	3
Hepatitis A IG		
Contact prophylaxis	0.02 mL/kg (3.3 mg IgG/kg) IM	3
International travel	0.06 mL/kg (10 mg IgG/kg) IM	3
Hepatitis B IG	0.06 mL/kg (10 mg IgG/kg) IM	3
Rabies IG	20 IU/kg (22 mg IgG/kg) IM	4
Measles prophylaxis IG		
Standard (i.e., nonimmunocompromised) contact	0.25 mL/kg (40 mg IgG/kg) IM	5
Immunocompromised contact	0.50 mL/kg (80 mg IgG/kg) IM	6
Blood transfusion		
Red blood cells (RBCs), washed	10 mL/kg negligible IgG/kg intravenously (IV)	None
RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	3
Packed RBCs (hematocrit 65%)§	10 mL/kg (60 mg IgG/kg) IV	6
Whole blood (hematocrit 35%–50%)§	10 mL/kg (80–100 mg IgG/kg) IV	6
Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	7
Cytomegalovirus intravenous immune globulin (IGIV)	150 mg/kg maximum	6
IGIV		
Replacement therapy for immune deficiencies¶	300–400 mg/kg IV¶	8
Immune thrombocytopenic purpura	400 mg/kg IV	8
Postexposure varicella prophylaxis**	400 mg/kg IV	8
Immune thrombocytopenic purpura	1000 mg/kg IV	10
Kawasaki disease	2 g/kg IV	11

* This table is not intended for determining the correct indications and dosages for using antibody-containing products. Unvaccinated persons might not be fully protected against measles during the entire recommended interval, and additional doses of immune globulin or measles vaccine might be indicated after measles exposure. Concentrations of measles antibody in an immune globulin preparation can vary by manufacturer's lot. Rates of antibody clearance after receipt of an immune globulin 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.

† Contains antibody only to respiratory syncytial virus

§ Assumes a serum IgG concentration of 16 mg/mL.

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

** The investigational product VariZIG, similar to licensed VZIG, is a purified human immune globulin preparation made from plasma containing high levels of anti-varicella antibodies (immunoglobulin class G [IgG]). When indicated, health-care providers should make every effort to obtain and administer VariZIG. In situations in which administration of VariZIG does not appear possible within 96 hours of exposure, administration of immune globulin intravenous (IGIV) should be considered as an alternative. IGIV also should be administered within 96 hours of exposure. Although licensed IGIV preparations are known to contain anti-varicella antibody titers, the titer of any specific lot of IGIV that might be available is uncertain because IGIV is not routinely tested for antiviral antibodies. The recommended IGIV dose for postexposure prophylaxis of varicella is 400 mg/kg, administered once. For pregnant women who cannot receive VariZIG within 96 hours of exposure, clinicians can choose either to administer IGIV or closely monitor the women for signs and symptoms of varicella and institute treatment with acyclovir if illness occurs. (Source: CDC. A new product for postexposure prophylaxis available under an investigational new drug application expanded access protocol. MMWR 2006;55:209–10).

Interchangeability of Vaccines from Different Manufacturers

Certain vaccines are available from different manufacturers, and these vaccines usually are not identical in antigen content or 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, HepB, and hepatitis A (HepA) vaccines produce a satisfactory antibody response after a complete primary series (41–44). All brands of Hib conjugate, HepB,[§] and HepA vaccines are interchangeable within

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

their respective series. If different brands of Hib conjugate vaccine are administered, 3 doses are considered adequate for the primary series among infants. If PRP-OMP is used, the primary series consists of 2 doses. After completing the primary series, any Hib conjugate vaccine can be used for the booster dose at age 12–18 months.

Data are limited about the safety, immunogenicity, and efficacy of using acellular pertussis (e.g., 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[®] followed by Infanrix[®] for the remaining dose(s) is comparable to 3 doses of Tripedia with regard to immunogenicity, as measured by antibodies to diphtheria, tetanus, and pertussis toxoid, and filamentous hemagglutinin (45). 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. Whenever feasible, the same brand of DTaP vaccine should be used for all doses of the vaccination series. If vaccination providers do not know or have available the type of DTaP vaccine previously administered to a child, any DTaP vaccine should be used to continue or complete the series. For vaccines in general, vaccination should not be deferred because the brand used for previous doses is not available or is unknown (27,46).

Lapsed Vaccination Schedule

Vaccination providers should administer vaccines as close to the recommended intervals as possible. However, longer-than-recommended intervals between doses do not reduce final antibody concentrations, although protection might not be attained until the recommended number of doses has been administered. With the exception of 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.

Unknown or Uncertain Vaccination Status

Vaccination providers frequently encounter persons who do not have adequate documentation of vaccinations. Providers should only accept written, dated records as evidence of vaccination. With the exception of influenza vaccine and PPV (47,48), self-reported doses of vaccine without written documentation should not be accepted. 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 immunization information systems (IIS), and searching for a

personally held record. If records cannot be located, these persons should be considered susceptible and should be 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).

Contraindications and Precautions

Contraindications and precautions to vaccination dictate circumstances when vaccines should not be administered. The majority of precautions are temporary, and the vaccination can be administered later. A contraindication is a condition in a recipient that increases the risk for a serious adverse reaction. A vaccine should not be administered when a contraindication is present. For example, administering influenza vaccine to a person with an anaphylactic allergy to egg protein could cause serious illness in or death of the recipient.

National standards for pediatric vaccination practices have been established and include true contraindications and precautions to vaccination (Table 5) (1). The only contraindication applicable to all vaccines is a history of a severe allergic reaction after a previous dose of vaccine or to a vaccine constituent (unless the recipient has been desensitized). In addition, severely immunocompromised persons should generally not receive live vaccines. Children who experience encephalopathy within 7 days after administration of a previous dose of diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP), DTaP, or Tdap not attributable to another identifiable cause should not receive further doses of a vaccine that contains pertussis. Because of the theoretical risk for the fetus, women known to be pregnant should generally not receive live-attenuated virus vaccines.

A precaution is a condition in a recipient that might increase the risk for a serious adverse reaction or that 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). 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 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 because the benefit of protection from the vaccine outweighs the risk for an adverse reaction. For example, caution should be exercised in vaccinating a child with DTaP who, within 48 hours of receipt of a previous dose of DTP or DTaP, experienced fever of >104°F (>40.5°C); had persistent, inconsolable crying for 3 or more hours; collapsed or experienced a shock-like state; or had a seizure <3 days after receiving the previous dose of DTP or DTaP. How-

TABLE 5. Contraindications and precautions* to commonly used vaccines

Vaccine	True contraindications and precautions*	Untrue (vaccines can be administered)
General for all routine vaccines, including diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP); pediatric diphtheria-tetanus toxoid (DT); adult tetanus-diphtheria toxoid (Td); tetanus-reduced-diphtheria toxoid and acellular pertussis vaccine (Tdap), inactivated poliovirus vaccine (IPV); measles-mumps-rubella vaccine (MMR); <i>Haemophilus influenzae</i> type b vaccine (Hib); hepatitis A vaccine; hepatitis B vaccine; varicella vaccine; Rotavirus vaccine, pneumococcal conjugate vaccine (PCV); inactivated influenza vaccine (TIV); live-attenuated influenza vaccine (LAIV) pneumococcal polysaccharide vaccine (PPV); meningococcal conjugate vaccine (MCV4); meningococcal polysaccharide vaccine (MPSV); human papillomavirus vaccine (HPV); and herpes zoster vaccine (HZ)	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precautions Moderate or severe acute illness with or without fever</p>	<p>Mild acute illness with or without fever</p> <p>Mild-to-moderate local reaction (i.e., swelling, redness, and soreness); low-grade or moderate fever after previous dose</p> <p>Lack of previous physical examination in well-appearing person</p> <p>Current antimicrobial therapy[†]</p> <p>Convalescent phase of illness</p> <p>Preterm birth (hepatitis B vaccine is an exception in certain circumstances)[§]</p> <p>Recent exposure to an infectious disease</p> <p>History of penicillin allergy, other nonvaccine allergies, relatives with allergies, receiving allergen extract immunotherapy</p> <p>Breast feeding</p>
DTaP	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>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</p> <p>Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy: defer DTaP until neurologic status clarified and stabilized</p> <p>Precautions Temperature of $\geq 105^{\circ}\text{F}$ ($\geq 40.5^{\circ}\text{C}$) for ≤ 48 hours after vaccination with a previous dose of DTP or DTaP</p> <p>Collapse or shock-like state (i.e., hypotonic hyporesponsive episode) ≤ 48 hours after receiving a previous dose of DTP/DTaP</p> <p>Seizure ≤ 3 days after receiving a previous dose of DTP/DTaP[¶]</p> <p>Persistent, inconsolable crying lasting ≥ 3 hours within 48 hours after receiving a previous dose of DTP/DTaP</p> <p>Guillain-Barré syndrome (GBS) < 6 weeks after previous dose of tetanus toxoid-containing vaccine</p> <p>Moderate or severe acute illness with or without fever</p>	<p>Temperature of $\leq 104^{\circ}\text{F}$ ($< 40.5^{\circ}\text{C}$), fussiness, or mild drowsiness after a previous dose of diphtheria toxoid-tetanus toxoid-pertussis vaccine (DTP/DTaP)</p> <p>Family history of seizures[¶]</p> <p>Family history of sudden infant death syndrome</p> <p>Family history of an adverse event after DTP or DTaP administration</p> <p>Stable neurologic conditions (e.g., cerebral palsy, well-controlled seizure disorder, developmental delay)</p>
DT, Td	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precautions GBS < 6 weeks after previous dose of tetanus toxoid-containing vaccine</p> <p>Moderate or severe acute illness with or without fever</p>	

TABLE 5. (Continued) Contraindications and precautions* to commonly used vaccines

Vaccine	True contraindications and precautions*	Untrue (vaccines can be administered)
Tdap	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Encephalopathy (e.g., coma, decreased level of consciousness, and prolonged seizures) not attributable to another identifiable cause within 7 days of administration of previous dose of DTP, DTaP or Tdap</p> <p>Precautions Moderate or severe acute illness with or without fever</p> <p>GBS ≤ 6 weeks after a previous dose of tetanus toxoid containing vaccine</p> <p>Progressive or unstable neurological disorder, uncontrolled seizures or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized</p> <p>History of arthus-type hypersensitivity reactions following a previous dose of tetanus toxoid-containing vaccine. Defer vaccination until at least 10 years have elapsed since the last tetanus toxoid-containing vaccine</p>	<p>Temperature of $>104^{\circ}$ F ($>40.5^{\circ}$ C) for ≤ 48 hours after vaccination with a previous dose of DTP or DTaP</p> <p>Collapse or shock-like state (i.e., hypotonic hyporesponsive episode) ≤ 48 hours after receiving a previous dose of DTP/DTaP</p> <p>Seizure ≤ 3 days after receiving a previous dose of DTP/DTaP[¶]</p> <p>Persistent, inconsolable crying lasting ≥ 3 hours within 48 hours after receiving a previous dose of DTP/DTaP</p> <p>History of extensive limb swelling after DTP/DTaP/Td that is not an arthus-type reaction</p> <p>Stable neurologic disorder</p> <p>Brachial neuritis</p> <p>Latex allergy that is not anaphylactic</p> <p>Breast feeding</p> <p>Immunosuppression</p>
IPV	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precautions Pregnancy</p> <p>Moderate or severe acute illness with or without fever</p>	<p>Previous receipt of one or more doses of oral polio vaccine</p>
MMR**	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Pregnancy</p> <p>Known severe immunodeficiency (e.g., hematologic and solid tumors; receiving chemotherapy; congenital immunodeficiency; long-term immunosuppressive therapy;^{††} or patients with human immunodeficiency virus [HIV] infection who are severely immunocompromised)</p> <p>Precautions Recent (≤ 11 months) receipt of antibody-containing blood product (specific interval depends on product)^{¶¶}</p> <p>History of thrombocytopenia or thrombocytopenic purpura</p> <p>Moderate or severe acute illness with or without fever</p>	<p>Positive tuberculin skin test</p> <p>Simultaneous tuberculosis skin testing^{§§}</p> <p>Breast feeding</p> <p>Pregnancy of recipient's mother or other close or household contact</p> <p>Recipient is childbearing-age female</p> <p>Immunodeficient family member or household contact</p> <p>Asymptomatic or mildly symptomatic HIV infection</p> <p>Allergy to eggs</p>
Hib	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Aged < 6 weeks</p> <p>Precautions Moderate or severe acute illness with or without fever</p>	

TABLE 5. (Continued) Contraindications and precautions* to commonly used vaccines

Vaccine	True contraindications and precautions*	Untrue (vaccines can be administered)
Hepatitis B	<p>Contraindication Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precautions Infant weighing <2000 g[§] Moderate or severe acute illness with or without fever</p>	<p>Pregnancy</p> <p>Autoimmune disease (e.g., systemic lupus erythematosus or rheumatoid arthritis)</p>
Hepatitis A	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precautions Pregnancy Moderate or severe acute illness with or without fever</p>	
Varicella	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component Substantial suppression of cellular immunity Pregnancy</p> <p>Precautions Recent (≤ 11 months) receipt of antibody-containing blood product (specific interval depends on product)^{¶¶} Moderate or severe acute illness with or without fever</p>	<p>Pregnancy of recipient's mother or other close or household contact</p> <p>Immunodeficient family member or household contact^{***}</p> <p>Asymptomatic or mildly symptomatic HIV infection</p> <p>Humoral immunodeficiency (e.g., agammaglobulinemia)^{†††}</p>
PCV	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precaution Moderate or severe acute illness with or without fever</p>	
TIV	<p>Contraindication Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precaution Moderate or severe acute illness with or without fever</p>	<p>Nonsevere (e.g., contact) allergy to latex or thimerosal</p> <p>Concurrent administration of coumadin or aminophylline</p>
LAIV	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component Pregnancy Known severe immunodeficiency (e.g., hematologic and solid tumors; receiving chemotherapy; congenital immunodeficiency; long-term immunosuppressive therapy;^{††} or patients with human immunodeficiency virus [HIV] infection who are severely immunocompromised) Previous history of GBS Certain chronic medical conditions^{§§§}</p> <p>Precaution Moderate or severe acute illness with or without fever</p>	

TABLE 5. (Continued) Contraindications and precautions* to commonly used vaccines

Vaccine	True contraindications and precautions*	Untrue (vaccines can be administered)
PPV	<p>Contraindication Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precaution Moderate or severe acute illness with or without fever</p>	History of invasive pneumococcal disease or pneumonia
MCV4	<p>Contraindications Severe allergic reaction (e.g., anaphylaxis) after a previous vaccine dose or to a vaccine component</p> <p>Precautions Moderate or severe acute illness with or without fever History of Guillain-Barré syndrome (if not at high risk for meningococcal disease)</p>	
MPSV	<p>Contraindications Severe allergic reaction after a previous dose or to a vaccine component</p> <p>Precautions Moderate or severe acute illness with or without fever</p>	
HPV	<p>Contraindications Severe allergic reaction after a previous dose or to a vaccine component</p> <p>Precautions Moderate or severe acute illness with or without fever Pregnancy</p>	
Rotavirus	<p>Contraindications Severe allergic reaction after a previous dose or to a vaccine component</p> <p>Precautions Moderate or severe acute illness with or without fever Immunosuppression Receipt of an antibody-containing blood product within 6 weeks^{¶¶¶} Preexisting gastrointestinal disease Previous history of intussusception</p>	<p>Preterm births</p> <p>Immunosuppression in household contacts</p> <p>Pregnant household contacts</p>

* 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.

