known as memory T cells, are T lymphocytes that have a memory of a previous immune response. The secondary response depends on immunologic memory after the first exposure mediated by both T and B lymphocytes. Infection with measles or varicella vaccine strains has been shown to evoke a cell-mediated in addition to a humoral response.

Many pathogens replicate at mucosal surfaces before host invasion and may induce secretory IgA along the respiratory and gastrointestinal mucous membranes and at other localized sites (e.g., polio, rubella, influenza, rotavirus). IgA antibodies are efficient at virus neutralization (e.g., polio), fix complement through the alternative pathway (e.g., cholera), prevent adsorption of organisms to the intestinal wall (e.g., *Escherichia coli,* cholera), and can lyse gram-negative bacteria (with the aid of both complement and lysozyme).[34] Current parenteral, especially inactivated, vaccines rarely induce high levels of secretory IgA antibodies.

MEASUREMENT OF THE IMMUNE RESPONSE

Response to vaccines is often gauged by measuring the appearance and concentration of specific serum antibodies.[35] For some viral vaccines, such as those for measles and rubella, the presence of circulating antibodies correlates with clinical protection. Although this has served as a dependable indicator of immunity, seroconversion measures only the humoral parameter of the immune response. Secondary vaccine failure occurs when an individual who previously had developed an adequate immune response loses protection over time. This waning immunity can be attributed to a loss of long-lived memory B or T cells in the absence of repeated exposure to the pathogen. Evaluating persistence of antibody has been used to determine the duration of vaccine-induced immunity for those diseases for which antibody is judged to be a good correlate of protection. However, the absence of measurable antibody may not mean that the individual is unprotected. Although a fall in titer occurs, on revaccination or challenge a rapid secondary response is observed in IgG antibodies, with little or no detectable IgM response, suggesting persistent protection. With some vaccines and toxoids, the mere presence of antibodies is not sufficient to ensure clinical protection, but rather a minimal circulating level of antibody is required (e.g., 0.01 IU/mL of tetanus antitoxin). Functional antibody is important in assessing immunity to bacterial polysaccharide vaccines. Opsonophagocytic activity is considered the assay of choice for monitoring vaccine response[36] because the vaccines also induce nonfunctional antibodies that are detected in standard enzyme immunosorbent assay (EIA), although the EIA can be used as a proxy. Some immune responses may not in themselves confer immunity but may be sufficiently associated with protection that they remain useful proxy measures of protective immunity (e.g., vibriocidal serum antibodies in cholera). The measurement of cell-mediated immunity, which would be helpful in assessing the degree of ongoing protection in many circumstances, usually is limited to research laboratories and to only a few vaccines.

VACCINE DEVELOPMENT

Most vaccines in use today have been developed by empirical techniques.[37] For live-attenuated viral vaccines, organisms are repeatedly passaged in various tissue culture cell lines to reduce virulent properties while maintaining immunogenicity. Inactivated vaccines usually have been developed by growing microorganisms, followed by concentration, purification, and inactivation, not necessarily in that order. Component vaccines usually are derived from chemical separation of the needed component from the parent organism.

Future vaccines are likely to be derived from new methods of biotechnology, especially recombinant techniques. Currently available hepatitis B vaccines were developed by cloning the HBsAg gene into yeast, leading to synthesis of HBsAg within the yeast cell. Other new approaches for producing vaccines include live vectors, in which one or more genes encoding critical determinants of immunity from pathogenic microorganisms are inserted into the genome of the vector, followed by the administration of the vector as a component of the vaccine. These vectors may include viruses, such as poxviruses (vaccinia or canarypox), or bacteria, such as *Salmonella* or bacillus Calmette-Guérin (BCG). Additional newer techniques include microencapsulation of critical antigens in polymers, which can lead to sustained release or pulse release over prolonged periods, mimicking the effect of multiple injections of an antigen over a several-month interval. New technologies also include use of nucleic acids, which encode critical antigens. Injection of the DNA, combined with administration of a protein at a later point in time, leads to production of antigen without risk for producing whole infectious organisms. LAIV was developed using genetic reassortment of the genes encoding two of the surface glycoproteins from wild virus isolates with six other genes contributed from a cold-adapted, temperature-sensitive influenza strain. Similar techniques were used to develop bovine rotavirus vaccines.[38] Last, newer technologies focus on the development of adjuvants to help stimulate the immune response.[39]

General Principles of Immunization

Introduction and widespread use of vaccines resulted in global eradication of smallpox, elimination of poliomyelitis caused by wild viruses in the United States and most of the countries of the world, and dramatic reductions in the incidence rates of other diseases (Tables 316.1 and 316.2). Measles and rubella are no longer considered endemic in the Americas.[40,41] Measles and rubella have been reduced by greater than 90% in developed countries and, if global vaccination efforts can be sustained, may eventually be eliminated from many countries. The World Health Assembly had established a goal to eradicate polio from the world by the end of 2000.[42] Although that goal was not achieved, by the end of 2016 only three countries in the world had never interrupted wild poliovirus transmission (www.polioeradication.org).[43] The last case of polio caused by wild virus in the Western Hemisphere was in 1991; four of the six regions of the World Health Organization (WHO)—American, European, Southeast Asian, and Western Pacific—have been certified free of wild poliovirus.[44–46] Global use of hepatitis B vaccine in infants may have an impact comparable to that of other vaccines in childhood. Hib vaccines have only recently come into widespread use, but disease incidence has been reduced markedly in many developed countries.[47–50] Reductions based on historical estimates have been achieved for congenital rubella syndrome and Hib invasive disease.[51] Despite these successes, cases of measles and pertussis continue to occur in the United States (see Table 316.1). All measles cases are the result of

TABLE 316.1 Representative 20th-Century Morbidity Cases in 2017 and Change

DISEASE	20th CENTURY ANNUAL MORBIDITY[a]	2017 REPORTED CASES[b]	PERCENT DECREASE
Smallpox	29,005	0	100%
Diphtheria	21,053	0	100%
Measles	530,217	120	>99%
Mumps	162,344	6109	96%
Pertussis	200,752	18,975	91%
Polio (paralytic)	16,316	0	100%
Rubella	47,745	7	>99%
Congenital rubella syndrome	152	5	99%
Tetanus	580	33	94%
Haemophilus influenzae	20,000	33[c]	>99%

[a]From Roush SW, Murphy TV; Vaccine-Preventable Disease Table Working Group. Historical comparisons of morbidity and mortality for vaccine-preventable diseases in the United States. *JAMA*. 2007;298:2155–2163.
[b]Centers for Diease Control and Prevention. *National Notifiable Diseases Surveillance System, 2017 Annual Tables of Infectious Disease Data.* Atlanta: CDC Division of Health Informatics and Surveillance; 2018.
[c]*H. influenzae* type b (Hib) at <5 years of age. An additional 10 cases of Hib are estimated to have occurred among the 203 notifications of *H. influenzae* (<5 years of age) with unknown serotype.

TABLE 316.2 Representative 20th-Century Morbidity Cases in 2016 and Change

DISEASE	PREVACCINE ERA ANNUAL ESTIMATE	2016 ESTIMATE (UNLESS OTHERWISE SPECIFIED)	PERCENT DECREASE
Hepatitis A	117,333[a]	4000[b]	97%
Hepatitis B (acute)	66,232[a]	20,900[b]	68%
Pneumococcus (invasive)			
All ages	63,067[a]	30,400[c]	52%
<5 yr of age	16,069[a]	1700[c]	89%
Rotavirus (hospitalizations, <3 yr of age)	62,500[d]	30,625[e]	51%
Varicella	4,085,120[a]	102,128[f]	98%

[a]Rousch SW, Murphy TV; Vaccine-Prevenatable Disease Table Working Group. Historical comparisons of morbidity and mortality for vaccine-preventable diseases in the United States. *JAMA.* 2007;298:2155–2163.
[b]Centers for Disease Control and Prevention. Viral hepatitis surveillance—United States, 2016.
[c]Centers for Disease Control and Prevention. Active bacterial core surveillance 2016 (unpublished).
[d]Cortese MM, Parashar UD; Centers for Disease Control and Prevention. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2009;58(RR-2):1-25.
[e]New Vaccine Surveillance Network 2017 data (unpublished); US rotavirus disease now has a biennial pattern.
[f]Centers for Disease Control and Prevention. Varicella Program 2017 data (unpublished).

international importations, some of which spread within the US population, whereas pertussis remains endemic.

