

This chapter discusses best practices related to vaccine timing and spacing, dosing, adverse reactions, and contraindications and precautions for routinely recommended vaccines in the United States. A more thorough discussion of issues common to the use of multiple vaccines and non-routinely recommended vaccines (e.g., rabies, smallpox) can be found in the *General Best Practice Guidelines for Immunization: Best Practices Guidance of the Advisory Committee on Immunization Practices*. Information about recommended travel vaccines (e.g., yellow fever, typhoid) can be found in CDC's *Yellow Book*.

Timing and Spacing of Vaccines

Timing and spacing of vaccine doses are two of the most important considerations for the appropriate use of vaccines. Specific circumstances commonly encountered in immunization practice are the intervals between doses of the same vaccine, simultaneous and nonsimultaneous administration of different vaccines, and the intervals between antibody-containing blood products and live attenuated vaccines (particularly measles- and varicella-containing vaccines).

Interval Between Doses of the Same Vaccine

Most vaccines in the immunization schedule require two or more doses for development of an adequate and persistent antibody response. Vaccinations are recommended beginning with the youngest age group at risk for a disease for whom vaccine efficacy and safety have been demonstrated. Studies have demonstrated that following the recommended ages and intervals between doses of the same antigen(s) provides optimal protection. As a general rule, decreasing the interval between doses in a multiple-dose vaccine series may interfere with antibody response and protection.

For routine vaccination, vaccine doses should not be administered earlier than the minimum ages or at less than the minimum intervals. However, exceptions may occasionally be necessary. One exception involves administering a dose up to 4 days before the minimum age or interval to avoid missing an opportunity to vaccinate. The patient may have come to the office early or for an appointment not specifically for vaccination. In these situations, the provider can consider administering the vaccine earlier than the minimum age or interval. However, if the provider has confidence that the patient will return for a later visit, it is preferable to reschedule vaccination on or after the recommended minimum age or interval. If the patient is new to the provider or habitually misses appointments, it may be preferable to administer the vaccine early. These early doses administered within 4 days of

NOTES

NOTES

the minimum age or interval are considered valid. In certain situations, state or local requirements might mandate doses of selected vaccines be administered on or after specific ages, superseding this 4-day grace period. Doses administered 5 days or more before the minimum age or interval should not be counted as valid and should be repeated as age-appropriate.

Other exceptions are administering doses in a vaccine series at shorter intervals than recommended when a person is behind schedule and needs to be brought up to date quickly or when international travel is pending. In these cases, an accelerated schedule using the minimum age or minimum interval criteria can be used. An example is an infant age 6 through 11 months receiving 1 dose of MMR vaccine prior to international travel (not to be considered valid as part of the routinely recommended series) or administering the second dose of measles vaccine before age 4 years during a measles outbreak (considered valid as long as a minimum interval of at least 4 weeks from the prior dose was heeded and the child was age 12 months or older).

In some cases, a scheduled dose of vaccine may be administered late. A late dose should be administered at the next visit. Available data indicate intervals between doses that are longer than those routinely recommended do not affect seroconversion rates or titers when the schedule is completed. Therefore, it is not necessary to restart a series or add doses of any vaccine because of an extended interval between doses.

Simultaneous and Nonsimultaneous Vaccine Administration

Simultaneous Administration of Different Vaccines

Simultaneous administration (i.e., administration of two or more vaccines on the same day) of all recommended vaccines is important because it increases the probability that an individual will be fully vaccinated at the appropriate age. It is also an important part of immunization practice when a health care provider is uncertain that a patient will return for additional doses of vaccine.

As a general rule, almost all vaccines can be administered at the same visit. Exceptions to this include:

- PCV13 (Pevnar 13) vaccine and MenACWY-D (Menactra) vaccine should not be administered simultaneously to persons with functional or anatomic asplenia or HIV. Menactra brand meningococcal conjugate vaccine is thought to interfere with the antibody response to Pevnar 13. When both Pevnar 13 and Menactra are indicated, Pevnar 13 should be administered first, followed by Menactra at least 4 weeks later.

