Chapter 52: Vaccines, Toxoids, and Other Immunobiologics

INTRODUCTION

- *Vaccines* are substances administered to generate a protective immune response. They can be live attenuated or killed.
- *Toxoids* are inactivated bacterial toxins. They retain the ability to stimulate the formation of antitoxins, which are antibodies directed against the bacterial toxin.
- *Adjuvants* are inert substances, such as aluminum salts (ie, alum), which enhance vaccine antigenicity by prolonging antigen absorption.
- *Immune sera* are sterile solutions containing antibody derived from human (immunoglobulin [Ig]) or equine (antitoxin) sources.

VACCINE AND TOXOID RECOMMENDATIONS

- The childhood, adolescent, and adult immunization schedules are updated frequently and published annually. Recommendations for the use of influenza vaccine are issued annually. Healthcare providers involved in primary care and immunization delivery must keep themselves abreast of these changes in a systematic way. Electronic newsletters and browsing reliable websites are efficient methods for obtaining information (**Table 52-1**).
- In general, killed vaccines can be administered simultaneously at separate sites. Killed and live-attenuated vaccines may be administered simultaneously at separate sites. If they cannot be administered simultaneously, they can be administered at any interval between doses with the exception of cholera (killed) and yellow fever (live) vaccines, which should be given at least 3 weeks apart. If live vaccines are not administered simultaneously, their administration should be separated by at least 4 weeks.
- Administration of live vaccines, such as rubella or varicella, are deferred until postpartum and are routinely recommended for new mothers who do not have evidence of immunity prior to hospital discharge. These live vaccines can be administered without regard to administration of Rho(D) Ig (RDIg) in the postpartum period. Pregnant women should receive Tdap during the late second trimester or third trimester of pregnancy. Additionally, Tdap is recommended for all new mothers who have not received a Tdap before because household contacts are frequently implicated as the source of pertussis infection in a young infant.
- In general, severely immunocompromised individuals should not receive live vaccines.
- Patients with chronic conditions that cause limited immunodeficiency (eg, renal disease, diabetes, liver disease, and asplenia) and who are not receiving immunosuppressants may receive live-attenuated and killed vaccines, as well as toxoids.
- Patients with active malignant disease may receive killed vaccines or toxoids but should not be given live vaccines. Live virus vaccines may be administered to persons with leukemia who have not received chemotherapy for at least 3 months.
- If a person has been receiving high-dose corticosteroids or has had a course lasting longer than 2 weeks, then at least 1 month should pass before immunization with live virus vaccines.
- Responses to live and killed vaccines generally are suboptimal for human immune deficiency virus (HIV)–infected patients and decrease as the disease progresses.
- Whenever possible, transplant patients should be immunized before transplantation. Live vaccines generally are not given after transplantation.

TABLE 52-1

Web Resources for Vaccine Information

Recommended Internet sites for vaccine information	
http://www.cdc.gov/vaccines/	Vaccines and Immunizations
	Centers for Disease Control and Prevention
www.immunize.org	Immunization Action Coalition
www.nfid.org/	National Foundation for Infectious Diseases
www.cdc.gov/mmwr/	Morbidity and Mortality Weekly Report
http://www.nationalacademies.org/hmd/	The National Academies of Sciences, Engineering, and Medicine. Health and Medicine Division
http://www.hrsa.gov/vaccinecompensation/	Vaccine Injury Compensation Program
http://www.chop.edu/centers-programs/vaccine-education-center/	Vaccine Education Center
	Children's Hospital of Philadelphia
https://vaers.hhs.gov/index.html	Vaccine Adverse Event Reporting System
Recommended electronic newsletters	
www.immunize.org/express	The Immunization Action Coalition's newsletter
www.cdc.gov/mmwr/	Morbidity and Mortality Weekly Report

DIPHTHERIA TOXOID ADSORBED AND DIPHTHERIA ANTITOXIN

- Two strengths of diphtheria toxoid are available: pediatric strength (D) and adult strength (d), which contain less antigen. Primary immunization with D is indicated for children older than 6 weeks. Generally, D is given along with tetanus and acellular pertussis (DTaP) vaccines at 2, 4, and 6 months of age, and then at 15–18 months and 4–6 years of age.
- For nonimmunized adults, a complete three-dose series of diphtheria toxoid should be administered, with the first two doses given at least 4 weeks apart and the third dose 6–12 months after the second. One dose in the series should be Tdap. The combined preparation, tetanus–diphtheria (Td), is recommended in adults because it contains less diphtheria toxoid than DTaP, with fewer reactions seen from the diphtheria preparation. Booster doses are given every 10 years.
- Adverse effects to diphtheria toxoid include mild to moderate tenderness, erythema, and induration at the injection site.

