**IMMUNOLOGY / DERMATOLOGY / OPTHALMOLOGY**

**Required Readings**

1. Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR. January 28, 2011; Vol 60(RR02); 1-60

<http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf>

Introduction

CDC recommends routine vaccination to prevent 17 vaccine-preventable diseases that occur in infants, children, adolescents, or adults

Timing and Spacing of Immunobiologics

* *General Principles for Vaccine Scheduling*

Optimal response to a vaccine depends on multiple factors, including the type of vaccine, age of the recipient, and immune status of the recipient.

Recommendations for the age at which vaccines are administered are influenced by age-specific risks for disease, age-specific risks for complications, age-specific responses to vaccination, and potential interference with the immune response by passively transferred maternal antibodies

Certain products, including inactivated vaccines, toxoids, recombinant subunit vaccines, polysaccharide conjugate vaccines, and live vaccines, require **≥2 doses** to elicit an adequate antibody response.

Tetanus and diphtheria toxoids require **booster** doses to maintain protective antibody concentrations

Unconjugated polysaccharide vaccines do not induce T-cell memory, and addi­tional doses (although they elicit the same or a lower antibody concentration) might increase the level of protection.

Conjugation with a protein carrier improves the effectiveness of polysaccharide vaccines by inducing T-lymphocyte–dependent immunologic function. Many vaccines that stimulate both cell-mediated immunity and neutralizing antibodies (e.g., live, attenuated virus vaccines) usually can induce prolonged immunity, even if antibody titers decline over time

Approximately 90%–95% of recipients of a single dose of certain live vaccines administered by injection at the recom­mended age (i.e., measles, rubella, and yellow fever vaccines) develop protective antibodies, generally within 14 days of the dose.

For varicella and mumps vaccines, 80%–85% of vac­cinees are protected after a single dose. However, because a limited proportion (5%–15%) of measles, mumps, and rubella (MMR) or varicella vaccinees fail to respond to 1 dose, a sec­ond dose is recommended to provide another opportunity to develop immunity (97 – 99% response)

The *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Immunization Schedule* are revised annually

* *Spacing of Multiple Doses of the Same Antigen*

Administration at recommended ages and in accordance with recommended intervals between doses of multidose antigens provide optimal protection.

In clinical practice, vaccine doses occasionally are administered at intervals less than the minimum interval or at ages younger than the minimum age. Doses administered too close together (shorter intervals) or at too young an age (younger) can lead to a suboptimal immune response. However, administering a dose a few days earlier the minimum interval or age is unlikely to have a sub­stantially negative effect on the immune response to that dose.

Vaccine doses administered ≤4 days before the minimum inter­val or age are considered valid; however, local or state mandates might supersede this **4-day guideline**.

Because of the unique schedule for **rabies vaccine**, the 4-day guideline does not apply to this vaccine

Doses of any vaccine administered ≥5 days earlier than the minimum interval or age should not be counted as valid doses and should be repeated as age appropriate.

*Shorter interval* - The repeat dose should be spaced after the invalid dose by the recommended minimum interval

*Younger age* - If the first dose in a series is given ≥5 days before the recom­mended minimum age, the dose should be repeated on or after the date when the child reaches at least the minimum age.

If the vaccine is a live vaccine, ensuring that a minimum interval of 28 days has elapsed from the invalid dose is recommended.

* *Simultaneous Administration*

Simultaneous administration of vaccines is defined as administering more than one vaccine on the same clinic day, at different anatomic sites, and not combined in the same syringe.

With some exceptions, simultaneously administering the most widely used live and inactivated vaccines has produced seroconversion rates and rates for adverse reactions similar to those observed when the vaccines are administered separately

There is no exact limit on the number of injections, with a little flexibility, a provider can ensure that the primary series doses are given without administering too many injections at each visit.