Pneumococcal conjugate vaccines (PCVs) have had a marked impact on invasive pneumococcal disease in countries where they have been used widely in children.[52,53] Decreases in disease were observed not only in children but also in adults, who presumably are not being exposed to infectious children because the latter have had vaccine-type pneumococcal carriage eliminated by vaccination.

Modern vaccines are safe and generally effective. Each vaccine is associated with some adverse effects, which are usually mild, and only rarely life-threatening. No vaccine is 100% effective. Consequently, some persons who have received a complete vaccine or toxoid series may acquire disease after exposure. The effectiveness of vaccines recommended for universal use in children is well defined, with most vaccines protecting more than 80% of recipients after a primary series.

In most studies, acellular pertussis vaccines range in efficacy from 63% to 99% during the first few years after vaccination.[54,55,56] One dose of varicella vaccine is 95% or more effective against severe varicella but is less effective against varicella of any severity.[57,58] With some vaccines, antibody may wane, but immunologic memory is sufficient to prevent disease if the individual is exposed (e.g., hepatitis B).[59] However, for some diseases with short incubation periods (e.g., meningococcal disease), waning antibody after vaccination is associated with waning protection. This waning has occurred with meningococcal conjugate vaccines, resulting in the need for modification of the originally recommended vaccine schedule with the addition of a second dose.[60] Another example of loss of durability has occurred with the Tdap (tetanus, diphtheria, and acellular pertussis) and DTaP (diphtheria and tetanus toxoids and acellular pertussis) vaccines, in which protection begins to wane a few years after administration.[61–63]

Although high efficacy of each of these vaccines is apparent, there has been substantial controversy about reported adverse events temporally associated with vaccination. Because of these controversies, the IOM reviewed available information, and between 1991 and 2013 published multiple reports.[64–67] In the 1991 and 1994 studies, the IOM found insufficient evidence to indicate a causal relationship between DTaP and permanent neurologic damage, and the IOM favored rejection of a causal relationship between combined diphtheria and tetanus toxoids (DT) and encephalopathy and between conjugate Hib vaccines and early-onset Hib disease. The IOM also concluded that the evidence establishes a causal relationship between MMR and thrombocytopenia, between rubella vaccine and acute arthritis, between DT and brachial neuritis, and between a variety of vaccines and anaphylaxis. In 2004 the IOM reported the relationships between a variety of disorders and vaccines (www.iom.edu/Activities/PublicHealth/ImmunizationSafety.aspx).[67,68] The IOM panel concluded that evidence did not support a relationship between MMR or thimerosal and autism, between multiple immunizations and heterologous infections, between multiple immunizations and type 1 diabetes, or between hepatitis B vaccine and incident or relapsed multiple sclerosis. In 2011 the IOM looked at the relationship of vaccines with many conditions that are reported after vaccination and, in most cases, found no evidence to support such associations. The IOM specifically found evidence to support rejection of an association between MMR vaccine and autism. Likewise, it found evidence to reject an association between IIV and asthma. In 2013 the IOM studied the impact of giving multiple vaccines to an individual in accordance with Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC), American Academy of Pediatrics (AAP), and American Academy of Family Physicians (AAFP) recommendations and found no evidence of a safety concern with adhering to the childhood schedule.[69]

Development of vaccines consists of four phases. Initial studies typically are conducted in animal models to demonstrate protection (or at least production of antibodies) and relative safety. These are called *preclinical studies*. Then limited numbers of doses are administered to humans to demonstrate antibody production and safety (phase I). After this phase, clinical trials in humans are conducted in a limited number of people to select optimal vaccine schedules and to demonstrate further safety (phase II). Larger trials are conducted to demonstrate efficacy (phase III). Because of their limited size, these field trials can be expected to detect adverse events that occur only relatively frequently (1 per 1000 doses or higher). After clinical trials, licensure may be sought. In the United States, vaccine production is regulated by the Center for Biologics Evaluation and Research (CBER) of the US Food and Drug Administration (FDA). Only after a vaccine has been found to be safe and effective is it licensed for use. Postmarketing surveillance (phase IV) is necessary to detect rare adverse events associated with vaccination and to monitor safety of vaccination practices, such as simultaneous immunization.

There is no direct evidence of risk to the fetus when pregnant women are given vaccines routinely recommended during pregnancy by ACIP. The benefit of IIV to the pregnant mother and the fetus outweighs any risk of vaccination to the mother or the fetus.[70] Some vaccines are recommended for pregnant women in order to provide passive immunity to their fetuses so that when the child is born, the child is protected before active immunity can be induced through direct vaccination of the infant. Thus, Tdap and nonlive influenza vaccine is recommended during each pregnancy.[6,70,71] Most live-virus vaccines induce viremia, which at least theoretically could result in infection of the fetus, so live-virus vaccines are not administered to pregnant women except in unusual circumstances, when potential benefit clearly outweighs the risk.

The decision to administer a vaccine involves assessment of risks of disease, benefits of vaccination, and risks associated with vaccination. The relative balance of risks and benefits may change over time; consequently, continuing assessment of vaccines is essential. Recommendations for vaccine use are developed by several different bodies: ACIP develops recommendations for vaccines for children, adolescents, and adults in the civilian population in conjunction with professional societies. These recommendations are updated annually and are available at www.cdc.gov/vaccines/schedules/hcp/index.html. Since 2011, the ACIP process for making vaccine recommendations has included a careful evaluation of the strength of the evidence supporting recommendations, which is known as GRADE (Grading of Recommendations, Assessment, Development and Evaluation; www.cdc.gov/vaccines/acip/recs/GRADE/

table-refs.html). The Committee on Infectious Diseases (COID) of the AAP (the "Red Book " committee) develops recommendations for vaccine use in infants, children, and adolescents.[72] Since 1995, ACIP, the AAP, and the AAFP have collaborated to issue a harmonized childhood immunization schedule, which is updated annually. The childhood immunization schedule consists of three parts: one based on age, a second that is a catch-up schedule for children who are behind on their immunizations, and a third that is based on underlying medical conditions (Fig. 316.1).[73] ACIP also annually issues an adult immunization schedule in two parts: (1) recommendations based on age group and (2) recommendations based on underlying medical conditions (Figs. 316.2 to 316.4), which can be found at www.cdc.gov/vaccines/schedules/hcp/adult.html. The Adult Immunization Schedule for 2018 was harmonized with the AAFP, the American College of Obstetricians and Gynecologists, the American College of Physicians, and the American College of Nurse-Midwives.

CURRENTLY AVAILABLE IMMUNIZING AGENTS

Tables 316.3 and 316.4 list currently licensed immunizing agents and immunoglobulins. This section presents brief information about most immunizing agents, primary indications for use, relative efficacy, number and spacing of doses required, known adverse effects, and precautions and contraindications for use. Package inserts and specific references and recommendations should be consulted for more detailed information. In addition to these licensed products, several other vaccines are under development and may become available.

Vaccines

Adenovirus Vaccine

Adenovirus vaccine contains live adenovirus types 4 and 7. It is recommended only for military personnel who are 17 through 50 years of age. It is taken as two oral tablets (one dose). Serious adverse events possibly associated with receipt of vaccine included hematuria, gastroenteritis, gastritis, pneumonia, and hematochezia.