† Antibacterial drugs and mefloquine might interfere with Ty21a oral typhoid vaccine, and certain antiviral drugs might interfere with varicella-containing and live-attenuated influenza virus vaccine.

§ Hepatitis B vaccination should be deferred for infants weighing <2000 g if the mother is documented to be hepatitis B surface antigen (HBsAg)-negative at the time of the infant's birth. Vaccination can commence at chronological age 1 month. For infants born to HBsAg-positive women, hepatitis B immunoglobulin and hepatitis B vaccine should be administered at or soon after birth, regardless of weight.

¶ Acetaminophen or other appropriate antipyretic can be administered to infants and children with a history of previous seizures at the time of DTaP vaccination and every 4 hours for 24 hours thereafter to reduce the possibility of postvaccination fever (**Source:** American Academy of Pediatrics. Active immunization. In: Pickering LK, Baker CJ, Long SS, McMillan J. eds. 2006 red book: report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006).

** 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.

†† 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.

§§ Measles vaccination might suppress tuberculin reactivity temporarily. Measles-containing vaccine can be administered on the same day as tuberculin skin testing. If testing cannot be performed until after the day of MMR vaccination, the test should be postponed for ≥ 4 weeks after the vaccination. If an urgent need exists to skin test, do so with the understanding that reactivity might be reduced by the vaccine.

¶¶¶ See text for details

TABLE 5. (Continued) Contraindications and precautions* to commonly used vaccines

Vaccine	True contraindications and precautions*	Untrue (vaccines can be administered)
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*** If a vaccinee experiences a presumed vaccine-related rash 7–25 days after vaccination, avoid direct contact with immunocompromised persons for the duration of the rash, if possible.

††† Vaccine should be deferred for the appropriate interval if replacement IG products are being administered (Table 4).

§§§ For details, see CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2006;55:No. RR-10.

¶¶¶ Rotavirus vaccine (RV) should be deferred for 6 weeks after receipt of an antibody-containing product if possible. However, if the 6-week deferral would cause the first dose of RV to be scheduled for age ≥ 13 weeks, a shorter deferral interval should be used to ensure the first dose of RV is administered no later than age 13 weeks.

ever, administering a pertussis-containing vaccine should be considered if the risk for pertussis is increased (e.g., during a pertussis outbreak) (27). These precautions do not apply to administration of tetanus-reduced-diphtheria-acellular-pertussis vaccine for adolescents and adults. The presence of a moderate or severe acute illness with or without a fever is a precaution to administration of all vaccines (Table 5).

Clinicians or other health-care providers might inappropriately consider certain conditions or circumstances to be true contraindications or precautions to vaccination. This misconception results in missed opportunities to administer recommended vaccines (49). Likewise, clinicians and other health-care providers might fail to understand what constitutes a true contraindication or precaution and might administer a vaccine when it should be withheld. This practice can result in an increased risk for an adverse reaction to the vaccine. Among the most common conditions often inappropriately considered contraindications are diarrhea, minor upper-respiratory tract illnesses (including otitis media) with or without fever, mild-to-moderate local reactions to a previous dose of vaccine, current antimicrobial therapy, and the convalescent phase of an acute illness (Table 5).

The decision to administer or delay vaccination because of a current or recent acute illness depends on severity of symptoms and etiology of the disease. All vaccines can be administered to persons with minor acute illness (e.g., diarrhea or mild upper-respiratory tract infection with or without fever). Studies indicate that failure to vaccinate children with minor illnesses can seriously impede vaccination efforts (50–52). Among persons whose compliance with medical care cannot be ensured, use of every opportunity to provide appropriate vaccinations is critical.

The safety and efficacy of vaccinating persons who have mild illnesses have been documented (53–56). Vaccination should not be delayed because of the presence of mild respiratory tract illness or other acute illness with or without fever.

Persons with moderate or severe acute illness should be vaccinated as soon as the acute illness has improved, after screening for contraindications. This precaution avoids superimposing adverse effects of the vaccine on the underlying illness or causing diagnostic confusion between manifes-

tations of the underlying illness and possible adverse effects of vaccination.

Routine physical examinations and procedures (e.g., measuring temperatures) are not prerequisites for vaccinating persons who appear to be healthy. Asking the parent or guardian if the child is ill and then postponing vaccination for children with moderate-to-severe illness or proceeding with vaccination if no contraindications exist are appropriate procedures in childhood vaccination programs.

A family history of seizures or other central nervous system disorders is not a contraindication to administration of pertussis or other vaccines. However, delaying pertussis vaccination for infants and children with a history of previous seizures until the child's neurologic status has been assessed is prudent. Pertussis vaccine should not be administered to infants with evolving neurologic conditions until the condition has stabilized (Table 5) (27).

Vaccine Administration

Infection Control and Sterile Technique

Persons administering vaccines should follow appropriate precautions to minimize risk for spread of disease. Hands should be cleansed with an alcohol-based waterless antiseptic hand rub or washed with soap and water between each patient contact (57). Occupational Safety and Health Administration (OSHA) regulations do not require gloves to be worn when administering vaccinations, unless persons administering vaccinations are likely to come into contact with potentially infectious body fluids or have open lesions on their hands. Needles used for injections must be sterile and disposable to minimize the risk for contamination. 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. Different vaccines should never be mixed in the same syringe unless specifically licensed for such use, and no attempt should be made to transfer between syringes.

To prevent inadvertent needle-stick injury or reuse, needles and syringes should be discarded immediately after use in labeled, puncture-proof containers located in the same room where the vaccine is administered. Needles should not be recapped before being placed in the container. Safety needles or needle-free injection devices should be used if available to reduce the risk for injury.

Injection Route and Injection Site

With the exception of *Bacillus Calmette-Guerin* (BCG) vaccine, injectable vaccines are administered by the intramuscular and subcutaneous route. The method of administration of injectable vaccines is determined, in part, by the presence of adjuvants in some vaccines. The term adjuvant refers to a vaccine component distinct from the antigen that enhances the immune response to the antigen. The majority of vaccines containing an adjuvant (e.g., DTaP, DT, Td, Tdap, PCV, Hib, HepA, HepB, and human papillomavirus [HPV]) should be injected into a muscle because administration sub-

cutaneously or intradermally can cause local irritation, induration, skin discoloration, inflammation, and granuloma formation. Anthrax vaccine, an inactivated vaccine with adjuvant, is an exception to this rule and is recommended to be administered subcutaneously. Routes of administration are recommended by the manufacturer for each immunobiologic (Table 6). Deviation from the recommended route of administration might reduce vaccine efficacy (58,59) or increase local adverse reactions (60–62).

Intramuscular Injections and 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 (60). Appropriate needle length depends on age and body mass.

TABLE 6: Dose and route of administration for selected vaccines

Vaccines	Dose	Route
Diphtheria, tetanus, pertussis (DTaP, DT, Td, Tdap)	0.5 mL	Intramuscular (IM)
Diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B vaccine (DTaP-IPV-HepB)	0.5 mL	IM
Diphtheria, tetanus, acellular pertussis, <i>haemophilus influenzae</i> type b vaccine (DTaP-Hib)	0.5 mL	IM
<i>Haemophilus influenzae</i> type b (Hib)	0.5 mL	IM
<i>Haemophilus influenzae</i> type b – Hepatitis B (Hib-HepB)	0.5 mL	IM
Hepatitis A (HepA)	≤18 yrs: 0.5 mL ≥19 yrs: 1.0 mL	IM
HepB	≤19 yrs: 0.5 mL* ≥20 yrs: 1.0 mL	IM
HepA/HepB	≥18 yrs: 1.0 mL	IM
Influenza, live attenuated	0.5 mL	Intranasal spray
Influenza, trivalent inactivated	6–35 mos: 0.25 mL ≥3 yrs: 0.5 mL	IM
Measles, mumps, rubella	0.5 mL	Subcutaneous (SC)
Measles, mumps, rubella, varicella	0.5 mL	SC
Meningococcal conjugate	0.5 mL	IM
Meningococcal polysaccharide	0.5 mL	SC
Pneumococcal conjugate	0.5 mL	IM
Pneumococcal polysaccharide	0.5 mL	IM or SC
Human papillomavirus	0.5 mL	IM
Polio, inactivated	0.5 mL	IM or SC
Rotavirus	2.0 mL	Oral
Varicella	0.5 mL	SC
Zoster	0.7 mL	SC

* Persons aged 11–15 years can be administered Recombivax HB® (Merck) 1.0 mL (adult formulation) on a 2-dose schedule. Adapted from: Immunization Action Coalition (<http://www.immunize.org>).

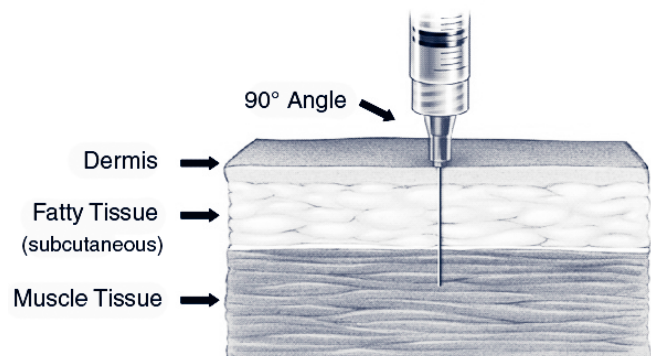
For all intramuscular injections, the needle should be long enough to reach the muscle mass and prevent vaccine from seeping into subcutaneous tissue, but not so long as to involve underlying nerves, blood vessels, or bone (59,63–65). Vaccinators should be familiar with the anatomy of the area into which 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 7).

Decision on needle size 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). Aspiration before injection of vaccines or toxoids (i.e., pulling back on the syringe plunger after needle insertion, before injection) is not required because no large blood vessels exist at the recommended injection sites.

Infants (Aged <12 Months)

For the majority of infants, the anterolateral aspect of the thigh is the recommended site for injection because it provides a large muscle mass (Figure 2). The muscles of the buttock have not been used for administration of vaccines in infants and children because of concern about potential injury to the sciatic nerve, which is well documented after injection of antimicrobial agents into the buttock. If the gluteal muscle must be used, care should be taken to define the ana-

FIGURE 1. Intramuscular needle insertion



Adapted from California Immunization Branch

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



Adapted from Minnesota Department of Health

TABLE 7. Needle length and injection site of intramuscular injections

Birth–18 years		
Age	Needle length	Injection site
Newborn*	5/8" (16mm) [†]	Anterolateral thigh
Infant 1–12 months	1" (25mm)	Anterolateral thigh
Toddler 1 – 2 years	1"–1 1/4" (25–32 mm) 5/8" [†] –1" (16–25 mm)	Anterolateral thigh [§] Deltoid muscle of the arm
Child/adolescent 3–18 years	5/8" [†] –1" (16–25 mm) 1"–1 1/4" (25–32 mm)	Deltoid muscle of the arm [§] Anterolateral thigh
Aged ≥19 Years		
Sex/weight	Needle length	Injection site
Male and female <60 kg (130 lbs)	1" (25mm) [¶]	Deltoid muscle of the arm
Female 60–90 kg (130–200 lbs)	1"–1 1/2" (25–38 mm)	
Male 60–118 kg (130–260 lbs)		
Female >90 kg (200 lbs)	1 1/2" (38 mm)	
Male >118 kg (260 lbs)		

* Newborn = first 28 days of life.

[†] If skin stretched tight, subcutaneous tissues not bunched.

[§] Preferred site.

[¶] Certain experts recommend a 5/8" (16 mm) needle for males and females who weigh <60 kg (130 lbs).

Adapted from: Poland GA, Borrud A, Jacobsen RM, et al. Determination of deltoid fat pad thickness: implications for needle length in adult immunization. JAMA 1997;277: 1709–11.

tomic landmarks.⁴ Injection technique is the most important parameter to ensure efficient intramuscular vaccine delivery. If the subcutaneous and muscle tissue are bunched to minimize the chance of striking bone (63), a 1-inch needle is required to ensure intramuscular administration in infants. For the majority of infants, a 1-inch, 22–25-gauge needle is sufficient to penetrate muscle in an infant's thigh. For newborn (first 28 days of life) and premature infants, a 5/8 inch long needle usually is adequate if the skin is stretched flat between thumb and forefinger and the needle inserted at a 90-degree angle to the skin (65).

Toddlers and Older Children (Aged 12 Months–10 Years)

The deltoid muscle should be used if the muscle mass is adequate. The needle size for deltoid site injections can range from 22–25 gauge and from 5/8 to 1 inch on the basis of the size of the muscle and the thickness of adipose tissue at the injection site (Figure 3). A 5/8-inch needle is adequate only for the deltoid muscle and only if the skin is stretched flat between thumb and forefinger and the needle inserted at a 90-degree angle to the skin. For toddlers, the anterolateral thigh can be used, but the needle should be at least 1 inch in length.

Adolescents and Adults (Aged >11 Years)

For adults and adolescents, the deltoid muscle is recommended for routine intramuscular vaccinations. The antero-

⁴If 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.

FIGURE 3. Intramuscular site of administration: deltoid



Adapted from Minnesota Department of Health

lateral thigh also can be used. For men and women weighing <130 lbs (<60 kg) a 5/8–1-inch needle is sufficient to ensure intramuscular injection. For women weighing 130–200 lbs (60–90 kg) and men 130–260 lbs (60–118kg), a 1–1½-inch needle is needed. For women weighing >200 lbs (>90 kg) or men weighing >260 lbs (>118 kg), a 1½-inch needle is required (Table 7) (64).

Subcutaneous Injections

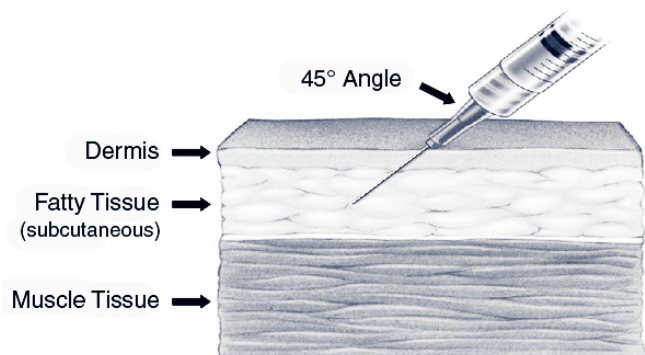
Subcutaneous injections are administered at a 45-degree angle usually into the thigh for infants aged <12 months and in the upper-outer triceps area of persons aged ≥12 months. Subcutaneous injections can be administered into the upper-outer triceps area of an infant, if necessary. A 5/8-inch, 23–25-gauge needle should be inserted into the subcutaneous tissue (Figures 4 and 5).