- PCV13 (Pevnar 13) vaccine and PPSV23 (Pneumovax 23) vaccine should not be administered at the same visit; studies show a better immune response when Pevnar 13 is administered before Pneumovax 23. When both Pevnar 13 and Pneumovax 23 are indicated, Pevnar 13 should be administered first, and Pneumovax 23 should be administered either at least 8 weeks later or at least 1 year later, depending on the age and health conditions of the vaccine recipient.
- Varicella (VAR [Varivax]) vaccine should not be administered simultaneously with smallpox vaccine.

Combination vaccines are generally preferred over simultaneous administration of single-component vaccines. Combination vaccines contain components that can be divided into independently available routine vaccines and can reduce the number of injections needed. Considerations for using combination vaccines should include an assessment of the number of injections, availability of vaccine, likelihood of improved vaccination coverage, likelihood of patient return, and issues regarding storage and cost. Considerations should also include patient choice and the potential for adverse events.

There is an increased risk of febrile seizures following the first dose of the combination measles, mumps, rubella, varicella (MMRV [ProQuad]) vaccine compared with separate administration of MMR vaccine (MMR-II) and VAR vaccine (Varivax). For the first dose, MMR and varicella vaccines should be administered separately for children age 12 through 47 months unless the parent or caregiver expresses a preference for MMRV vaccine.

Nonsimultaneous Administration of Live Vaccines

If any combination of live, injected vaccines (MMR-II, ProQuad, Varivax) or live, attenuated influenza vaccine (LAIV [FluMist]) is not administered simultaneously, the vaccine doses should be separated by at least 4 weeks. This interval is intended to reduce or eliminate interference from the vaccine administered first with the vaccine administered later. If any two of these vaccines are administered at an interval of less than 4 weeks, then the vaccine administered second should be repeated in 4 weeks or serologic testing should be performed following MMR-II and ProQuad to confirm their effectiveness (serologic testing is not recommended following FluMist or Varivax vaccines).

Live vaccines administered by the oral route (e.g., typhoid TY21a, [Vivotif], rotavirus, and adenovirus vaccines) are not believed to interfere with parenteral or intranasal live vaccines or with each other. Therefore, they may be administered simultaneously with or at any time before or after other live vaccines.

NOTES

NOTES

Vaccines and Antibody-Containing Products

Antibody, in the form of immune globulin, might be administered simultaneously with or around the same time as certain vaccines; for example, as postexposure prophylaxis for certain diseases, such as hepatitis B, rabies, and tetanus. Immune response to some live attenuated vaccines can be affected by receipt of immune globulin, depending on the type of vaccine, amount of antibody, and timing of administration. Immune response to inactivated vaccines are generally not affected by antibody-containing products. Inactivated vaccines can be administered before, after, or at the same time as the antibody products. However, the presence of circulating antibody to a vaccine antigen might reduce or eliminate the immune response to that vaccine. The vaccine antigen should be administered at a site distant from where the immune globulin was injected.

Live, Attenuated Injectable Vaccines

Live, attenuated vaccines must replicate to produce an immune response. Antibody against injected live vaccine antigen may interfere with replication. If measles, mumps, and rubella (MMR [MMR-II]), varicella (VAR [Varivax]), or combination measles, mumps, rubella, and varicella (MMRV [ProQuad]) vaccines must be administered around the same time as antibody, the two must be separated by enough time to prevent the antibody from interfering with viral replication. If these live vaccines are administered first, it is necessary to wait at least 2 weeks before administering the antibody. If the interval between the vaccine and antibody is less than 2 weeks, the recipient should be tested for immunity or the vaccine dose should be repeated. If the antibody is administered first, it is necessary to wait until the antibody has waned before administering the vaccine. This will reduce the chance of interference by the antibody.

An exception to the waiting period for antibody to wane before vaccination is the low dose of RhoGam or Rhophylac (anti-Rho(D) globulin) or any other blood product administered to women who do not have evidence of immunity to rubella or varicella during the last trimester of pregnancy or at delivery. Although passively acquired antibodies can interfere with the response to rubella vaccine, the low dose of anti-Rho(D) globulin has not been demonstrated to reduce the response to the rubella vaccine. These women should receive MMR-II, Varivax, or ProQuad as indicated immediately after delivery and, if possible, be tested 3 or more months later to ensure immunity to rubella and, if necessary, to measles.

