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General Recommendations on Immunization

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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DEFINITIONS

Immunobiologic: Immunobiologics include antigenic substances, such as vaccines and toxoids, or antibody-containing preparations, such as 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:

a) **Vaccine**: A suspension of live (usually attenuated) or inactivated microorganisms (e.g., bacteria, viruses, or rickettsiae) 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., killed *Bordetella pertussis* or live attenuated viruses). For a list of licensed vaccines, see Table 1.

b) **Toxoid:** A modified bacterial toxin that has been made nontoxic, but retains the ability to stimulate the formation of antitoxin. For a list of licensed toxoids, see Table 1.

c) **Immune globulin (IG):** A sterile solution containing antibodies 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, IG is primarily indicated for routine maintenance of immunity of certain immunodeficient persons and for passive immunization against measles and hepatitis A. IG does not transmit hepatitis B virus, human immunodeficiency virus (HIV), or other infectious diseases. For a list of immune globulins, see Table 2.

d) **Intravenous immune globulin (IGIV):** A product derived from blood plasma from a donor pool similar to the IG pool, but prepared so it is suitable for intravenous use. IGIV does not transmit infectious diseases. It is primarily used for replacement therapy in primary antibody-deficiency disorders, for the treatment of Kawasaki disease, immune thrombocytopenic purpura, hypogammaglobulinemia in chronic lymphocytic leukemia, and some cases of HIV infection. For a list of intravenous immune globulins, see Table 2.

e) **Specific immune globulin:** 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, and cytomegalovirus immune globulin). Like IG and IGIV, these preparations do not transmit infectious diseases. For a list of specific immune globulins, see Table 2.

f) **Antitoxin:** A solution of antibodies (e.g., diphtheria antitoxin and botulinum antitoxin) derived from the serum of animals immunized with specific antigens. Antitoxins are used to confer passive immunity and for treatment. For a list of antitoxins, see Table 2.

Vaccination and Immunization

Vaccination and *vaccine* derive from *vaccinia*, the virus once used as smallpox vaccine. Thus, *vaccination* originally meant inoculation with vaccinia virus to make a person immune to smallpox. Vaccination currently denotes the physical act of administering any vaccine or toxoid.

Immunization is a more inclusive term denoting the process of inducing or providing immunity artificially by administering an immunobiologic. Immunization can be active or passive.

Active immunization is the production of antibody or other immune responses through the administration of a vaccine or toxoid. *Passive immunization* means the provision of temporary immunity by the administration of preformed antibodies. Three types of immunobiologics are administered for passive immunization: a) pooled human IG or IGIV, b) specific immune globulin preparations, and c) antitoxins.

Although persons often use *vaccination* and *immunization* interchangeably in reference to active immunization, the terms are not synonomous because the administration of an immunobiologic cannot be automatically equated with the development of adequate immunity.

General Recommendations on Immunization

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Summary

This revision of the General Recommendations on Immunization *updates the 1989 statement (*1*). Changes in the immunization schedule for infants and children include recommendations that the third dose of oral polio vaccine be administered routinely at 6 months of age rather than at age 15 months and that measles-mumps-rubella vaccine be administered routinely to all children at 12–15 months of age. Other updated or new sections include a) a listing of vaccines and other immunobiologics available in the United States by type and recommended routes, advice on the proper storage and handling of immunobiologics, a section on the recommended routes for administration of vaccines, and discussion of the use of jet injectors; b) revisions in the guidelines for spacing administration of immune globulin preparations and live virus vaccines, a discussion of vaccine interactions and recommendations for the simultaneous administration of multiple vaccines, a section on the interchangeability of vaccines from different manufacturers, and a discussion of hypersensitivity to vaccine components; c) a discussion of vaccination during pregnancy, a section on breast-feeding and vaccination, recommendations for the vaccination of premature infants, and updated schedules for immunizing infants and children (including recommendations for the use of* Haemophilus influenzae *type b conjugate vaccines); d) sections on the immunization of hemophiliacs and immunocompromised persons; e) discussion of the Standards for Pediatric Immunization Practices (including a new table of contraindications and precautions to vaccination), information on the National Vaccine Injury Compensation Program, the Vaccine Adverse Events Reporting System, and Vaccine Information Pamphlets; and f) guidelines for vaccinating persons without documentation of immunization, a section on vaccinations received outside the United States, and a section on reporting of vaccine-preventable diseases. These recommendations are based on information available before publishing and are not comprehensive for each vaccine. The most recent Advisory Committee on Immunization Practices (ACIP) recommendations for each specific vaccine should be consulted for more details.*

Additional copies of this document and other ACIP statements can be purchased from Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20202-9325. Telephone: (202) 783-3238

INTRODUCTION

Recommendations for vaccinating infants, children, and adults are based on characteristics of immunobiologics, scientific knowledge about the principles of active and passive immunization and the epidemiology of diseases, and judgments by public

health officials and specialists in clinical and preventive medicine. Benefits and risks are associated with the use of all immunobiologics: no vaccine is completely safe or completely effective. Benefits of vaccination range from partial to complete protection against the consequences of infection, ranging from asymptomatic or mild infection to severe consequences, such as paralysis or death. Risks of vaccination range from common, minor, and inconvenient side effects to rare, severe, and life-threatening conditions. Thus, recommendations for immunization practices balance scientific evidence of benefits, costs, and risks to achieve optimal levels of protection against infectious disease. These recommendations describe this balance and attempt to minimize risk by providing information regarding dose, route, and spacing of immunobiologics and delineating situations that warrant precautions or contraindicate the use of these immunobiologics. These recommendations are for use only in the United States because vaccines and epidemiologic circumstances often differ in other countries. *Individual circumstances may warrant deviations from these recommendations*. The relative balance of benefits and risks can change as diseases are controlled or eradicated. For example, because smallpox has been eradicated throughout the world, the risk of complications associated with smallpox vaccine (vaccinia virus) now outweighs any theoretical risk of contracting smallpox or related viruses for the general population. Consequently, smallpox vaccine is no longer recommended routinely for civilians or most military personnel. Smallpox vaccine is now recommended only for selected laboratory and health-care workers with certain defined exposures to these viruses (*2*).

IMMUNOBIOLOGICS

The specific nature and content of immunobiologics can differ. When immunobiologics against the same infectious agents are produced by different manufacturers, active and inert ingredients in the various products are not always the same. Practitioners are urged to become familiar with the constituents of the products they use.

Suspending Fluids

These may be sterile water, saline, or complex fluids containing protein or other constituents derived from the medium or biologic system in which the vaccine is produced (e.g., serum proteins, egg antigens, and cell-culture-derived antigens).

Preservatives, Stabilizers, Antibiotics

These components of vaccines, antitoxins, and globulins are used to inhibit or prevent bacterial growth in viral cultures or the final product, or to stabilize the antigens or antibodies. Allergic reactions can occur if the recipient is sensitive to one of these additives (e.g., mercurials [thimerosal], phenols, albumin, glycine, and neomycin).

Adjuvants

Many antigens evoke suboptimal immunologic responses. Efforts to enhance immunogenicity include mixing antigens with a variety of substances or adjuvants (e.g., aluminum adjuvants such as aluminum phosphate or aluminum hydroxide).

Storage and Handling of Immunobiologics

Failure to adhere to recommended specifications for storage and handling of immunobiologics can make these products impotent (*3*). Recommendations included in a product's package inserts, including reconstitution of vaccines, should be followed closely to assure maximum potency of vaccines. Vaccine quality is the shared responsibility of all parties from the time the vaccine is manufactured until administration. In general, all vaccines should be inspected and monitored to assure that the cold chain has been maintained during shipment and storage. Vaccines should be stored at recommended temperatures immediately upon receipt. Certain vaccines, such as oral polio vaccine (OPV) and yellow fever vaccine, are very sensitive to increased temperature. Other vaccines are sensitive to freezing, including diphtheria and tetanus toxoids and pertussis vaccine, adsorbed (DTP), diphtheria and tetanus toxoids and acellular pertussis vaccine, adsorbed (DTaP), diphtheria and tetanus toxoids for pediatric use (DT), tetanus and diphtheria toxoids for adult use (Td), inactivated poliovirus vaccine (IPV), *Haemophilus influenzae* type b conjugate vaccine (Hib), hepatitis B vaccine, pneumococcal vaccine, and influenza vaccine. Mishandled vaccine may not be easily distinguished from potent vaccine. When in doubt about the appropriate handling of a vaccine, contact the manufacturer.

ADMINISTRATION OF VACCINES

General Instructions

Persons administering vaccines should take the necessary precautions to minimize risk for spreading disease. They should be adequately immunized against hepatitis B, measles, mumps, rubella, and influenza. Tetanus and diphtheria toxoids are recommended for all persons. Hands should be washed before each new patient is seen. Gloves are not required when administering vaccinations, unless the persons who administer the vaccine will come into contact with potentially infectious body fluids or have open lesions on their hands. Syringes and needles used for injections must be sterile and preferably disposable to minimize the risk of contamination. A separate needle and syringe should be used for each injection. Different vaccines should not be mixed in the same syringe unless specifically licensed for such use.* Disposable needles and syringes should be discarded in labeled, puncture-proof containers to prevent inadvertent needlestick injury or reuse.

Routes of administration are recommended for each immunobiologic (Table 1). To avoid unnecessary local or systemic effects and to ensure optimal efficacy, the practitioner should not deviate from the recommended routes. Injectable immunobiologics should be administered where there is little likelihood of local, neural, vascular, or tissue injury. In general, vaccines containing adjuvants should be injected into the muscle mass; when administered subcutaneously or intradermally they can cause local irritation, induration, skin discoloration, inflammation, and granuloma formation. Before the vaccine is expelled into the body, the needle should be inserted into the

* The only vaccines currently licensed to be mixed in the same syringe by the person administering the vaccine are PRP-T *Haemophilus influenzae* type b conjugate vaccine, lyophilized, which can be reconstituted with DTP vaccine produced by Connaught. This PRP-T/DTP combination was licensed by the FDA on November 18, 1993.