FIGURE 4. Subcutaneous site of administration: triceps



Adapted from Minnesota Department of Health

FIGURE 5. Subcutaneous needle insertion



Adapted from California Immunization Branch

Multiple Vaccinations

If multiple vaccines are administered at a single visit, administration of each preparation at a different anatomic site is desirable. For infants and younger children, if more than two vaccines must be injected in a single limb, the thigh is the preferred site because of the greater muscle mass; the injections should be sufficiently separated (i.e., 1 inch or more if possible) so that any local reactions can be differentiated (60,66). 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], HepB and hepatitis B immunoglobulin [HBIG]), separate anatomic sites should be used for each injection. The location of each injection should be documented in the patients' medical record.

Jet Injection

Jet injectors (JIs) are needle-free devices that drive liquid medication through a nozzle orifice, creating a narrow stream under high pressure that penetrates skin to deliver a drug or vaccine into intradermal, subcutaneous, or intramuscular tissues (67,68). JIs have the potential to reduce the frequency of needle-stick injuries to health-care workers (69) and to overcome the improper reuse and other drawbacks of needles and syringes in economically developing countries (70–72). JIs have been safe and effective for administering different live and inactivated vaccines for viral and bacterial diseases (72). The immune responses generated are equivalent to, and occasionally greater than, immune responses induced by needle injection. However, local reactions or injury (e.g., redness, induration, pain, blood, and ecchymosis at the injection site) can be more frequent when vaccines are delivered by JIs compared with needle injection (68,72).

In the 1990s, a new generation of JIs was introduced with disposable cartridges serving as dose chambers and nozzle (72). With the provision of a new sterile cartridge for each patient and correct use, these devices avoid the safety concerns for multiple-use–nozzle devices (72–76). These devices should be used in accordance with their labeling for intradermal, subcutaneous, or intramuscular administration.

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), ingestion of sweet liquids, breast feeding, cooling of the injection site, and topical or oral analgesia, can help infants or children cope with the

discomfort associated with vaccination (77,78). Pretreatment (30–60 minutes before injection) with 5% topical lidocaine-prilocaine emulsion can decrease the pain of vaccination by causing superficial anesthesia (79,80). Evidence indicates that this cream does not interfere with the immune response to MMR (81). Topical lidocaine-prilocaine emulsion should not be used on infants aged <12 months who are receiving treatment with methemoglobin-inducing agents because of the possible development of methemoglobinemia (82).

Acetaminophen has been used among children to reduce the discomfort and fever associated with DTP vaccination (83). However, acetaminophen can cause formation of methemoglobin and might interact with lidocaine-prilocaine cream if used concurrently (82). 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 (84).

Nonstandard Vaccination Practices

Recommendations for route, site, and dosage of immunobiologics are derived from data from clinical trials, from practical experience, and from 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 (85), the immunogenicity of HepB is substantially lower when the gluteal rather than the deltoid site is used for administration (58). HepB administered intradermally can result in a lower seroconversion rate and final titer of hepatitis B surface antibody than when administered by the deltoid intramuscular route (86,87). HepB administered by any route other than intramuscularly, or in adults at any site other than the deltoid or anterolateral thigh, should not be counted as valid and should be repeated. Similarly, doses of rabies vaccine administered in the gluteal site should not be counted as valid doses and should be repeated (88). Meningococcal conjugate vaccine (MCV4) should be administered intramuscularly; however, revaccination is not necessary when administered subcutaneously (89). Inactivated influenza vaccine is immunogenic when administered in a lower than standard dose by the intradermal (ID) route to healthy adult volunteers (90). However, the immunogenicity for persons aged ≥ 60 years is inadequate, and variance from the recommended route and dose is not recommended.

Live-attenuated injectable vaccines (e.g., MMR, varicella, and yellow fever) and certain inactivated vaccines (e.g., meningococcal polysaccharide and anthrax) are recommended by the manufacturers to be administered by subcutaneous injection.

tion. PPV and IPV are recommended by the manufacturer to be administered by the subcutaneous or intramuscular route. Response to vaccines recommended by the subcutaneous route probably will not be affected if the vaccines are administered by the intramuscular rather than subcutaneous route. Repeating doses of vaccine administered by the intramuscular route rather than by the subcutaneous route is not necessary.

Administering volumes smaller than that recommended (e.g., split doses) can result in inadequate protection. Using larger than recommended dosages can be hazardous because of excessive local or systemic concentrations of antigens or other vaccine constituents. Using reduced doses administered at multiple immunization visits that equal a full dose or using smaller divided doses are not endorsed or recommended. 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 been achieved.

Preventing Adverse Reactions

Vaccines are intended to produce active immunity to specific antigens. An adverse reaction is an untoward effect that occurs after a vaccination that is extraneous to the vaccine's primary purpose of producing immunity. Vaccine adverse reactions are classified by three general categories: local, systemic, and allergic (91). Local reactions are usually the least severe and most frequent. Systemic reactions (e.g., fever) occur less frequently than local reactions. Serious allergic reactions (e.g., anaphylaxis) are the most severe and least frequent. Severe adverse reactions are rare.

Persons who administer vaccines should screen their patients for contraindications and precautions to the vaccine before each dose of vaccine is administered (Table 5). Screening can be facilitated by consistent use of screening questionnaires, which are available from certain state vaccination programs and other sources (e.g., the Immunization Action Coalition at <http://www.immunize.org>).

Syncope (vasovagal or vasodepressor reaction) can occur after vaccination, most commonly among adolescents and young adults. During 1990–2004, a total of 3,168 reports to Vaccine Adverse Event Reporting System (VAERS) were coded as syncope; 35% of these episodes were reported among persons aged 10–18 years (CDC, unpublished data, 2005). Approximately 14% of reported syncopal episodes resulted in hospitalization because of injury or medical evaluation. Serious injury, including skull fracture and cerebral hemorrhage, has resulted from syncopal episodes after vaccination (92). A review of syncope after vaccination indicated that 63% of syncopal episodes occurred ≤ 5 minutes after vaccination, and

89% occurred within 15 minutes after vaccination (93). Although syncopal episodes are uncommon and severe allergic reactions are rare, vaccine providers should strongly consider observing patients for 15 minutes after they are vaccinated (94). If syncope develops, patients should be observed until the symptoms resolve.

Managing Acute Vaccine Reactions

Although rare after vaccination, the immediate onset and life-threatening nature of an anaphylactic reaction require that all personnel and facilities providing vaccinations have procedures in place for managing a reaction. All vaccine providers should be familiar with the office emergency plan and be certified in cardiopulmonary resuscitation. Epinephrine and equipment for maintaining an airway should be available for immediate use.

Anaphylaxis usually begins within minutes of vaccine administration (95,96). Rapidly recognizing and initiating treatment are required to prevent possible progression to cardiovascular collapse. If flushing, facial edema, urticaria, itching, swelling of the mouth or throat, wheezing, difficulty breathing, or other signs of anaphylaxis occur, the patient should be placed in a recumbent position with the legs elevated. Treatment options for management of anaphylaxis using pharmaceuticals have been recommended (Table 8) (94,97). Maintenance of an airway and oxygen administration might be necessary. Arrangements should be made for immediate transfer to an emergency facility for further evaluation and treatment.

Occupational Safety Regulations

Bloodborne diseases (e.g., hepatitis B, hepatitis C, and human immunodeficiency virus [HIV]) are occupational hazards for physicians and other health-care providers. To reduce the incidence of needle-stick injury and the consequent risk for bloodborne diseases acquired from patients, the Needlestick Safety and Prevention Act was enacted in November 2000. The Act directed OSHA to strengthen its existing bloodborne pathogen standards. Those standards were revised and became effective in April 2001 (69). These federal regulations require that safer injection devices (e.g., needle-shielding syringes or needle-free injectors) be used for injectable vaccination in all clinical settings. The rules also require that records be kept documenting injuries caused by medical sharps and that nonmanagerial employees be involved in the evaluation and selection of safer devices to be procured.

Needle-shielding or needle-free devices that might satisfy the occupational safety regulations for administering inject-

TABLE 8. Treatment of anaphylaxis with intramuscular or oral pharmaceuticals

Drug	Dosage
Child	
Primary regimen	
Epinephrine 1:1000 (aqueous) (1 mg/mL)*	0.01 mg/kg up to 0.5 mg (administer 0.01 mL/kg/dose up to 0.5 mL) intramuscularly (IM) repeated every 10–20 minutes up to 3 doses
Secondary regimen	
Diphenhydramine	1–2 mg/kg oral, IM, or intravenously (IV), every 4–6 hours (maximum single dose: 100 mg)
Hydroxyzine	0.5–1 mg/kg oral, IM, every 4–6 hours (maximum single dose: 100 mg)
Prednisone	1.5–2 mg/kg oral (maximum single dose: 60 mg); use corticosteroids as long as needed
Adult	
Primary regimen	
Epinephrine 1:1000 (aqueous)*	0.01 mg/kg up to 0.5 mg (give 0.01 mL/kg/dose up to 0.5 mL) IM repeated every 10–20 minutes up to 3 doses
Secondary regimen	
Diphenhydramine	1–2 mg/kg up to 100 mg IM or oral, every 4–6 hours

* If agent causing anaphylactic reaction was administered by injection, epinephrine can be injected into the same site to slow absorption. Adapted from American Academy of Pediatrics. Passive immunization. In: Pickering LK, Baker CJ, Long SS, McMillan J. Red Book: 2006 Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006. Immunization Action Coalition. Medical Management of Anaphylaxis in Adult Patients. Available at <http://www.immunize.org/catg.d/p3082.pdf>, and Mosby's Drug Consult 2005.

able vaccines are available in the United States (72,98,99).** Additional information about implementation and enforcement of these regulations is available from OSHA (<http://www.osha.gov/pls/oshaweb>).

Storage and Handling of Immunobiologics

Failure to adhere to recommended specifications for storage and handling of immunobiologics can reduce their potency, resulting in an inadequate immune response in the recipient. Recommendations in the product package inserts, including methods for reconstitution of the vaccine, should be followed carefully. 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 upon delivery and monitored during storage to ensure that the cold chain has been maintained. Vaccines should continue to be stored at recommended temperatures immediately upon receipt until use.

Storage Temperature

The majority of recommended vaccines require storage temperatures of 35°F–46°F (2°C–8°C), and they must not be exposed to freezing temperatures (100). Certain vaccines are

sensitive to freezing temperatures because they contain an aluminum adjuvant (e.g., anthrax, DTaP, DT, Td, Tdap, Hib [PRP-OMP], HepA, HepB, PCV, rabies, and HPV) that precipitates when exposed to temperatures of $\leq 32^{\circ}\text{F}$ ($\leq 0^{\circ}\text{C}$) (100,101). Other vaccines (e.g., MMR, varicella, MMRV, LAIV, and yellow fever) lose potency when exposed to increased temperature because they contain live viruses (Table 9).

Vaccine storage units must be carefully selected, used properly, and consistently monitored to ensure that recommended temperatures are maintained. Refrigerators without freezers and stand-alone freezers (either manual defrost or automatic defrost) usually perform best at maintaining the precise temperatures required for vaccine storage, and such single-purpose units sold for home use are less expensive alternatives to medical specialty equipment (100). A combination refrigerator/freezer unit sold for home use is acceptable for storage of limited quantities of vaccines if the refrigerator and freezer compartments each have a separate external door. In these units, a freezer thermostat usually controls the freezer temperature and a refrigerator thermostat controls the volume of freezer temperature air entering the refrigerator, possibly resulting in different temperature zones within the refrigerator. In such units, vaccines should not be stored on the top shelf near the cold air outlet from the freezer to the refrigerator (usually located at the top of the refrigerator compartment). Any refrigerator or freezer used for vaccine storage must maintain the required temperature range year-round, be large enough to hold the year's largest inventory, and be dedicated to storage of biologics. Before use of the refrigerator for vaccine storage, the temperature should be measured in various

**Internet sites with device listings are identified for information purposes only. CDC, the U.S. Public Health Service, and the Department of Health and Human Services do not endorse any specific device or imply that the devices listed would all satisfy the needle-stick prevention regulations.

TABLE 9. Vaccine storage temperature recommendations

Vaccines	Vaccine storage temperature	Diluent storage temperature	Instructions
Diphtheria-tetanus, or pertussis-containing vaccines	35°F–46°F (2°C–8°C) Do not freeze	No diluent*	Aluminum adjuvant – irreversible loss of potency with exposure to freezing temperature
<i>Haemophilus influenzae</i> type b conjugate vaccines (Hib)	35°F–46°F (2°C–8°C) Do not freeze	35°F–46°F (2°C–8°C) Do not freeze	Several vaccine types with different thermostability profiles†
Hepatitis A and hepatitis B vaccines	35°F–46°F (2°C–8°C) Do not freeze	No diluent	Aluminum adjuvant – irreversible loss of potency with exposure to freezing temperature
Inactivated polio vaccine	35°F–46°F (2°C–8°C) Do not freeze	No diluent	Data on thermostability properties of this vaccine are lacking
Meningococcal conjugate vaccine	35°F–46°F (2°C–8°C) Do not freeze	No diluent	Data on thermostability properties of this vaccine are lacking. Do not expose to light
Meningococcal polysaccharide vaccine	35°F–46°F (2°C–8°C) Do not freeze	Data are lacking on ideal pre-reconstitution storage requirements. After reconstitution, vaccine should be stored at 35°F–46°F (2°C–8°C). Do not freeze	Freeze dried (lyophilized) vaccine. Data on the effect of freezing temperatures on potency are lacking
Pneumococcal conjugate vaccine	35°F–46°F (2°C–8°C) Do not freeze	No diluent	Aluminum adjuvant – irreversible loss of potency with exposure to freezing temperatures
Pneumococcal polysaccharide vaccine	35°F–46°F (2°C–8°C) Do not freeze	No diluent	Data on thermostability properties of this vaccine are lacking
Measles, mumps, and rubella vaccine in the lyophilized (freeze-dried) state§	35°F–46°F (2°C–8°C) Lyophilized (freeze dried) vaccine can be stored at freezer temperature	35°F–77°F (2°C–25°C) Can be refrigerated or stored at room temperature	Protect from light or temperatures above the recommended range
Measles, mumps, rubella, and varicella vaccine	≤5°F (≤15°C)	35°F–77°F (2°C–25°C) Can be refrigerated or stored at room temperature	Protect from light
Trivalent inactivated influenza vaccine	35°F–46°F (2°C–8°C) Do not freeze	No diluent	Data on the thermostability properties of this vaccine are lacking
Live-attenuated influenza vaccine	≤5°F (≤15°C)	No diluent	Do not expose to temperatures above the recommended range
Varicella vaccine	≤5°F (≤15°C)	35°F–77°F (2°C–25°C) Can be refrigerated or stored at room temperature	Do not expose to light or temperatures above the recommended range
Herpes zoster vaccine	≤5°F (≤15°C)	35°F–77°F (2°C–25°C) Can be refrigerated or stored at room temperature	Protect from light
Rotavirus	35°F–46°F (2°C–8°C) Do not freeze	No diluent	Protect from light
Human papillomavirus vaccine	35°F–46°F (2°C–8°C) Do not freeze	No diluent	Protect from light

* DTaP–Tripedia® is sometimes used as a diluent for ActHib®

† ActHIB® (Aventis Pasteur, Lyon, France) in the lyophilized state is not expected to be affected detrimentally by freezing temperatures, although no data are available.