Some blood products contain negligible antibody or type-specific antibody which do not interfere with vaccine replication. These products can be administered at any time

before or after administration of MMR or varicella-containing vaccines. Palivizumab (Synagis), used to prevent respiratory syncytial virus (RSV) infection in some infants and young children, contains antibody directed only at RSV. Washed red blood cells contain a negligible amount of antibody.

Live, Attenuated Oral and Intranasal Vaccines

Rotavirus vaccines (RV1 [Rotarix] and RV5 [RotaTeq]) and LAIV (FluMist) are not known to be affected by the administration of immune globulin or blood products. They may be administered simultaneously with blood products or separated from them by any interval.

Doses

Many factors influence the number of doses recommended in a vaccine series, including the type of vaccine, epidemiology of the disease, and host factors (e.g., age, presence of underlying diseases). For live, injected vaccines, the first dose administered at the recommended age usually provides protection. An additional dose is administered to provide another opportunity for vaccine response in the small proportion of recipients who do not respond to the first dose. For instance, approximately 95% of recipients respond to a single dose of measles vaccine. The second dose is administered to ensure that nearly 100% of persons are immune. Immunity following live vaccines is long-lasting, and booster doses are usually not necessary.

For inactivated vaccines, the first dose administered at the recommended age usually does not provide protection (hepatitis A vaccine is an exception). A protective immune response may not develop until after dose 2 or 3. For inactivated vaccines, antibody titers may decrease below protective levels after a few years. This phenomenon is most notable with pertussis vaccine. Tetanus and diphtheria vaccine-induced immunity also wanes. For these vaccines, a booster dose is administered to raise antibody back to protective levels.

Not all inactivated vaccines require boosting throughout the lifetime. For example, additional doses of *Haemophilus influenzae* type b vaccine are not required after completion of the infant primary series and booster dose because *H. influenzae* type b disease is rare in persons older than age 5 years. Hepatitis B vaccine does not require boosting in immunocompetent persons because of immunologic memory of the vaccine and the long incubation period for hepatitis B. Immunologic memory produces an “autoboost,” which means exposure to the virus causes the established immune memory to respond faster than the virus can cause disease.

NOTES

NOTES

Adverse Reactions Following Vaccination

An adverse reaction or side effect is an untoward effect caused by a vaccine. An adverse reaction is different from a vaccine adverse event. Vaccine adverse event refers to any medical event that occurs following vaccination. An adverse event could be a true adverse reaction or a coincidental event, with further investigation needed to distinguish between them. Health care providers are required by law to report certain adverse events after vaccination. Details on reporting adverse events after vaccination can be found at <https://vaers.hhs.gov/>

Allergic reactions may be caused by the vaccine antigen itself or some other vaccine component, such as cell culture material or a stabilizer, preservative, or antibiotic used to inhibit bacterial growth. Severe allergic reactions (e.g., anaphylaxis) may be life-threatening but fortunately are rare. The risk of an allergic reaction can be decreased by effective screening prior to vaccination. All providers who administer vaccines must have an emergency protocol, supplies, and training to treat anaphylaxis.

Local adverse reactions (e.g., pain, swelling, and redness at the injection site) are the most common adverse reactions following vaccination. They generally occur within a few hours of the injection and are usually mild and self-limited. Local reactions may occur with up to 80% of vaccine doses, depending on the type of vaccine. On rare occasions, local reactions may be severe. These reactions, referred to as Arthus reactions, are most frequently seen with diphtheria and tetanus toxoids. Arthus reactions are not allergic reactions. They are believed to be due to high titers of antibody, usually caused by too many doses of toxoid.