TABLE 1. Licensed vaccines and toxoids available in the United States, by type and recommended routes of administration

Vaccine	Type	Route
Adenovirus*	Live virus	Oral
Anthrax†	Inactivated bacteria	Subcutaneous
Bacillus of Calmette and Guérin (BCG)	Live bacteria	Intradermal/percutaneous
Cholera	Inactivated bacteria	Subcutaneous or intradermal§
Diphtheria-tetanus-pertussis (DTP)	Toxoids and inactivated whole bacteria	Intramuscular
DTP-*Haemophilus influenzae* type b conjugate (DTP-Hib)	Toxoids, inactivated whole bacteria, and bacterial polysaccharide conjugated to protein	Intramuscular
Diphtheria-tetanus-acellular pertussis (DTaP)	Toxoids and inactivated bacterial components	Intramuscular
Hepatitis B	Inactive viral antigen	Intramuscular
Haemophilus influenzae type be conjugate (Hib)¶	Bacterial polysaccharide conjugated to protein	Intramuscular
Influenza	Inactivated virus or viral components	Intramuscular
Japanese encephalitis	Inactivated virus	Subcutaneous
Measles	Live virus	Subcutaneous
Measles-mumps-rubella (MMR)	Live virus	Subcutaneous
Meningococcal	Bacterial polysaccharides of serotypes A/C/Y/W-135	Subcutaneous
Mumps	Live virus	Subcutaneous
Pertussis†	Inactivated whole bacteria	Intramuscular
Plague	Inactivated bacteria	Intramuscular
Pneumococcal	Bacterial polysaccharides of 23 pneumococcal types	Intramuscular or subcutaneous
Poliovirus vaccine, inactivated (IPV)	Inactivated viruses of all 3 serotypes	Subcutaneous
Poliovirus vaccine, oral (OPV)	Live viruses of all 3 serotypes	Oral
Rabies	Inactivated virus	Intramuscular or intradermal**
Rubella	Live virus	Subcutaneous
Tetanus	Inactivated toxin (toxoid)	Intramuscular††
Tetanus-diphtheria (Td or DT)§§	Inactivated toxins (toxoids)	Intramuscular††
Typhoid (parenteral)	Inactivated bacteria	Subcutaneous¶¶
(Ty21a oral)	Live bacteria	Oral
Varicella***	Live virus	Subcutaneous
Yellow fever	Live virus	Subcutaneous

* Available only to the U.S. Armed Forces.
† Distributed by the Division of Biologic Products, Michigan Department of Public Health.
§ The intradermal dose is lower than the subcutaneous dose.
¶ The recommended schedule for infants depends on the vaccine manufacturer; consult the package insert and ACIP recommendations for specific products.
** The intradermal dose of rabies vaccine, human diploid cell (HDCV), is lower than the intramuscular dose and is used only for preexposure vaccination. **Rabies vaccine, adsorbed (RVA) should not be used intradermally.**
†† Preparations with adjuvants should be administered intramuscularly.
§§ Td=tetanus and diphtheria toxoids for use among persons ≥7 years of age. Td contains the same amount of tetanus toxoid as DTP or DT, but contains a smaller dose of diphtheria toxoid. DT=tetanus and diphtheria toxoids for use among children <7 years of age.
¶¶ Booster doses may be administered intradermally unless vaccine that is acetone-killed and dried is used.
*** A live, attenuated varicella vaccine is currently under consideration for licensure. This vaccine may be available for use through a special study protocol to any physician requesting it for certain pediatric patients with acute lymphocytic leukemia. Additional information about eligibility criteria and vaccine administration is available from the Varivax Coordinating Center; telephone: (215) 283-0897 (*4*).

TABLE 2. Immune globulins and antitoxins* available in the United States, by type of antibodies and indications for use

Immunobiologic	Type	Indication(s)
Botulinum antitoxin	Specific equine antibodies	Treatment of botulism
Cytomegalovirus immune globulin, intravenous (CMV-IGIV)	Specific human antibodies	Prophylaxis for bone marrow and kidney transplant recipients
Diphtheria antitoxin	Specific equine antibodies	Treatment of respiratory diphtheria
Immune globulin (IG)	Pooled human antibodies	Hepatitis A pre- and post-exposure prophylaxis; measles post-exposure prophylaxis
Immune globulin, intravenous (IGIV)	Pooled human antibodies	Replacement therapy for antibody deficiency disorders; immune thrombocytopenic purpura (ITP); hypogammaglobulinemia in chronic lymphocytic leukemia; Kawasaki disease
Hepatitis B immune globulin (HBIG)	Specific human antibodies	Hepatitis B post-exposure prophylaxis
Rabies immune globulin† (HRIG)	Specific human antibodies	Rabies post-exposure management of persons not previously immunized with rabies vaccine
Tetanus immune globulin (TIG)	Specific human antibodies	Tetanus treatment; post-exposure prophylaxis of persons not adequately immunized with tetanus toxoid
Vaccinia immune globulin (VIG)	Specific human antibodies	Treatment of eczema vaccinatum, vaccinia necrosum, and ocular vaccinia
Varicella zoster immune globulin (VZIG)	Specific human antibodies	Post-exposure prophylaxis of susceptible immunocompromised persons, certain susceptible pregnant women, and perinatally exposed newborn infants

*Immune globulin preparations and antitoxins are administered intramuscularly unless otherwise indicated.
†HRIG is administered around the wounds in addition to the intramuscular injection.

injection site and the syringe plunger should be pulled back—if blood appears in the needle hub, the needle should be withdrawn and a new site selected. The process should be repeated until no blood appears.

Subcutaneous Injections

Subcutaneous injections are usually administered into the thigh of infants and in the deltoid area of older children and adults. A 5/8- to 3/4-inch, 23- to 25-gauge needle should be inserted into the tissues below the dermal layer of the skin.

Intramuscular Injections

The preferred sites for intramuscular injections are the anterolateral aspect of the upper thigh and the deltoid muscle of the upper arm. *The buttock should not be used routinely for active vaccination of infants, children, or adults because of the potential risk of injury to the sciatic nerve (5*). In addition, injection into the buttock has been associated with decreased immunogenicity of hepatitis B and rabies vaccines in adults, presumably because of inadvertent subcutaneous injection or injection into deep fat tissue (*6*). If the buttock is used for passive immunization when large volumes are to be injected or multiple doses are necessary (e.g., large doses of immune globulin [IG]), the central region should be avoided; only the upper, outer quadrant should be used, and the needle should be directed anteriorly (i.e., not inferiorly or perpendicular to the skin) to minimize the possibility of involvement with the sciatic nerve (*7*).

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 endanger underlying neurovascular structures or bone. Vaccinators should be familiar with the structural anatomy of the area into which they are injecting vaccine. An individual decision on needle size and site of injection must be made for each person based on age, the volume of the material to be administered, the size of the muscle, and the depth below the muscle surface into which the material is to be injected.

Infants (<12 months of age). Among most infants, the anterolateral aspect of the thigh provides the largest muscle mass and is therefore the recommended site. However, the deltoid can also be used with the thigh; for example, when multiple vaccines must be administered at the same visit. In most cases, a 7/8- to 1-inch, 22- to 25-gauge needle is sufficient to penetrate muscle in the thigh of a 4-month-old infant. The free hand should bunch the muscle, and the needle should be directed inferiorly along the long axis of the leg at an angle appropriate to reach the muscle while avoiding nearby neurovascular structures and bone.

Toddlers and Older Children. The deltoid may be used if the muscle mass is adequate. The needle size can range from 22 to 25 gauge and from 5/8 to 1¼ inches, based on the size of the muscle. As with infants, the anterolateral thigh may be used, but the needle should be longer—generally ranging from 7/8 to 1¼ inches.

Adults. The deltoid is recommended for routine intramuscular vaccination among adults, particularly for hepatitis B vaccine. The suggested needle size is 1 to 1½ inches and 20 to 25 gauge.

Intradermal Injections

Intradermal injections are generally administered on the volar surface of the forearm, except for human diploid cell rabies vaccine (HDCV) for which reactions are less severe when administered in the deltoid area. With the bevel facing upwards, a 3/8- to 3/4-inch, 25- or 27-gauge needle can be inserted into the epidermis at an angle parallel to the long axis of the forearm. The needle should be inserted so the entire bevel penetrates the skin and the injected solution raises a small bleb. Because of the small amounts of antigen used in intradermal injections, care must be taken not to inject the vaccine subcutaneously because it can result in a suboptimal immunologic response.

Multiple Vaccinations

If more than one vaccine preparation is administered or if vaccine and an immune globulin preparation are administered simultaneously, it is preferable to administer each at a different anatomic site. It is also preferable to avoid administering two intramuscular injections in the same limb, especially if DTP is one of the products administered. However, if more than one injection must be administered in a single limb, the thigh is usually the preferred site because of the greater muscle mass; the injections should be sufficiently separated (i.e., 1–2 inches apart) so that any local reactions are unlikely to overlap (*8,9*).

Jet Injectors

Jet injectors that use the same nozzle tip to vaccinate more than one person (multiple-use nozzle jet injectors) have been used worldwide since 1952 to administer vaccines when many persons must be vaccinated with the same vaccine within a short time period. These jet injectors have been generally considered safe and effective for delivering vaccine if used properly by trained personnel; the safety and efficacy of vaccine administered by these jet injectors are considered comparable to vaccine administered by needle and syringe.

The multiple-use nozzle jet injector most widely used in the United States (Ped-o-Jet) has never been implicated in transmission of bloodborne diseases. However, the report of an outbreak of hepatitis B virus (HBV) transmission following use of one type of multiple-use nozzle jet injector in a weight loss clinic and laboratory studies in which blood contamination of jet injectors has been simulated have caused concern that the use of multiple-use nozzle jet injectors may pose a potential hazard of bloodborne-disease transmission to vaccine recipients (*10*). This potential risk for disease transmission would exist if the jet injector nozzle became contaminated with blood during an injection and was not properly cleaned and disinfected before subsequent injections. The potential risk of bloodborne-disease transmission would be greater when vaccinating persons at increased risk for bloodborne diseases such as HBV or human immunodeficiency virus (HIV) infection because of behavioral or other risk factors (*11,12*).

Multiple-use nozzle jet injectors can be used in certain situations in which large numbers of persons must be rapidly vaccinated with the same vaccine, the use of needles and syringes is not practical, and state and/or local health authorities judge that the public health benefit from the use of the jet injector outweighs the small potential risk of bloodborne-disease transmission. This potential risk can be minimized

by training health-care workers before the vaccine campaign on the proper use of jet injectors and by changing the injector tip or removing the jet injector from use if there is evidence of contamination with blood or other body fluid. In addition, mathematical and animal models suggest that the potential risk for bloodborne-disease transmission can be substantially reduced by swabbing the stationary injector tip with alcohol or acetone after each injection. It is advisable to consult sources experienced in the use of jet injectors (e.g., state or local health departments) before beginning a vaccination program in which these injectors will be used. Manufacturer's directions for use and maintenance of the jet injector devices should be followed closely.

Newer models of jet injectors that employ single-use disposable nozzle tips should not pose a potential risk of bloodborne disease transmission if used appropriately.

Regurgitated Oral Vaccine

Infants may sometimes fail to swallow oral preparations (e.g., oral poliovirus vaccine [OPV]) after administration. If, in the judgment of the person administering the vaccine, a substantial amount of vaccine is spit out, regurgitated, or vomited shortly after administration (i.e., within 5–10 minutes), another dose can be administered at the same visit. If this repeat dose is not retained, neither dose should be counted, and the vaccine should be re-administered at the next visit.

Non-Standard Vaccination Practices

The recommendations on route, site, and dosages of immunobiologics are derived from theoretical considerations, experimental trials, and clinical experience. The Advisory Committee on Immunization Practices (ACIP) strongly discourages any variations from the recommended route, site, volume, or number of doses of any vaccine.