§ MMR in the lyophilized state is not affected detrimentally by freezing temperatures.

Adapted from Atkinson WL, Pickering LK, Watson JC, Peter G. General Immunization Practices. In: Plotkin SA, Orenstein WA, eds. Vaccine. 4th ed. Philadelphia: Elsevier; 2004. p. 1357-86 and CDC. Guidelines for maintaining and managing the vaccine cold chain. MMWR 2003;52:1023–5.

locations within the refrigerator compartment to document that a stable temperature can be maintained (Table 9) within the compartment (102). The refrigerator temperature should be set at the midpoint of the recommended range (i.e., 40°F [5°C]) (103,104). Frequent opening and closing of doors can cause fluctuations of storage temperature; food, beverages, and clinical specimens should not be stored in vaccine storage units.

Temperature Monitoring

Temperature monitoring is a critical component of cold chain management. One person in the office should be assigned primary responsibility for maintaining temperature logs (Figure 6), with a second person assigned as backup. Temperatures for both the refrigerator and freezer should be docu-

mented twice a day and recorded. The backup person should review the log each week. Temperature logs should be maintained for 3 years unless state or local statutes mandate a longer time period. An automated monitoring system that alerts staff when a temperature deviation occurs is optimal. However, even if an automated monitoring system is used, temperatures should still be manually checked and recorded twice a day.

Thermometers should be placed in a central location in each compartment near the vaccine. Different types of thermometers can be used, including standard fluid-filled, minimum-maximum, and continuous chart recorder thermometers (Table 10). Standard fluid-filled thermometers are the simplest and least expensive products, but some models might

FIGURE 6. Sample temperature log

Temperature Log for Vaccines (Fahrenheit)

Month/Year: _____ Days 1–15

***Instructions:** Place an "X" in the box that corresponds with the temperature. The hatched zones represent unacceptable temperature ranges. If the temperature recorded is in the hatched zone: 1. **Store the vaccine** under proper conditions as quickly as possible. 2. **Call the vaccine manufacturer(s)** to determine whether the potency of the vaccine(s) has been affected. 3. **Call the immunization program at your local health department** for further assistance: (____) _____. and 4. **Document the action taken** on the reverse side of this log.

Day of Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15															
Exact Time																														
°F Temp	am pm	am pm	am pm	am pm	am pm	am pm	am pm	am pm	am pm	am pm	am pm	am pm	am pm	am pm	am pm															
≥49°	Take immediate action if temperature is in shaded section*																													
48°																														
47°																														
46°																														
45°																														
44°																														
43°																														
42°																														
41°																														
40°																														
39°																														
38°																														
37°																														
36°																														
35°																														
Refrigerator temperature	Take immediate action if temperature is in shaded section*																													
34°																														
33°																														
32°																														
31°																														
30°																														
29°																														
≤28°																														
Freezer temp																Take immediate action if temperature is in shaded section*														
≥8°																														
7°																														
6°																														
5°																														
4°																														
≤3°																														
Room temp																														
Staff Initials																														

Adapted by the Immunization Action Coalition courtesy of the Michigan Department of Community Health

www.immunize.org/catg.d/p3039.pdf • Item #P3039 (11/05)

TABLE 10. Comparison of thermometers used to monitor vaccine temperatures

Thermometer type	Advantages	Disadvantages
Standard fluid-filled	<ul style="list-style-type: none"> • Inexpensive and simple to use • Thermometers encased in biosafe liquids can reflect vaccine temperatures more accurately than those directly exposed to the air 	<ul style="list-style-type: none"> • Accurate within a range of (+/-1° C) • No information about duration of out-of-temperature exposure • No information on minimum/maximum temperatures • Cannot be recalibrated at routine intervals • Inexpensive models might perform poorly
Minimum-maximum	<ul style="list-style-type: none"> • Inexpensive • Monitors temperature range 	<ul style="list-style-type: none"> • Accurate within a range of (+/-1° C.) • No information about the duration of out-of-range temperature • Cannot be recalibrated at routine intervals
Continuous chart recorder	<ul style="list-style-type: none"> • Most accurate • Continuous 24-hour readings of temperature range and duration • Can be recalibrated at regular intervals 	<ul style="list-style-type: none"> • Most expensive • Requires most training and maintenance

Adapted from CDC. Guidelines for maintaining and managing the vaccine cold chain. MMWR 2003;52:1023–25; and Langley A, Grant S, eds. Proceedings of the National Vaccine Storage Workshop; June 28–30, 2003; Brisbane, Australia. Maroochydoore Queensland Health; 2004.

perform poorly. Product temperature thermometers (i.e., those encased in biosafe liquids) generally reflect refrigerator temperature more accurately. Minimum-maximum thermometers monitor the temperature range. Continuous chart recorder thermometers monitor temperature range and duration and can be recalibrated at specified intervals. All thermometers used for monitoring vaccine storage temperatures should be calibrated and certified by an appropriate agency (e.g., National Institute of Standards and Technology or the American Society for Testing and Materials). Because all thermometers are calibrated as part of the manufacturing process, this recommendation refers to a second calibration process that occurs after manufacturing but before marketing and is documented with a certificate that comes with the product.

Response to Out-of-Temperature-Range Storage

An out-of-range temperature reading should prompt immediate action. A plan should be developed to transfer vaccine to a predesignated alternative emergency storage site if a temperature problem cannot be resolved immediately (i.e., unit unplugged or door left open). Vaccine should be marked “do not use” and moved to the alternate site. After the vaccine has been moved, determine if the vaccine is still useable by contacting the manufacturer or state/local health department. Changes to vaccine exposed to temperatures outside of the recommended range and that affects its immunogenicity usually are not apparent visually.

Expiration Dates and Windows

All vaccines have an expiration date determined by the manufacturer that must be observed. When vaccines are removed from storage, physicians and health-care providers should note whether an expiration window exists for vaccine stored at room temperature or at an intermediate temperature. For example, live-attenuated influenza vaccine that is stored frozen must be discarded after 60 hours at refrigerator temperature. An expiration window also applies to vaccines that have been reconstituted. For example, after reconstitution, MMR vaccine must be administered within 8 hours and must be kept at refrigerator temperature during this time. Doses of expired vaccines that are administered inadvertently generally should not be counted as valid and should be repeated. Additional information about expiration dates is available at <http://www.cdc.gov/nip>.

Multidose Vials

Certain vaccines (i.e., DT, Td, Typhoid Vi, meningococcal polysaccharide vaccine [MPSV], TIV, JE, MMR, IPV, and yellow fever) might be distributed in multidose vials. For multidose vials that do not require reconstitution, after entering the vial, the remaining doses in a multidose vial can be administered until the expiration date printed on the vial or vaccine packaging if the vial has been stored correctly and the vaccine is not visibly contaminated, unless otherwise specified by the manufacturer. Multidose vials that require reconstitution must be used within an interval specified by the manufacturer. After reconstitution, the new expiration date should be written on the vial.

Prefilling Syringes

ACIP discourages the routine practice of prefiling syringes because of the potential for administration errors. The majority of vaccines have a similar appearance after being drawn into a syringe. Vaccine doses should not be drawn into a syringe until immediately before administration. When the syringes are filled, the type of vaccine, lot number, and date of filling must be labeled on each syringe, and the doses should be administered as soon as possible after filling. In certain circumstances in which a single vaccine type is being used (e.g., in advance of a community influenza vaccination campaign), filling a small number of syringes can be considered. Unused syringes filled by the end user (i.e., not filled by the manufacturer) should be discarded at the end of the vaccination session. In addition to administration errors, prefiling of syringes is a concern because FDA does not license administration syringes for vaccine storage. When in doubt about the appropriate handling of a vaccine, vaccination providers should contact the manufacturer.

As a general rule, vaccines that have been mishandled or stored at inappropriate temperatures should not be administered. Guidance for specific situations is available from the state health department or CDC. For certain vaccines (i.e., MMR, MMRV, or varicella vaccine), a serologic test can be performed and, if evidence of immunity can be documented for all antigens, revaccination is not necessary.

Altered Immunocompetence

General Principles

Altered immunocompetence is a term often used synonymously with immunosuppression and immunocompromise that includes conditions commonly classified as primary immunodeficiency and secondary immunodeficiency.

Primary immunodeficiencies generally are inherited and include conditions defined by an absence or quantitative deficiency of cellular and/or humoral components that provide immunity. Examples include congenital immunodeficiency diseases (e.g., X-linked agammaglobulinemia), severe combined immunodeficiency disease, and chronic granulomatous disease. Secondary immunodeficiency generally is acquired and is defined by loss or qualitative deficiency in cellular and humoral immune components that occurs as a result of a disease process or its therapy. Examples of secondary immune deficiency include HIV infection, hematopoietic malignancies, treatment with radiation, and treatment with immunosuppressive drugs, including alkylating agents and antimetabolites. The degree to which immunosuppressive

drugs cause clinically significant immunodeficiency generally is dose-related and varies by drug. Primary and secondary immunodeficiencies might display a combination of deficits in both cellular and humoral immunity. In this report, the general term altered immunocompetence also will be used to include conditions such as asplenia and chronic renal disease and treatments with therapeutic monoclonal antibodies (specifically the tumor-necrosis-factor alpha inhibitors) (105–110) and prolonged high-dose corticosteroids.

Determination of altered immunocompetence is important to the vaccine provider because the incidence or severity of certain vaccine-preventable diseases is higher in persons with altered immunocompetence; therefore, certain vaccines (e.g., inactivated influenza and pneumococcal vaccines) are recommended specifically for persons with these diseases (47,111–113). Vaccines might be less effective during the period of altered immunocompetence. Live vaccines generally should be deferred until immune function has improved. Inactivated vaccines administered during the period of altered immunocompetence might need to be repeated after immune function has improved. Finally, persons with altered immunocompetence might be at increased risk for an adverse reaction after administration of live-attenuated vaccines because of reduced ability to mount an effective immune response.

The degree of altered immunocompetence in a patient should be determined by a physician. The challenge for clinicians and other health-care providers is in 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 11). 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 (tetanus, diphtheria, and response to pneumococcal vaccine). 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+ versus CD8+ lymphocytes), and tests that measure T-lymphocyte proliferation in response to specific or nonspecific stimuli (e.g., lymphocyte proliferation assays) (114–115). 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

TABLE 11. Vaccination of persons with primary and secondary immune deficiencies

Category	Specific immunodeficiency	Contraindicated vaccines*	Risk-specific recommended vaccines*	Effectiveness and comments
Primary				
B-lymphocyte (humoral)	Severe antibody deficiencies (e.g., X-linked agammaglobulinemia and common variable immunodeficiency)	Oral poliovirus (OPV) [†] Smallpox Live-attenuated influenza vaccine (LAIV) BCG Ty21a (live oral typhoid)	Pneumococcal Influenza (TIV) Consider measles and varicella vaccination	The effectiveness of any vaccine will be uncertain if it depends only on the humoral response; intravenous immune globulin 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 [†] Other live-vaccines appear to be safe	Pneumococcal Influenza (TIV)	All vaccines probably effective. Immune response may be attenuated
T-lymphocyte (cell-mediated and humoral)	Complete defects (e.g., severe combined immunodeficiency [SCID] disease, complete DiGeorge syndrome)	All live vaccines ^{§,¶}	Pneumococcal Influenza (TIV)	Vaccines may be ineffective
	Partial defects (e.g., the majority of patients with DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia)	All live vaccines ^{§,¶}	Pneumococcal Meningococcal <i>Haemophilus influenzae</i> type b (Hib) (if not administered in infancy) Influenza (TIV)	Effectiveness of any vaccine depends on degree of immune suppression
Complement	Deficiency of early components (C1, C2, C3, and C4)	None	Pneumococcal Meningococcal Influenza (TIV)	All routine vaccines probably effective
	Deficiency of late components (C5-C9) and C3, properdin, factor B	None	Pneumococcal Meningococcal Influenza (TIV)	All routine vaccines probably effective
Phagocytic function	Chronic granulomatous disease, leukocyte adhesion defect, and myeloperoxidase deficiency	Live bacterial vaccines [§]	Pneumococcal** Influenza (TIV) (to decrease secondary bacterial infection)	All inactivated vaccines safe and probably effective Live viral vaccines probably safe and effective
Secondary				
	Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)	OPV Smallpox BCG LAIV Withhold MMR and varicella in severely immunocompromised persons	Influenza (TIV) Pneumococcal Consider Hib (if not administered in infancy) and meningococcal vaccination.	Measles, mumps, rubella (MMR, varicella, and all inactivated vaccines, including inactivated influenza, might be effective) ^{††}
	Malignant neoplasm, transplantation, immunosuppressive or radiation therapy	Live viral and bacterial, depending on immune status	Influenza (TIV) Pneumococcal	Effectiveness of any vaccine depends on degree of immune suppression

TABLE 11. (Continued) Vaccination of persons with primary and secondary immune deficiencies

Category	Specific immunodeficiency	Contraindicated vaccines*	Risk-specific recommended vaccines*	Effectiveness and comments
Secondary	Asplenia	None	Pneumococcal Meningococcal Hib (if not administered in infancy)	All routine vaccines probably effective.
	Chronic renal disease	LAIV	Pneumococcal Influenza (TIV) Hepatitis B	All routine vaccines probably effective.

* Other vaccines that are universally or routinely recommended should be administered if not contraindicated.

† OPV is no longer available for routine use in the United States.

§ Live bacterial vaccines: BCG, and Ty21a *Salmonella typhi* vaccine.

¶ Live viral vaccines: MMR, OPV, LAIV, yellow fever, and varicella, including MMRV and HZ vaccine, and vaccinia (smallpox). Smallpox vaccine is not recommended for children or the general public.