Systemic adverse reactions (e.g., fever, myalgia, rash, headache) may occur following vaccination. Adverse reactions such as fever or rash following live, attenuated vaccines may be similar to a mild form of the natural disease, with symptoms produced from viral replication. Systemic adverse reactions are usually mild and occur 3 through 21 days after the vaccine was administered. Systemic adverse reactions from live attenuated vaccines are seen at longer intervals following vaccine administration because they are caused by replication of vaccine virus in the body, which occurs over several days. FluMist may cause upper respiratory symptoms rather than influenza-like symptoms since it replicates in the mucous membranes of the nose and throat and not in the lungs. Systemic adverse reactions were relatively frequent with diphtheria-tetanus-whole-cell-pertussis (DTP) vaccine, which contained a whole-cell pertussis component. Systemic adverse events are less common with acellular pertussis vaccine.

Contraindications and Precautions to Vaccination

Contraindications and precautions to vaccination generally dictate circumstances when vaccines should not be administered. Some contraindications and precautions are temporary, and the vaccine can be administered later.

Contraindications

A contraindication is a health condition in the recipient that increases the likelihood of a serious adverse reaction to a vaccine. For instance, administering MMR-II vaccine to a person with a true anaphylactic allergy to gelatin could cause serious illness or death in the recipient. In general, vaccines should not be administered when a contraindication is present.

Medical conditions that are contraindications to vaccination include:

- A severe allergic reaction (e.g., anaphylaxis) to a vaccine component is a contraindication to any vaccine containing that component, and a severe allergy following a dose of vaccine is a contraindication to subsequent doses of that vaccine.
- Severe immunosuppression is a contraindication to live, attenuated vaccines.
- A history of intussusception is a contraindication to rotavirus vaccination.
- Encephalopathy not due to another identifiable cause and occurring within 7 days of pertussis vaccination is a contraindication to subsequent doses of pertussis-containing vaccine.

Use of aerosolized steroids, such as inhalers for asthma, is not a contraindication to vaccination; nor are alternate-day, rapidly tapering, and short (less than 14 days) high-dose schedules, topical formulations, and physiologic replacement steroid dose schedules.

Precautions

A precaution is a health condition in the recipient that might increase the chance or severity of a serious adverse reaction, might compromise the ability of the vaccine to produce immunity (such as administering measles vaccine to a person with passive immunity to measles from a blood transfusion), or might cause diagnostic confusion. Injury could result, but the chance of this happening is less than with a contraindication. In general, vaccines should be deferred when a precaution is

NOTES

NOTES

present. However, situations may arise when the benefit of protection from the vaccine outweighs the risk of an adverse reaction, and a provider may decide to administer the vaccine.

Medical conditions that are precautions to vaccination include:

- Moderate or severe acute illness, with or without fever, is a precaution for all vaccines.
- Guillain-Barré syndrome (GBS) occurring 6 weeks or less after a previous dose of a tetanus toxoid-containing vaccine is a precaution for tetanus toxoid-containing vaccines.
- GBS occurring 6 weeks or less after a previous dose of influenza vaccine is a precaution for influenza vaccines.
- History of thrombocytopenia or thrombocytopenic purpura is a precaution for MMR vaccine.
- Chronic gastrointestinal disease, or altered immunocompetence other than SCID are precautions for rotavirus vaccine. Spina bifida or bladder exstrophy are precautions for Rotarix (RV1) but not for RotaTeq RV5 vaccine.
- Recent receipt of antibody-containing blood products is a precaution for MMR- and varicella-containing vaccines.
- History of Arthus-type hypersensitivity reaction after a previous dose of diphtheria toxoid or tetanus toxoid vaccine is a precaution to these vaccines; vaccination should be deferred until at least 10 years have elapsed since the last tetanus-toxoid-containing vaccine.
- Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, or progressive encephalopathy is a precaution for DTaP and Tdap vaccination; individual clinical decision-making should be used to guide revaccination until neurologic status has been clarified and stabilized.

Family History of Adverse Events

With few exceptions, family medical history is not a contraindication or precaution to vaccines. A family history of immunosuppression in first-degree relatives (i.e., parents or siblings) is a contraindication to MMR and varicella-containing vaccines unless the potential vaccine recipient's immunocompetence has been verified either clinically or by a laboratory. A family history of seizures is a precaution for MMRV vaccination.