TETANUS TOXOID, TETANUS TOXOID ADSORBED, AND TETANUS IMMUNOGLOBULIN

- In children, primary immunization against tetanus is usually done in conjunction with diphtheria and pertussis vaccination using DTaP or a combination vaccine that includes other antigens. A 0.5-mL dose is recommended at 2, 4, 6, and 15–18 months of age.

- In children 7 years and older and in adults who have not been previously immunized, a series of three 0.5-mL doses of Td is administered intramuscularly (IM) initially. The first two doses are given 1–2 months apart and the third dose 6–12 months later. Boosters are recommended every 10 years.
- Tetanus toxoid may be given to immunosuppressed patients if indicated.
- Tetanus Ig (TIg) is used to provide passive tetanus immunization after the occurrence of traumatic wounds in nonimmunized or suboptimally immunized persons (**Table 52-2**). A dose of 250–500 units is administered IM. When administered with tetanus toxoid, separate sites for administration should be used.
- TIg is also used for the treatment of tetanus. In this setting, a single dose of 3000–6000 units is administered IM.

TABLE 52-2

Tetanus Prophylaxis

Vaccination History	Clean, Minor Wounds		All Other Wounds	
	Td[a]	TIG	Td[a]	TIG
Unknown or fewer than three doses	Yes	No	Yes	Yes
Three or more doses	No[a,b]	No	No[a,c]	No

[a]A single dose of Tdap should be used for the next dose of tetanus–diphtheria toxoid for individuals aged >10 years.

[b]Yes, if more than 10 years since last dose.

[c]Yes, if more than 5 years since last dose.

HAEMOPHILUS INFLUENZAE TYPE B VACCINES

- *Haemophilus influenzae* type b (Hib) vaccines currently in use are conjugate products, consisting of either a polysaccharide or oligosaccharide of polyribosylribitol phosphate (PRP) covalently linked to a protein carrier.
- Hib conjugate vaccines are indicated for routine use in all infants and children younger than 5 years.
- The primary series of Hib vaccination consists of 0.5-mL IM doses at 2, 4, and 6 months of age. If PRP-OMP (PRP conjugated to an outer membrane protein) is used, it should be given at ages 2 and 4 months. A booster dose is recommended at age 12–15 months.
- For infants 7–11 months of age who have not been vaccinated, three doses of Hib vaccine should be given: two doses spaced 4 weeks apart and then a booster dose at age 12–15 months (but at least 8 weeks since the second dose). For unvaccinated children ages 12–14 months, two doses should be given, with an interval of 2 months between doses. In a child older than 15 months, a single dose of any of the four conjugate vaccines is indicated.

HEPATITIS VACCINES

- Information on hepatitis vaccines can be found in Chapter 25.

HUMAN PAPILLOMAVIRUS VACCINE

- ACIP recommends HPV vaccine for the prevention of HPV-related disease in individuals aged 9–26 years. Individuals who start the HPV series between the ages of 9 and 14 years should receive two doses separated by 6 months. This vaccine is administered as a three-dose series using a schedule of 0, 1–2, and 6 months for individuals who start the series at age 15 years or older. The vaccines are recommended for adolescents aged 11–12 years and catch-up immunization for individuals aged 13–26 years.
- The ACIP recommended shared clinical decision-making for HPV vaccine for individuals aged 27–45 years. The vaccine is administered as a three-dose series (0, 1–2, and 6 months).
- The vaccine is well tolerated, with injection site reactions and headache and fatigue occurring as commonly as in placebo groups.

INFLUENZA VIRUS VACCINE

- See Chapter 41 for information regarding influenza vaccination.

MEASLES VACCINE

- Measles vaccine is a live-attenuated vaccine that is administered for primary immunization to persons 12–15 months of age or older, usually as a combination of measles, mumps, and rubella (MMR). A second dose is recommended at 4–6 years of age.
- Measles-containing vaccine should not be given to pregnant women or immunosuppressed patients. An exception is HIV-infected patients, who are at very high risk for severe complications if they develop measles.
- The vaccine should not be given within 1 month of any other live vaccine unless the vaccine is given on the same day (as with the MMR vaccine).
- Measles vaccine is indicated in all persons born after 1956 or in those who lack documentation of wild virus infection by either history or antibody titers.