** Pneumococcal vaccine is not indicated for children with chronic granulomatous disease.

†† HIV-infected children should receive IG after exposure to measles, and can receive varicella and measles vaccine if CD4+ lymphocyte count is >15%. Modified from American Academy of Pediatrics. Passive Immunization. In: Pickering LK, ed. Red Book: 2006 Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006, and CDC. Use of vaccines and immune globulins in persons with altered immunocompetence: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1993;42 (No. RR-4).

inactivated vaccines is more complicated and might require consultation with an infectious disease or immunology specialist.

Altered Immunocompetence as an Indication to Receive a Vaccine

Persons with altered immunocompetence generally are advised to receive TIV and polysaccharide-based vaccines (i.e., PCV, PPV, MCV4, MPSV, and Hib vaccines) on the basis of demonstrated effectiveness and an increased risk for disease if the vaccine is withheld.

Pneumococcal Vaccines

Two types of vaccine against invasive pneumococcal disease are available in the United States: PCV and PPV. PCV is routinely recommended for all children beginning at age 2 months. PCV is not recommended for persons aged >59 months. PPV is approved for persons aged ≥2 years with certain underlying medical conditions (including altered immunocompetence) and routinely for persons aged ≥65 years. Complete recommendations on use of PCV and PPV are available in the Recommended Child and Adolescent Immunization Schedule and the Recommended Adult Immunization Schedule (113,116).

Influenza Vaccine

Two types of influenza vaccine are available in the United States: TIV and LAIV. Vaccination with TIV is indicated specifically for persons with altered immunocompetence, including HIV infection. LAIV usually is contraindicated for persons

with altered immunocompetence, although healthy persons with anatomic or functional asplenia and household and other close contacts of persons with altered immunocompetence can receive this vaccine.

Meningococcal Vaccine

Two types of meningococcal vaccine are available in the United States: MCV4 and MPSV. Persons with asplenia, C3 complement deficiency (117), or terminal complement component deficiency are at increased risk for meningococcal disease and should receive MCV4 or MPSV. Persons with HIV infection can elect to receive MCV4 or MPSV. MCV4 is licensed for persons aged 11–55 years^{††}; children aged 2–10 years or persons aged ≥56 years should receive MPSV.

Haemophilus influenzae type b Vaccine

Hib conjugate vaccines are available in single or combined antigen preparations. Hib vaccine is recommended routinely for all children through age 59 months. However, a single dose of Hib vaccine also can be considered for asplenic older children, adolescents, and adults who did not receive the vaccine series in childhood. Clinicians and other health-care providers might consider use of Hib vaccine among persons with HIV infection who did not receive the vaccine as an infant or in childhood (112).

††A supplement to the original MCV4 vaccine Biologics License Agreement was submitted to FDA in March 2005, for use of MCV4 in children aged 2–10 years.

Vaccination of Contacts of Persons with Altered Immunocompetence

Household and other close contacts of persons with altered immunocompetence should receive all age-appropriate vaccines, with the exception of live OPV and smallpox vaccine. MMR, varicella, and rotavirus vaccines should be administered to susceptible household and other close contacts of immunocompromised patients when indicated. MMR vaccine viruses are not transmitted to contacts, and transmission of varicella vaccine is rare (6,118). No special precautions are needed unless the varicella vaccine recipient has a rash after vaccination, in which case direct contact with susceptible household contacts should be avoided until the rash resolves (8,119). To minimize potential rotavirus transmission, all members of the household should employ hand hygiene measures after contact with feces of a rotavirus-vaccinated infant for at least 1 week (19). Household and other close contacts of persons with altered immunocompetence should receive annual influenza vaccination. LAIV can be administered to otherwise eligible contacts (47).

Vaccination with Inactivated Vaccines

All inactivated vaccines can be administered safely to persons with altered immunocompetence whether the vaccine is a killed whole organism or a recombinant, subunit, toxoid, polysaccharide, or polysaccharide protein-conjugate vaccine. If inactivated vaccines are indicated for persons with altered immunocompetence, the usual doses and schedules are recommended. However, the effectiveness of such vaccinations might be suboptimal.

Except for influenza vaccine, which should be administered annually (47), vaccination during chemotherapy or radiation therapy should be avoided if possible because antibody response might be suboptimal. However, administration of inactivated vaccines during chemotherapy or radiation is not contraindicated. Patients vaccinated within 2 weeks before starting immunosuppressive therapy or while receiving immunosuppressive therapy should be considered unvaccinated and should be revaccinated at least 3 months after therapy is discontinued if immune competence has been restored.

Vaccination with Live-Attenuated Vaccines

Severe complications have followed vaccination with live-attenuated viral and live-attenuated bacterial vaccines among persons with altered immunocompetence (120–127). Persons with most forms of altered immunocompetence should not receive live vaccines (MMR, varicella vaccine, LAIV, yellow

fever vaccine, oral typhoid, BCG, and rotavirus) except in certain circumstances. Patients with leukemia, lymphoma, or other malignancies whose disease is in remission and whose chemotherapy has been terminated for at least 3 months can receive live-virus vaccines.

Children with defects in phagocyte function (e.g., chronic granulomatous disease or myeloperoxidase deficiency) can receive live-attenuated viral vaccines in addition to inactivated vaccines, but should not receive live-attenuated bacterial vaccines (e.g., BCG and Ty21a oral typhoid vaccine). Children with deficiencies in complement or with asplenia can receive live-attenuated viral and live-attenuated bacterial vaccines (94).

Persons with severe cell-mediated immune deficiency should not receive live attenuated vaccines. However, children with HIV infection are at increased risk for complications of primary varicella and herpes zoster compared with immunocompetent children (118,128). Limited data among HIV-infected children (specifically CDC class N1, N2, A1, A2, B1, or B2) with age-specific CD4⁺ lymphocyte percentages of >15% indicate that varicella vaccine is immunogenic, effective, and safe (129). Varicella vaccine should be considered for children meeting these criteria. Eligible children should receive 2 doses of varicella vaccine with a 3-month interval between doses (118).

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 (130–133). Therefore, MMR vaccination is recommended for all asymptomatic HIV-infected persons who do not have evidence of severe immunosuppression (age-specific CD4⁺ lymphocyte percentages of >15%) and for whom measles vaccination would otherwise be indicated. Similarly, MMR vaccination should be considered for mildly symptomatic (Pediatric Category A1, A2 or Adolescent/adult Category A) (129,134) HIV-infected persons who do not have evidence of severe immunosuppression (age-specific CD4⁺ lymphocyte percentages of >15%) for whom measles vaccination would otherwise be indicated.

HIV-infected persons who are receiving regular doses of IGIV might not respond to varicella vaccine or MMR or its individual component vaccines because of the continued presence of passively acquired antibody. However, because of the potential benefit, MMR and varicella vaccines should be considered approximately 2 weeks before the next scheduled dose of IGIV (if not otherwise contraindicated), although an optimal immune response might not occur depending on the dose and interval since the previous dose of IGIV. Unless serologic testing indicates that specific antibodies have been produced,

vaccination should be repeated (if not otherwise contraindicated) after the recommended interval (Table 4). An additional dose of IGIV should be considered for persons on maintenance IGIV therapy who are exposed to measles or varicella 3 or more weeks after administering a standard dose (100–400 mg/kg body weight) of IGIV.

Persons with impaired humoral immunity (e.g., hypogammaglobulinemia or dysgammaglobulinemia) should receive varicella vaccine (118,135). However, the majority of persons with these disorders also receive periodic doses of IGIV. Appropriate spacing should be maintained between administration of IGIV and varicella vaccine to prevent an inadequate response to vaccination caused by the presence of neutralizing antibodies from the IGIV. Household and other close contacts of persons with altered immunocompetence should receive all age appropriate vaccines, with the exception of live OPV and smallpox vaccine.

Recipients of Hematopoietic Stem Cell Transplant

Hematopoietic stem cell transplantation (HSCT) results in immunosuppression from the hematopoietic ablative therapy preceding transplant, from drugs used to prevent or treat graft-versus-host disease, and in certain cases from the underlying disease process necessitating transplantation (136). HSCT involves ablation of the bone marrow with 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) decline 1–4 years after autologous or allogeneic HSCT if the recipient is not revaccinated. HSCT 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, HSCT recipients should be revaccinated routinely after HSCT, regardless of the source of the transplanted stem cells (136). Revaccination with inactivated vaccines should begin 12 months after HSCT, except inactivated influenza vaccine, which should be administered beginning at least 6 months after HSCT and annually thereafter for the life of the patient. PPV should be administered at 12 and 24 months after HSCT. Data are limited about the use of heptavalent PCV in this population. Sequential administration of 2 doses of heptavalent pneumococcal conjugate vaccine followed by a dose of pneumococcal polysaccharide vaccine (with 8 weeks between doses) can be considered, especially for children aged <60 months. A 3-dose regimen of Hib vaccine should be administered at ages 12, 14, and 24

months after transplantation for all age groups (136). MMR vaccine should be administered 24 months after transplantation if the HSCT recipient is immunocompetent. Because of insufficient experience using varicella vaccine among HSCT recipients, physicians should assess the immune status of each recipient on a case-by-case basis and determine the risk for infection before using these vaccines. If a decision is made to vaccinate with varicella vaccine, the vaccine should be administered a minimum of 24 months after transplantation if the HSCT recipient is presumed to be immunocompetent (137).

Situations in Which Some Degree of Immunodeficiency Might be Present

Asplenia and use of corticosteroids or certain drugs have the potential to be immunosuppressive and in each, some degree of altered immunocompetence is presumed to exist.

Anatomic or Functional Asplenia

Persons with anatomic (e.g., surgical removal or congenital absence) or functional (as occurs with sickle cell disease) asplenia are at increased risk for infection by encapsulated bacteria, especially with *S. pneumoniae* (pneumococcus), *N. meningitidis* (meningococcus), and Hib (26,48,117). Persons with anatomic or functional asplenia should receive pneumococcal vaccine, depending on their age and previous pneumococcal vaccination status, as recommended (29,48,113,116).

Meningococcal vaccine is recommended for persons with anatomic or functional asplenia. Children aged 2–10 years and persons aged ≥ 56 years should receive MPSV. MCV4 is approved for persons aged 11–55 years^{††} and is preferred for persons in this age group, but MPSV is an acceptable alternative (117). A second dose of MPSV can be considered at least 5 years after the initial dose. The duration of immunity after MCV4 is not known, but is thought to be long-lasting like other conjugate vaccines, and revaccination is not recommended.

No efficacy data are available on which to base a recommendation about use of Hib vaccine for older children and adults with the chronic conditions associated with an increased risk for Hib disease. However, studies suggest good immunogenicity in patients who have sickle cell disease or have had splenectomies; administering Hib vaccine to these patients is not contraindicated (112).

Pneumococcal, meningococcal, and Hib vaccines should be administered at least 2 weeks before elective splenectomy, if possible. If vaccines are not administered before surgery, they should be administered as soon as the person's condition stabilizes after the procedure.

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. Corticosteroid therapy usually is not a contraindication to administering live-virus vaccine when administration is short-term (i.e., <2 weeks); a low-to-moderate dose (<20 mg or prednisone or equivalent per day); long-term, alternate-day treatment with short-acting preparations; maintenance physiologic doses (replacement therapy); or administered topically (skin or eyes), inhaled, or by intra-articular, bursal, or tendon injection (138). No evidence of increased severity of reactions to live-attenuated vaccines has been reported among persons receiving corticosteroid therapy by aerosol, and such therapy is not a reason to delay vaccination. The immunosuppressive effects of steroid treatment vary, but 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 ≥2 weeks as sufficiently immunosuppressive to raise concern about the safety of vaccination with live-virus vaccines (112,138). Corticosteroids used in greater than physiologic doses also can reduce the immune response to vaccines. Vaccination providers should wait at least 1 month after discontinuation of high dose systemically absorbed corticosteroid therapy administered for more than 2 weeks before administering a live-virus vaccine.

Other Immunosuppressive Drugs

Whenever feasible, clinicians should provide all indicated vaccines to all persons 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, solid tumors, or after solid organ transplant 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 might need to be readministered after immune competence is regained. Persons vaccinated before chemotherapy for leukemia, lymphoma, other malignancies, or radiation generally are thought to retain immune memory after treatment, although revaccination following chemotherapy for acute lymphoblastic leukemia might be indicated (139). Revaccination of a person after chemotherapy or radiation therapy is not thought to be necessary if the previous vaccination occurred before therapy and not during the therapy, with the exception of recipients of HSCT, who should be revaccinated as recommended previ-

ously. Determination of the level of immune memory and the need for revaccination should be made by the treating physician.

Inactivated vaccines can be administered during low dose intermittent or maintenance therapy of immunosuppressive drugs. The safety and efficacy of live-attenuated vaccines during such therapy is unknown. Physicians should carefully weigh the risks for and benefits of providing injectable live vaccines to adult patients on low-dose therapies for chronic autoimmune disease. The safety and efficacy of live-attenuated vaccines administered concurrently with recombinant human immune mediators and immune modulators is unknown. Evidence that use of therapeutic monoclonal antibodies, especially the antitumor necrosis factor agents adalimumab, infliximab, and etanercept, causes reactivation of latent tuberculosis infection and tuberculosis disease and predisposes to other opportunistic infections suggests caution in the use of live vaccines in patients receiving these drugs (105–110). Until additional information becomes available, avoidance of live attenuated vaccines during intermittent or low dose chemotherapy or other immunosuppressive therapy is prudent, unless the benefit of vaccination outweighs the hypothetical increased risk for an adverse reaction after vaccination.

Special Situations

Concurrently Administering Antimicrobial Agents and Vaccines

With limited exceptions, using an antimicrobial agent is not a contraindication to vaccination. Antimicrobial agents have no effect on the response to live-attenuated vaccines, except live oral Ty21a typhoid vaccine, and have no effect on inactivated, recombinant subunit, or polysaccharide vaccines or toxoids. Ty21a typhoid vaccine should not be administered to persons receiving antimicrobial agents until 24 hours after any dose of antimicrobial agent (20).

Antiviral drugs used for treatment or prophylaxis of influenza virus infections have no effect on the response to inactivated influenza vaccine (47). However, live-attenuated influenza vaccine should not be administered until 48 hours after cessation of therapy using antiviral influenza drugs. If feasible, antiviral medication should not be administered for 2 weeks after LAIV administration (47). Antiviral drugs active against herpesviruses (e.g., acyclovir or valacyclovir) might reduce the efficacy of live-attenuated varicella vaccine. These drugs should be discontinued at least 24 hours before administration of varicella-containing vaccines, if possible.

The antimalarial drug mefloquine could affect the immune response to oral Ty21a typhoid vaccine if both are taken si-

multaneously (140). To minimize this effect, administering Ty21a typhoid vaccine at least 24 hours before or after a dose of mefloquine is prudent.