Contraindications and Precautions in Persons with Specific Health Conditions

Persons with a History of Allergic Reactions

A severe allergic reaction (e.g., anaphylaxis) following a dose of vaccine is a contraindication for a subsequent dose of that vaccine. Anaphylactic reactions are mediated by IgE, occur within minutes or hours of receiving the vaccine, and require emergency medical attention. Anaphylaxis involves two or more organ systems (dermatologic, cardiovascular, respiratory, and/or gastrointestinal) simultaneously. Symptoms and signs of anaphylactic reactions include generalized urticaria (hives), swelling of the mouth and throat, difficulty breathing, wheezing, hypotension, or shock. Anaphylaxis after vaccination occurs rarely and can often be prevented by appropriate screening.

Persons may be allergic to a vaccine antigen or to a vaccine component such as an animal protein, antibiotic, preservative, or stabilizer. The most common animal protein allergen is egg protein found in influenza vaccines prepared using embryonated chicken eggs. Asking persons whether they can eat eggs without adverse effects is a reasonable way to screen for those who might be at risk if they receive egg-containing influenza vaccines. Persons with a history of egg allergy who have experienced only hives after exposure to egg should receive influenza vaccine. Influenza vaccine may also be administered to persons who report having had reactions to egg involving symptoms other than hives (such as swelling of the throat and mouth, difficulty breathing, lightheadedness, or recurrent emesis) or who required epinephrine or another emergency medical intervention. If egg-containing influenza vaccine is administered to persons who report having had reactions to egg involving symptoms other than hives, it should be administered in an inpatient or outpatient medical setting and supervised by a health care provider able to recognize and manage severe allergic conditions. A previous severe allergic reaction to influenza vaccine, regardless of the component suspected of being responsible for the reaction, is a contraindication to future receipt of the vaccine.

Studies show that children who have a history of severe allergy to eggs rarely have reactions to MMR-II and ProQuad vaccine. This is probably because measles and mumps vaccine viruses are both grown in chick embryo fibroblasts, not actually in eggs. It appears gelatin, not egg, might be the cause of allergic reactions to MMR-II. Children with egg allergies may be vaccinated with MMR-II or ProQuad without prior skin testing.

Certain vaccines contain trace amounts of neomycin. Persons who have experienced an anaphylactic reaction to neomycin should not receive these vaccines. Most often, neomycin allergy

NOTES

Immunosuppression

Live, attenuated vaccines can cause severe or fatal reactions in immunosuppressed persons due to uncontrolled replication of the vaccine virus. Live vaccines should usually not be administered to severely immunosuppressed persons with congenital immunodeficiency, leukemia, lymphoma, or generalized malignancy. However, persons with isolated B-cell deficiency may receive varicella vaccine. Generally, the provider treating an immunosuppressed patient should determine the severity of that patient’s immunosuppression.

Certain drugs can also cause immunosuppression. For instance, persons receiving cancer treatment with alkylating agents, antimetabolites, or radiation therapy should not receive live vaccines. Live vaccines can be administered after chemotherapy or radiation therapy has been discontinued for at least 3 months. In addition, persons receiving large doses of corticosteroids should not receive live vaccines. This includes persons receiving 20 milligrams or more of prednisone daily or 2 milligrams or more of prednisone per kilogram of body weight per day for 14 days or longer.

The safety and efficacy of live, attenuated vaccines administered concurrently with recombinant human immune mediators and immune modulators are not known. There is evidence that use of therapeutic monoclonal antibodies, especially the anti-tumor necrosis factor (TNF) agents (e.g., adalimumab, infliximab, etanercept, golimumab, and certolizumab pegol), may lead to reactivation of latent tuberculosis infection and disease. These agents might also predispose persons to other opportunistic infections. Because these drugs vary dramatically in the scope and number of immune-system-targeted components, it is prudent to avoid administering live, attenuated vaccines while patients are taking these drugs. For vaccination against seasonal influenza, inactivated injectable alternatives are available.