***Examples***:

Depending on which vaccines are administered during the first year of life, a child might receive up to nine injections at the 12- through 15-month visit:

MMR

Varicella

Hib

PCV

Pediatric diphtheria and DTaP

IPV

Hepatitis A

Hepatitis B

Influenza vaccines

To reduce the number of injec­tions at the 12- through 15-month visit (before the child’s first birthday)

Hepatitis B series

3 doses of IPV

The majority of children aged 1 year who have received 2 Hib vaccine doses (polyribosylribitol phosphate-meningococcal outer membrane protein [PRP-OMP]) or 3 Hib vaccine doses (PRP-tetanus [PRP-T]) and 3 previous doses of DTaP and PCV have protection against Hib, diphtheria, pertussis, tetanus, and pneumococcus, which lasts throughout infancy (*21,22*).

* *Combination Vaccines*

Combination vaccines merge equivalent component vac­cines into single products to prevent more than one disease or to protect against multiple strains of infectious agents causing the same disease.

Licensed combination vaccines can be used whenever any components of the combination are indicated and its other components are not contraindicated and if licensed by the Food and Drug Administration (FDA) for that dose in the series.

**Potential advantages** of combination vaccines include

1) Improved vaccine coverage rates

2) Timely vaccination coverage for children who are behind the schedule

3) Reduced shipping and stocking costs

4) Reduced costs for extra health-care visits necessitated by deferral of vaccination

5) Facilitation of additional new vaccines into vaccination programs

**Potential disadvantages** of combination vaccines include the following

1. Adverse events that might occur more frequently after administration of a combination vaccine

Ex: Combination measles, mumps, rubella, and varicella (MMRV) vaccine

Combination DTaP-hepatitis B-IPV vaccine

2) Confusion and uncer­tainty about selection of vaccine combinations and schedules for subsequent doses, especially when vaccinations are given by multiple providers who might be using different products

3) Reduced immunogenicity of one or more components

4) Extra doses of certain antigens in the fixed product (e.g., a provider who uses DTaP-hepatitis B-IPV vaccine will give an extra dose of hepatitis B component)

5) A shorter shelf-life than the individual component vaccines.

The economic impact of the use of combination vaccines is unclear because combination products have the potential for either increased or decreased costs compared with single-antigen component vaccines.

* **Licensed Combination Vaccines**

In this report, a combination vaccine is defined as a prod­uct containing components that can be divided equally into independently available routine vaccines.

A dash ( - ) between vaccine products indicates that products are supplied in their final form by the manufacturer and do not require mixing or reconstitution by the user.

A slash ( / ) indicates that the products must be mixed or reconstituted by the user.

Seven combination vaccines for which separate antigens or antigen combinations exist have been licensed by FDA since 1996 in the United States

* **Combination Vaccines and FDA Licensure**

Only combination vaccines licensed by FDA should be used.

Vaccination providers should not combine separate vaccines into the same syringe to administer together unless mixing is indicated for the patient’s age and is explicitly specified on the FDA-approved product label inserts.

Only two combination vaccines (DTaP-IPV/Hib vaccine, marketed as Pentacel, and DTaP/Hib, marketed as TriHibit) contain separate antigen components for which FDA approves mixing by the user.

* **Interchangeability of Formulations**

FDA generally licenses a combination vaccine based on studies demonstrating that the product’s immunogenicity (or efficacy) and safety are comparable or equivalent to monova­lent or combination products licensed previously.

FDA licensure also generally indicates that a combination vaccine may be used interchangeably with monovalent formulations and other combination products with similar component antigens produced by the same manufacturer to continue the vaccination series.

* **Interchangeability of Combination Vaccines from Different Manufacturers**

Licensure of a vaccine by FDA does not necessarily indicate that the vaccine is interchangeable with products from other manufacturers.

Such data are ascertained and interpreted more readily for diseases with known correlates of protective immu­nity (e.g., specific serologic markers). For diseases without such surrogate laboratory markers, prelicensure field vaccine efficacy (phase III) trials or postlicensure surveillance generally are required to determine protection

* *Nonsimultaneous Administration*

There is no evidence that **inactivated vaccines** interfere with the immune response to other inactivated vaccines or to live vaccines. Any inactivated vaccine can be administered either simultaneously or at any time before or after a different inac­tivated vaccine or live vaccine (Table 3).