Anthrax Vaccine

Anthrax vaccine (AVA) is prepared from microaerophilic cultures of an avirulent nonencapsulated strain of *Bacillus anthracis.* The vaccine is a cell-free filtrate that contains a mixture of components, including protective antigen (the antigen that is thought to confer immunity) and other bacterial products adsorbed to aluminum hydroxide. Because of concerns about potential use of *B. anthracis* as a biologic warfare agent, vaccination of selected members of the US Armed Forces was begun in 1998. After the intentional release of anthrax in the United States in 2001, anthrax vaccine was recommended for civilians at risk for repeated exposure to *B. anthracis* spores, including laboratory personnel handling environmental specimens and performing confirmatory testing for *B. anthracis* in selected laboratories and workers making repeated entries into sites known to be contaminated with *B. anthracis* spores. Anthrax vaccine also was used after exposure, in conjunction with antimicrobial prophylaxis, under an investigational protocol.[74] Groups for whom preexposure vaccination is recommended include persons working with production quantities of *B. anthracis* cultures or in activities with a high potential for aerosol production and selected other workers at high risk for exposure to *B. anthracis* spores.[75] Efficacy has been demonstrated in protection against cutaneous disease. Data on clinical efficacy against inhaled anthrax in humans are limited, but available human and animal data are consistent with protection.[76] The vaccine induces antibodies in greater than 90% of adults who received the currently recommended primary course of three IM injections given at time zero, 4 weeks, and 6 months, with boosters at 12 months and 18 months, followed by annual boosters.[75,77] A controlled study of a vaccine similar to the currently available vaccine demonstrated protective efficacy against cutaneous disease of 93% among mill workers.[78] Experience suggests that two doses of vaccine confer some protection.[79] Mild

TABLE 316.3 Currently Available Vaccines and Toxoids and Year Licensed

PRODUCT	YEAR LICENSED
Adenovirus vaccine, live, attenuated	2014
Anthrax vaccine adsorbed	1972
Calmette-Guérin bacillus vaccine; live, attenuated	1950
Cholera vaccine, live, attenuated	2016
Dengue tetravalent vaccine, live	2019
Diphtheria and tetanus toxoids and acellular pertussis vaccine	1991
Diphtheria and tetanus toxoids adsorbed (pediatric use, DT)	1949
Diphtheria and tetanus toxoids and acellular pertussis vaccine absorbed, *Haemophilus* B conjugate vaccine, and inactivated polio vaccine combined	2008
Diphtheria and tetanus toxoids and acellular pertussis vaccine absorbed and inactivated polio vaccine combined	2008
Diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (recombinant), and inactivated poliovirus vaccine combined	2002
Haemophilus influenzae type b conjugate vaccine	1987
Hepatitis A vaccine	1995
Hepatitis A inactivated and hepatitis B (recombinant) vaccine	2001
Hepatitis B recombinant vaccine	1987
Human papillomavirus vaccine	2006
Influenza virus vaccine (cell culture)	2013
Influenza virus vaccine (inactivated)	1945
Influenza virus vaccine; live, attenuated, intranasal	2003
Influenza virus vaccine; recombinant hemagglutinin	2014
Japanese encephalitis vaccine	2009
Measles virus vaccine; live, attenuated	1963
Measles, mumps, rubella, varicella; live, attenuated	2005
Measles, mumps, and rubella virus vaccine; live, attenuated	1971

TABLE 316.3 Currently Available Vaccines and Toxoids and Year Licensed[a]—cont'd

PRODUCT	YEAR LICENSED
Meningococcal polysaccharide (serogroups A, C, Y, and W) conjugated to diphtheria toxoid	2005
Pneumococcal conjugate vaccine (13-valent)	2010
Pneumococcal polysaccharide vaccine (23-valent)	1983
Poliomyelitis vaccine (inactivated, enhanced potency)	1987
Rabies vaccine (human diploid)	1980
Recombinant zoster vaccine	2017
Rotavirus vaccine, live, attenuated	2006
Rubella virus vaccine, live, attenuated	1969
Serogroup B meningococcal vaccine	2014
Smallpox vaccine, live, attenuated	2007
Tetanus and diphtheria toxoids, adsorbed (adult use, Td)	1955
Tetanus toxoid adsorbed	1949
Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, absorbed	2005
Typhoid vaccine (polysaccharide)	1994
Typhoid vaccine; live, attenuated (oral)	1990
Varicella vaccine; live, attenuated	1995
Yellow fever vaccine; live, attenuated	1953
Zoster vaccine; live, attenuated	2006

[a]As of January 2017.

TABLE 316.4 Immune Globulin Preparations Made From Human Plasma[a]

NAME	ABBREVIATION	ROUTE OF ADMINISTRATION	YEAR LICENSED
Anthrax immune globulin		Intravenous	2015
Botulism intravenous immune globulin	BabyBIG	Intravenous	2003
Cytomegalovirus immune globulin intravenous	CMV IGIV	Intravenous	1990
Hepatitis B immune globulin	HBIG	Intramuscular	1977
Immune globulin	IG	Intramuscular	1943
Immune globulin intravenous	IGIV	Intravenous	1981
Immune globulin subcutaneous	IGSC	Subcutaneous	2006
Rabies immune globulin	RIG	Intramuscular	1974
Tetanus immune globulin	TIG	Intramuscular	1957
Vaccinia immune globulin intravenous	VIG-IGIV	Intravenous	2005
Varicella-zoster immune globulin	VariZIG	Intramuscular	2012[c]

[a]Antitoxin preparations from animal sera other than humans are available for botulism and diphtheria.
[b]As of January 2017.
[c]A previous preparation of varicella-zoster IG (VZIG) was licensed in 1980.

local reactions at the site of injection occur in about 30% of recipients. Studies of adverse events after injection of the alum-precipitated vaccine, which is the precursor to the AVA vaccine, demonstrate that more severe local reactions occur infrequently (<4%) and systemic reactions are rare (0.2%). Surveillance for adverse events in the military program revealed no pattern of serious adverse events.[80,81] Adverse events, including injection site reaction incidence and duration, were less often seen after IM injection compared with subcutaneous injection.[77] The IM route of administration is indicated for preexposure use.[75] Vaccines containing only recombinant protective antigen are under active development and may be less reactogenic than the current vaccine.[82,83] In the event of exposure to anthrax spores, the recommended postexposure prophylaxis (PEP) regimen is three doses of AVA administered at 0, 2, and 4 weeks, combined with 60 days of antibiotics.[75]

Bacillus Calmette-Guérin Vaccine

BCG vaccine contains living Calmette-Guérin bacillus, an attenuated strain of *Mycobacterium bovis*. In many countries, BCG is used in infants and young children to prevent disseminated tuberculosis infection. In the United States, use of BCG is recommended only in special circumstances because the general risk for infection is low. BCG vaccination can also result in conversion of the purified protein derivative (PPD) or Mantoux tuberculin skin test, thereby removing one of the most important indicators of tuberculosis infection (tuberculin conversion). However, the association of a positive PPD skin test result after immunization with BCG in childhood tends to fade over time, and most individuals will have a PPD reaction of less than 10 mm by 10 years later. BCG does not cross react with the interferon-γ release assay (IGRA), so the IGRA is the preferred test over the PPD for diagnosis of tuberculosis in patients older than 4 years who have received BCG.[84] The IGRA is not as sensitive in children 4 years or younger and requires a blood draw. Although BCG is widely used throughout the world, there has been much controversy regarding its efficacy. Studies have suggested that the vaccine is effective, particularly for preventing complications of disseminated tuberculosis in young children.[85–87] In

Text continued on p. 3785

Table 1 Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger United States, 2019