Varying from the recommended route and site can result in a) inadequate protection (e.g., when hepatitis B vaccine is administered in the gluteal area rather than the deltoid muscle or when vaccines are administered intradermally rather than intramuscularly) and b) increased risk for reactions (e.g., when DTP is administered subcutaneously rather than intramuscularly). Administration of volumes smaller than those recommended, such as split doses, can result in inadequate protection. Use of larger than the recommended dose can be hazardous because of excessive local or systemic concentrations of antigens or other vaccine constituents. The use of multiple reduced doses that together equal a full immunizing dose or the use of smaller divided doses is not endorsed or recommended. The serologic response, clinical efficacy, and frequency and severity of adverse reactions with such schedules have not been adequately studied. Any vaccination using less than the standard dose or a nonstandard route or site of administration should not be counted, and the person should be revaccinated according to age. If a medically documented concern exists that revaccination may result in an increased risk of adverse effects because of repeated prior exposure from nonstandard vaccinations, immunity to most relevant antigens can be tested serologically to assess the need for revaccination.

AGE AT WHICH IMMUNOBIOLOGICS ARE ADMINISTERED

Recommendations for the age at which vaccines are administered (Tables 3–5) are influenced by several factors: age-specific risks of disease, age-specific risks of

TABLE 3. Recommended schedule for routine active vaccination of infants and children*

Vaccine	At birth (before hospital discharge)	1–2 months	2 months†	4 months	6 months	6–18 months	12–15 months	15 months	4–6 years (before school entry)
Diphtheria-tetanus-pertussis§			DTP	DTP	DTP			DTaP/DTP¶	DTaP/DTP
Polio, live oral			OPV	OPV	OPV**				OPV
Measles-mumps-rubella							MMR		MMR††
Haemophilus influenzae type b conjugate									
HbOC/PRP-T §,§§			Hib	Hib	Hib		Hib¶¶		
PRP-OMP§§			Hib	Hib			Hib¶¶		
Hepatitis B***									
Option 1	HepB	HepB†††				HepB†††			
Option 2		HepB†††		HepB†††		HepB†††			

* See Table 4 for the recommended immunization schedule for infants and children up to their seventh birthday who do not begin the vaccination series at the recommended times or who are >1 month behind in the immunization schedule.

† Can be administered as early as 6 weeks of age.

§ Two DTP and Hib combination vaccines are available (DTP/HbOC [TETRAMUNE™]; and PRP-T [ActHIB™, OmniHIB™] which can be reconstituted with DTP vaccine produced by Connaught).

¶ This dose of DTP can be administered as early as 12 months of age provided that the interval since the previous dose of DTP is at least 6 months. *Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) is currently recommended only for use as the fourth and/or fifth doses of the DTP series among children aged 15 months through 6 years (before the seventh birthday)*. Some experts prefer to administer these vaccines at 18 months of age.

** The American Academy of Pediatrics (AAP) recommends this dose of vaccine at 6–18 months of age.

†† The AAP recommends that two doses of MMR should be administered by 12 years of age with the second dose being administered preferentially at entry to middle school or junior high school.

§§ HbOC: [HibTITER®] (Lederle Praxis). PRP-T: [ActHIB™, OmniHIB™] (Pasteur Merieux). PRP-OMP: [PedvaxHIB®] (Merck, Sharp, and Dohme). A DTP/Hib combination vaccine can be used in place of HbOC/PRP-T.

¶¶ After the primary infant Hib conjugate vaccine series is completed, any of the licensed Hib conjugate vaccines may be used as a booster dose at age 12–15 months.

*** For use among infants born to HBsAg-negative mothers. The first dose should be administered during the newborn period, preferably before hospital discharge, but no later than age 2 months. Premature infants of HBsAg-negative mothers should receive the first dose of the hepatitis B vaccine series at the time of hospital discharge or when the other routine childhood vaccines are initiated. (All infants born to HBsAg-positive mothers should receive immunoprophylaxis for hepatitis B as soon as possible after birth.)

††† Hepatitis B vaccine can be administered simultaneously at the same visit with DTP (or DTaP), OPV, Hib, and/or MMR.

TABLE 4. Recommended accelerated immunization schedule for infants and children <7 years of age who start the series late* or who are >1 month behind in the immunization schedule† (i.e., children for whom compliance with scheduled return visits cannot be assured)

Timing	Vaccine(s)	Comments
First visit (≥ 4 mos of age)	DTP§, OPV, Hib¶,§, Hepatitis B, MMR (should be given as soon as child is age 12–15 mos)	All vaccines should be administered simultaneously at the appropriate visit.
Second visit (1 month after first visit)	DTP§, Hib¶,§, Hepatitis B	
Third visit (1 month after second visit)	DTP§, OPV, Hib¶,§	
Fourth visit (6 weeks after third visit)	OPV	
Fifth visit (≥6 mos after third visit)	DTaP§ or DTP, Hib¶,§, Hepatitis B	
Additional visits (Age 4–6 yrs)	DTaP§ or DTP, OPV, MMR	Preferably at or before school entry.
(Age 14–16 yrs)	Td	Repeat every 10 yrs through-out life.

DTP	Diphtheria-tetanus-pertussis
DTaP	Diphtheria-tetanus-acellular pertussis
Hib	Haemophilus influenzae type b conjugate
MMR	Measles-mumps-rubella
OPV	Poliovirus vaccine, live oral, trivalent
Td	Tetanus and diphtheria toxoids (for use among persons ≥7 years of age

* If initiated in the first year of life, administer DTP doses 1, 2, and 3 and OPV doses 1, 2, and 3 according to this schedule; administer MMR when the child reaches 12–15 months of age.

† See individual ACIP recommendations for detailed information on specific vaccines.

§ Two DTP and Hib combination vaccines are available (DTP/HbOC [TETRAMUNE™]; and PRP-T [ActHIB™, OmniHIB™] which can be reconstituted with DTP vaccine produced by Connaught). DTaP preparations are currently recommended only for use as the fourth and/or fifth doses of the DTP series among children 15 months through 6 years of age (before the seventh birthday). DTP and DTaP should not be used on or after the seventh birthday.

¶ The recommended schedule varies by vaccine manufacturer. For information specific to the vaccine being used, consult the package insert and ACIP recommendations. Children beginning the Hib vaccine series at age 2–6 months should receive a primary series of three doses of HbOC [HibTITER®] (Lederle-Praxis), PRP-T [ActHIB™, OmniHIB™] (Pasteur Merieux; SmithKline Beecham; Connaught), or a licensed DTP-Hib combination vaccine; **or** two doses of PRP-OMP [PedvaxHIB®] (Merck, Sharp, and Dohme). An additional booster dose of any licensed Hib conjugate vaccine should be administered at 12–15 months of age **and** at least 2 months after the previous dose. Children beginning the Hib vaccine series at 7–11 months of age should receive a primary series of two doses of an HbOC, PRP-T, or PRP-OMP-containing vaccine. An additional booster dose of any licensed Hib conjugate vaccine should be administered at 12–18 months of age **and** at least 2 months after the previous dose. Children beginning the Hib vaccine series at ages 12–14 months should receive a primary series of one dose of an HbOC, PRP-T, or PRP-OMP-containing vaccine. An additional booster dose of any licensed Hib conjugate vaccine should be administered 2 months after the previous dose. Children beginning the Hib vaccine series at ages 15–59 months should receive one dose of any licensed Hib vaccine. Hib vaccine should not be administered after the fifth birthday except for special circumstances as noted in the specific ACIP recommendations for the use of Hib vaccine.

TABLE 5. Recommended immunization schedule for persons ≥7 years of age not vaccinated at the recommended time in early infancy*

Timing	Vaccine(s)	Comments
First visit	Td†, OPV§ MMR¶, and Hepatitis B**	Primary poliovirus vaccination is not routinely recommended for persons ≥18 years of age.
Second visit (6–8 weeks after first visit)	Td, OPV, MMR††,¶, Hepatitis B**	
Third visit (6 months after second visit)	Td, OPV, Hepatitis B**	
Additional visits	Td	Repeat every 10 years throughout life.

MMR Measles-mumps-rubella
OPV Poliovirus vaccine, live oral, trivalent
Td Tetanus and diphtheria toxoids (for use among persons ≥7 years of age)

* See individual ACIP recommendations for details.

† The DTP and DTaP doses administered to children <7 years of age who remain incompletely vaccinated at age ≥7 years should be counted as prior exposure to tetanus and diphtheria toxoids (e.g., a child who previously received two doses of DTP needs only one dose of Td to complete a primary series for tetanus and diphtheria).

§ When polio vaccine is administered to previously unvaccinated persons ≥18 years of age, inactivated poliovirus vaccine (IPV) is preferred. For the immunization schedule for IPV, see specific ACIP statement on the use of polio vaccine.

¶ Persons born before 1957 can generally be considered immune to measles and mumps and need not be vaccinated. Rubella (or MMR) vaccine can be administered to persons of any age, particularly to nonpregnant women of childbearing age.

** Hepatitis B vaccine, recombinant. Selected high-risk groups for whom vaccination is recommended include persons with occupational risk, such as health-care and public-safety workers who have occupational exposure to blood, clients and staff of institutions for the developmentally disabled, hemodialysis patients, recipients of certain blood products (e.g., clotting factor concentrates), household contacts and sex partners of hepatitis B virus carriers, injecting drug users, sexually active homosexual and bisexual men, certain sexually active heterosexual men and women, inmates of long-term correctional facilities, certain international travelers, and families of HBsAg-positive adoptees from countries where HBV infection is endemic. Because risk factors are often not identified directly among adolescents, universal hepatitis B vaccination of teenagers should be implemented in communities where injecting drug use, pregnancy among teenagers, and/or sexually transmitted diseases are common.

†† The ACIP recommends a second dose of measles-containing vaccine (preferably MMR to assure immunity to mumps and rubella) for certain groups. Children with no documentation of live measles vaccination after the first birthday should receive two doses of live measles-containing vaccine not less than 1 month apart. In addition, the following persons born in 1957 or later should have documentation of measles immunity (i.e., two doses of measles-containing vaccine [at least one of which being MMR], physician-diagnosed measles, or laboratory evidence of measles immunity): a) those entering post-high school educational settings; b) those beginning employment in health-care settings who will have direct patient contact; and c) travelers to areas with endemic measles.

complications, ability of persons of a given age to respond to the vaccine(s), and potential interference with the immune response by passively transferred maternal antibody. In general, vaccines are recommended for the youngest age group at risk for developing the disease whose members are known to develop an adequate antibody response to vaccination.

SPACING OF IMMUNOBIOLOGICS

Interval Between Multiple Doses of Same Antigen

Some products require administration of more than one dose for development of an adequate antibody response. In addition, some products require periodic reinforcement or booster doses to maintain protection. In recommending the ages and intervals for multiple doses, the ACIP considers risks from disease and the need to induce or maintain satisfactory protection (Tables 3–5).