Limited data are available regarding interference between live vaccines used in the United States. The immune response to **one live-virus vaccine** might be impaired if administered within 28 days (i.e., 4 weeks) of another live-virus vaccine.

To minimize the potential risk for interference, injectable or nasally administered live vaccines not administered on the same day should be administered ≥4 weeks apart (Table 3).

* *Spacing of Vaccines and Antibody-Containing Products*
* **Live Vaccines**

Ty21a typhoid, yellow fever, LAIV, zoster, and rotavirus vaccines may be administered at any time before, concurrent with, or after administration of any immune globulin, hyper­immune globulin, or intravenous immune globulin (IGIV) (55). Blood (e.g., whole blood, packed red blood cells, and plasma) and other antibody-containing blood products (e.g., immune globulin, hyperimmune globulin, and IGIV) can inhibit the immune response to measles and rubella vaccines for ≥3 months.

Therefore, after an antibody-containing product is received, live vaccines (other than yellow fever, oral Ty21a typhoid, LAIV, zoster, and rotavirus) should be delayed until the passive antibody has degraded (Table 4).

* **Inactivated Vaccines**

Antibody-containing products interact less with inactivated vaccines, toxoids, recombinant subunit, and polysaccharide vaccines than with live vaccines (61). Therefore, administering inactivated vaccines and toxoids either simultaneously with or at any interval before or after receipt of an antibody-containing product should not substantially impair development of a protective antibody response (Table 4).

Contraindications and Precautions

The only contraindication applicable to all vaccines is a history of a severe allergic reaction (i.e., anaphylaxis) after a previous dose of vaccine or to a vaccine component (unless the recipient has been desensitized; see Special Situations section).

In addition, severely immunocompromised persons generally should not receive live vaccines.

Children who experienced encephalopathy within 7 days after administration of a pre­vious dose of diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP), DTaP, or Tdap not attributable to another identifiable cause should not receive additional doses of a vaccine that contains pertussis. Because of the theoreti­cal risk to the fetus, women known to be pregnant generally should not receive live, attenuated virus vaccines (see Special Situations section).

In general, vaccinations should be deferred when a precaution is present. However, a vaccination might be indicated in the presence of a precaution if the benefit of protection from the vaccine outweighs the risk for an adverse reaction. For example a dose of DTaP should be considered for a person in a com­munity with a pertussis outbreak even if that person previously developed Guillain-Barré syndrome after a dose.

Among the most common conditions mistakenly considered to be con­traindications are diarrhea, minor upper respiratory tract illnesses (including otitis media) with or without fever, mild to moderate local reactions to a previous dose of vaccine, current antimicrobial therapy, and being in the convalescent phase of an acute illness.

Preventing and Managing Adverse Reactions

Benefit and Risk Communication

The National Childhood Vaccine Injury Act of 1986†† requires that vaccine information materials be developed for each vaccine covered by the act. These materials, known as vaccine information statements (VISs), must be provided by all public and private vaccination providers each time a vaccine is administered.

Preventing Adverse Reactions

Vaccine adverse reactions are classified as

1) Local

2) Systemic

3) Allergic

Local reactions (e.g., redness) are usually the least severe and most frequent.

Systemic reactions (e.g., fever) occur less frequently than local reactions

Severe allergic reactions (e.g., anaphylaxis) are the least frequent reactions.

**Syncope** (vasovagal or vasodepressor reaction) can occur after vaccination (within 15 minutes of vaccine administration) and is most common among adolescents and young adults. In 2005, the Vaccine Adverse Event Reporting System (VAERS) began detecting a trend of increasing syncope reports that coincided with the licensure of three vaccines for adolescents: human papillomavirus (HPV), MCV4, and Tdap (77). Of particular concern among adolescents has been the risk for serious secondary injuries, including skull fracture and cerebral hemorrhage.