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

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16 yrs	17-18 yrs
Hepatitis B (HepB)	1st dose	2nd dose			3rd dose												
Rotavirus (RV) RV1 (2-dose series); RV5 (3-dose series)			1st dose	2nd dose	See Notes												
Diphtheria, tetanus, & acellular pertussis (DTaP: <7 yrs)			1st dose	2nd dose	3rd dose			4th dose				5th dose					
Haemophilus influenzae type b (Hib)			1st dose	2nd dose	See Notes		3rd or 4th dose, See Notes										
Pneumococcal conjugate (PCV13)			1st dose	2nd dose	3rd dose		4th dose										
Inactivated poliovirus (IPV: <18 yrs)			1st dose	2nd dose	3rd dose							4th dose					
Influenza (IIV)					Annual vaccination 1 or 2 doses									Annual vaccination 1 dose only			
or													or				
Influenza (LAIV)											Annual vaccination 1 or 2 doses			Annual vaccination 1 dose only			
Measles, mumps, rubella (MMR)					See Notes		1st dose					2nd dose					
Varicella (VAR)							1st dose					2nd dose					
Hepatitis A (HepA)					See Notes		2-dose series, See Notes										
Meningococcal (MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)			See Notes											1st dose		2nd dose	
Tetanus, diphtheria, & acellular pertussis (Tdap: ≥7 yrs)														Tdap			
Human papillomavirus (HPV)														See Notes			
Meningococcal B														See Notes			
Pneumococcal polysaccharide (PPSV23)											See Notes						

Range of recommended ages for all children

Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision-making

No recommendation

FIG. 316.1 (A) Recommended child and adolescent immunization schedule for ages 18 years or younger, United States, 2019. (B) Catch-up immunization schedule for persons aged 4 months to 18 years who start late or who are more than 1 month behind—United States, 2019. (C) Footnotes for both schedules. (D) Child and adolescent schedule by medical and other indications, United States, 2019. *(From Centers for Disease Control and Prevention. Recommended child and adolescent immunization schedule for ages 18 years or younger, United States, 2019.* www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html. *Accessed February 8, 2019.)*

Table 2 Catch-up immunization schedule for persons aged 4 months—18 years who start late or who are more than 1 month behind, United States, 2019

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

Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
Children age 4 months through 6 years					
Hepatitis B	Birth	**4 weeks**	**8 weeks *and* at least 16 weeks after first dose.** Minimum age for the final dose is 24 weeks.		
Rotavirus	6 weeks Maximum age for first dose is 14 weeks, 6 days	**4 weeks**	**4 weeks** Maximum age for final dose is 8 months, 0 days.		
Diphtheria, tetanus, and acellular pertussis	6 weeks	**4 weeks**	**4 weeks**	**6 months**	**6 months**
Haemophilus influenzae type b	6 weeks	**No further doses needed** if first dose was administered at age 15 months or older. **4 weeks** if first dose was administered before the 1st birthday. **8 weeks (as final dose)** if first dose was administered at age 12 through 14 months.	**No further doses needed** if previous dose was administered at age 15 months or older. **4 weeks** if current age is younger than 12 months ***and*** first dose was administered at younger than age 7 months, ***and*** at least 1 previous dose was PRP-T (ActHib, Pentacel, Hiberix) or unknown. **8 weeks *and* age 12 through 59 months (as final dose)** if current age is younger than 12 months ***and*** first dose was administered at age 7 through 11 months; OR if current age is 12 through 59 months ***and*** first dose was administered before the 1st birthday, ***and*** second dose administered at younger than 15 months; OR if both doses were PRP-OMP (PedvaxHIB; Comvax) ***and*** were administered before the 1st birthday.	**8 weeks (as final dose)** This dose only necessary for children age 12 through 59 months who received 3 doses before the 1st birthday.	
Pneumococcal conjugate	6 weeks	**No further doses needed** for healthy children if first dose was administered at age 24 months or older. **4 weeks** if first dose administered before the 1st birthday. **8 weeks (as final dose for healthy children)** if first dose was administered at the 1st birthday or after.	**No further doses needed** for healthy children if previous dose administered at age 24 months or older. **4 weeks** if current age is younger than 12 months and previous dose given at <7 months old. **8 weeks (as final dose for healthy children)** if previous dose given between 7-11 months (wait until at least 12 months old); OR if current age is 12 months or older and at least 1 dose was given before age 12 months.	**8 weeks (as final dose)** This **dose** only necessary for children age 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age.	
Inactivated poliovirus	6 weeks	**4 weeks**	4 weeks if current age is < 4 years. 6 months (as final dose) if current age is 4 years or older.	**6 months** (minimum age 4 years for final dose).	
Measles, mumps, rubella	12 months	**4 weeks**			
Varicella	12 months	**3 months**			
Hepatitis A	12 months	**6 months**			
Meningococcal	2 months MenACWY-CRM 9 months MenACWY-D	**8 weeks**	See Notes	See Notes	
Children and adolescents age 7 through 18 years					
Meningococcal	Not Applicable (N/A)	**8 weeks**			
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis	7 years	**4 weeks**	**4 weeks** if first dose of DTaP/DT was administered before the 1st birthday. **6 months (as final dose)** if first dose of DTaP/DT or Tdap/Td was administered at or after the 1st birthday.	**6 months** if first dose of DTaP/DT was administered before the 1st birthday.	
Human papillomavirus	9 years	**Routine dosing intervals are recommended.**			
Hepatitis A	N/A	**6 months**			
Hepatitis B	N/A	**4 weeks**	**8 weeks *and*** at least 16 weeks after first dose.		
Inactivated poliovirus	N/A	**4 weeks**	**6 months** A fourth dose is not necessary if the third dose was administered at age 4 years or older and at least 6 months after the previous dose.	A fourth dose of IPV is indicated if all previous doses were administered at <4 years or if the third dose was administered <6 months after the second dose.	
Measles, mumps, rubella	N/A	**4 weeks**			
Varicella	N/A	**3 months** if younger than age 13 years. **4 weeks** if age 13 years or older.			

FIG. 316.1, cont'd

Continued

Notes Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2019

For vaccine recommendations for persons 19 years of age and older, see the Recommended Adult Immunization Schedule.

Additional information

- Consult relevant ACIP statements for detailed recommendations at www.cdc.gov/vaccines/hcp/acip-recs/index.html.
- For information on contraindications and precautions for the use of a vaccine, consult the General Best Practice Guidelines for Immunization and relevant ACIP statements at www.cdc.gov/vaccines/hcp/acip-recs/index.html.
- For calculating intervals between doses, 4 weeks = 28 days. Intervals of ≥4 months are determined by calendar months.
- Within a number range (e.g., 12–18), a dash (–) should be read as "through."
- Vaccine doses administered ≤4 days before the minimum age or interval are considered valid. Doses of any vaccine administered ≥5 days earlier than the minimum age or minimum interval should not be counted as valid and should be repeated as age-appropriate. The repeat dose should be spaced after the invalid dose by the recommended minimum interval. For further details, see Table 3-1, Recommended and minimum ages and intervals between vaccine doses, in General Best Practice Guidelines for Immunization at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html.
- Information on travel vaccine requirements and recommendations is available at wwwnc.cdc.gov/travel/.
- For vaccination of persons with immunodeficiencies, see Table 8-1, Vaccination of persons with primary and secondary immunodeficiencies, in General Best Practice Guidelines for Immunization at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html, and Immunization in Special Clinical Circumstances (In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018:67–111).
- For information regarding vaccination in the setting of a vaccine-preventable disease outbreak, contact your state or local health department.
- The National Vaccine Injury Compensation Program (VICP) is a no-fault alternative to the traditional legal system for resolving vaccine injury claims. All routine child and adolescent vaccines are covered by VICP except for pneumococcal polysaccharide vaccine (PPSV23). For more information, see www.hrsa.gov/vaccinecompensation/index.html.