Longer-than-recommended intervals between doses do not reduce final antibody concentrations. Therefore, an interruption in the immunization schedule does not require reinstitution of the entire series of an immunobiologic or the addition of extra doses. However, administering doses of a vaccine or toxoid at less than the recommended minimum intervals may decrease the antibody response and therefore should be avoided. Doses administered at less than the recommended minimum intervals should not be considered part of a primary series.

Some vaccines produce increased rates of local or systemic reactions in certain recipients when administered too frequently (e.g., adult Td, pediatric DT, tetanus toxoid, and rabies vaccines). Such reactions are thought to result from the formation of antigen-antibody complexes. Good recordkeeping, maintaining careful patient histories, and adherence to recommended schedules can decrease the incidence of such reactions without sacrificing immunity.

Simultaneous Administration

Experimental evidence and extensive clinical experience have strengthened the scientific basis for administering certain vaccines simultaneously (*13–16*). Many of the commonly used vaccines can safely and effectively be administered simultaneously (i.e., on the same day, *not* at the same anatomic site). Simultaneous administration is important in certain situations, including a) imminent exposure to several infectious diseases, b) preparation for foreign travel, and c) uncertainty that the person will return for further doses of vaccine.

Killed vaccines

In general, inactivated vaccines can be administered simultaneously at separate sites. However, when vaccines commonly associated with local or systemic reactions (e.g., cholera, parenteral typhoid, and plague) are administered simultaneously, the reactions might be accentuated. When feasible, it is preferable to administer these vaccines on separate occasions.

Live vaccines

The simultaneous administration of the most widely used live and inactivated vaccines has not resulted in impaired antibody responses or increased rates of adverse reactions. Administration of combined measles-mumps-rubella (MMR) vaccine yields results similar to administration of individual measles, mumps, and rubella vaccines at different sites. Therefore, there is no medical basis for administering these vaccines separately for routine vaccination instead of the preferred MMR combined vaccine.

Concern has been raised that oral live attenuated typhoid (Ty21a) vaccine theoretically might interfere with the immune response to OPV when OPV is administered simultaneously or soon after live oral typhoid vaccine (*17*). However, no published data exist to support this theory. Therefore, if OPV and oral live typhoid vaccine are needed at the same time (e.g., when international travel is undertaken on short notice), both vaccines may be administered simultaneously or at any interval before or after each other.

Routine childhood vaccines

Simultaneous administration of all indicated vaccines is important in childhood vaccination programs because it increases the probability that a child will be fully immunized at the appropriate age. During a recent measles outbreak, one study indicated that about one third of measles cases among unvaccinated preschool children could have been prevented if MMR had been administered at the same time another vaccine had been received (*18*).

The simultaneous administration of routine childhood vaccines does not interfere with the immune response to these vaccines. When administered at the same time and at separate sites, DTP, OPV, and MMR have produced seroconversion rates and rates of side effects similar to those observed when the vaccines are administered separately (*13*). Simultaneous vaccination of infants with DTP, OPV (or IPV), and either Hib vaccine or hepatitis B vaccine has resulted in acceptable response to all antigens (*14–16*). Routine simultaneous administration of DTP (or DTaP), OPV (or IPV), Hib vaccine, MMR, and hepatitis B vaccine is encouraged for children who are the recommended age to receive these vaccines and for whom no specific contraindications exist at the time of the visit, unless, in the judgment of the provider, complete vaccination of the child will not be compromised by administering different vaccines at different visits. Simultaneous administration is particularly important if the child might not return for subsequent vaccinations. Administration of MMR and Hib vaccine at 12–15 months of age, followed by DTP (or DTaP, if indicated) at age 18 months remains an acceptable alternative for children with caregivers known to be compliant with other health-care recommendations and who are likely to return for future visits; hepatitis B vaccine can be administered at either of these two visits. DTaP may be used instead of DTP only for the fourth and fifth dose for children 15 months of age through 6 years (i.e., before the seventh birthday). Individual vaccines should not be mixed in the same syringe unless they are licensed for mixing by the U.S. Food and Drug Administration (FDA).*

*The only vaccines currently licensed to be mixed in the same syringe by the person administering the vaccine are PRP-T *Haemophilus influenzae* type b conjugate vaccine, lyophilized, which can be reconstituted with DTP vaccine produced by Connaught. This PRP-T/DTP combination was licensed by the FDA on November 18, 1993.

Other vaccines

The simultaneous administration of pneumococcal polysaccharide vaccine and whole-virus influenza vaccine elicits a satisfactory antibody response without increasing the incidence or severity of adverse reactions in adults (*19*). Simultaneous administration of pneumococcal vaccine and split-virus influenza vaccine can be expected to yield satisfactory results in both children and adults.

Hepatitis B vaccine administered with yellow fever vaccine is as safe and efficacious as when these vaccines are administered separately (*20*). Measles and yellow fever vaccines have been administered together safely and with full efficacy of each of the components (*21*).

The antibody response of yellow fever and cholera vaccines is decreased if administered simultaneously or within a short time of each other. If possible, yellow fever and cholera vaccinations should be separated by at least 3 weeks. If time constraints exist and both vaccines are necessary, the injections can be administered simultaneously or within a 3-week period with the understanding that antibody response may not be optimal. Yellow fever vaccine is required by many countries and is highly effective in protecting against a disease with substantial mortality and for which no therapy exists. The currently used cholera vaccine provides limited protection of brief duration; few indications exist for its use.

Antimalarials and vaccination

The antimalarial mefloquine (Lariam®) could potentially affect the immune response to oral live attenuated typhoid (Ty21a) vaccine if both are taken simultaneously (*17,22,23*). To minimize this effect, it may be prudent to administer Ty21a typhoid vaccine at least 24 hours before or after a dose of mefloquine. Because chloroquine phosphate (and possibly other structurally related antimalarials such as mefloquine) may interfere with the antibody response to HDCV when HDCV is administered by the intradermal dose/route, HDCV should not be administered by the intradermal dose/route when chloroquine, mefloquine, or other structurally related antimalarials are used (*24–26*).

Nonsimultaneous Administration

Inactivated vaccines generally do not interfere with the immune response to other inactivated vaccines or to live vaccines except in certain instances (e.g., yellow fever and cholera vaccines). In general, an inactivated vaccine can be administered either simultaneously or at any time before or after a different inactivated vaccine or live vaccine. However, limited data have indicated that prior or concurrent administration of DTP vaccine may enhance anti-PRP antibody response following vaccination with certain *Haemophilus influenzae* type b conjugate vaccines (i.e., PRP-T, PRP-D, and HbOC) (*27–29*). For infants, the immunogenicity of PRP-OMP appears to be unaffected by the absence of prior or concurrent DTP vaccination (*28,30*).

Theoretically, the immune response to one live-virus vaccine might be impaired if administered within 30 days of another live-virus vaccine; however no evidence exists for currently available vaccines to support this concern (*31*). Whenever possible, live-virus vaccines administered on different days should be administered at least 30 days apart (Table 6). However, OPV and MMR vaccines can be administered at any time

before, with, or after each other, if indicated. Live-virus vaccines can interfere with the response to a tuberculin test (*32–34*). Tuberculin testing, if otherwise indicated, can be done either on the same day that live-virus vaccines are administered or 4–6 weeks later.

Immune Globulin

Live vaccines

OPV and yellow fever vaccines can be administered at any time before, with, or after the administration of immune globulin or specific immune globulins (e.g., hepatitis B immune globulin [HBIG] and rabies immune globulin [RIG]) (Table 7) (*35*). The concurrent administration of immune globulin should not interfere with the immune response to oral Ty21a typhoid vaccine.

Previous recommendations, based on data from persons who received low doses of immune globulin, have stated that MMR and its individual component vaccines can be administered as early as 6 weeks to 3 months after administration of immune globulin (*1,36*). However, recent evidence suggests that high doses of immune globulin can inhibit the immune response to measles vaccine for more than 3 months (*37,38*). Administration of immune globulin can also inhibit the response to rubella vaccine (*37*). The effect of immune globulin preparations on the response to mumps and varicella vaccines is unknown, but commercial immune globulin preparations contain antibodies to these viruses.

Blood (e.g., whole blood, packed red blood cells, and plasma) and other antibody-containing blood products (e.g., immune globulin; specific immune globulins; and immune globulin, intravenous [IGIV]) can diminish the immune response to MMR or its individual component vaccines. Therefore, after an immune globulin preparation is received, these vaccines should not be administered before the recommended interval (Tables 7 and 8). However, the postpartum vaccination of rubella-susceptible women with rubella or MMR vaccine should not be delayed because anti-Rho(D) IG (human) or any other blood product was received during the last trimester of

TABLE 6. Guidelines for spacing the administration of live and killed antigens

Antigen combination	Recommended minimum interval between doses
≥2 Killed antigens	None. May be administered simultaneously or at any interval between doses.*
Killed and live antigens	None. May be administered simultaneously or at any interval between doses.†
≥2 Live antigens	4-week minimum interval if not administered simultaneously.§ However, oral polio vaccine can be administered at any time before, with, or after measles-mumps-rubella, if indicated.

* If possible, vaccines associated with local or systemic side effects (e.g., cholera, parenteral typhoid, and plague vaccines) should be administered on separate occasions to avoid accentuated reactions.

† Cholera vaccine with yellow fever vaccine is the exception. If time permits, these antigens should not be administered simultaneously, and at least 3 weeks should elapse between administration of yellow fever vaccine and cholera vaccine. If the vaccines must be administered simultaneously or within 3 weeks of each other, the antibody response may not be optimal.

§ If oral live typhoid vaccine is indicated (e.g., for international travel undertaken on short notice), it can be administered before, simultaneously with, or after OPV.

TABLE 7. Guidelines for spacing the administration of immune globulin preparations* and vaccines

Simultaneous administration		Nonsimultaneous administration		
		Immunobiologic administered		
Immunobiologic combination	Recommended minimum interval between doses	First	Second	Recommended minimum interval between doses
Immune globulin and killed antigen	None. May be given simultaneously at different sites or at any time between doses.	Immune globulin	Killed antigen	None
		Killed antigen	Immune globulin	None
Immune globulin and live antigen	Should generally not be administered simultaneously.† If simultaneous administration of measles-mumps-rubella [MMR], measles-rubella, and monovalent measles vaccine is unavoidable, administer at different sites and revaccinate or test for seroconversion after the recommended interval (Table 8).	Immune globulin	Live antigen	Dose related†,§
		Live antigen	Immune globulin	2 weeks

*Blood products containing large amounts of immune globulin (such as serum immune globulin, specific immune globulins [e.g., TIG and HBIG], intravenous immune globulin [IGIV], whole blood, packed red cells, plasma, and platelet products).

†Oral polio virus, yellow fever, and oral typhoid (Ty21a) vaccines are exceptions to these recommendations. These vaccines may be administered at any time before, after, or simultaneously with an immune globulin-containing product without substantially decreasing the antibody response (*35*).