The time health care providers should wait to administer a live-virus vaccine after immune modulator drugs have been discontinued is not specified by the Advisory Committee on Immunization Practices (ACIP) or other authoritative guidelines. No basis exists for interpreting laboratory studies of immune parameters with vaccines’ safety or efficacy. Lymphocyte-depleting agents such as alemtuzumab and rituximab may cause prolonged immunosuppression. Both inactivated and live vaccines should be withheld at least 6 months following therapy with anti-B cell antibodies. Some experts recommend longer than 6 months following anti-B cell antibodies. The optimal time for restarting immunosuppressive therapy after vaccination with live vaccines has not been studied, but the Infectious Diseases Society of America (IDSA) recommends waiting at least 1 month.

NOTES

- Revaccination with inactivated vaccines, including influenza vaccine, should begin 6 months after HCT. However, influenza vaccine may be administered as early as 4 months after HCT, if needed.
- Three doses of Prevnar 13 should be administered 3-6 months after HCT, followed by a dose of PPSV23.
- A dose of MenACWY should also be administered 6 months after HCT.

Invalid Contraindications and Precautions to Vaccination

Sometimes certain conditions or circumstances are inappropriately considered to be contraindications or precautions to vaccination. Such conditions or circumstances are known as invalid contraindications and these misperceptions result in missed opportunities to administer needed vaccines. Some of the most common invalid contraindications are mild illnesses, pregnancy, breastfeeding, allergies that are not anaphylactic in nature, and certain aspects of the patient’s family history.

Mild Illness

Children with a mild acute illness, such as a low-grade fever, an upper respiratory infection (URI), otitis media, or mild diarrhea, should be vaccinated on schedule.

Low-grade fever is not a contraindication to vaccination. Measuring temperature is not necessary before vaccination if the patient does not appear ill and does not report currently being ill. ACIP has not defined a body temperature above which vaccines should not be administered. The decision to vaccinate should be based on the overall evaluation of the person rather than an arbitrary body temperature.

Nonanaphylactic Allergy

If an allergy to a vaccine component is not severe (e.g., is not anaphylaxis), it is not a contraindication to that vaccine. Only a severe allergic reaction (e.g., anaphylaxis) to a vaccine component is a true contraindication to vaccination.

Allergy to Products Not Present in Vaccines

There is no contraindication or precaution for persons with nonspecific allergies, duck or feather allergies, or penicillin allergy, or for persons who have relatives with allergies or those taking allergy shots. Anyone with these allergies can and should be vaccinated. No vaccine available in the United States contains duck antigen or penicillin.

NOTES

NOTES

Antimicrobial Therapy

Antimicrobials do not influence the immune response to most vaccines. However, antiviral drugs may affect vaccine replication in some circumstances. FluMist should not be administered until 48 hours after cessation of oseltamivir and zanamivir, 5 days after cessation of peramivir, and 17 days after baloxavir. If possible, antiviral drugs (acyclovir, famciclovir) that are active against herpesviruses should be discontinued 24 hours before administration of a varicella-containing vaccine.

Breastfeeding

Breastfeeding does not decrease the response to any routinely recommended childhood vaccine and is not a contraindication to vaccination; however, breastfeeding is a precaution for yellow fever vaccine. Breastfeeding also does not extend or improve the passive immunity to vaccine-preventable disease that is provided by maternal antibody.

Household Contacts of Pregnant or Immunosuppressed Persons

Being a household contact of a pregnant woman or immunosuppressed person is usually not a contraindication to vaccination. In fact, it is critical that healthy household contacts of pregnant women and immunosuppressed persons be vaccinated. Vaccination of healthy contacts reduces the chance that pregnant women and immunosuppressed persons will be exposed to vaccine-preventable diseases.

Most routinely recommended vaccines, including live vaccines (MMR-II, Varivax, RotaTeq/Rotarix, and FluMist), can be administered to persons who are household contacts of pregnant or immunosuppressed persons. If a varicella vaccine recipient has a rash after vaccination, direct contact with susceptible household contacts with altered immunocompetence should be avoided until the rash resolves. All members of the household should wash their hands after changing the diaper of an infant who received rotavirus vaccine. This minimizes rotavirus transmission, as shedding may occur up to one month after the last dose. FluMist should not be administered to close contacts and caregivers of severely immunosuppressed persons who require a protected environment.