Diphtheria, tetanus, and pertussis (DTaP) vaccination (minimum age: 6 weeks [4 years for Kinrix or Quadracel])

Routine vaccination

- 5-dose series at 2, 4, 6, 15–18 months, 4–6 years
  - **Prospectively:** Dose 4 may be given as early as age 12 months if at least 6 months have elapsed since dose 3.
  - **Retrospectively:** A 4th dose that was inadvertently given as early as 12 months may be counted if at least 4 months have elapsed since dose 3.

Catch-up vaccination

- Dose 5 is not necessary if dose 4 was administered at age 4 years or older.
- For other catch-up guidance, see Table 2.

Haemophilus influenzae type b vaccination (minimum age: 6 weeks)

Routine vaccination

- **ActHIB, Hiberix, or Pentacel:** 4-dose series at 2, 4, 6, 12–15 months
- **PedvaxHIB:** 3-dose series at 2, 4, 12–15 months

Catch-up vaccination

- **Dose 1 at 7–11 months:** Administer dose 2 at least 4 weeks later and dose 3 (final dose) at 12–15 months or 8 weeks after dose 2 (whichever is later).
- **Dose 1 at 12–14 months:** Administer dose 2 (final dose) at least 8 weeks after dose 1.
- **Dose 1 before 12 months and dose 2 before 15 months:** Administer dose 3 (final dose) 8 weeks after dose 2.
- **2 doses of PedvaxHIB before 12 months:** Administer dose 3 (final dose) at 12–59 months and at least 8 weeks after dose 2.
- **Unvaccinated at 15–59 months:** 1 dose
- For other catch-up guidance, see Table 2.

Special situations

- **Chemotherapy or radiation treatment:**
  12–59 months
  - Unvaccinated or only 1 dose before age 12 months: 2 doses, 8 weeks apart
  - 2 or more doses before age 12 months: 1 dose at least 8 weeks after previous dose

  Doses administered within 14 days of starting therapy or during therapy should be repeated at least 3 months after therapy completion.
- **Hematopoietic stem cell transplant (HSCT):**
  - 3-dose series 4 weeks apart starting 6 to 12 months after successful transplant regardless of Hib vaccination history
- **Anatomic or functional asplenia (including sickle cell disease):**
  12–59 months
  - Unvaccinated or only 1 dose before 12 months: 2 doses, 8 weeks apart
  - 2 or more doses before 12 months:1 dose at least 8 weeks after previous dose

  Unvaccinated persons age 5 years or older*
  - 1 dose
- **Elective splenectomy:**
  Unvaccinated persons age 15 months or older*
  - 1 dose (preferably at least 14 days before procedure)
- **HIV infection:**
  12–59 months
  - Unvaccinated or only 1 dose before age 12 months: 2 doses, 8 weeks apart
  - 2 or more doses before age 12 months: 1 dose at least 8 weeks after previous dose

  Unvaccinated persons age 5–18 years*
  - 1 dose
- **Immunoglobulin deficiency, early component complement deficiency:**
  12–59 months
  - Unvaccinated or only 1 dose before age 12 months: 2 doses, 8 weeks apart
  - 2 or more doses before age 12 months: 1 dose at least 8 weeks after previous dose

**Unvaccinated* = Less than routine series (through 14 months) OR no doses (14 months or older)

FIG. 316.1, cont'd

Notes

Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2019

Hepatitis A vaccination (minimum age: 12 months for routine vaccination)

Routine vaccination

- 2-dose series (**Havrix** 6–12 months apart or **Vaqta** 6–18 months apart, minimum interval 6 months); a series begun before the 2nd birthday should be completed even if the child turns 2 before the second dose is administered.

Catch-up vaccination

- Anyone 2 years of age or older may receive HepA vaccine if desired. Minimum interval between doses: 6 months
- Adolescents 18 years and older may receive the combined HepA and HepB vaccine, **Twinrix**, as a 3-dose series (0, 1, and 6 months) or 4-dose series (0, 7, and 21–30 days, followed by a dose at 12 months).

International travel

- Persons traveling to or working in countries with high or intermediate endemic hepatitis A (wwwnc.cdc.gov/travel/):
  - **Infants age 6–11 months**: 1 dose before departure; revaccinate with 2 doses, separated by 6–18 months, between 12 to 23 months of age.
  - **Unvaccinated age 12 months and older**: 1st dose as soon as travel considered

Special situations

At risk for hepatitis A infection: 2-dose series as above

- **Chronic liver disease**
- **Clotting factor disorders**
- **Men who have sex with men**
- **Injection or non-injection drug use**
- **Homelessness**
- **Work with hepatitis A virus** in research laboratory or nonhuman primates with hepatitis A infection
- **Travel** in countries with high or intermediate endemic hepatitis A
- **Close, personal contact with international adoptee** (e.g., household or regular babysitting) in first 60 days after arrival from country with high or intermediate endemic hepatitis A (administer dose 1 as soon as adoption is planned, at least 2 weeks before adoptee's arrival)

Hepatitis B vaccination (minimum age: birth)

Birth dose (monovalent HepB vaccine only)

- **Mother is HBsAg-negative:** 1 dose within 24 hours of birth for **all** medically stable infants ≥2,000 grams. Infants <2,000 grams: administer 1 dose at chronological age 1 month or hospital discharge.
- **Mother is HBsAg-positive:**
  - Administer **HepB vaccine** and **0.5 mL of hepatitis B immune globulin (HBIG)** (at separate anatomic sites) within 12 hours of birth, regardless of birth weight. For infants <2,000 grams, administer 3 additional doses of vaccine (total of 4 doses) beginning at age 1 month.
  - Test for HBsAg and anti-HBs at age 9–12 months. If HepB series is delayed, test 1–2 months after final dose.
- **Mother's HBsAg status is unknown:**
  - Administer **HepB vaccine** within 12 hours of birth, regardless of birth weight.
  - For infants <2,000 grams, administer **0.5 mL of HBIG** in addition to HepB vaccine within 12 hours of birth. Administer 3 additional doses of vaccine (total of 4 doses) beginning at age 1 month.
  - Determine mother's HBsAg status as soon as possible. If mother is HBsAg-positive, administer **0.5 mL of HBIG** to infants ≥2,000 grams as soon as possible, but no later than 7 days of age.

Routine series

- 3-dose series at 0, 1–2, 6–18 months (use monovalent HepB vaccine for doses administered before age 6 weeks)
- Infants who did not receive a birth dose should begin the series as soon as feasible (see Table 2).
- Administration of **4 doses** is permitted when a combination vaccine containing HepB is used after the birth dose.
- **Minimum age** for the final (3rd or 4th) dose: 24 weeks
- **Minimum intervals:** dose 1 to dose 2: 4 weeks / dose 2 to dose 3: 8 weeks / dose 1 to dose 3: 16 weeks (when 4 doses are administered, substitute "dose 4" for "dose 3" in these calculations)

Catch-up vaccination

- Unvaccinated persons should complete a 3-dose series at 0, 1–2, 6 months.
- Adolescents age 11–15 years may use an alternative 2-dose schedule with at least 4 months between doses (adult formulation **Recombivax HB** only).
- Adolescents 18 years and older may receive a 2-dose series of HepB **(Heplisav-B)** at least 4 weeks apart.
- Adolescents 18 years and older may receive the combined HepA and HepB vaccine, **Twinrix**, as a 3-dose series (0, 1, and 6 months) or 4-dose series (0, 7, and 21–30 days, followed by a dose at 12 months).
- For other catch-up guidance, see Table 2.