§The duration of interference of immune globulin preparations with the immune response to the measles component of the MMR, measles-rubella, and monovalent measles vaccine is dose-related (Table 8).

pregnancy or at delivery. These women should be vaccinated immediately after delivery and, if possible, tested at least 3 months later to ensure immunity to rubella and, if necessary, to measles.

If administration of an immune globulin preparation becomes necessary because of imminent exposure to disease, MMR or its component vaccines can be administered simultaneously with the immune globulin preparation, although vaccine-induced immunity might be compromised. The vaccine should be administered at a site remote from that chosen for the immune globulin inoculation. Unless serologic testing indicates that specific antibodies have been produced, vaccination should be repeated after the recommended interval (Tables 7 and 8).

If administration of an immune globulin preparation becomes necessary after MMR or its individual component vaccines have been administered, interference can

TABLE 8. Suggested intervals between administration of immune globulin preparations for various indications and vaccines containing live measles virus*

Indication	Dose (including mg IgG/kg)	Suggested interval before measles vaccination (months)
Tetanus (TIG)	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 prophylaxis (HBIG)	0.06 mL/kg (10 mg IgG/kg) IM	3
Rabies prophylaxis (HRIG)	20 IU/kg (22 mg IgG/kg) IM	4
Varicella prophylaxis (VZIG)	125 units/10 kg (20–40 mg IgG/kg) IM (maximum 625 units)	5
Measles prophylaxis (IG)		
Normal 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) IV	0
RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	3
Packed RBCs (Hct 65%)†	10 mL/kg (60 mg IgG/kg) IV	6
Whole blood (Hct 35–50%)†	10 mL/kg (80–100 mg IgG/kg) IV	6
Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	7
Replacement of humoral immune deficiencies	300–400 mg/kg IV§ (as IGIV)	8
Treatment of:		
ITP¶	400 mg/kg IV (as IGIV)	8
ITP¶	1000 mg/kg IV (as IGIV)	10
Kawasaki disease	2 grams/kg IV (as IGIV)	11

*This table is not intended for determining the correct indications and dosage for the use of immune globulin preparations. Unvaccinated persons may not be fully protected against measles during the entire suggested interval and additional doses of immune globulin and/or measles vaccine may be indicated following measles exposure. The concentration of measles antibody in a particular immune globulin preparation can vary by lot. The rate of antibody clearance following receipt of an immune globulin preparation can also vary. The 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 following a dose of 80 mg IgG/kg (*37*).

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

§Measles vaccination is recommended for children with HIV infection but is contraindicated in patients with congenital disorders of the immune system.

¶Immune (formally, idiopathic) thrombocytopenic purpura.

occur. Usually, vaccine virus replication and stimulation of immunity will occur 1–2 weeks after vaccination. Thus, if the interval between administration of any of these vaccines and subsequent administration of an immune globulin preparation is <14 days, vaccination should be repeated after the recommended interval (Tables 7 and 8), unless serologic testing indicates that antibodies were produced.

Killed vaccines

Immune globulin preparations interact less with inactivated vaccines and toxoids than with live vaccines (*39*). Therefore, administration of inactivated vaccines and toxoids either simultaneously with or at any interval before or after receipt of immune globulins should not substantially impair the development of a protective antibody response. The vaccine or toxoid and immune globulin preparation should be administered at different sites using the standard recommended dose of corresponding vaccine. Increasing the vaccine dose volume or number of vaccinations is not indicated or recommended.

Interchangeability of Vaccines from Different Manufacturers

When at least one dose of a hepatitis B vaccine produced by one manufacturer is followed by subsequent doses from a different manufacturer, the immune response has been shown to be comparable with that resulting from a full course of vaccination with a single vaccine (*11,40*).

Both HDCV and rabies vaccine, adsorbed (RVA) are considered equally efficacious and safe and, when used as licensed and recommended, are considered interchangeable during the vaccine series. *RVA should not be used intradermally*. The full 1.0-mL dose of either product, administered by intramuscular injection, can be used for both preexposure and postexposure prophylaxis (*25*).

When administered according to their licensed indications, different diphtheria and tetanus toxoids and pertussis vaccines as single antigens or various combinations, as well as the live and inactivated polio vaccines, also can be used interchangeably. However, published data supporting this recommendation are generally limited (*41*).

Currently licensed *Haemophilus influenzae* type b conjugate vaccines have been shown to induce different temporal patterns of immunologic response in infants (*42*). Limited data suggest that infants who receive sequential doses of different vaccines produce a satisfactory antibody response after a complete primary series (*43–45*). The primary vaccine series should be completed with the same Hib vaccine, if feasible. However, if different vaccines are administered, a total of three doses of Hib vaccine is considered adequate for the primary series among infants, and any combination of Hib conjugate vaccines licensed for use among infants (i.e., PRP-OMP, PRP-T, HbOC, and combination DTP-Hib vaccines) may be used to complete the primary series. Any of the licensed conjugate vaccines can be used for the recommended booster dose at 12–18 months of age (Tables 3 and 4).

HYPERSENSITIVITY TO VACCINE COMPONENTS

Vaccine components can cause allergic reactions in some 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). The responsible vaccine components can derive from a) vaccine antigen, b) animal protein, c) antibiotics, d) preservatives, and e) stabilizers.

The most common animal protein allergen is egg protein found in vaccines prepared using embryonated chicken eggs (e.g., influenza and yellow fever vaccines) or chicken embryo cell cultures (e.g., measles and mumps vaccines). 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 not. 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 measles, mumps, yellow fever, and influenza vaccines. Protocols requiring caution have been developed for testing and vaccinating with measles, mumps, and MMR vaccines those persons with anaphylactic reactions to egg ingestion (*46–49*). A regimen for administering influenza vaccine to children with egg hypersensitivity and severe asthma has also been developed (*50*). Rubella vaccine is grown in human diploid cell cultures and can safely be administered to persons with histories of severe allergy to eggs or egg proteins.

Some vaccines contain trace amounts of antibiotics (e.g., neomycin) to which patients may be hypersensitive. The information provided in the vaccine package insert should be carefully reviewed before deciding if the uncommon patient with such hypersensitivity should receive the vaccine(s). No currently recommended vaccine contains penicillin or penicillin derivatives.

MMR and its individual component vaccines contain trace amounts of neomycin. Although the amount present is less than would usually be used for the skin test to determine hypersensitivity, 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. A history of delayed-type reactions to neomycin is not a contraindication for these vaccines.

Certain parenteral bacterial vaccines such as cholera, DTP, plague, and typhoid are frequently associated with local or systemic adverse effects, such as redness, soreness, and fever. These reactions are difficult to link with a specific sensitivity to vaccine components and appear to be toxic rather than hypersensitive. Urticarial or anaphylactic reactions in DTP, DT, Td, or tetanus toxoid recipients have been reported rarely. When these reactions are reported, appropriate skin tests can be performed to determine sensitivity to tetanus toxoid before its use is discontinued (*51*). Alternatively, serologic testing to determine immunity to tetanus can be performed to evaluate the need for a booster dose of tetanus toxoid.

Exposure to vaccines containing the preservative thimerosal (e.g., DTP, DTaP, DT, Td, Hib, hepatitis B, influenza, and Japanese encephalitis) can lead to induction of hypersensitivity. However, most patients do not develop reactions to thimerosal given as a component of vaccines even when patch or intradermal tests for thimerosal indicate hypersensitivity. Hypersensitivity to thimerosal usually consists of local delayed-type hypersensitivity reactions (*52,53*).

VACCINATION OF PRETERM INFANTS

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 (Tables 3 and 4). Birthweight and size generally are not factors in deciding whether to postpone routine vaccination of a clinically stable premature infant (*54–56*). The full recommended dose of each vaccine should be used. Divided or reduced doses are not recommended (*57*). To prevent the theoretical risk of poliovirus transmission in the hospital, the administration of OPV should be deferred until discharge.

Any premature infant born to a hepatitis B surface antigen (HBsAg)-positive mother should receive immunoprophylaxis with hepatitis B vaccine and HBIG beginning at or shortly after birth. For premature infants of HBsAg-negative mothers, the optimal timing of hepatitis B vaccination has not been determined. Some studies suggest that decreased seroconversion rates might occur in some premature infants with low birthweights (i.e., <2000 grams) following administration of hepatitis B vaccine at birth (*58*). Such low birthweight premature infants of HBsAg-negative mothers should receive the hepatitis B vaccine series, which can be initiated at discharge from the nursery if the infant weighs at least 2000 grams or at 2 months of age along with DTP, OPV, and Hib vaccine.

BREAST-FEEDING AND VACCINATION

Neither killed nor live vaccines affect the safety of breast-feeding for mothers or infants. Breast-feeding does not adversely affect immunization and is not a contraindication for any vaccine. Breast-fed infants should be vaccinated according to routine recommended schedules (*59–61*).

Inactivated or killed vaccines do not multiply within the body. Therefore they should pose no special risk for mothers who are breast-feeding or for their infants. Although live vaccines do multiply within the mother's body, most have not been demonstrated to be excreted in breast milk. Although rubella vaccine virus may be transmitted in breast milk, the virus usually does not infect the infant, and if it does, the infection is well tolerated. There is no contraindication for vaccinating breast-feeding mothers with yellow fever vaccine. Breast-feeding mothers can receive OPV without any interruption in the feeding schedule.

VACCINATION DURING PREGNANCY

Risk from vaccination during pregnancy is largely theoretical. The benefit of vaccination among pregnant women usually outweighs the potential risk when a) the risk for disease exposure is high, b) infection would pose a special risk to the mother or fetus, and c) the vaccine is unlikely to cause harm.

Combined tetanus and diphtheria toxoids are the only immunobiologic agents routinely indicated for susceptible pregnant women. 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 unimmunized or only partially immunized against tetanus should complete the primary series. Depending on when a woman

seeks prenatal care and the required interval between doses, one or two doses of Td can be administered before delivery. Women for whom the vaccine is indicated but who have not completed the required three-dose series during pregnancy should be followed up after delivery to assure they receive the doses necessary for protection.

There is no convincing evidence of risk from vaccinating pregnant women with other inactivated virus or bacteria vaccines or toxoids. Hepatitis B vaccine is recommended for women at risk for hepatitis B infection, and influenza and pneumococcal vaccines are recommended for women at risk for infection and for complications of influenza and pneumococcal disease.

OPV can be administered to pregnant women who are at substantial risk of imminent exposure to natural infection (*62*). Although OPV is preferred, IPV may be considered if the complete vaccination series can be administered before the anticipated exposure. Pregnant women who must travel to areas where the risk for yellow fever is high should receive yellow fever vaccine. In these circumstances, the small theoretical risk from vaccination is far outweighed by the risk of yellow fever infection (*21,63*). Known pregnancy is a contraindication for rubella, measles, and mumps vaccines. Although of theoretical concern, no cases of congenital rubella syndrome or abnormalities attributable to a rubella vaccine virus infection have been observed in infants born to susceptible mothers who received rubella vaccine during pregnancy.