Preterm Birth

Vaccines should be started on schedule based on the child's chronological age. Preterm infants have been shown to respond adequately to vaccines used in infancy.

Studies demonstrate that decreased seroprotection rates might occur among infants with low birth weight (less than 2,000 grams) after administration of hepatitis B vaccine at birth.

However, by the chronological age of 1 month, all preterm infants, regardless of initial birth weight or gestational age, are likely to respond as adequately as older and larger infants.

Tuberculin Skin Test

Persons who need a tuberculin skin test (TST) can and should be vaccinated. All vaccines can be administered on the same day as a TST or at any time after a TST is administered. For most vaccines, there are no TST timing restrictions.

MMR-containing vaccine may decrease the response to a TST, potentially causing a false-negative response in someone who has a tuberculosis infection. MMR-II can be administered the same day as a TST, but if MMR-II has been administered and 1 or more days have elapsed, it is recommended in most situations to wait at least 4 weeks before administering a routine TST. There is no information available on the effect of varicella-containing vaccine or FluMist on a TST. Until such information is available, it is prudent to apply the same rules for spacing measles-containing vaccine and TST to varicella-containing vaccine and FluMist.

An interferon-gamma release assay (IGRA) tuberculosis test may be affected by live vaccines, so it is prudent to apply the same spacing rules as for TST and live vaccines.

Screening for Contraindications and Precautions to Vaccination

The key to preventing serious adverse reactions after vaccination is effective screening. Every patient should be screened for contraindications and precautions before administering any vaccine dose. Effective screening can be accomplished by asking a few questions:

Is the patient sick today?

There is no evidence that acute illness reduces vaccine efficacy or increases vaccine adverse events. However, as a precaution, if there is a moderate or severe acute illness, all vaccines should be deferred until the illness has improved. Mild illnesses (such as otitis media, URIs, and diarrhea) are *not* contraindications or precautions to vaccination and recommended vaccines should be administered on time.

Does the patient have allergies to medications, food, a vaccine component, or latex?

It may be more efficient to inquire about allergies in a generic way (i.e., allergies to any food or medication) rather than to inquire about allergies to specific vaccine components. Most persons will not be familiar with minor components of vaccines, but they should know if they or their child have had an allergic

NOTES

NOTES

reaction to a food or medication that was severe enough to require medical attention. If a person reports anaphylaxis after eating eggs, a specific protocol should be followed that includes determining the symptoms experienced. For information on egg allergies and influenza vaccination, please refer to the most recent ACIP influenza vaccination recommendations.

Has the patient experienced any reaction after receiving a vaccination?

A history of severe allergic reaction such as urticaria, wheezing or difficulty breathing, or circulatory collapse or shock (not fainting) following a previous dose of vaccine or to a vaccine component is a contraindication to further doses. A local adverse reaction (redness or swelling at the injection site) is not a contraindication to subsequent doses.

Some reactions after vaccination (e.g., Arthus reactions after a previous dose of diphtheria toxoid-containing or tetanus toxoid-containing vaccine) are considered as precautions to receiving further vaccine doses. ACIP recommends for persons with a history of Arthus-type hypersensitivity reactions after a previous dose of tetanus or diphtheria toxoid-containing vaccines should defer vaccination until at least 10 years have elapsed since the last tetanus toxoid-containing vaccine. Usually vaccines are deferred when a precaution is present. However, situations may arise when the benefit outweighs the risk (e.g., during a community pertussis outbreak).

Has the patient experienced a brain or other nervous system problem including seizures?

DTaP and Tdap are contraindicated for persons who have a history of encephalopathy not attributed to an identifiable cause within 7 days following DTaP, DTP, or Tdap vaccination. An unstable or progressive neurologic problem is a precaution for the use of DTaP and Tdap. Children with stable neurologic disorders (including seizures) unrelated to vaccination may be vaccinated as usual.

A history of GBS is a precaution for tetanus toxoid-containing and influenza vaccines, if it occurred within 6 weeks following a dose of the specific vaccine.

A personal or family history of febrile or afebrile seizures is a precaution for ProQuad vaccine. Simultaneous administration of MMR-II and Varivax is not associated with an increased risk of fever or seizures and is, therefore, preferred to ProQuad in children age 12 through 47 months.