MENINGOCOCCAL VACCINES

- There are two meningococcal conjugate vaccines: Menactra is licensed for individuals 9 months–55 years old and Menveo for those 2 months–55 years old. They are recommended for all children 11–12 years old with a second dose at 16 years of age.
- The vaccine is indicated in high-risk populations such as those exposed to the disease, those in the midst of uncontrolled outbreaks, travelers to an area with epidemic hyperendemic meningococcal disease, and individuals who have terminal complement deficiencies or asplenia. Reimmunization at 5-year intervals is recommended for individuals who are at high risk. The polysaccharide vaccine should be reserved for those older than 55 years who require immunization.
- Also, there are two meningococcal serogroup B vaccines (Trumenba and Bexsero), and are licensed for individuals 10–25 years of age. Either vaccine is recommended for individuals at high risk for invasive meningococcal disease.

MUMPS VACCINE

- The vaccine (usually given in conjunction with measles and rubella, MMR) is given beginning at age 12–15 months, with a second dose prior to entry into elementary school.
- Two doses of mumps vaccine are recommended for school-age children, international travelers, college students, and healthcare workers born after 1956.
- Postexposure vaccination is of no benefit.
- Mumps vaccine should not be given to pregnant women or immunosuppressed patients. The vaccine should not be given within 6 weeks (preferably 3 months) of administration of Ig.

PERTUSSIS VACCINE

- Acellular pertussis vaccine is usually administered in combination with diphtheria and tetanus toxoids (as DTaP).
- The primary immunization series for pertussis vaccine consists of four doses given at ages 2, 4, 6, and 15–18 months. A booster dose is recommended at age 4–6 years. Pertussis vaccine is administered in combination with diphtheria and tetanus (DTaP). Administration of an acellular pertussis-containing vaccine is also recommended for adolescents once between ages 11 and 18 years and a single dose of Tdap should be administered to all adults.
- Tdap should be administered to females in their late second or third trimester of pregnancy. Tdap should also be administered to all close contacts, including household contacts and out of home care providers.
- Systemic reactions, such as moderate fever, occur in 3%–5% of those receiving vaccines. Very rarely, high fever, febrile seizures, persistent crying spells, and hypotonic hyporesponsive episodes occur after vaccination.
- There are only two contraindications to pertussis administration: (1) an immediate anaphylactic reaction to a previous dose and (2) encephalopathy within 7 days of a previous dose, with no evidence of other cause.

PNEUMOCOCCAL VACCINES

- Pneumococcal polysaccharide vaccine is a mixture of capsular polysaccharides from 23 of the most prevalent types of *Streptococcus pneumoniae* seen in the United States (PPV23). The vaccine is administered IM or subcutaneously as a single 0.5 mL dose.
- Pneumococcal vaccine (PPV23) is recommended for the following immunocompetent persons:

  ✔ Persons 65 years or older. If an individual received vaccine more than 5 years earlier and was younger than 65 at the time of administration, revaccination should be given.

  ✔ Persons ages 2–64 years with chronic illness.

  ✔ Persons ages 2–64 years with functional or anatomical asplenia. When splenectomy is planned, pneumococcal vaccine should be given at least 2 weeks before surgery. A single revaccination is recommended at 5 years in subjects older than 10 years and at 3 years in subjects younger than 10 years).

  ✔ Persons aged 19–64 years who smoke cigarettes or have asthma.

  ✔ Persons with cochlear implants.

- Pneumococcal vaccination (PPV23) is recommended for immunocompromised persons 2 years of age or older with:

  ✔ HIV infection

  ✔ Leukemia, lymphoma, Hodgkin disease, or multiple myeloma

  ✔ Generalized malignancy

  ✔ Chronic renal failure of nephritic syndrome

  ✔ Patients receiving immunosuppressive therapy

  ✔ Organ or bone marrow transplant recipients

- Because children younger than 2 years do not respond adequately to the pneumococcal polysaccharide vaccine, a pneumococcal conjugate vaccine was created (PCV13).

- PCV 13 valent (Prevnar-13) is administered as a 0.5-mL IM injection at 2, 4, and 6 months of age and between 12 and 15 months of age. A single dose of PCV13 should be administered to children aged 6–18 years with sickle cell disease or splenic dysfunction, HIV infection, immunocompromising conditions, cochlear implant, or cerebral spinal fluid leak should be immunized. It is also licensed for individuals aged 50 years and older.