Tuberculosis Screening and Skin Test Reactivity

Measles illness, severe acute or chronic infections, HIV infection, and malnutrition can create a relatively anergic state during which the tuberculin skin test (TST) (previously referred to as purified protein derivative [PPD] skin test) might give a false negative reaction (141–143). Although any live attenuated measles vaccine can theoretically suppress TST reactivity, the degree of suppression is probably less than that occurring from acute infection from wild-type measles virus. Although routine TST screening of all children is no longer recommended, TST screening is sometimes needed at the same time as administering a measles-containing vaccine (e.g., for well-child care, school entrance, or for employee health reasons).

TST and measles-containing vaccine can be administered at the same visit (preferred option). Simultaneously administering 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 TST will remove the concern of any theoretical but transient suppression of TST reactivity from the vaccine.

TST screening can be performed and read before administering the measles-containing vaccine. This option is the least favored because it will delay receipt of the measles-containing vaccine.

No data exist for the potential degree of TST suppression that might be associated with other injectable, live-attenuated virus vaccines (e.g., varicella and 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. Because of similar concerns about smallpox vaccine and TST suppression, a TST should not be performed until four weeks after smallpox vaccination (144).

TST reactivity in the absence of tuberculosis disease is not a contraindication to administration of any vaccine, including live-attenuated virus vaccines. Tuberculosis disease is not a contraindication to vaccination, unless the person is moderately or severely ill. Although no studies have reported the

effect of MMR vaccine on persons with untreated tuberculosis, a theoretical basis exists for concern that measles vaccine might exacerbate the disease tuberculosis (6). As a result, before administering MMR to persons with untreated active tuberculosis, initiating antituberculosis therapy is advisable (7). Considering if concurrent immunosuppression (e.g., immunosuppression caused by HIV infection) is a concern before administering live attenuated vaccines also is prudent.

Severe Allergy to Vaccine Components

Vaccine components can cause allergic reactions among certain recipients. These reactions can be local or systemic and can include mild-to-severe anaphylaxis or anaphylactic-like responses (e.g., generalized urticaria or hives, wheezing, swelling of the mouth and throat, difficulty breathing, hypotension, and shock). Allergic reactions might be caused by the vaccine antigen, residual animal protein, antimicrobial agents, preservatives, stabilizers, or other vaccine components (145). Components of each vaccine are listed in the respective package insert. An extensive listing of vaccine components, their use, and the vaccines that contain each component has been published (146) and is also available from CDC's National Center for Immunization and Respiratory Diseases (proposed) (<http://www.cdc.gov/nip>).

The most common animal protein allergen is egg protein, which is found in influenza and yellow fever vaccines, which are prepared using embryonated chicken eggs. Ordinarily, persons who are able to eat eggs or egg products safely can receive these vaccines; persons with histories of anaphylactic or anaphylactic-like allergy to eggs or egg proteins should generally not receive these vaccines. Asking persons if they can eat eggs without adverse effects is a reasonable way to determine who might be at risk for allergic reactions from receiving yellow fever and influenza vaccines. A regimen for administering influenza vaccine to children with egg hypersensitivity and severe asthma has been developed (147).

Measles and mumps vaccine viruses are grown in chick embryo fibroblast tissue culture. Persons with a serious egg allergy can receive measles- or mumps-containing vaccines without skin testing or desensitization to egg protein (6). Rubella and varicella vaccines are grown in human diploid cell cultures and can safely be administered to persons with histories of severe allergy to eggs or egg proteins. The rare serious allergic reactions after measles or mumps vaccination or MMR are not believed to be caused by egg antigens, but to other components of the vaccine (e.g., gelatin) (148–151). MMR, MMRV, and their component vaccines and other vaccines contain hydrolyzed gelatin as a stabilizer. Extreme caution should be used when administering vaccines that contain

gelatin to persons who have a history of an anaphylactic reaction to gelatin or gelatin-containing products. Before administering gelatin-containing vaccines to such persons, skin testing for sensitivity to gelatin can be considered. However, no specific protocols for this approach have been published.

Certain vaccines contain trace amounts of antimicrobial agents or other preservatives (e.g., neomycin or thimerosal) to which patients might be severely allergic. The information provided in the vaccine package insert should be reviewed carefully before deciding if the rare patient with such allergies should receive the vaccine. No licensed vaccine contains penicillin or penicillin derivatives.

Certain vaccines contain trace amounts of neomycin. Persons who have experienced anaphylactic reactions to neomycin should not receive these vaccines. Most often, neomycin allergy is a contact dermatitis, a manifestation of a delayed type (cell-mediated) immune response, rather than anaphylaxis (152,153). A history of delayed type reactions to neomycin is not a contraindication for administration of these vaccines.

Thimerosal is an organic mercurial compound in use since the 1930s and is added to certain immunobiologic products as a preservative. A joint statement issued by the U.S. Public Health Service and the American Academy of Pediatrics (AAP) in 1999 (154) and agreed to by the American Academy of Family Physicians (AAFP) later in 1999, established the goal of removing thimerosal as soon as possible from vaccines routinely recommended for infants. Although no evidence exists of any harm caused by low levels of thimerosal in vaccines and the risk was only theoretical (155), this goal was established as a precautionary measure.

The public is concerned about the health effects of mercury exposure of any type, and the elimination of mercury from vaccines was judged a feasible means of reducing an infant's total exposure to mercury in a world where other environmental sources of exposure are more difficult or impossible to eliminate (e.g., common foods like tuna). Since mid-2001, vaccines routinely recommended for infants have been manufactured without thimerosal as a preservative. 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 trace thimerosal, in which thimerosal no longer functions as a preservative, and in formulations that contain thimerosal. Thimerosal that acts as a preservative 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 (<http://www.fda.gov/cber/vaccine/thimerosal.htm>).

Receiving thimerosal-containing vaccines might lead to induction of allergy. However, limited scientific basis exists for this assertion (145). Allergy to thimerosal usually consists of local delayed type hypersensitivity reactions (156–158). Thimerosal elicits positive delayed type hypersensitivity patch tests in 1%–18% of persons tested, but these tests have limited or no clinical relevance (159–160). 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 (160). A localized or delayed type hypersensitivity reaction to thimerosal is not a contraindication to receipt of a vaccine that contains thimerosal.

Latex Allergy

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

The most common type of latex sensitivity is contact-type (type 4) allergy, usually as a result of prolonged contact with latex-containing gloves (161). However, injection-procedure-associated latex allergies among patients with diabetes mellitus have been described (162–164). Allergic reactions (including anaphylaxis) after vaccination procedures are rare (165). Only one known report of an allergic reaction after administering HepB to a patient with known severe allergy (anaphylaxis) to latex has been published (166).

If a person reports a severe (anaphylactic) allergy to latex, vaccines supplied in vials or syringes that contain natural rubber should not be administered unless the benefit of vaccination outweighs the risk for a potential allergic reaction. For latex allergies other than anaphylactic allergies (e.g., a history of contact allergy to latex gloves), vaccines supplied in vials or syringes that contain dry natural rubber or natural rubber latex can be administered.

Vaccination of Preterm Infants

In the majority of cases, infants born prematurely, regardless of birthweight, should be vaccinated at the same chronological age and according to the same schedule and precautions as full-term infants and children. Birthweight and size are not factors in deciding whether to postpone routine vaccination of a clinically stable preterm infant (167–171), except for HepB. The full recommended dose of each vaccine should be used. Divided or reduced doses are not recommended (173).

Decreased seroconversion rates might occur among certain preterm infants with low birthweights (i.e., <2,000 g) after administration of HepB at birth (173). However, by chronological age 1 month, all preterm infants, regardless of initial birth weight or gestational age, are likely to respond as adequately as older and larger infants (174–176). Preterm infants born to HBsAg-positive mothers and mothers with unknown HBsAg status must receive immunoprophylaxis with HepB and HBIG within 12 hours after birth. If these infants weigh <2,000 g at birth, the initial vaccine dose should not be counted towards completion of the HepB series, and 3 additional doses of HepB should be administered, beginning when the infant is aged 1 month. Preterm infants weighing <2,000 g and born to HBsAg-negative mothers should receive the first dose of the HepB series at chronological age 1 month or at hospital discharge. (30)

Breast Feeding and Vaccination

Neither inactivated nor live vaccines administered to a lactating woman affect the safety of breast feeding for women or their infants. Breast feeding does not adversely affect immunization and is not a contraindication for any vaccine, with the exception of smallpox vaccine. Limited data indicate that breast feeding can enhance the response to certain vaccine antigens (177). Breast-fed infants should be vaccinated according to recommended schedules (178–180).

Although live vaccines multiply within the mother's body, the majority have not been demonstrated to be excreted in human milk (181). Although rubella vaccine virus might be 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 (182). Inactivated, recombinant, subunit, polysaccharide, conjugate vaccines and toxoids pose no risk for mothers who are breast feeding or for their infants.

Vaccination During Pregnancy

Risk for a developing fetus from vaccination of the mother during pregnancy primarily is theoretical. No evidence exists of risk from vaccinating pregnant women with inactivated

virus or bacterial vaccines or toxoids (183,184). Live vaccines pose a theoretical risk to the fetus. Benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high, when infection would pose a risk to the mother or fetus, and when the vaccine is unlikely to cause harm.

Recommendations for vaccination during pregnancy can be found in the adult immunization schedule (113). Pregnant women should receive Td vaccine if indicated. Previously vaccinated pregnant women who have not received a Td vaccination within the last 10 years should receive a booster dose. Pregnant women who are not vaccinated or only partially immunized against tetanus should complete the primary series (28,112). Women for whom the vaccine is indicated but who have not completed the recommended 3-dose series during pregnancy should receive follow-up after delivery to ensure the series is completed. Pregnant adolescents and adults who received the last tetanus-containing vaccine <10 years previously are generally recommended to receive Tdap after delivery. To prevent neonatal tetanus, pregnant adolescents who received the last dose of tetanus-toxoid containing vaccine ≥ 10 years previously should generally receive Td in preference to Tdap while they are pregnant (28), although Tdap is not contraindicated during pregnancy.

Women in the second and third trimesters of pregnancy are at increased risk for hospitalization from influenza. Therefore, routine influenza vaccination is recommended for all women who will be pregnant (in any trimester) during influenza season (usually November–March in the United States) (47).

IPV can be administered to pregnant women who are at risk for exposure to wild-type poliovirus infection (4). HepB is recommended for pregnant women at risk for hepatitis B virus infection (30). HepA, pneumococcal polysaccharide, meningococcal conjugate, and meningococcal polysaccharide vaccines should be considered for women at increased risk for those infections (48,117,185). Pregnant women who must travel to areas where the risk for yellow fever is high should receive yellow fever vaccine because the limited theoretical risk from vaccination is substantially outweighed by the risk for yellow fever infection (24,186).

Pregnancy is a contraindication for smallpox (vaccinia), measles, mumps, rubella, and varicella-containing vaccines. Smallpox (vaccinia) vaccine is the only vaccine known to cause harm to a fetus when administered to a pregnant woman. In addition to the vaccinee herself, smallpox (vaccinia) vaccine should not be administered to a household contact of a pregnant woman (144). Although of theoretical concern, no cases of congenital rubella or varicella syndrome or abnormalities

attributable to fetal infection have been observed among infants born to susceptible women who received rubella or varicella vaccines during pregnancy (6,187). 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 be pregnant; 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 (6,39,188). Routine pregnancy testing of women of childbearing age before administering a live-virus vaccine is not recommended (6). If vaccination of an unknowingly pregnant woman occurs or if she becomes pregnant within 4 weeks after MMR or varicella vaccination, she should be counseled about the theoretical basis of concern for the fetus; however, MMR or varicella vaccination during pregnancy should not be regarded as a reason to terminate pregnancy (6,8,189).

Persons who receive MMR vaccine do not transmit the vaccine viruses to contacts (6). Transmission of varicella vaccine virus to contacts is extremely rare (118). MMR and varicella vaccines should be administered when indicated to the children and other household contacts of pregnant women (6,8).

All pregnant women should be evaluated for immunity to rubella and varicella and be tested for the presence of HBsAg in every pregnancy (6,30,39). Women susceptible to rubella and varicella should be vaccinated immediately after delivery. A woman found to be HBsAg-positive should be followed carefully to ensure that the infant receives HBIG and begins the hepatitis B vaccine series no later than 12 hours after birth and that the infant completes the recommended HepB vaccine series on schedule (30). No known risk exists for the fetus from passive immunization of pregnant women with immune globulin preparations.

Persons Vaccinated Outside the United States, Including Internationally Adopted Children

The ability of a clinician to determine that a person is protected on the basis of their country of origin and their records alone is limited. Vaccines administered outside the United States can generally be accepted as valid if the schedule was similar to that recommended in the United States (i.e., minimum ages and intervals). 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 the

person's age at the time of vaccination are comparable to U.S. recommendations. Although vaccines with inadequate potency have been produced in other countries (190,191), the majority of vaccines used worldwide is produced with adequate quality control standards and are potent.

The number of U.S. families adopting children from outside the United States has increased substantially in recent years (192). Adopted children's birth countries often have vaccination schedules that differ from the recommended childhood immunization schedule in the United States. Differences in the U.S. immunization 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 about 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 Eastern Europe determined that 67% of children with documentation of more than 3 doses of DTP before adoption had nonprotective titers to these antigens. By contrast, children adopted from these countries who received vaccination in the community (not only from orphanages) and who possessed records of 1 or more doses of DTP exhibited protective titers 67% of the time (193). However, antibody testing was performed by using a hemagglutination assay, which tends to underestimate protection and cannot directly be compared with antibody concentration (194). Data are likely to remain limited for countries other than the People's Republic of China, Russia, and Eastern Europe because of the limited number of adoptees from other countries.

Clinicians and other health-care providers can follow one of multiple approaches if a question exists about whether vaccines administered to an international adoptee were immunogenic. Repeating the vaccinations is an acceptable option. Doing so usually is safe and avoids the need to obtain and interpret serologic tests. If avoiding unnecessary injections is desired, judicious use of serologic testing might be helpful in determining which vaccinations are needed. For some vaccines, the most readily available serologic tests cannot document protection against infection. These recommendations provide guidance on possible approaches to evaluation and revaccination for each vaccine recommended universally for children in the United States (Table 12). Clinicians and other health-care providers should ensure that household contacts of internationally adoptees are adequately vaccinated, particularly for measles and hepatitis B.