Managing Acute Vaccine Reactions

Anaphylaxis usually begins within minutes of vaccine administration. Rapid recognition and initiation of treatment are required to prevent possible progression to car­diovascular collapse. If flushing, facial edema, urticaria, itching, swelling of the mouth or throat, wheezing, dyspnea, or other signs or symptoms of anaphylaxis occur, the patient should be placed in a recumbent position with the legs elevated if possible. Administration of epinephrine is the management of choice.

Reporting Adverse Events After Vaccination

These events range from com­mon, minor, local reactions to rare, severe, allergic reactions (e.g., anaphylaxis).

The Vaccine Adverse Event Reporting System (VAERS)

There are three ways to report to VAERS:

1. Submit the report online via a secure website at https://vaers.hhs.gov/esub/step1,

2. Fax a completed VAERS form to 877-721-0366, or

3. Mail a completed VAERS form: VAERS, P.O. Box 1100, Rockville, MD 20849-1100.

Altered Immunocompetence

General Principles

Altered immunocompetence, a term often used synony­mously with immunosuppression and immunocompromise, can be classified as primary or secondary.

**Primary immunodefi­ciencies** generally are inherited and include conditions defined by an absence or quantitative deficiency of cellular or humoral components or both that provide immunity. Examples include congenital immunodeficiency diseases such as X-linked agam­maglobulinemia, severe combined immunodeficiency disease, and chronic granulomatous disease.

**Secondary immunodefi­ciency** generally is acquired and is defined by loss or qualitative deficiency in cellular or humoral immune components that occurs as a result of a disease process or its therapy. Examples of secondary immunodeficiency include HIV infection, hematopoietic malignancies, treatment with radiation, and treatment with immunosuppressive drugs including alkylating agents and antimetabolites.

Primary and sec­ondary immunodeficiencies might include a combination of deficits in both cellular and humoral immunity. In this report, the general term altered immunocompetence also is used to include conditions such as asplenia and chronic renal disease, and treatments with therapeutic monoclonal antibodies (spe­cifically, the tumor necrosis factor inhibitors) and prolonged administration of high-dose corticosteroids.

Vaccines might be less effective during the period of altered immunocompetence.

Live vaccines might need to be deferred until immune function has improved.

Inactivated vaccines administered during the period of altered immuno­competence might need to be repeated after immune function has improved.

In addition, persons with altered immuno­competence might be at increased risk for an adverse reaction after administration of live, attenuated vaccines because of uninhibited replication.

Altered Immunocompetence as an Indication to Receive a Vaccine

* Pneumococcal Vaccines

PCV (pneumococcal conjugate vaccine) is recom­mended routinely for all children beginning at age 2 months. PCV

is recommended routinely up to age 59 months (5 yrs) for healthy children and up to 71 months (6 yrs) for children with conditions that place them at high risk for invasive disease from *Streptococcus pneumoniae*.

PPSV (pneumococcal polysaccharide vaccine) PPSV is licensed for persons aged ≥2 years and recommended for persons with certain underlying medical condi­tions (including altered immunocompetence) and for all persons aged ≥65 years.

* Influenza Vaccines

Vaccination with TIV (trivalent influenza vaccine) is recommended specifi­cally for persons with altered immunocompetence, including HIV infection.

LAIV (live, attenuated influenza vaccine) usually is contraindicated for persons with altered immunocompetence, although healthy persons with anatomic or functional asplenia and household and other close contacts of persons with altered immunocompetence can receive this vaccine.

* Meningococcal Vaccines

MCV4 (quadrivalent meningococcal conjugate vaccine) or MPSV4 (quadrivalent meningococcal polysaccharide vaccine) - Persons with asplenia, C3 complement deficiency, or persistent complement component deficiency are at increased risk for meningococcal disease and should receive MCV4 or MPSV4.

Quadrivalent MCV4 is licensed for persons aged 2–55 years;

Persons aged ≥56 years should receive MPSV4.

* Hib Vaccines

Hib conjugate vaccines are available in single or combined antigen preparations.

Hib vaccine is recommended routinely for all children through age 59 months (4.9 yrs). However, a single dose of Hib vaccine also may be considered for asplenic older children, adolescents, and adults who did not receive the vaccine series in childhood.