Human papillomavirus vaccination (minimum age: 9 years)

Routine and catch-up vaccination

- HPV vaccination routinely recommended for all adolescents **age 11–12 years (can start at age 9 years)** and through age 18 years if not previously adequately vaccinated
- 2- or 3-dose series depending on age at initial vaccination:
  - **Age 9 through 14 years at initial vaccination**: 2-dose series at 0, 6–12 months (minimum interval: 5 months; repeat dose if administered too soon)
  - **Age 15 years or older at initial vaccination**: 3-dose series at 0, 1–2 months, 6 months (minimum intervals: dose 1 to dose 2: 4 weeks / dose 2 to dose 3: 12 weeks / dose 1 to dose 3: 5 months; repeat dose if administered too soon)
- If completed valid vaccination series with any HPV vaccine, no additional doses needed

Special situations

- **Immunocompromising conditions, including HIV infection:** 3-dose series as above
- **History of sexual abuse or assault:** Start at age 9 years
- **Pregnancy:** HPV vaccination not recommended until after pregnancy; no intervention needed if vaccinated while pregnant; pregnancy testing not needed before vaccination

Inactivated poliovirus vaccination (minimum age: 6 weeks)

Routine vaccination

- 4-dose series at ages 2, 4, 6–18 months, 4–6 years; administer the final dose on or after the 4th birthday and at least 6 months after the previous dose.
- 4 or more doses of IPV can be administered before the 4th birthday when a combination vaccine containing IPV is used. However, a dose is still recommended after the 4th birthday and at least 6 months after the previous dose.

Catch-up vaccination

- In the first 6 months of life, use minimum ages and intervals only for travel to a polio-endemic region or during an outbreak.
- IPV is not routinely recommended for U.S. residents 18 years and older.

Series containing oral polio vaccine (OPV), either mixed OPV-IPV or OPV-only series:

- Total number of doses needed to complete the series is the same as that recommended for the U.S. IPV schedule. See www.cdc.gov/mmwr/volumes/66/wr/mm6601a6.htm?s_cid=mm6601a6_w.

FIG. 316.1, cont'd

Continued

Notes — Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2019

- Only trivalent OPV (tOPV) counts toward the U.S. vaccination requirements. For guidance to assess doses documented as "OPV," see www.cdc.gov/mmwr/volumes/66/wr/mm6606a7.htm?s_cid=mm6606a7_w.
- For other catch-up guidance, see Table 2.

Influenza vaccination (minimum age: 6 months [IIV], 2 years [LAIV], 18 years [RIV])

Routine vaccination

- 1 dose any influenza vaccine appropriate for age and health status annually (2 doses separated by at least 4 weeks for **children 6 months–8 years** who did not receive at least 2 doses of influenza vaccine before July 1, 2018)

Special situations

- **Egg allergy, hives only**: Any influenza vaccine appropriate for age and health status annually
- **Egg allergy more severe than hives** (e.g., angioedema, respiratory distress): Any influenza vaccine appropriate for age and health status annually in medical setting under supervision of health care provider who can recognize and manage severe allergic conditions
- **LAIV should not be used for** those with a history of severe allergic reaction to any component of the vaccine (excluding egg) or to a previous dose of any influenza vaccine, children and adolescents receiving concomitant aspirin or salicylate-containing medications, children age 2 through 4 years with a history of asthma or wheezing, those who are immunocompromised due to any cause (including immunosuppression caused by medications and HIV infection), anatomic and functional asplenia, cochlear implants, cerebrospinal fluid-oropharyngeal communication, close contacts and caregivers of severely immunosuppressed persons who require a protected environment, pregnancy, and persons who have received influenza antiviral medications within the previous 48 hours.

Measles, mumps, and rubella vaccination (minimum age: 12 months for routine vaccination)

Routine vaccination

- 2-dose series at 12–15 months, 4–6 years
- Dose 2 may be administered as early as 4 weeks after dose 1.

Catch-up vaccination

- Unvaccinated children and adolescents: 2 doses at least 4 weeks apart
- The maximum age for use of *MMRV* is 12 years.

Special situations

International travel

- **Infants age 6–11 months:** 1 dose before departure; revaccinate with 2 doses at 12–15 months (12 months for children in high-risk areas) and dose 2 as early as 4 weeks later.
- **Unvaccinated children age 12 months and older:** 2-dose series at least 4 weeks apart before departure

Meningococcal serogroup A,C,W,Y vaccination (minimum age: 2 months [MenACWY-CRM, Menveo], 9 months [MenACWY-D, Menactra])

Routine vaccination

- 2-dose series: 11–12 years, 16 years

Catch-up vaccination

- Age 13–15 years: 1 dose now and booster at age 16–18 years (minimum interval: 8 weeks)
- Age 16–18 years: 1 dose

Special situations

Anatomic or functional asplenia (including sickle cell disease), HIV infection, persistent complement component deficiency, eculizumab use:

- **Menveo**
  - Dose 1 at age 8 weeks: 4-dose series at 2, 4, 6, 12 months
  - Dose 1 at age 7–23 months: 2-dose series (dose 2 at least 12 weeks after dose 1 and after the 1st birthday)
  - Dose 1 at age 24 months or older: 2-dose series at least 8 weeks apart
- **Menactra**
  - **Persistent complement component deficiency:**
    - Age 9–23 months: 2 doses at least 12 weeks apart
    - Age 24 months or older: 2 doses at least 8 weeks apart
  - **Anatomic or functional asplenia, sickle cell disease, or HIV infection:**
    - **Age 9–23 months**: Not recommended
    - **24 months or older**: 2 doses at least 8 weeks apart
    - **Menactra** must be administered at least 4 weeks after completion of PCV13 series.

Travel in countries with hyperendemic or epidemic meningococcal disease, including countries in the African meningitis belt or during the Hajj (wwwnc.cdc.gov/travel/)**:**

- Children age less than 24 months:
  - **Menveo (age 2–23 months):**
    - Dose 1 at 8 weeks: 4-dose series at 2, 4, 6, 12 months
    - Dose 1 at 7–23 months: 2-dose series (dose 2 at least 12 weeks after dose 1 and after the 1st birthday)
  - **Menactra (age 9–23 months):**
    - 2-dose series (dose 2 at least 12 weeks after dose 1; dose 2 may be administered as early as 8 weeks after dose 1 in travelers)
- Children age 2 years or older: 1 dose **Menveo** or **Menactra**

First-year college students who live in residential housing (if not previously vaccinated at age 16 years or older) or military recruits:

- 1 dose **Menveo** or **Menactra**

Note: Menactra should be administered either before or at the same time as DTaP. For MenACWY booster dose recommendations for groups listed under "Special situations" above and additional meningococcal vaccination information, see meningococcal *MMWR* publications at www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html.

Meningococcal serogroup B vaccination (minimum age: 10 years [MenB-4C, Bexsero; MenB-FHbp, Trumenba])

Clinical discretion

- MenB vaccine may be administered based on individual clinical decision to **adolescents not at increased risk** age 16–23 years (preferred age 16–18 years):
- **Bexsero:** 2-dose series at least 1 month apart
- **Trumenba:** 2-dose series at least 6 months apart; if dose 2 is administered earlier than 6 months, administer a 3rd dose at least 4 months after dose 2.

Special situations

Anatomic or functional asplenia (including sickle cell disease), persistent complement component deficiency, eculizumab use:

- **Bexsero:** 2-dose series at least 1 month apart
- **Trumenba:** 3-dose series at 0, 1–2, 6 months

Bexsero and **Trumenba** are not interchangeable; the same product should be used for all doses in a series.
For additional meningococcal vaccination information, see meningococcal *MMWR* publications at www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html.

FIG. 316.1, cont'd

Notes

Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2019

Pneumococcal vaccination (minimum age: 6 weeks [PCV13], 2 years [PPSV23])

Routine vaccination with PCV13

- 4-dose series at 2, 4, 6, 12–15 months

Catch-up vaccination with PCV13

- 1 dose for healthy children age 24–59 months with any incomplete* PCV13 series
- For other catch-up guidance, see Table 2.

Special situations

High-risk conditions below: When both PCV13 and PPSV23 are indicated, administer PCV13 first. PCV13 and PPSV23 should not be administered during same visit.

Chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure); chronic lung disease (including asthma treated with high-dose, oral corticosteroids); diabetes mellitus:

Age 2–5 years

- Any incomplete* series with:
  - 3 PCV13 doses: 1 dose PCV13 (at least 8 weeks after any prior PCV13 dose)
  - Less than 3 PCV13 doses: 2 doses PCV13 (8 weeks after the most recent dose and administered 8 weeks apart)
- No history of PPSV23: 1 dose PPSV23 (at least 8 weeks after any prior PCV13 dose)

Age 6–18 years

- No history of PPSV23: 1 dose PPSV23 (at least 8 weeks after any prior PCV13 dose)

Cerebrospinal fluid leak, cochlear implant:

Age 2–5 years

- Any incomplete* series with:
  - 3 PCV13 doses: 1 dose PCV13 (at least 8 weeks after any prior PCV13 dose)
  - Less than 3 PCV13 doses: 2 doses PCV13, 8 weeks after the most recent dose and administered 8 weeks apart
- No history of PPSV23: 1 dose PPSV23 (at least 8 weeks after any prior PCV13 dose)

Age 6–18 years

- No history of either PCV13 or PPSV23: 1 dose PCV13, 1 dose PPSV23 at least 8 weeks later
- Any PCV13 but no PPSV23: 1 dose PPSV23 at least 8 weeks after the most recent dose of PCV13
- PPSV23 but no PCV13: 1 dose PCV13 at least 8 weeks after the most recent dose of PPSV23

Sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiency; HIV infection; chronic renal failure; nephrotic syndrome; malignant neoplasms, leukemias, lymphomas, Hodgkin disease, and other diseases associated with treatment with immunosuppressive drugs or radiation therapy; solid organ transplantation; multiple myeloma:

Age 2–5 years

- Any incomplete* series with:
  - 3 PCV13 doses: 1 dose PCV13 (at least 8 weeks after any prior PCV13 dose)
  - Less than 3 PCV13 doses: 2 doses PCV13 (8 weeks after the most recent dose and administered 8 weeks apart)
- No history of PPSV23: 1 dose PPSV23 (at least 8 weeks after any prior PCV13 dose) and a 2nd dose of PPSV23 5 years later

Age 6–18 years

- No history of either PCV13 or PPSV23: 1 dose PCV13, 2 doses PPSV23 (dose 1 of PPSV23 administered 8 weeks after PCV13 and dose 2 of PPSV23 administered at least 5 years after dose 1 of PPSV23)
- Any PCV13 but no PPSV23: 2 doses PPSV23 (dose 1 of PPSV23 administered 8 weeks after the most recent dose of PCV13 and dose 2 of PPSV23 administered at least 5 years after dose 1 of PPSV23)
- PPSV23 but no PCV13: 1 dose PCV13 at least 8 weeks after the most recent PPSV23 dose and a 2nd dose of PPSV23 administered 5 years after dose 1 of PPSV23 and at least 8 weeks after a dose of PCV13

Chronic liver disease, alcoholism:

Age 6–18 years

- No history of PPSV23: 1 dose PPSV23 (at least 8 weeks after any prior PCV13 dose)

*An incomplete series is defined as not having received all doses in either the recommended series or an age-appropriate catch-up series. See Tables 8, 9, and 11 in the ACIP pneumococcal vaccine recommendations (www.cdc.gov/mmwr/pdf/rr/rr5911.pdf) for complete schedule details.

Rotavirus vaccination (minimum age: 6 weeks)

Routine vaccination

- **Rotarix:** 2-dose series at 2 and 4 months.
- **RotaTeq:** 3-dose series at 2, 4, and 6 months.

If any dose in the series is either **RotaTeq** or unknown, default to 3-dose series.

Catch-up vaccination

- Do not start the series on or after age 15 weeks, 0 days.
- The maximum age for the final dose is 8 months, 0 days.
- For other catch-up guidance, see Figure 2.

Tetanus, diphtheria, and pertussis (Tdap) vaccination (minimum age: 11 years for routine vaccination, 7 years for catch-up vaccination)

Routine vaccination

- **Adolescents age 11–12 years:** 1 dose Tdap
- **Pregnancy:** 1 dose Tdap during each pregnancy, preferably in early part of gestational weeks 27–36
- Tdap may be administered regardless of the interval since the last tetanus- and diphtheria-toxoid-containing vaccine.

Catch-up vaccination

- **Adolescents age 13–18 years who have not received Tdap:** 1 dose Tdap, then Td booster every 10 years
- **Persons age 7–18 years not fully immunized with DTaP:** 1 dose Tdap as part of the catch-up series (preferably the first dose); if additional doses are needed, use Td.
- **Children age 7–10 years** who receive Tdap inadvertently or as part of the catch-up series should receive the routine Tdap dose at 11–12 years.
- **DTaP inadvertently given after the 7th birthday:**
  - **Child age 7–10 years**: DTaP may count as part of catch-up series. Routine Tdap dose at 11–12 should be administered.
  - **Adolescent age 11–18 years**: Count dose of DTaP as the adolescent Tdap booster.
- For other catch-up guidance, see Table 2.
- For information on use of Tdap or Td as tetanus prophylaxis in wound management, see www.cdc.gov/mmwr/volumes/67/rr/rr6702a1.htm.

Varicella vaccination (minimum age: 12 months)

Routine vaccination

- 2-dose series: 12–15 months, 4–6 years
- Dose 2 may be administered as early as 3 months after dose 1 (a dose administered after a 4-week interval may be counted).

Catch-up vaccination

- Ensure persons age 7–18 years without evidence of immunity (see *MMWR* at www.cdc.gov/mmwr/pdf/rr/rr5604.pdf) have 2-dose series:
  - **Ages 7–12 years**: routine interval: 3 months (minimum interval: 4 weeks)
  - **Ages 13 years and older**: routine interval: 4–8 weeks (minimum interval: 4 weeks).
  - The maximum age for use of *MMRV* is 12 years.

FIG. 316.1, cont'd

Continued

Table 3 Recommended Child and Adolescent Immunization Schedule by Medical Indication United States, 2019

VACCINE	INDICATION									
			HIV infection CD4+ count[1]							
	Pregnancy	Immunocompromised status (excluding HIV infection)	<15% and total CD4 cell count of <200/mm3	≥15% and total CD4 cell count of ≥200/mm3	Kidney failure, end-stage renal disease, on hemodialysis	Heart disease, chronic lung disease	CSF leaks/ cochlear implants	Asplenia and persistent complement component deficiencies	Chronic liver disease	Diabetes
Hepatitis B										
Rotavirus		SCID[2]								
Diphtheria, tetanus, & acellular pertussis (DTaP)										
Haemophilus influenzae type b										
Pneumococcal conjugate										
Inactivated poliovirus										
Influenza (IIV)										
or										
Influenza (LAIV)						Asthma, wheezing: 2-4yrs[3]				
Measles, mumps, rubella										
Varicella										
Hepatitis A										
Meningococcal ACWY										
Tetanus, diphtheria, & acellular pertussis (Tdap)										
Human papillomavirus										
Meningococcal B										
Pneumococcal polysaccharide										

- Vaccination according to the routine schedule recommended
- Recommended for persons with an additional risk factor for which the vaccine would be indicated
- Vaccination is recommended, and additional doses may be necessary based on medical condition. See Notes.
- Contraindicated or use not recommended—vaccine should not be administered because of risk for serious adverse reaction
- Precaution—vaccine might be indicated if benefit of protection outweighs risk of adverse reaction
- Delay vaccination until after pregnancy if vaccine indicated
- No recommendation

1 For additional information regarding HIV laboratory parameters and use of live vaccines, see the General Best Practice Guidelines for Immunization "Altered Immunocompetence" at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html, and Table 4-1 (footnote D) at: www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html.
2 Severe Combined Immunodeficiency
3 LAIV contraindicated for children 2–4 years of age with asthma or wheezing during the preceding 12 months.