TABLE 12. Approaches to the evaluation and vaccination of internationally adopted children with no or questionable vaccination records

Vaccine	Recommended approach	Alternative approach
Measles, mumps, and rubella (MMR)	Revaccinate with MMR	Serologic testing for immunoglobulin G (IgG) antibody to measles, mumps, and rubella
<i>Haemophilus influenzae</i> type b (Hib)	Age-appropriate revaccination	—
Hepatitis A	Age-appropriate revaccination	Serologic testing for IgG antibody to hepatitis A virus
Hepatitis B (Hep B)	Age-appropriate revaccination and serologic testing for HBsAg*	—
Poliovirus	Revaccinate with inactivated poliovirus vaccine (IPV)	Serologic testing for neutralizing antibody to poliovirus types 1, 2, and 3 (limited availability)
Diphtheria and tetanus toxoids and acellular pertussis (DTaP)	Revaccination with DTaP, with serologic testing for specific IgG antibody to tetanus and diphtheria toxins in the event of a severe local reaction	Children 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
Varicella	Age-appropriate vaccination of children who lack evidence of varicella immunity	—
Pneumococcal conjugate	Age-appropriate vaccination	—

* Very rarely, Hep B vaccine can give a false positive HBsAg result up to 18 days following vaccination; therefore, blood should be drawn to test for HBsAg before vaccinating (CDC. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices [ACIP]; Part I: Immunization in Infants, Children, and Adolescents. MMWR 2005;54[No. RR-16]).

MMR Vaccine

The simplest approach to resolving concerns about MMR vaccination among internationally adopted children is to revaccinate with 1 or 2 doses of MMR vaccine, depending on the child's age. Serious adverse events after MMR vaccinations are rare (6). 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 (6). Alternatively, serologic testing for immunoglobulin G (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 child 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 used). If a child whose record indicates receipt of MMR at age ≥ 12 months has a protective

concentration of antibody to measles, no additional vaccination is needed unless required for school entry.

Hib Vaccine

Interpretation of a serologic test to verify protection from Hib bacteria for children vaccinated >2 months previously can be difficult to interpret. Because the number of vaccinations needed for protection decreases with age and adverse events are rare (26), age-appropriate vaccination should be provided. Hib vaccination is not recommended routinely for children aged ≥ 5 years (116).

Hepatitis A Vaccine

Children without documentation of HepA vaccination or serologic evidence of immunity should be vaccinated on arrival if aged ≥ 12 months (185).

Hepatitis B Vaccine

Children not known to be vaccinated for hepatitis B should receive an age-appropriate series of HepB. A child whose records indicate receipt of 3 or more doses of vaccine can be considered protected, and additional doses are not needed if 1 or more doses were administered at age ≥ 24 weeks. Chil-

dren who received their last HepB dose at age <24 weeks should receive an additional dose at age ≥ 24 weeks. Children who have received fewer than 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 in which HBV is highly endemic should be tested for HBsAg, regardless of vaccination status. 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 not already immune.

Poliovirus Vaccine

The simplest approach is to revaccinate internationally adopted children with IPV according to the U.S. schedule. Adverse events after IPV are rare (4). Children appropriately vaccinated with 3 doses of OPV in economically developing countries might have suboptimal seroconversion, including to type 3 poliovirus (180). Serologic testing for neutralizing antibody to poliovirus types 1, 2, and 3 can be obtained commercially and at certain state health department laboratories. Children with protective titers against all three types do not need revaccination and should complete the schedule as age-appropriate.

DTaP Vaccine

Vaccination providers can revaccinate a child with DTaP vaccine without regard to recorded doses; however, one concern about this approach is that data indicate increased rates of local adverse reactions after the fourth and fifth doses of DTP or DTaP (46). 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^{§§} indicates that further 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 or more 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 can be considered valid, and the vaccination series should be completed as age-appropriate. Indeterminate antibody concentration might indicate

immunologic memory but antibody waning; serology can be repeated after a booster dose if the vaccination provider wants to avoid revaccination with a complete series.

Alternately, for a child whose records indicate receipt of 3 or more 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 a protective concentration is obtained, the recorded doses can be considered valid and the vaccination series completed as age-appropriate. Children with indeterminate concentration after a booster dose should be revaccinated with a complete series.

Varicella Vaccine

Varicella vaccine is not administered in the majority of countries. A child who lacks reliable evidence of varicella immunity should be vaccinated as age-appropriate (8,116).

Pneumococcal Vaccines

PCV and PPV are not administered in the majority of countries and should be administered as age-appropriate or as indicated by the presence of underlying medical conditions (29,48).

Vaccinating Persons with Bleeding Disorders and Persons Receiving Anticoagulant Therapy

Because of the risk for hematoma formation after injections, intramuscular injections are often avoided among persons with bleeding disorders by using the subcutaneous or intradermal routes for vaccines that are administered normally by the intramuscular route. HepB administered intramuscularly to 153 persons with hemophilia by using a 23-gauge needle or smaller, followed by steady pressure to the site for 1–2 minutes, resulted in a 4% bruising rate with no patients requiring factor supplementation (195). Whether antigens that produce more local reactions (e.g., pertussis) would produce an equally low rate of bruising is unknown.

When HepB or any other intramuscular vaccine is indicated for a patient with a bleeding disorder or a person receiving anticoagulant therapy, the vaccine should be administered intramuscularly if, in the opinion of a physician familiar with the patient's bleeding risk, the vaccine can be administered with reasonable safety by this route. If the patient receives antihemophilia or similar therapy, intramuscular vaccinations can be scheduled shortly after such therapy is administered. A fine needle (23 gauge or smaller) should be used for the vaccination and firm pressure applied to the site, without rubbing, for at least 2 minutes. The patient or family should be instructed concerning the risk for hematoma from the injection.

^{§§}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.

Vaccination Records

Consent to Vaccinate

The National Childhood Vaccine Injury Act of 1986 (42 U.S.C. § 300aa-26) requires that all health-care providers in the United States who administer any vaccine covered by the Act⁴⁴ must provide a copy of the relevant, current edition of the vaccine information materials that have been produced by CDC before administering each dose of the vaccine. Vaccine information statements (VIS) are available at <http://www.cdc.gov/nip/publications/VIS/default.htm> and <http://www.immunize.org/vis>. VIS must be provided to the parent or legal representative of any child or to any adult to whom the physician or other health-care provider intends to administer the vaccine. The act does not require that a signature be obtained, but documentation of consent is recommended or required by certain state or local authorities.

Provider Records

Documentation of patient vaccinations helps ensure that persons in need of a vaccine receive it and that adequately vaccinated patients are not administered excess doses, possibly increasing the risk for local adverse events (e.g., tetanus toxoid). Serologic test results for vaccine-preventable diseases (e.g., those for rubella screening and antibody to hepatitis B surface antigen) and documented episodes of adverse events also should be recorded in the permanent medical record of the vaccine recipient.

Health-care providers who administer vaccines covered by the National Childhood Vaccine Injury Act are required 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. In addition, the provider is required to record the edition date of the VIS distributed and the date those materials were provided. In the Act, the term health-care provider is defined as 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 same information should be kept for all vaccines, not just for those required by the National Childhood Vaccine Injury Act.

⁴⁴As of May 2006, vaccines covered by the act include diphtheria, tetanus, pertussis, measles, mumps, rubella, poliovirus, HepB, Hib, varicella, pneumococcal conjugate, HepA, trivalent inactivated influenza vaccine, and pentavalent RV.

Patients' Personal Records

Official childhood vaccination records have been adopted by every state, 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. A permanent vaccination record card should be established for each newborn infant and maintained by the parent or guardian. In certain states, these cards are distributed to new mothers before discharge from the hospital. Using vaccination record cards for adolescents and adults also is encouraged. Standardized adult vaccination records are available at <http://www.immunize.org>.

Immunization Information Systems

IISs 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 increased vaccination coverage by consolidating vaccination records of children from multiple providers, generating reminder and recall vaccination notices for each child, and providing official vaccination forms and vaccination coverage assessments (196). A fully operational IIS also can prevent duplicate vaccinations, limit missed appointments, reduce vaccine waste, and reduce staff time required to produce or locate vaccination records or certificates. The National Vaccine Advisory Committee strongly encourages development of community- or state-based IISs and recommends that vaccination providers participate in these systems whenever possible (196). One of the national health objectives for 2010 is 95% participation of children aged <6 years in a fully operational population-based IIS (objective 20.1) (197).

Reporting Adverse Events after Vaccination

Modern vaccines are safe and effective; however, adverse events have been reported after administration of all vaccines (91). These events range from frequent, minor, local reactions to extremely rare, severe, systemic illness (e.g., anaphylaxis). Establishing evidence for cause-and-effect relations on the basis of case reports and case series alone is impossible because temporal association alone does not necessarily indicate causation. Unless the symptom or syndrome that occurs after vaccination is clinically or pathologically distinctive, more detailed epidemiologic studies to compare the incidence of

the event among vaccinees with the incidence among unvaccinated persons are necessary. Reporting adverse events to public health authorities, including serious events, is a key stimulus to developing studies to confirm or refute a causal association with vaccination. More complete information about adverse reactions to a specific vaccine is available in the ACIP recommendations for that vaccine and in a specific statement on vaccine adverse reactions (91).

The National Childhood Vaccine Injury Act requires health-care providers to report selected events occurring after vaccination to VAERS. Events for which reporting is required appear in the Reportable Events Table.^{***} Persons other than health-care providers also can report adverse events to VAERS. All clinically significant adverse events other than those that must be reported or that occur after administration of vaccines not covered by the Act also should be reported to VAERS, even if the physician or other health-care provider is uncertain they are related causally to vaccination. VAERS forms and instructions are available in the FDA Drug Bulletin by contacting VAERS (800-822-7967), or from the VAERS website (<http://www.vaers.hhs.gov/vaers.htm>).

National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program, established by the National Childhood Vaccine Injury Act, is a no-fault system in which persons thought to have suffered an injury or death 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 a Reportable Events Table listing the vaccines covered by the program and the injuries, disabilities, illnesses, and conditions (including death) 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. 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 table if they prove causation. Injuries after administration of vaccines not listed in the legislation authorizing the program are not eligible for compen-

sation through the program. Additional information is available from the National Vaccine Injury Compensation Program, Health Resources and Services Administration, Parklawn Building, Room 11C-26, 5600 Fishers Lane, Rockville, MD 20857; telephone: 800-338-2382; Website: <http://www.hrsa.gov/osp/vicp>.

Persons wanting to file a claim for vaccine injury should contact the following: U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, DC 20005; telephone: 202-357-6400.

Benefit and Risk Communication

Parents, guardians, legal representatives, and adolescent and adult patients should be informed about the benefits of and risks for vaccines in understandable language. Opportunity for questions should be provided before each vaccination. Discussion of the benefits of and risks for vaccination is sound medical practice and is required by law.

The National Childhood Vaccine Injury Act requires that vaccine information materials be developed for each vaccine covered by the Act. These materials, known as Vaccine Information Statements, must be provided by all public and private vaccination providers each time a vaccine is administered. Copies of Vaccine Information Statements are available from state health authorities responsible for vaccination, or they can be obtained from CDC's National Center for Immunization and Respiratory Disease (proposed) website (<http://www.cdc.gov/nip>). Translations of Vaccine Information Statements into languages other than English are available from certain state vaccination programs and from the Immunization Action Coalition website (<http://www.immunize.org>).

Health-care providers should anticipate that certain parents or patients will question the need for or safety of vaccination, refuse certain vaccines, or even reject all vaccinations. A limited number of persons might have religious or personal objections to vaccinations. Others might want to enter into a dialogue about the risks for and benefits of certain vaccines. Having a basic understanding of how patients view vaccine risk and developing effective approaches in dealing with vaccine safety concerns when they arise is 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, perceived ability to control those risks, and their risk preference. Increasingly, through the media and nonauthoritative Internet sites, decisions about risk are based on inaccurate information. Only through direct dialogue with parents and by using available

^{***}The Reportable Events Table can be obtained from the Vaccine Injury Compensation Program Internet site at <http://vaers.hhs.gov/reportable.htm>.

resources can health-care providers prevent acceptance of media reports and information from nonauthoritative Internet sites as scientific fact.

When a parent or patient initiates a discussion about a vaccine controversy, 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, recognizing that for certain persons, risk assessment and decision-making are difficult and confusing. Certain vaccines might be acceptable to the resistant parent. Their concerns should then be addressed using the VIS and offering other resource materials (e.g., information available on the National Center for Immunization and Respiratory Diseases (proposed) website [<http://www.cdc.gov/nip>]).

Although a limited number of providers might exclude from their practice those patients who question or refuse vaccination, the more effective public health strategy is to identify common ground and discuss measures that need to be followed if the patient's decision is to defer vaccination. As part of a strong recommendation, health-care providers can reinforce key points about each vaccine, including safety, and emphasize risks encountered by unvaccinated children. Parents should be advised of state laws pertaining to school or child-care entry, which might require that unvaccinated children be excluded from school or child care during outbreaks. Documentation of these discussions in the patient's record, including the refusal to receive certain vaccines (i.e., informed refusal), might reduce any potential liability if a vaccine-preventable disease occurs in the unvaccinated patient.

Vaccination Programs

The best way to reduce vaccine-preventable diseases is to have a highly immune population. Universal vaccination is a critical part of quality health care and should be accomplished through routine and intensive vaccination programs implemented in physicians' offices and in public health clinics. Programs should be established and maintained in all communities to ensure vaccination of all children at the recommended age. In addition, appropriate vaccinations should be available for all adolescents and adults.

Physicians and other pediatric vaccination providers should adhere to the standards for child and adolescent vaccination practices (1). These standards define appropriate vaccination practices for both the public and private sectors. The standards provide guidance on practices that will result in eliminating barriers to vaccination. These include practices aimed at eliminating unnecessary prerequisites for receiving vacci-

nations, eliminating missed opportunities to vaccinate, improving procedures to assess vaccination needs, enhancing knowledge about vaccinations among parents and providers, and improving the 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. Physicians and other health-care providers should simultaneously administer as many vaccine doses as possible, as indicated on the Recommended Child and Adolescent Immunization Schedule (116).

Standards of practice also have been published to increase vaccination coverage among adults (2). These standards include ensuring vaccine availability, routine review of vaccination status, communicating risks for and benefits to the patient, using standing orders, and recommending simultaneous administration of all indicated doses according to the Recommended Adult Immunization Schedule (113).

Every visit to a physician or other health-care provider can be an opportunity to update a patient's vaccination status with needed vaccinations. Official health agencies should take necessary steps, including, when appropriate, developing and enforcing child care and school vaccination requirements, to ensure that students at all grade levels (including college) and children in day care centers are protected against vaccine-preventable diseases. Agencies also should encourage institutions (e.g., hospitals and long-term-care facilities) to adopt policies about the appropriate vaccination of patients, residents, and employees (198).

Dates of vaccination (day, month, and year) should be recorded on institutional vaccination records (e.g., records kept in schools and day care centers). These records will facilitate assessments that a primary vaccination series has been completed according to an appropriate schedule and that needed booster doses have been administered at the appropriate time.

The independent, nonfederal Task Force on Community Preventive Services (the Task Force), 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 and the applicability to specific populations and settings and the potential barriers to implementation. This information is available 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 (199–202). Using the results of their review, the Task Force made recommendations about the use of these interventions (202). Several interventions were identified and recommended on the basis of published evidence. The interventions and the recommendations are summarized in this report (Table 13).

Vaccine Information Sources

In addition to these general recommendations, other sources are available that contain specific and updated vaccine information.