Vaccination of Contacts of Persons with Altered Immunocompetence

Household contacts and other close contacts of persons with altered immunocompetence may receive all age-appropriate vaccines, with the exception of smallpox vaccine.

Vaccines should be administered to susceptible household contacts and other close contacts of immunocompromised patients when indicated:

MMR, varicella

Rotavirus

Annual influenza (LAIV)

Vaccination with Inactivated Vaccines

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

Except for inactivated influenza vaccine, vaccination during chemotherapy or radiation therapy should be avoided if pos­sible because antibody response might be suboptimal. Patients vaccinated within 14 days before starting immunosuppressive therapy or while receiving immunosuppressive therapy should be considered unimmunized and should be revaccinated at least 3 months after therapy is discontinued if immune competence has been restored.

Vaccination with Live, Attenuated Viral and Bacterial Vaccines

Severe complications have followed vaccination with live, attenuated viral and live, attenuated bacterial vaccines among persons with altered immunocompetence. Persons with most forms of altered immunocompetence should not receive live vaccines

MMR

Varicella

MMRV

LAIV

Zoster

Yellow fever

Ty21a oral typhoid

BCG

Rotavirus

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

Persons with severe cell-mediated immunodeficiency should not receive live, attenuated viral or bacterial vaccines. However, two factors support vaccination of HIV-exposed or HIV-infected infants:

1) The HIV diagnosis might not be established in infants born to HIV-infected mothers before the age of the first rotavirus vaccine dose (only 1.5% to 3% of HIV-exposed infants in the United States will be determined to be HIV-infected)

2) Vaccine strains of rotavirus are considerably attenuated.

Children with HIV infection are at increased risk for com­plications from varicella and herpes zoster compared with immunocompetent children. Limited data among HIV-infected children (specifically CDC class N, A, or B with age-specific CD4+ T-lymphocyte percentages of ≥15%) indicate that varicella vaccine is immunogenic, effective, and safe. Varicella vaccine should be considered for chil­dren who meet these criteria. Eligible children should receive 2 doses of varicella vaccine with a 3-month interval between doses. Doses separated by <3 months are invalid for persons with altered immunocompetence.

MMR vac­cination is recommended for all asymptomatic or mildly symptomatic HIV-infected persons who do not have evidence of severe immunosuppres­sion (age-specific CD4+ T-lymphocyte percentages of ≥15%) and for whom measles vaccination would otherwise be indi­cated.

HIV-infected persons who are receiving regular doses of IGIV (Immune globulin intravenous) might not respond to varicella vaccine or MMR vac­cine because of the continued presence of passively acquired antibody. However, because of the potential benefit, MMR and varicella vaccines should be considered approximately 14 days before the next scheduled dose of IGIV

Patients with leukemia, lymphoma, or other malignancies whose disease is in remission, who have restored immunocom­petence, and whose chemotherapy has been discontinued for **at least 3 months** can receive live-virus vaccines.

Zoster incidence is higher in persons with altered immuno­competence. Zoster vaccine is contraindicated in persons with primary or acquired immunodeficiency (e.g., lymphoma, leu­kemia, tumors involving bone marrow, and patients receiving chemotherapy) and some patients with AIDS.

Conditions or Drugs that Might Cause Immunodeficiencies

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

Anatomic or Functional Asplenia

Persons with anatomic asplenia (e.g., surgical removal or congenital absence of the spleen) or functional asplenia (as occurs in persons with sickle cell disease) are at increased risk for infection by encapsulated bacteria, especially by S. pneu­moniae (pneumococcus), N. meningitidis (meningococcus), and Hib (Haemophilus influenzae type b).

Children aged <5 years with anatomic or functional asplenia should receive an age-appropriate series of PCV (pneumococcal conjugate vaccine).

Persons aged ≥2 years should receive 2 doses of PPSV separated by 5 years (pneumococcal polysaccharide vaccine)

Quadrivalent meningococcal conjugate vaccine

MCV4 (Menactra) for persons aged 2 – 55 yrs

MCV4 (Menveo) only for ages 11 – 55 yrs

MPSV4 (Quadrivalent meningococcal polysaccharide vaccine) for persons ≥ 56 yrs

A 3-year interval to the next dose is recommended for children at high risk who receive their first dose at ages 2–6 years.