FIG. 316.1, cont'd

the United States, use of BCG should be considered for individuals, such as infants, whose skin test results are negative and who have prolonged, close contact with patients with active tuberculosis who are untreated, are ineffectively treated, or have antibiotic-resistant infection. BCG also may be considered for health care providers in areas in which multidrug-resistant *Mycobacterium tuberculosis* infection has become a significant problem.[88]

A single dose of vaccine is administered intradermally or by the percutaneous route. (The Tice strain licensed in the United States is approved only for percutaneous administration.) Known adverse reactions include regional adenitis, disseminated BCG infection, and osteitis caused by the BCG organism. Adenitis occurs in about 1% to 10% of vaccinees, whereas disseminated infections and osteitis are quite rare (about 1 case per 1 million vaccinees). The risk for developing osteitis after BCG vaccination varies by country; in one review, this risk ranged from 0.01 cases per million vaccinees in Japan to 32.5 and 43.4 cases per million vaccinees in Sweden and Finland, respectively.[89] Immunocompromised individuals should not receive the vaccine because of increased risk for disseminated BCG infection.[88]

Cholera Vaccine

A killed whole-cell cholera vaccine was available in the United States from the 1940s until 2001. [90] Killed whole-cell vaccines are still available in some countries, and improved killed vaccines are licensed in some countries. Two oral whole-cell inactivated vaccines, including one that is combined with the B subunit of cholera toxin, are available in some parts of the world, as is an oral live-attenuated vaccine with a critical moiety of the gene for the cholera toxin deleted.[91,91a] Killed oral cholera vaccines are increasingly being used as important components of cholera prevention in epidemic and endemic settings. A live oral vaccine (CVD 103-HgR or Vaxchora, manufactured by PaxVax) was licensed in the United States in 2016. The vaccine is administered as a single dose with a buffer salt to neutralize stomach acid. It is recommended for travelers 18 to 64 years of age to an area of active cholera transmission. Vaxchora should be administered 8 hours or more after a dose of oral typhoid vaccine.

Diphtheria Toxoid

Diphtheria toxoid is a purified preparation of inactivated diphtheria toxin. It is highly effective in inducing antibodies that will prevent disease, although antibodies may not prevent acquisition or carriage of the organism. In the United States, the toxoid is available in adsorbed form, combined with tetanus toxoid (adult formulation, Td, and pediatric formulation, DT) or with tetanus toxoid and acellular pertussis vaccine (DTaP, childhood formulation; or Tdap, adult formulation). Single-antigen diphtheria toxoid is not distributed in the United States. Two dosage formulations are available: one for use in children through 6 years of age, and one for use in older children and adults. The adult formulation has a lower concentration of diphtheria toxoid (≤2.5 limit of flocculation units [Lf]) than the childhood formulation (6.7–25 Lf) because local reactions are thought to relate to both age and dosage. With all formulations, levels of antitoxin considered protective are induced in more than 90% of recipients who complete the schedule.[54,92,93]

Immunization against diphtheria is recommended for all residents in the United States. For children younger than 7 years with no contraindications to pertussis immunization, DTaP is recommended, and the primary series is three doses administered 4 to 8 weeks apart, followed by a first booster dose 6 to 12 months later and a second booster dose at school entry (4–6 years of age). For infants with contraindications to pertussis vaccine, DT is administered in the same schedule as DTaP (see "Pertussis-Containing Vaccine" and Fig. 316.1). The primary immunizing series of DT (for children 1–6 years of age) or Td (for older children and adults) consists of at least two doses administered 4 to 8 weeks apart, followed by a third dose 6 to 12 months later. There is no need to restart a series if the schedule is interrupted; the next dose in the series should be given. Booster doses of Td should be given every 10 years. All persons 11 years and older should receive one dose of Tdap, which can serve as one of the recommended booster doses for diphtheria and tetanus. Persons 7 years or older not fully vaccinated with DTaP vaccine should receive one dose of Tdap as part of a catch-up series. If the dose is administered at 7 through 10 years of age, another dose of Tdap should be administered at 11 or 12 years of age. Tdap should be administered to pregnant women during every pregnancy, optimally early between gestational ages 27 weeks and 36 weeks.[71] Tdap administered during pregnancy provides passive immunity to the fetus and should protect newborns and young infants before they have time to make an active immune response to DTaP. Known adverse effects of diphtheria toxoid include local reactions and mild or moderate systemic reactions such as fever; anaphylaxis occurs rarely. Brachial neuritis appears to be a rare consequence of immunization and is most likely due to tetanus toxoid.[65] The only contraindications are in individuals who previously have had severe hypersensitivity reactions after diphtheria or tetanus toxoids or, if combined with pertussis, have had previous similar adverse events to those antigens.

Haemophilus influenzae Type b Vaccine (Hib)

Conjugated vaccines to prevent Hib invasive disease were first licensed at the end of 1987 and have replaced the earlier polysaccharide vaccines because they elicit substantially higher antibody titers and are effective in young infants.[94] The polysaccharide in these vaccines is covalently linked to protein carriers, converting them from T-lymphocyte–independent antigens to T-lymphocyte–dependent antigens. There are four available conjugate vaccines licensed for use in infants.[95] Three are single-component vaccines for prevention of Hib disease. Carrier proteins include a *Neisseria meningitidis* outer membrane protein complex (PRP-OMP) for PedVaxHib and tetanus toxoid (PRP-T) for ActHIB and Hiberix. PRP-OMP has been demonstrated to be 95% effective in a clinical trial in infants. PRP-T has been licensed for use in infants because it elicits comparable antibody responses to other conjugate vaccines that have been shown to be highly effective. A combination vaccine, DTaP-IPV/Hib, is licensed for any of the recommended first four doses during the first 2 years of life (www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm174757.htm and www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm172502.htm).[96]

The Hib component of DTaP-IPV contains PRP-T as the conjugate. PRP-OMP behaves differently from PRP-T, inducing high levels of antibody after a single dose. A second dose 2 months later increases those levels; less benefit appears to be derived from a third dose.[94] The basic series for PRP-OMP is two doses given 2 months apart beginning at 2 months of age, followed by a booster dose at 12 to 15 months of age.[94] PRP-OMP is preferred in American Indian/Alaska Native populations because of the younger peak in disease incidence. In contrast, PRP-T does not induce substantial antibody levels until the second dose, and high levels of protection are achieved only after three doses 2 months apart. The basic series for PRP-T starts at 2 months of age with three doses 2 months apart, followed by a booster dose at 12 to 15 months of age.[94] Although use of a single conjugate vaccine for the primary series is recommended, several studies have suggested that mixed sequences of Hib conjugate vaccines induce an adequate immune response.[97–99] Thus, for infants younger than 6 months, three doses of any licensed Hib vaccine administered at 2-month intervals should confer protection; a booster dose is given at 12 to 15 months of age.

For healthy infants starting immunization at 7to 11 months, two doses of any of the Hib vaccines licensed for infants should be given with at least 4 weeks between the two doses, followed by a booster dose at 12 to 15 months, provided that at least 2 months have elapsed since the second dose. Any of the conjugates can be used for the booster dose.[94]

Healthy children beginning immunization at 12 to 14 months of age can receive two doses of any conjugate, with the second dose given at least 2 months after the first dose. Healthy children who initially are immunized at 15 months or older need only one dose of any of the conjugate vaccines. Unimmunized children aged 60 months or older do not need catch-up vaccination.

High-risk conditions include functional or anatomic asplenia and immunosuppression, particularly IgG2 subclass deficiency, early complement component deficiency, HIV infection, receipt of chemotherapy or radiation therapy for malignant neoplasms, and receipt of a hematopoietic stem cell transplant (HSCT). Children who will be undergoing splenectomy and are age 15 months or older who are unvaccinated or incompletely vaccinated (which means they have received fewer doses

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