Persons who receive measles, mumps, or rubella vaccines can shed these viruses but generally do not transmit them. These vaccines can be administered safely to the children of pregnant women. Although live polio virus is shed by persons recently vaccinated with OPV (particularly after the first dose), this vaccine can also be administered to the children of pregnant women because experience has not revealed any risk of polio vaccine virus to the fetus.

All pregnant women should be evaluated for immunity to rubella and tested for the presence of HBsAg. Women susceptible to rubella should be vaccinated immediately after delivery. A woman infected with HBV should be followed carefully to assure the infant receives HBIG and begins the hepatitis B vaccine series shortly after birth.

There is no known risk to the fetus from passive immunization of pregnant women with immune globulin preparations. Further information regarding immunization of pregnant women is available in the American College of Obstetricians and Gynecologists Technical Bulletin Number 160, October 1991. This publication is available from the American College of Obstetricians and Gynecologists, Attention: Resource Center, 409 12th Street SW, Washington, DC 20024–2188.

ALTERED IMMUNOCOMPETENCE

The ACIP statement on vaccinating immunocompromised persons summarizes recommendations regarding the efficacy, safety, and use of specific vaccines and immune globulin preparations for immunocompromised persons (*64*). ACIP statements on individual vaccines or immune globulins also contain additional information regarding these issues.

Severe immunosuppression can be the result of congenital immunodeficiency, HIV infection, leukemia, lymphoma, generalized malignancy or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids. Severe complications have followed vaccination with live, attenuated virus vaccines and live

bacterial vaccines among immunocompromised patients (*65–71*). In general, these patients should not receive live vaccines except in certain circumstances that are noted below. In addition, OPV should not be administered to any household contact of a severely immunocompromised person. If polio immunization is indicated for immunocompromised patients, their household members, or other close contacts, IPV should be administered. MMR vaccine is not contraindicated in the close contacts of immunocompromised patients. The degree to which a person is immunocompromised should be determined by a physician.

Limited studies of MMR vaccination in HIV-infected patients have not documented serious or unusual adverse events. Because measles may cause severe illness in persons with HIV infection, MMR vaccine is recommended for all asymptomatic HIV-infected persons and should be considered for all symptomatic HIV-infected persons. HIV-infected persons on regular IGIV therapy may not respond to MMR or its individual component vaccines because of the continued presence of passively acquired antibody. However, because of the potential benefit, measles vaccination should be considered approximately 2 weeks before the next monthly dose of IGIV (if not otherwise contraindicated), although an optimal immune response is unlikely to occur. Unless serologic testing indicates that specific antibodies have been produced, vaccination should be repeated (if not otherwise contraindicated) after the recommended interval (Table 8).

An additional dose of IGIV should be considered for persons on routine IGIV therapy who are exposed to measles ≥3 weeks after administration of a standard dose (100–400 mg/kg) of IGIV.

Killed or inactivated vaccines can be administered to all immunocompromised patients, although response to such vaccines may be suboptimal. All such childhood vaccines are recommended for immunocompromised persons in usual doses and schedules; in addition, certain vaccines such as pneumococcal vaccine or Hib vaccine are recommended specifically for certain groups of immunocompromised patients, including those with functional or anatomic asplenia.

Vaccination during chemotherapy or radiation therapy should be avoided because antibody response is poor. Patients vaccinated while on immunosuppressive therapy or in the 2 weeks before starting therapy should be considered unimmunized and should be revaccinated at least 3 months after therapy is discontinued. Patients with leukemia in remission whose chemotherapy has been terminated for 3 months may receive live-virus vaccines.

The exact amount of systemically absorbed corticosteroids and the duration of administration needed to suppress the immune system of an otherwise healthy child are not well defined. Most experts agree that steroid therapy usually does not contraindicate administration of live virus vaccine when it is short term (i.e., <2 weeks); low to moderate dose; long-term, alternate-day treatment with short-acting preparations; maintenance physiologic doses (replacement therapy); or administered topically (skin or eyes), by aerosol, or by intra-articular, bursal, or tendon injection (*64*). Although of recent theoretical concern, no evidence of increased severe reactions to live vaccines has been reported among persons receiving steroid therapy by aerosol, and such therapy is not in itself a reason to delay vaccination. The immunosuppressive effects of steroid treatment vary, but many clinicians consider a dose equivalent to either 2 mg/kg of body weight or a total of 20 mg per day of prednisone as sufficiently

immunosuppressive to raise concern about the safety of vaccination with live virus vaccines (*64*). Corticosteroids used in greater than physiologic doses also can reduce the immune response to vaccines. Physicians should wait at least 3 months after discontinuation of therapy before administering a live-virus vaccine to patients who have received high systemically absorbed doses of corticosteroids for ≥2 weeks.

VACCINATION OF PERSONS WITH HEMOPHILIA

Persons with bleeding disorders such as hemophilia have an increased risk of acquiring hepatitis B and at least the same risk as the general population of acquiring other vaccine-preventable diseases. However, because of the risk of hematomas, intramuscular injections are often avoided among persons with bleeding disorders by using the subcutaneous or intradermal routes for vaccines that are normally administered by the intramuscular route. Hepatitis B vaccine administered intramuscularly to 153 hemophiliacs using a 23-gauge needle, followed by steady pressure to the site for 1 to 2 minutes, has resulted in a 4% bruising rate with no patients requiring factor supplementation (*72*). Whether an antigen that produces more local reactions, such as pertussis, would produce an equally low rate of bruising is unknown.

When hepatitis B or any other intramuscular vaccine is indicated for a patient with a bleeding disorder, it 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 other similar therapy, intramuscular vaccination can be scheduled shortly after such therapy is administered. A fine needle (≤23 gauge) can 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 of hematoma from the injection.

MISCONCEPTIONS CONCERNING TRUE CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

Some health-care providers inappropriately consider certain conditions or circumstances to be true contraindications or precautions to vaccination. This misconception results in missed opportunities to administer needed vaccines. Likewise, providers may fail to understand what constitutes a true contraindication or precaution and may administer a vaccine when it should be withheld. This practice can result in an increased risk of an adverse reaction to the vaccine.

Standards for Pediatric Immunization Practice

National standards for pediatric immunization practices have been established and include true contraindications and precautions to vaccination (Table 9) (*73*). True contraindications, applicable to all vaccines, include a history of anaphylactic or anaphylactic-like reactions to the vaccine or a vaccine constituent (unless the recipient has been desensitized) and the presence of a moderate or severe illness with or without a fever. Except as noted previously, severely immunocompromised persons should not receive live vaccines. Persons who developed an encephalopathy within 7 days of administration of a previous dose of DTP or DTaP should not receive further

TABLE 9. Guide to contraindications and precautions to vaccinations*

True contraindications and precautions	Not contraindications (vaccines may be administered)
General for all vaccines (DTP/DTaP, OPV, IPV, MMR, Hib, Hepatitis B)	
Contraindications	**Not contraindications**
Anaphylactic reaction to a vaccine contraindicates further doses of that vaccine	Mild to moderate local reaction (soreness, redness, swelling) following a dose of an injectable antigen
Anaphylactic reaction to a vaccine constituent contraindicates the use of vaccines containing that substance	Mild acute illness with or without low-grade fever
Moderate or severe illnesses with or without a fever	Current antimicrobial therapy
	Convalescent phase of illnesses
	Prematurity (same dosage and indications as for normal, full-term infants)
	Recent exposure to an infectious disease
	History of penicillin or other nonspecific allergies or family history of such allergies
DTP/DTaP	
Contraindications	**Not contraindications**
Encephalopathy within 7 days of administration of previous dose of DTP	Temperature of <40.5 C (105 F) following a previous dose of DTP
Precautions†	Family history of convulsions§
Fever of ≥40.5°C (105°F) within 48 hrs after vaccination with a prior dose of DTP	Family history of sudden infant death syndrome
Collapse or shocklike state (hypotonic-hyporesponsive episode) within 48 hrs of receiving a prior dose of DTP	Family history of an adverse event following DTP administration
Seizures within 3 days of receiving a prior dose of DTP§	
Persistent, inconsolable crying lasting ≥3 hrs within 48 hrs of receiving a prior dose of DTP	
OPV¶	
Contraindications	**Not contraindications**
Infection with HIV or a household contact with HIV	Breast-feeding
Known altered immunodeficiency (hematologic and solid tumors; congenital immunodeficiency; and long-term immunosuppressive therapy)	Current antimicrobial therapy
Immunodeficient household contact	Diarrhea
Precaution†	
Pregnancy	

TABLE 9. Guide to contraindications and precautions to vaccinations* — Continued

True contraindications and precautions	Not contraindications (vaccines may be administered)
IPV	
Contraindication Anaphylactic reaction to neomycin or streptomycin **Precaution†** Pregnancy	
MMR¶	
Contraindications Anaphylactic reactions to egg ingestion and to neomycin** Pregnancy Known altered immunodeficiency (hematologic and solid tumors; congenital immunodeficiency; and long-term immunosuppressive therapy) **Precaution†** Recent immune globulin administration (see Table 8)	**Not contraindications** Tuberculosis or positive PPD skin test Simultaneous TB skin testing†† Breast-feeding Pregnancy of mother of recipient Immunodeficient family member or household contact Infection with HIV Nonanaphylactic reactions to eggs or neomycin
Hib	
Contraindication None identified	**Not a contraindication** History of Hib disease
Hepatitis B	
Contraindication Anaphylactic reaction to common baker's yeast	**Not a contraindication** Pregnancy

* This information is based on the recommendations of the Advisory Committee on Immunization Practices (ACIP) and those of the Committee on Infectious Diseases (Red Book Committee) of the American Academy of Pediatrics (AAP). Sometimes these recommendations vary from those contained in the manufacturer's package inserts. For more detailed information, providers should consult the published recommendations of the ACIP, AAP, and the manufacturer's package inserts.

† The events or conditions listed as precautions, although not contraindications, should be carefully reviewed. The benefits and risks of administering a specific vaccine to an individual under the circumstances should be considered. If the risks are believed to outweigh the benefits, the vaccination should be withheld; if the benefits are believed to outweigh the risks (for example, during an outbreak or foreign travel), the vaccination should be administered. Whether and when to administer DTP to children with proven or suspected underlying neurologic disorders should be decided on an individual basis. It is prudent on theoretical grounds to avoid vaccinating pregnant women. However, if immediate protection against poliomyelitis is needed, OPV is preferred, although IPV may be considered if full vaccination can be completed before the anticipated imminent exposure.

§ Acetaminophen given before administering DTP and thereafter every 4 hours for 24 hours should be considered for children with a personal or family history of convulsions in siblings or parents.

¶ No data exist to substantiate the theoretical risk of a suboptimal immune response from the administration of OPV and MMR within 30 days of each other.