A 5-year interval is recom­mended for persons at high risk who receive their first dose at age ≥7 years.

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

Corticosteroids

Corticosteroid therapy usually is not a contraindica­tion to administering live-virus vaccine when administration is

1) Short term (i.e., <14 days)

2) A low to moderate dose (<20 mg of prednisone or equivalent per day)

3) Long-term, alternate-day treatment with short-acting preparations

4) Maintenance physiologic doses (replacement therapy); **or**

5) Topical (skin or eyes), inhaled, or by intraarticular, bursal, or tendon injection.

Although the immunosuppressive effects of steroid treatment vary, the majority of clinicians consider a dose equivalent to **either** ≥2 mg/kg of body weight **or** ≥20 mg/day of prednisone or equivalent for persons who weigh >10 kg when administered for ≥14 days as sufficiently immunosuppressive to raise concern about the safety of vaccination with live-virus vaccines

Other Immunosuppressive Drugs

When feasible, clinicians should administer all indicated vac­cines to all persons before initiation of chemotherapy, before treatment with other immunosuppressive drugs, and before radiation or splenectomy.

Live, attenu­ated vaccines should not be administered for at least 3 months after such immunosuppressive therapy.

Inactivated vaccines administered during chemotherapy should be readministered after immune competence is regained.

Special Situations

Severe Allergy to Vaccine Components

Allergic reactions might be caused by the vaccine antigen, residual animal protein, antimicrobial agents, preservatives, stabiliz­ers, or other vaccine components.

The most common animal protein allergen is egg protein, which is found in influenza and yellow fever vaccines because they are prepared using embryonated chicken eggs.

Measles and mumps vaccine viruses are grown in chick embryo fibroblast tissue culture. However, persons with a severe egg allergy can receive measles- or mumps-containing vaccines without skin testing or desensitization to egg protein.

Rubella and varicella vaccines are grown in human diploid cell cultures and can safely be administered to persons with a severe allergy to eggs or egg proteins.

No licensed vac­cine contains penicillin or penicillin derivatives.

Persons who have had anaphylactic reactions to neomycin should not receive vaccines containing neomycin. Most often, a neomycin allergy is a contact dermatitis, a manifestation of a delayed-type (cell-mediated) immune response rather than anaphylaxis.

Thimerosal, an organic mercurial compound in use since the 1930s, is added to certain immunobiologics as a preserva­tive. Since mid-2001, vaccines routinely recommended for young infants have been manufactured without thimerosal as a preservative. Live, attenuated vaccines have never contained thimerosal. Thimerosal-free formulations of inactivated influ­enza vaccine are available. Inactivated influenza vaccine also is available in formulations with trace thimerosal, in which thimerosal remains as a manufacturing residual but does not function as a preservative, and in formulations that contain thimerosal as a preservative. Thimerosal at a preservative concentration is present in certain other vaccines that can be administered to children (e.g., Td and DT).

A local or delayed-type hypersensitivity reaction to thimerosal is not a contraindication to receipt of a vaccine that contains thimerosal.

Latex Allergy

Latex is sap from the commercial rubber tree. Latex contains naturally occurring impurities (e.g., plant proteins and pep­tides) that might be responsible for allergic reactions.

The most common type of latex sensitivity is a contact-type (type 4) allergy, usually as a result of prolonged contact with latex-containing gloves (176). However, latex allergies associated with injection procedures have been described among patients with diabetes mellitus.

Vaccination of Preterm Infants

In the majority of cases, preterm infants (infants born before 37 weeks’ gestation), regardless of birth weight, should be vaccinated at the same chronological age and according to the same schedule and using the same precautions as for full-term infants and children. Birth weight and size are not factors in deciding whether to vaccinate a clinically stable preterm infant (181–185), except for hepatitis B vaccination. The full recommended dose of each vaccine should be used. Divided or reduced doses are not recommended.