Does the patient have a long-term health problem with heart, lung, kidney, or metabolic disease (e.g., diabetes), asthma, a blood disorder, no spleen, complement

**component deficiency, a cochlear implant, or a CSF leak?
Is the patient on long-term aspirin therapy?**

These conditions are contraindications or precautions to LAIV. Age-appropriate inactivated or recombinant influenza vaccine is preferred for patients with these conditions.

Does the patient have cancer, leukemia, HIV/AIDS, or any other immune system problem?

Live virus vaccines (e.g., MMR-II, Varivax, MMRV, Rotarix and RotaTeq, and FluMist) are usually contraindicated in severely immunocompromised persons. However, there are exceptions. For example, MMR-II and Varivax are recommended for HIV-infected children who do not have evidence of severe immunosuppression.

Does the patient have a parent or sibling with an immune system problem?

MMR, VAR, and MMRV vaccines should not be given to a person with a family history of congenital or hereditary immunodeficiency in first-degree relatives (i.e., parents, siblings) unless the immune competence of the potential vaccine recipient has been clinically substantiated or verified by a laboratory.

Has the patient taken medications that affect the immune system, such as prednisone, other steroids, or anticancer drugs; drugs for the treatment of rheumatoid arthritis, Crohn’s disease, or psoriasis; or has the patient had radiation treatment?

Live-virus vaccines (e.g., MMR-II, Varivax, FluMist) should be postponed until after chemotherapy or long-term, high-dose steroid therapy has ended.

Has the patient received a transfusion of blood or blood products, immune (gamma) globulin, or an antiviral drug in the past year?

Certain live-virus vaccines (i.e., MMR-II, ProQuad, and Varivax) may need to be deferred following administration of blood products, depending on the type of blood product and the interval since the blood product was administered.

Is the person pregnant or is there a chance she could become pregnant during the next month?

Live-virus vaccines (e.g., MMR-II, Varivax, FluMist) are contraindicated during pregnancy because of the theoretical risk of virus transmission to the fetus. Sexually active young women who receive MMR-II or Varivax should be instructed to practice careful contraception for 1 month following receipt of either vaccine. On theoretical grounds, inactivated poliovirus vaccine should not be administered during pregnancy; however,

NOTES

General Best Practice Guidance for Immunization

NOTES

Notes section with 23 horizontal lines.

it may be administered if the risk of exposure (e.g., during travel to endemic disease areas) is imminent and immediate protection is needed. HPV vaccine should not be administered to pregnant women. There is no recommendation to administer *H. influenzae* type b vaccine (ActHIB, Hiberix, PedvaxHIB), pneumococcal conjugate vaccine (Prevna 13), or serogroup B meningococcal vaccine (Bexsero, Trumenba) to a pregnant woman. Hepatitis A vaccine (Havrix, Vaqta), hepatitis B vaccine (Engerix-B, Recombivax HB), and meningococcal conjugate vaccine (Menactra, Menveo), should be administered to pregnant women if routinely recommended or indicated. Data on use of HepB-CpG (Heplisav-B), MenACWY-TT (MenQuadfi), and the pneumococcal polysaccharide vaccine (Pneumovax 23) during pregnancy are limited.

Has the patient received vaccinations in the past 4 weeks?

A person who received either Flumist or a live, injectable vaccine (e.g., MMR-II, Varivax) in the past 4 weeks should wait 28 days before receiving another live vaccine. Inactivated vaccines may be administered at the same time or at any time before or after a live vaccine.

Has the patient (if the patient is a baby) ever had intussusception?

Intussusception is a contraindication for the rotavirus vaccine

General Best Practice Guidance for Immunization

2

NOTES

Plotkin S. Vaccines, vaccination and vaccinology. *J. Infect Dis* 2003;187(9):1349-59.

Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: a global perspective. *Biol Blood Marrow Transplant* 2009;15:1143-238.

Wood R, Berger M, Dreskin S, et al. An algorithm for treatment of patients with hypersensitivity reactions after vaccines. *Pediatrics* 2008;122(3):e771-7.