** Persons with a history of anaphylactic reactions following egg ingestion should be vaccinated only with caution. Protocols have been developed for vaccinating such persons and should be consulted. [J Pediatr 1983;102:196–9, J Pediatr 1988;113:504–6.]

†† Measles vaccination may temporarily suppress tuberculin reactivity. If testing can not be done the day of MMR vaccination, the test should be postponed for 4–6 weeks.

doses of DTP or DTaP. Persons infected with HIV, with household contacts infected with HIV, or with known altered immunodeficiency should receive IPV rather than OPV. Because of the theoretical risk to the fetus, women known to be pregnant should not receive MMR.

Certain conditions are considered precautions rather than true contraindications for vaccination. When faced with these conditions, some providers may elect to administer vaccine if they believe that the benefits outweigh the risks for the patient. For example, caution should be exercised in vaccinating a child with DTP who, within 48 hours of receipt of a prior dose of DTP, developed fever ≥40.5 C (105 F); had persistent, inconsolable crying for ≥3 hours; collapsed or developed a shock-like state; or had a seizure within 3 days of receiving the previous dose of DTP.

Conditions often inappropriately regarded as contraindications to vaccination are also noted (Table 9). Among the most important are diarrhea and minor upper-respiratory illnesses 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. Diarrhea is not a contraindication to OPV.

Febrile Illness

The decision to administer or delay vaccination because of a current or recent febrile illness depends on the severity of symptoms and on the etiology of the disease.

All vaccines can be administered to persons with minor illness such as diarrhea, mild upper-respiratory infection with or without low-grade fever, or other low-grade febrile illness. Studies suggest that failure to vaccinate children with minor illness can seriously impede vaccination efforts (*74–76*). Among persons whose compliance with medical care cannot be assured, it is particularly important to take every opportunity to provide appropriate vaccinations.

Most studies from developed and developing countries support the safety and efficacy of vaccinating persons who have mild illness (*77–79*). One large ongoing study in the United States has indicated that more than 97% of children with mild illnesses develop measles antibody after vaccination (*80*). Only one study has reported a somewhat lower rate of seroconversion (79%) to the measles component of MMR vaccine among children with minor, afebrile upper-respiratory infection (*81*). Therefore, vaccination should not be delayed because of the presence of mild respiratory illness or other illness with or without fever.

Persons with moderate or severe febrile illness should be vaccinated as soon as they have recovered from the acute phase of the illness. This precaution avoids superimposing adverse effects of the vaccine on the underlying illness or mistakenly attributing a manifestation of the underlying illness to the vaccine.

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

REPORTING OF ADVERSE EVENTS FOLLOWING VACCINATION

Modern vaccines are safe and effective. However, some adverse events have been reported following the administration of all vaccines. These events range from frequent, minor, local reactions to extremely rare, severe, systemic illness, such as paralysis associated with OPV. It is often impossible to establish evidence for cause-and-effect relationships on the basis of case reports alone because temporal association alone does not necessarily indicate causation. Unless the syndrome following vaccination is clinically or pathologically distinctive, more detailed epidemiologic studies to compare the incidence rates of the event in vaccinees with the incidence rates among unvaccinated persons may be necessary. Reporting of serious adverse events is extremely important to stimulate studies to confirm a causal association and to study risk factors for adverse events. More complete information on adverse reactions to a specific vaccine may be found in the ACIP recommendations for that vaccine.

Health-care providers are required to report selected events occurring after vaccination to the Vaccine Adverse Events Reporting System (VAERS). Persons other than health-care workers can also report adverse events to VAERS. Adverse events other than those that must be reported or that occur after administration of other vaccines, especially events that are serious or unusual, should also be reported to VAERS regardless of whether the provider thinks they are causally associated. VAERS forms and instructions are available in the *FDA Drug Bulletin* and the *Physicians' Desk Reference*, or by calling the 24-hour VAERS information recording at 1-800-822-7967.

VACCINE INJURY COMPENSATION

The National Vaccine Injury Compensation Program, established by the National Childhood Vaccine Injury Act of 1986, is a system under which compensation can be paid on behalf of a person who was injured or died as a result of receiving a vaccine. The program, which became effective on October 1, 1988, is intended as an alternative to civil litigation under the traditional tort system in that negligence need not be proven.

The law establishing the program also created a vaccine injury table, which lists the vaccines covered by the program and the injuries, disabilities, illnesses, and conditions (including death) for which compensation may be paid. The table also defines the period of time during which the first symptom or substantial aggravation of the injury must appear. Persons may be compensated for an injury listed in the established table or one that can be demonstrated to result from administration of a listed vaccine. Injuries following administration of vaccines not listed in the legislation authorizing the program are not eligible for compensation through the program. Additional information about the program is available from:

National Vaccine Injury Compensation Program
Health Resources and Services Administration
Parklawn Building, Room 8-05
5600 Fishers Lane
Rockville, MD 20857
Telephone: (800) 338-2382 (24-hour recording)

Persons wishing to file a claim for vaccine injury should call or write to:

U.S. Court of Federal Claims
717 Madison Place, NW
Washington, DC 20005
Telephone: (202) 219-9657

PATIENT INFORMATION

Parents, guardians, legal representatives, and adolescent and adult patients should be informed about the benefits and risks of vaccine in understandable language. Opportunity for questions and answers should be provided before each vaccination.

Vaccine Information Pamphlets

The National Childhood Vaccine Injury Act (NCVIA) requires that vaccine information materials be developed for each vaccine covered by the Act (DTP or component antigens, MMR or component antigens, IPV, and OPV). The resulting Vaccine Information Pamphlets must be used by *all public and private* providers of vaccines, although private providers may elect to develop their own materials. Such materials must contain the specific, detailed elements required by law. Copies of these pamphlets are available from individual providers and from state health authorities responsible for immunization (*82*).

Important Information Statements

CDC has developed Important Information Statements for the vaccines not covered by the NCVIA. These statements must be used in public health clinics and other settings where federally purchased vaccines are used. Copies can be obtained from state health authorities responsible for immunization. The use of similar statements in the private sector is encouraged.

IMMUNIZATION RECORDS

Provider Records

Documentation of patient vaccinations helps ensure that persons in need of vaccine receive it and that adequately vaccinated patients are not overimmunized, increasing the risk for hypersensitivity (e.g., tetanus toxoid hypersensitivity). Serologic test results for vaccine-preventable diseases (such as those for rubella screening) as well as documented episodes of adverse events also should be recorded in the permanent medical record of the vaccine recipient.

Health-care providers who administer one or more of the vaccines covered by NVICP are required to ensure that the permanent medical record of the recipient (or a permanent office log or file) states 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*. 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. The ACIP recommends that the above information be kept for *all* vaccines and not only for those required by the National Vaccine Injury Act.

Patient's Personal Record

Official immunization cards have been adopted by every state and the District of Columbia to encourage uniformity of records and to facilitate the assessment of immunization status by schools and child care centers. The records are also important tools in immunization education programs aimed at increasing parental and patient awareness of the need for vaccines. A permanent immunization record card should be established for each newborn infant and maintained by the parent. In many states, these cards are distributed to new mothers before discharge from the hospital. Some states are developing computerized immunization record systems.

Persons Without Documentation of Vaccinations

Health-care providers frequently encounter persons who have no adequate documentation of vaccinations. 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. If records cannot be located, such persons should be considered susceptible and should be started on the age-appropriate immunization schedule (Tables 4 and 5). The following guidelines are recommended:

- MMR, OPV (or IPV, if indicated), Hib, hepatitis B, and influenza vaccines can be administered because no adverse effects of repeated vaccination have been demonstrated with these vaccines.
- Persons who develop a serious adverse reaction after administration of DTP, DTaP, DT, Td, or tetanus toxoid should be individually assessed before the administration of further doses of these vaccines (see the ACIP recommendations for use of diphtheria, tetanus, and pertussis vaccines) (*14,83,84*).
- Pneumococcal vaccine should be administered, if indicated. In most studies, local reactions in adults after revaccination were similar compared with initial vaccination (see the ACIP recommendations for the use of Pneumococcal Polysaccharide Vaccine for further details) (*85*).

Acceptability of Vaccinations Received Outside the United States

The acceptability of vaccines received in other countries for meeting vaccination requirements in the United States depends on vaccine potency, adequate documentation of receipt of the vaccine, and the vaccination schedule used. Although problems with vaccine potency have occasionally been detected (most notably with tetanus

toxoid and OPV), the majority of vaccine used worldwide is from reliable local or international manufacturers. It is reasonable to assume that vaccine received in other countries was of adequate potency.

Thus, the acceptability of vaccinations received outside the United States depends primarily on whether receipt of the vaccine was adequately documented and whether the immunization schedule (i.e., age at vaccination and spacing of vaccine doses) was comparable with that recommended in the United States (Tables 3–5,10). The following recommendations are derived from current immunization guidelines in the United

TABLE 10. Minimum age for initial vaccination and minimum interval between vaccine doses, by type of vaccine

Vaccine	Minimum *age* for first dose*	Minimum *interval* from dose 1 to 2*	Minimum *interval* from dose 2 to 3*	Minimum *interval* from dose 3 to 4*
DTP (DT)†	6 weeks§	4 weeks	4 weeks	6 months
Combined DTP-Hib	6 weeks	1 month	1 month	6 months
DTaP*	15 months			6 months
Hib (primary series)				
HbOC	6 weeks	1 month	1 month	¶
PRP-T	6 weeks	1 month	1 month	¶
PRP-OMP	6 weeks	1 month	¶	
OPV	6 weeks§	6 weeks	6 weeks	
IPV**	6 weeks	4 weeks	6 months††	
MMR	12 months§§	1 month		
Hepatitis B	birth	1 month	2 months¶¶	

DTP	Diphtheria-tetanus-pertussis
DTaP	Diphtheria-tetanus-acellular pertussis
Hib	*Haemophilus influenza* type b conjugate
IPV	Inactivated poliovirus vaccine
MMR	Measles-mumps-rubella
OPV	Live oral polio vaccine

*These minimum acceptable ages and intervals may not correspond with the optimal recommended ages and intervals for vaccination. See tables 3–5 for the current recommended routine and accelerated vaccination schedules.

†DTaP can be used in place of the fourth (and fifth) dose of DTP for children who are at least 15 months of age. Children who have received all four primary vaccination doses before their fourth birthday should receive a fifth dose of DTP (DT) or DTaP at 4–6 years of age before entering kindergarten or elementary school **and** at least 6 months after the fourth dose. The total number of doses of diphtheria and tetanus toxoids should not exceed six each before the seventh birthday (*14*).

§The American Academy of Pediatrics permits DTP and OPV to be administered as early as 4 weeks of age in areas with high endemicity and during outbreaks.

¶The booster dose of Hib vaccine which is recommended following the primary vaccination series should be administered no earlier than 12 months of age **and** at least 2 months after the previous dose of Hib vaccine (Tables 3 and 4).