Preterm infants born to HBsAg-positive mothers and mothers with unknown HBsAg status must receive immunoprophylaxis with hepatitis B vaccine within 12 hours after birth. The initial vaccine dose should not be counted toward completion of the hepatitis B series, and 3 additional doses of hepatitis B vaccine should be administered, beginning when the infant is aged 1 month.

Infants weighing <2,000 g born to HBsAg-negative mothers should receive the first dose of the hepatitis B series at chronological age 1 month or at hospital discharge.

If a child aged at least 6 weeks has been in the hospital since birth, deferral of rotavirus vaccine is recommended until the time of discharge. The rotavirus vaccine series should not be initiated for infants aged ≥15 weeks, 0 days.

Breastfeeding and Vaccination

Neither inactivated nor live-virus vaccines administered to a lactating woman affect the safety of breastfeeding for women or their infants. Although live viruses in vaccines can replicate in vaccine recipients (i.e., the mother), the majority of live viruses in vaccines have been demonstrated not to be excreted in human milk.

Varicella vaccine virus has not been found in human milk (190). Although rubella vaccine virus might be excreted in human milk, the virus usually does not infect the infant.

Inactivated, recombinant, subunit, polysaccharide, and conjugate vaccines, as well as toxoids, pose no risk for mothers who are breastfeeding or for their infants.

Breastfeeding is a contraindication for **smallpox** vaccination of the mother because of the theoretical risk for contact trans­mission from mother to infant. **Yellow fever** vaccine should be avoided in breastfeeding women.

Vaccination During Pregnancy

Risk to a developing fetus from vaccination of the mother during pregnancy is theoretical. No evidence exists of risk to the fetus from vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids.

Live vaccines administered to a pregnant woman pose a theoretical risk to the fetus; therefore, live, attenuated virus and live bacterial vac­cines generally are contraindicated during pregnancy.

Pregnant women who received the last dose of tetanus-toxoid–containing vaccine >10 years previously should gener­ally receive Td rather than Tdap while they are pregnant, although Tdap is not contraindicated during pregnancy. A dose of Td during pregnancy ensures adequate tetanus immunity in the mother and prevents disease in both mother and infant.

Regardless of a recent Td vaccination, pregnant women who have not already received Tdap should receive a dose of Tdap as soon as possible after delivery to ensure pertussis immunity and reduce the risk for transmission to the newborn.

Women for whom Td is indicated but who did not complete the recommended 3-dose series during pregnancy should receive follow-up after delivery to ensure the series is completed.

Women in the second and third trimesters of pregnancy are at increased risk for hospitalization from influenza. Because vaccinating against influenza before the season begins is critical, and because predicting exactly when the season will begin is impossible, routine influenza vaccination is recom­mended for all women who are or will be pregnant (in any trimester) during influenza season, which in the United States is usually early October through late March.

IPV (inactivated poliovirus) can be administered to pregnant women who are at risk for exposure to wild-type poliovirus infection.

Hepatitis A, pneumococcal polysaccharide, meningococcal conjugate, and meningococcal polysaccharide vaccines should be considered for women at increased risk for those infections.

Pregnancy is a contraindication for **smallpox** (vaccinia) vac­cine and **measles**-, **mumps**-, **rubella**-, and **varicella**-containing vaccines. **Smallpox vaccine is the only vaccine known to harm a fetus when administered to a pregnant woman**.

Data from studies of children born to mothers vaccinated with rubella vaccine during pregnancy demonstrate rubella antibody levels in unvaccinated infants. This could represent passive transfer of maternal antibody or a fetal antibody response to vaccine virus infection in the fetus.

MMR and varicella vaccines should be administered when indicated to children and other household contacts of pregnant women. Infants living in households with pregnant women should be vaccinated with rotavirus vaccine according to the same schedule as infants in households without pregnant women.

A woman found to be HBsAg positive should be monitored carefully to ensure that the infant receives HBIG and begins the hepatitis B vaccine series no later than 12 hours after birth and that the infant completes the recommended hepatitis B vaccine series on schedule.