CDC-INFO Contact Center

The CDC-INFO contact center is supported by CDC's National Center for Immunization and Respiratory Diseases (proposed) and provides public health-related information, including vaccination information, for health-care providers and the public, 24 hours a day, seven days a week (Telephone

[English and Spanish]: 800-232-4636; Telephone [TTY]: 800-232-6348).

CDC's National Center for Immunization and Respiratory Diseases (proposed)

CDC's National Center for Immunization and Respiratory Diseases (proposed) website provides direct access to immunization recommendations of ACIP, vaccination schedules, vaccine safety information, publications, provider education and training, and links to other vaccination-related websites (<http://www.cdc.gov/nip>).

MMWR

ACIP recommendations 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. Electronic subscriptions are free (<http://www.cdc.gov/subscribe.html>). Printed subscriptions are available at

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TABLE 13. Summary of recommendations for interventions to improve coverage of vaccines recommended for routine use among children, adolescents, and adults*

Intervention	Recommendations
Interventions that increase community demand for immunization	
Client reminder or recall systems	Strongly recommended
Multicomponent interventions, including education	Strongly recommended
School, day care, and college-entry requirements	Recommended
Community education alone	Insufficient evidence
Clinic-based education	Insufficient evidence
Patient or family incentives or sanctions	Insufficient evidence
Client-held medical records	Insufficient evidence
Interventions that enhance access to vaccination services	
Reducing out-of-pocket costs	Strongly recommended
Enhancing access through the U.S. Department of Agriculture's Women, Infants, and Children program	Recommended
Home visits, outreach, and case management	Recommended
Enhancing access at day care centers	Insufficient evidence
Enhancing access at schools	Recommended
Expanding access in health-care settings	Recommended as part of multicomponent interventions only
Interventions that target providers	
Reminder or recall systems	Strongly recommended
Assessment and feedback	Strongly recommended
Standing orders	Strongly recommended
Provider education alone	Insufficient evidence

* Adapted from Task Force on Community Preventive Services. Recommendations regarding interventions to improve vaccination coverage in children, adolescents and adults. *Am J Prev Med* 2000;18:92–6, and Task Force on Community Preventive Services. Recommendations to improve targeted vaccination coverage among high-risk adults. *Am J Prev Med* 2005;28:231–7.

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 recommendations concerning infectious diseases and immunizations for infants, children, and adolescents (Telephone: 888-227-1770; Website: <http://www.aap.org>).

American Academy of Family Physicians (AAFP)

Information from the professional organization of family physicians is available at <http://www.aafp.org>.

Immunization Action Coalition

This source provides extensive free provider and patient information, including translations of Vaccine Information Statements into multiple languages. Printed materials are reviewed by CDC for technical accuracy (<http://www.immunize.org> and <http://vaccineinformation.org>).

National Network for Immunization Information

This information source is an affiliation of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, AAP, the American Nurses Association, the AAFP, the National Association of Pediatric Nurse Practitioners, the American College of Obstetricians and Gynecologists and the University of Texas Medical Branch. This source seeks to provide the public, health professionals, policy makers, and the media with up-to-date, scientifically valid information (<http://www.immunizationinfo.org>).

Vaccine Education Center

Located at the Children's Hospital of Philadelphia, this source provides patient and provider information (<http://www.vaccine.chop.edu>).

Institute for Vaccine Safety

Located at Johns Hopkins University School of Public Health, this source provides information about vaccine safety concerns and objective and timely information to physicians and health-care providers and parents (<http://www.vaccinesafety.edu>).

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

This organization provides information for clinicians, including the free personal digital assistant software called "Shots" which includes the childhood and adult schedule for Palm OS and for Windows handhelds (<http://www.immunizationed.org>).

State and Local Health Departments

State and local health departments provide technical advice through hotlines, electronic mail, and Internet sites, including printed information regarding vaccines and immunization schedules, posters, and other educational materials.

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Abbreviations Used in This Publication

AAFP	American Academy of Family Physicians	MCV4	meningococcal conjugate vaccine
AAP	American Academy of Pediatrics	MMR	measles, mumps, rubella vaccine
ACIP	Advisory Committee on Immunization Practices	MMRV	measles-mumps-rubella-varicella vaccine
DT	pediatric diphtheria-tetanus toxoid	MPSV	meningococcal polysaccharide vaccine
DTaP	pediatric diphtheria and tetanus toxoids and acellular pertussis vaccine	OPV	oral poliovirus vaccine
DTP	pediatric diphtheria and tetanus toxoids and whole-cell pertussis vaccine	OSHA	Occupational Safety and Health Administration
EIA/ELISA	enzyme immunoassay	PCV	pneumococcal conjugate vaccine
FDA	Food and Drug Administration	PPD	purified protein derivative
GBS	Guillain-Barré syndrome	PRP-OMP	<i>Haemophilus influenzae</i> type b-polyribosylribitol phosphate-meningococcal outer membrane protein conjugate
HBIG	hepatitis B immune globulin	PPV	pneumococcal polysaccharide vaccine
HbOC	<i>Haemophilus influenzae</i> type b-diphtheria CRM197 (CRM, cross-reactive material) protein conjugate	RV	pentavalent rotavirus vaccine
HBsAg	hepatitis B surface antigen	Td	adult tetanus-diphtheria toxoid
Hib	<i>Haemophilus influenzae</i> type b	Tdap	Tetanus reduced diphtheria acellular pertussis vaccine for adolescents and adults
HIV	human immunodeficiency virus	TST	tuberculin skin test
HPV	human papillomavirus	VAERS	Vaccine Adverse Event Reporting System
HSCT	hematopoietic stem cell transplant	VAPP	vaccine-associated paralytic poliomyelitis
IgG	immunoglobulin G	VICP	Vaccine Injury Compensation Program
IGIV	intravenous immune globulin	VIS	Vaccine Information Statement
IPV	inactivated poliovirus vaccine		
JI	jet injector		

Definitions Used in This Report

Adverse event. An untoward event that occurs after a vaccination that might be caused by the vaccine product or vaccination process. It includes events that are 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; 4) coincidental: the event was associated temporally with vaccination by chance or caused by underlying illness. Special studies are needed to determine if 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; 2000:707–32; 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.

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. The following are examples of immunobiologics:

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).

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

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.

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 4).

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).

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

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.

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Goals and Objectives

This *MMWR* provides general guidelines on immunization. The goal of this report is improve vaccination practices in the United States. Upon completion of this educational activity, the reader should be able to 1) identify valid contraindications for commonly used vaccines, 2) identify the minimum spacing between doses for vaccines routinely used in the United States, 3) describe recommended methods for administration of vaccines, and 4) identify evidence-based interventions shown to improve vaccination rates among children.

To receive continuing education credit, please answer all of the following questions.

1. **If a second dose of a live virus vaccine is determined to be invalid, when should another dose be administered?**
 - A. As soon as possible.
 - B. 28 days after the most recent valid dose.
 - C. 28 days from the invalid dose or a minimum interval from the invalid dose, whichever is longer.
 - D. A minimum interval from the most recent valid dose.
 - E. Never. You must start the series over.
2. **Which of the following is a permanent contraindication for all vaccines?**
 - A. Progressive neurologic disorder.
 - B. Pregnancy.
 - C. Severe allergic reaction to a previous dose of vaccine.
 - D. Family history of asthma.
 - E. Fever.
3. **Which factor is an important criterion for needle length for a subcutaneous injection?**
 - A. Body mass.
 - B. Site of injection.
 - C. Sex.
 - D. Age.
 - E. None of the above.
4. **Which test is NOT considered a suitable test to assess the level of altered immunocompetence?**
 - A. Immunoglobulin subclasses.
 - B. Pertussis titers.
 - C. Lymphocyte proliferation assays.
 - D. T-cell counts.
 - E. Antibody response to adult tetanus-diphtheria toxoid antigen.
5. **The combination measles-mumps-rubella-varicella (MMRV) vaccine...**
 - A. is an inactivated vaccine.
 - B. is contraindicated in pregnancy.
 - C. is recommended if a person has a contraindication to one of the single-antigen vaccines (like monovalent varicella vaccine).
 - D. must be refrigerated.
 - E. requires more injections than measles-mumps-rubella (MMR) vaccine.
6. **Which of the following strategy is not specifically recommended to improve vaccination coverage in children?**
 - A. Provision of vaccines at child care centers.
 - B. Enhancing access to vaccines at schools.
 - C. Laws requiring vaccines for school entry.
 - D. Enhancing access to vaccines through the Women, Infants, and Children program.
 - E. Reminder and recall systems.
7. **The minimum intervals for vaccines should be used...**
 - A. to schedule a patient's next visit.
 - B. to avoid simultaneous administration of vaccines.
 - C. to catch-up children that are behind on vaccine doses.
 - D. to avoid giving two injections at the same site.
 - E. by vaccine registries to construct recall messages for providers.
8. **Which is an acceptable way of alleviating the pain and discomfort of children as part of the vaccination process?**
 - A. Combining acetaminophen with topical EMLA therapy.
 - B. Distraction methods (e.g., blowing away the pain).
 - C. Telling children that vaccination doesn't hurt.
 - D. Assurance that most adverse reactions are mild.
 - E. None of the above.
9. **Which of the following is a contraindication to MMR vaccine?**
 - A. Positive tuberculin skin test (TST) skin test.
 - B. Simultaneous testing using TST.
 - C. Allergy to eggs.
 - D. Pregnancy.
 - E. A household contact with altered immunocompetence.
10. **If a storage unit has been found to be maintained at temperatures outside the recommended range for the vaccines contained within, which of the following would be an appropriate action?**
 - A. Discard all vaccines contained in the unit.
 - B. Continue using the vaccine after it has been transferred to another storage unit.
 - C. Mark the vaccine "Do not use" until more can be determined about the usability of the vaccine.
 - D. Shorten the expiration date by 1 month.
 - E. Recalibrate the thermometer.
11. **Which best describes your professional activities?**
 - A. Physician.
 - B. Nurse.
 - C. Health educator.
 - D. Office staff.
 - E. Other.
12. **I plan to use these recommendations as the basis for ... (Indicate all that apply.)**
 - A. health education materials.
 - B. insurance reimbursement policies.
 - C. local practice guidelines.
 - D. public policy.
 - E. other.
13. **Overall, the length of the journal report was...**
 - A. much too long.
 - B. a little too long.
 - C. just right.
 - D. a little too short.
 - E. much too short.
14. **After reading this report, I am confident I can identify valid contraindications for commonly used vaccines.**
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.

- 15. After reading this report, I am confident I can identify the minimum spacing between doses for vaccines routinely used in the United States.
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.
- 16. After reading this report, I am confident I can describe recommended methods for administration of vaccines.
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.
- 17. After reading this report, I am confident I can identify evidence-based interventions shown to improve vaccination rates among children.
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.
- 18. The learning outcomes (objectives) were relevant to the goals of this report.
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.

- 19. The instructional strategies used in this report (text, tables, and figures) helped me learn the material.
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.
- 20. The content was appropriate given the stated objectives of the report.
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.
- 21. The content expert(s) demonstrated expertise in the subject matter.
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.
- 22. Overall, the quality of the journal report was excellent.
 - A. Strongly agree.
 - B. Agree.
 - C. Undecided.
 - D. Disagree.
 - E. Strongly disagree.

(Continued on pg CE-4)

**MMWR Response Form for Continuing Education Credit
December 1, 2006/Vol. 55/No. RR-15**

**General Recommendations on Immunization:
Recommendations of the Advisory Committee
on Immunization Practices (ACIP)**

To receive continuing education credit, you must

1. provide your contact information (please print or type);
2. indicate your choice of CME, CME for nonphysicians, CEU, CNE, or CPE credit;
3. answer all of the test questions;
4. sign and date this form or a photocopy;
5. submit your answer form by **December 1, 2009**.

Failure to complete these items can result in a delay or rejection of your application for continuing education credit.

Detach or photocopy.

Check One

CME Credit

CME for nonphysicians Credit

CEU Credit

CNE Credit

CHES Credit

CPE Credit

Last Name (print or type) _____ First Name _____

Street Address or P.O. Box _____

Apartment _____ or _____ Suite _____

City _____ State _____ ZIP Code _____

Phone Number _____ Fax Number _____

E-Mail Address _____

Fill in the appropriate blocks to indicate your answers. Remember, you must answer all of the questions to receive continuing education credit!

1. [] A [] B [] C [] D [] E [] E	15. [] A [] B [] C [] D [] E [] E
2. [] A [] B [] C [] D [] E [] E	16. [] A [] B [] C [] D [] E [] E
3. [] A [] B [] C [] D [] E [] E	17. [] A [] B [] C [] D [] E [] E
4. [] A [] B [] C [] D [] E [] E	18. [] A [] B [] C [] D [] E [] E
5. [] A [] B [] C [] D [] E [] E	19. [] A [] B [] C [] D [] E [] E
6. [] A [] B [] C [] D [] E [] E	20. [] A [] B [] C [] D [] E [] E
7. [] A [] B [] C [] D [] E [] E	21. [] A [] B [] C [] D [] E [] E
8. [] A [] B [] C [] D [] E [] E	22. [] A [] B [] C [] D [] E [] E
9. [] A [] B [] C [] D [] E [] E	23. [] A [] B [] C [] D [] E [] E
10. [] A [] B [] C [] D [] E [] E	24. [] A [] B [] C [] D [] E [] E
11. [] A [] B [] C [] D [] E [] E	25. [] A [] B [] C [] D [] E [] E
12. [] A [] B [] C [] D [] E [] E	26. [] A [] B [] C [] D [] E [] E
13. [] A [] B [] C [] D [] E [] E	27. [] A [] B [] C [] D [] E [] E
14. [] A [] B [] C [] D [] E [] E	

Signature

Date / Completed Exam

23. These recommendations will improve the quality of my practice.

- A. Strongly agree.
- B. Agree.
- C. Undecided.
- D. Disagree.
- E. Strongly disagree.

24. The availability of continuing education credit influenced my decision to read this report.

- A. Strongly agree.
- B. Agree.
- C. Undecided.
- D. Disagree.
- E. Strongly disagree.

25. The *MMWR* format was conducive to learning this content.

- A. Strongly agree.
- B. Agree.
- C. Undecided.
- D. Disagree.
- E. Strongly disagree.

26. Do you feel this course was commercially biased? (*Indicate yes or no; if yes, please explain in the space provided.*)

- A. Yes.
- B. No.

27. How did you learn about the continuing education activity?

- A. Internet.
- B. Advertisement (e.g., fact sheet, *MMWR* cover, newsletter, or journal).
- C. Coworker/supervisor.
- D. Conference presentation.
- E. *MMWR* subscription.
- F. Other.

Correct answers for questions 1–10. 1. C; 2. C; 3. E; 4. B; 5. B; 6. A; 7. C; 8. B; 9. D; 10. C.

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