**See text to differentiate conventional inactivated poliovirus vaccine from enhanced-potency IPV.

††For unvaccinated adults at increased risk of exposure to poliovirus with <3 months but >2 months available before protection is needed, three doses of IPV should be administered at least 1 month apart.

§§Although the age for measles vaccination may be as young as 6 months in outbreak areas where cases are occurring in children <1 year of age, children initially vaccinated before the first birthday should be revaccinated at 12–15 months of age and an additional dose of vaccine should be administered at the time of school entry or according to local policy. Doses of MMR or other measles-containing vaccines should be separated by at least 1 month.

¶¶This final dose is recommended no earlier than 4 months of age.

States. They are based on minimum acceptable standards and may not represent optimal recommended ages and intervals.

Only doses of vaccine with written documentation of the date of receipt should be accepted as valid. Self-reported doses of vaccine without written documentation should not be accepted.

Because childhood vaccination schedules vary in different countries, the age at vaccination and the spacing of doses may differ from that recommended in the United States. The age at vaccination is particularly important for measles vaccine. In most developing countries, measles vaccine is administered at 9 months of age when seroconversion rates are lower than at ages 12–15 months. For this reason, children vaccinated against measles before their first birthday should be revaccinated at 12–15 months of age and again, depending on state or local policy, upon entry to primary, middle, or junior high school. Doses of MMR or other measles-containing vaccines should be separated by at least 1 month. Combined MMR vaccine is preferred. Children who received monovalent measles vaccine rather than MMR on or after their first birthday also should receive a primary dose of mumps and rubella vaccines.

In most countries, including the United States, the first of three regularly scheduled doses of OPV is administered at 6 weeks of age at the same time as DTP vaccine. However, in polio-endemic countries, an extra dose of OPV is often administered at birth or at ≤2 weeks of age. For acceptability in the United States, doses of OPV and IPV administered at ≥6 weeks (42 days) of age can be counted as a valid part of the vaccination series. For the primary vaccination series, each of the three doses of OPV should have been separated by a minimum of 6 weeks (42 days). If enhanced-potency IPV (available in the United States beginning in 1988) was received, the first two doses should have been separated by at least 4 weeks with at least 6 months between the second and third dose. If conventional inactivated poliovirus vaccine (available in the United States until 1988 and still used routinely in some countries [e.g., the Netherlands]) was used for the primary series, the first three doses should have been separated by at least 4 weeks with at least 6 months between the third and fourth dose. If both OPV and an inactivated poliovirus vaccine were received, the primary vaccination series should consist of a combined total of four doses of polio vaccine, unless the use of enhanced potency IPV can be verified. If OPV and enhanced-potency IPV were received, the primary series consists of a combined total of three doses of polio vaccine. Any dose of polio vaccine administered at the above recommended minimum intervals can be considered valid. Because the recommended polio vaccination schedule in many countries differs from that used in the United States, persons vaccinated outside the United States may need one or more additional doses of OPV (or enhanced-potency IPV) to meet current immunization guidelines in the United States.

Any dose of DTP vaccine or Hib vaccine administered at ≥6 weeks of age can be considered valid. The "booster" dose of Hib vaccine should not have been administered before age 12 months. The first three doses of DTP vaccine should have been separated by a minimum of 4 weeks, and the fourth dose should have been administered no less than 6 months after the third dose. Doses of Hib vaccine in the primary series should have been administered no less than 1 month apart. The booster dose of Hib vaccine should have been administered at least 2 months after the previous dose.

The first dose of hepatitis B vaccine can be administered as early as at birth and should have been separated from the second dose by at least 1 month. The final (third or fourth) dose should have been administered no sooner than 4 months of age and at least 2 months after the previous dose, although an interval of at least 4 months is preferable.

Any dose of vaccine administered at the recommended minimum intervals can be considered valid. Intervals longer than those recommended do not affect antibody titers and may be counted.

Immunization requirements for school entry vary by state. Specific state requirements should be consulted if vaccinations have been administered by schedules substantially different from those routinely recommended in the United States.

VACCINE PROGRAMS

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

Providers should strive to adhere to the *Standards for Pediatric Immunization Practices* (*74*). These Standards define appropriate immunization practices for both the public and private sectors. The Standards provide guidance on how to make immunization services more conducive to the needs of children through implementation of practices which will result in eliminating barriers to vaccination. These include practices aimed at eliminating unnecessary prerequisites for receiving vaccines, eliminating missed opportunities to vaccinate, improving procedures to assess a child's need for vaccines, enhancing knowledge about vaccinations among both parents and providers, and improving the management and reporting of adverse events. In addition, the Standards address the importance of tracking systems and the use of audits to monitor clinic/office immunization coverage levels among clients. The Standards are the goal to which all providers should strive to attain appropriate vaccination of all children.

Standards of practice have also been published to increase vaccination levels among adults (*86*). All adults should complete a primary series of tetanus and diphtheria toxoids and receive a booster dose every 10 years. Persons ≥65 years of age and all adults with medical conditions that place them at risk for pneumococcal disease or serious complications of influenza should receive pneumococcal polysaccharide vaccine and annual injections of influenza vaccine. Adult immunization programs should also provide MMR vaccine whenever possible to anyone susceptible to measles, mumps, or rubella. Persons born after 1956 who are attending college (or other post-high school educational institutions), who are newly employed in situations that place them at high risk for measles transmission (e.g., health-care facilities), or who are traveling to areas with endemic measles, should have documentation of having received two doses of live MMR on or after their first birthday or other evidence of immunity. All other young adults in this age group should have documentation of a single dose

of live MMR vaccine on or after their first birthday or have other evidence of immunity. Use of MMR causes no harm if the vaccinee is already immune to one or more of its components and its use ensures that the vaccinee has been immunized against three different diseases. In addition, widespread use of hepatitis B vaccine is encouraged for all persons who are or may be at increased risk (e.g., adolescents and adults who are either in a high-risk group or reside in areas with high rates of injecting drug use, teenage pregnancy, and/or sexually transmitted disease).

Every visit to a health-care provider is an opportunity to update a patient's immunization status with needed vaccines. Official health agencies should take necessary steps, including developing and enforcing school immunization requirements, to assure that students at all grade levels (including college students) and those in child care centers are protected against vaccine-preventable diseases. Agencies should also encourage institutions such as hospitals and long-term-care facilities to adopt policies regarding the appropriate vaccination of patients, residents, and employees.

Dates of vaccination (day, month, and year) should be recorded on institutional immunization records, such as those kept in schools and child care centers. This will facilitate assessments that a primary vaccine series has been completed according to an appropriate schedule and that needed boosters have been obtained at the correct time.

The ACIP recommends the use of "tickler" or recall systems by all health-care providers. Such systems should also be used by health-care providers who treat adults to ensure that at-risk persons receive influenza vaccine annually and that other vaccinations, such as Td, are administered as needed.

REPORTING VACCINE-PREVENTABLE DISEASES

Public health officials depend on the prompt reporting of vaccine-preventable diseases to local or state health departments by health-care providers to effectively monitor the occurrence of vaccine-preventable diseases for prevention and control efforts.

Nearly all vaccine-preventable diseases in the United States are notifiable; individual cases should be reported to local or state health departments. State health departments report these diseases each week to CDC. The local and state health departments and CDC use these surveillance data to determine whether outbreaks or other unusual events are occurring and to evaluate prevention and control strategies. In addition, CDC uses these data to evaluate the impact of national policies, practices, and strategies for vaccine programs.

SOURCES OF VACCINE INFORMATION

In addition to these general recommendations, other sources are available that contain specific and updated vaccine information. These sources include the following:

Official vaccine package circulars. Manufacturer-provided product-specific information approved by the FDA with each vaccine. Some of these materials are reproduced in the *Physician's Desk Reference (PDR)*.

Morbidity and Mortality Weekly Report (MMWR). Published weekly by CDC, MMWR contains regular and special ACIP recommendations on vaccine use and statements of vaccine policy as they are developed and reports of specific disease activity. Subscriptions are available through Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402–9235; Telephone: (202) 783-3238. Also available through MMS Publications, C.S.P.O. Box 9120, Waltham, MA 02254–9120; Telephone: (800) 843-6356.

Health Information for International Travel. This booklet is published annually by CDC as a guide to national requirements and contains recommendations for specific immunizations and health practices for travel to foreign countries. Purchase from the Superintendent of Documents (address above).

Advisory memoranda. Published as needed by CDC, these memoranda advise international travelers or persons who provide information to travelers about specific outbreaks of communicable diseases abroad. They include health information for prevention and specific recommendations for immunization. Memoranda and/or placement on mailing list are available from: Travelers' Health Section, Division of Quarantine MS-E03, National Center for Prevention Services (NCPS), CDC, Atlanta, GA 30333. The Division of Quarantine also maintains a 24-hour Travelers' Health Hotline voice information system that can be reached by dialing: (404) 332-4559.

The Report of the Committee on Infectious Diseases of the American Academy of Pediatrics (Red Book). This report, which contains recommendations on all licensed vaccines, is updated every 2–3 years—most recently in 1991. The next revision will be published in May 1994. Policy changes for individual recommendations for immunization practices are published as needed by the American Academy of Pediatrics in the journal **Pediatrics**. They are available from the American Academy of Pediatrics, Publications Division, 141 Northwest Point Boulevard, P.O. Box 927, Elk Grove Village, IL 60009–0927; Telephone: (708) 228-5005.

Control of Communicable Diseases in Man. This manual is published by the American Public Health Association every 5 years—most recently in 1990 (15th ed.). The manual contains information about infectious diseases, their occurrence worldwide, diagnoses and therapy, and up-to-date recommendations on isolation and other control measures for each disease presented. It is available from the American Public Health Association, 1015 Fifteenth Street, NW, Washington, DC 20005; Telephone: (202) 789-5600.

Guide for Adult Immunization (1990). Produced by the American College of Physicians for physicians caring for adults, this guide emphasizes use of vaccines in healthy adults and adults with specific disease problems. It is available from Subscriber Services, American College of Physicians, Independence Mall West, Sixth Street at Race, Philadelphia, PA 19106–1572; Telephone: (215) 351-2600 or (800) 523-1546. (A new edition should be published within 1994.)

Technical bulletins of the American College of Obstetricians and Gynecologists. These bulletins contain important information on immunization of pregnant women and are updated periodically. They are available from the American College of Obstetricians and Gynecologists, Attention: Resource Center, 409 12th Street, SW, Washington, DC 20024–2188.

State and many local health departments. These departments frequently provide technical advice, printed information on vaccines and immunization schedules, posters, and other educational materials.

National Immunization Program, CDC. This program maintains a 24-hour voice information hotline that provides technical advice on vaccine recommendations, disease outbreak control, and sources of immunobiologics. In addition, a course on the epidemiology, prevention, and control of vaccine preventable diseases is offered each year in Atlanta and in various states. For further information, contact CDC, National Immunization Program, Atlanta, GA 30333; Telephone: (404) 332-4553.

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