POLIOVIRUS VACCINES

- Two types of trivalent poliovirus vaccines are currently licensed for distribution in the United States: an enhanced inactivated poliovirus vaccine (IPV) and a live-attenuated, oral poliovirus vaccine (OPV). IPV is the recommended vaccine for the primary series and booster dose for children in the United States, whereas OPV is recommended in areas of the world that have circulating poliovirus.
- IPV is given to children ages 2, 4, and 6–18 months and 4–6 years. Primary poliomyelitis immunization is recommended for all children and young adults up to age 18 years. Allergies to any component of IPV, including streptomycin, polymyxin B, and neomycin, are contraindications to vaccine use.
- The routine use of OPV in the United States has been discontinued.

RUBELLA VACCINE

- The vaccine is given with measles and mumps vaccines (MMR) at 12–15 months of age, then at 4–6 years.
- The vaccine should not be given to immunosuppressed individuals, although MMR vaccine should be administered to young children with HIV without severe immunosuppression as soon as possible after their first birthday. The vaccine should not be given to individuals with anaphylactic reaction to neomycin.
- Although the vaccine has not been associated with congenital rubella syndrome, its use in pregnancy is contraindicated. Women should be counseled not to become pregnant for 4 weeks after vaccination.

VARICELLA VACCINE

- Varicella virus vaccine is recommended for all children 12–18 months of age, with a second dose prior to entering school between 4 and 6 years of age. It is also recommended for persons above this age if they have not had chickenpox. Persons ages 13 years and older should receive two doses separated by 4–8 weeks.
    - ✔ The vaccine is contraindicated in immunosuppressed or pregnant patients.
    - ✔ Children with asymptomatic or mildly symptomatic HIV should receive two doses of varicella vaccine 3 months apart.

ZOSTER VACCINE

- Two vaccines for the prevention of zoster are available, a live-attenuated vaccine (Zostavax) and a recombinant zoster vaccine (Shingrix). The recombinant zoster vaccine is 91% effective for preventing zoster and is currently the preferred product for use as recommended by the ACIP for use in immunocompetent individuals aged 50 years and older as a two-dose series at 0 and 2–6 months.
- Almost 80% of those who receive the recombinant vaccine report injection site pain with 9% of those reporting injection site reactions that interfere with their normal activities.

IMMUNOGLOBULIN

- Ig is available as both IM (IGIM) and IV (IGIV) preparations.
- **Table 52-3** lists the suggested dosages for IGIM in various disease states.

- The uses for IGIV are as follows:
  - ✔ Primary immunodeficiency states, including both antibody deficiencies and combined deficiencies
  - ✔ Idiopathic thrombocytopenia
  - ✔ Chronic lymphocytic leukemia in patients who have had a serious bacterial infection
  - ✔ Kawasaki disease (mucocutaneous lymph node syndrome)
  - ✔ Pediatric HIV infection
  - ✔ Allogeneic bone marrow transplant
  - ✔ Chronic inflammatory demyelinating polyneuropathy and multifocal motor neuropathy
  - ✔ Multifocal motor neuropathy
  - ✔ Kidney transplantation involving a recipient with high antibody concentrations or an ABO incompatible donor

TABLE 52-3

Indications and Dosage of Intramuscular Immunoglobulin in Infectious Diseases

Primary immunodeficiency states	1.2 mL/kg IM then 0.6 mL/kg every 2–4 weeks
Hepatitis A exposure	0.02 mL/kg IM within 2 weeks if <1 year or >39 years of age
Hepatitis A prophylaxis	0.02 mL/kg IM for exposure <3 months' duration
	0.06 mL/kg IM for exposure up to 5 months' duration
Hepatitis B exposure	0.06 mL/kg (HBIG preferred in known exposures)
Measles exposure	0.5 mL/kg (maximum dose 15 mL) as soon as possible

RHO(D) IMMUNOGLOBULIN

- Rho(D) Ig (RDIg) suppresses the antibody response and formation of anti-Rho(D) in Rho(D)-negative, D^u-negative women exposed to Rho(D)-positive blood and prevents the future chance of erythroblastosis fetalis in subsequent pregnancies with a Rho(D)-positive fetus.
- RDIg, when administered IM within 72 hours of delivery of a full-term infant, reduces active antibody formation from 1% to 0.2%.
- RDIg is also used in the case of a premenopausal woman who is Rho(D) negative and has inadvertently received Rho(D)-positive blood or blood products.
- RDIg may be used after abortion, miscarriage, amniocentesis, or abdominal trauma.

See Chapter 142, Vaccines, Toxoids, and Other Immunobiologics, authored by Mary S. Hayney, for a more detailed discussion of this topic.