



General Best Practice Guidelines for Immunization, Part I

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www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html

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General Best Practice Guidelines for Immunization



Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP)

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[Printer friendly version](#) [1.16 MB, 194 pages]

INTRODUCTION

Purpose and topics covered in this report...

METHODS

Method of development of: Timing and Spacing, Contraindications and Precautions, Preventing and Managing Adverse Reactions...

TIMING AND SPACING OF IMMUNOBIOLICS

Vaccine scheduling, supply and lapsed schedule, spacing of doses, simultaneous and nonsimultaneous administration, licensed combination



General Best
Practice
Guidelines

=

General
Recommendations

General Best Practice Guidelines for Immunization

- Timing and spacing
- Contraindications and precautions
- Preventing and managing adverse reactions to immunization
- Vaccine administration
- Storage and handling
- Altered immunocompetence
- Special situations
- Vaccination records
- Vaccination programs
- Vaccine information sources

General “Recommendations” on Immunization

- **Pink Book chapter**
 - Timing and spacing
 - Contraindications and precautions

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Timing
and
Spacing

Timing and Spacing Issues

- Interval between receipt of antibody-containing blood products and live vaccines
- Interval between doses of different vaccines not administered simultaneously
- Interval between subsequent doses of the same vaccine

Antibody-containing Blood Products

- Used to restore a needed component of blood or provide a passive immune response following disease exposure.
- Sometimes circumstance dictates the use of antibody-containing blood products along with a vaccine.

Antibody and Live Vaccines

General Rule

- Inactivated vaccines are generally not affected by circulating antibody to the antigen
- Live, attenuated vaccines might be affected by circulating antibody to the antigen – an effectiveness concern

Antibody Products and Measles- and Varicella-containing Vaccines

<u>Product given first</u>	<u>Action</u>
Vaccine	Wait 2 weeks before giving antibody
Antibody	Wait at least 3 months before giving vaccine

Appendix A24: Interval Between Antibody-Containing Products and Measles- and Varicella-Containing Vaccines

Appendix A

Recommended intervals between administration of immune globulin preparations and measles- or varicella-containing vaccine

Product / Indication	Dose, Including mg Immunoglobulin G (IgG)/kg body weight	Recommended Interval before measles or varicella-containing vaccine administration
Blood transfusion		
- Red blood cells (RBCs), washed	10 mL/kg (negligible IgG/kg) IV	None
- RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	3 months
- Packed RBCs (hematocrit 65%) ²	10 mL/kg (60 mg IgG/kg) IV	6 months
- Whole blood (hematocrit 35%-50%) ²	10 mL/kg (80-100 mg IgG/kg) IV	6 months
- Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	7 months
Botulinum Immune Globulin Intravenous (Human)	1.5 mL/kg (75 mg IgG/kg) IV	6 months
Cytomegalovirus IgIV	150 mg/kg maximum	6 months
Hepatitis A. IG		
- Contact prophylaxis	0.02 mL/kg (3.3 mg IgG/kg) IM	3 months
- International travel	0.06 mL/kg (10 mg IgG/kg) IM	3 months
Hepatitis B. IG (HBIG)	0.06 mL/kg (10 mg IgG/kg) IM	3 months
IgIV		
- Replacement therapy for immune deficiencies ³	300-400 mg/kg IV	8 months
- Immune thrombocytopenic purpura treatment	400 mg/kg IV	8 months
- Measles IG, contact prophylaxis (immunocompromised contact)	400 mg/kg IV	8 months
- Postexposure varicella prophylaxis	400 mg/kg IV	8 months
- Immune thrombocytopenic purpura treatment	1,000 mg/kg IV	10 months
Measles IG, contact prophylaxis		
- Standard (i.e., nonimmunocompromised) contact	0.5 mL/kg (80 mg IgG/kg) IM	6 months
Monoclonal antibody to respiratory syncytial virus F protein (Synagis™) ⁴	15 mg/kg (IM)	None
Rabies IG (RIG)	20 IU/kg (22 mg IgG/kg) IM	4 months
Tetanus IG (TIG)	250 units (10 mg IgG/kg) IM	3 months
Varicella IG ⁵	125 units/10 kg (60-200 mg IgG/kg) IM, maximum 625 units	5 months

This table is not intended for determining the correct indications and dosages for using antibody-containing products. Unvaccinated persons might not be fully protected against measles during the entire recommended interval, and additional doses of IG or measles vaccine might be indicated after measles exposure. Concentrations of measles antibody in an IG preparation can vary by manufacturer's lot. Rates of antibody clearance after receipt of an IG preparation also might vary. Recommended intervals are extrapolated from an estimated half-life of 30 days for passively acquired antibody and an observed interference with the immune response to measles vaccine for 5 months after a dose of 80 mg IgG/kg.

1. Does not include zoster vaccine. Zoster vaccine may be given with antibody-containing blood products.

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

3. Measles vaccination is recommended for children with mild or moderate immunosuppression from human immunodeficiency virus (HIV) infection, and varicella vaccination may be considered for children with mild or moderate immunosuppression from HIV, but both are contraindicated for persons with severe immunosuppression from HIV or any other immunosuppressive disorder.

4. Contains antibody only to respiratory syncytial virus.

5. Licensed VarIZIG is a purified human IG preparation made from plasma containing high levels of anti-varicella antibodies (IgG).

Adapted from Table 5, ACIP General Recommendations on Immunization

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Spacing of Antibody-containing Products and MMR and Varicella Vaccines

<u>Product</u>	<u>Interval</u>
Washed red blood cells	0 months
Hepatitis A (IG)	3 months
Measles prophylaxis (IG) (immunocompetent recipient)	6 months
Plasma/platelet products	7 months
Intravenous immune globulin (IGIV)	7-11 months

Exceptions to the General Rule

- Antibody-vaccine spacing recommendations apply specifically to MMR and varicella-containing vaccines
- Do NOT apply to:
 - Zoster vaccine (large amount of virus in the vaccine)
 - Yellow fever, oral typhoid vaccines (negligible antibody in the U.S. blood supply)
 - LAIV (viruses change annually)
 - Rotavirus (replication in GI tract)

Products Containing Type-specific or Negligible Antibody

□ Palivizumab (Synagis)

- Contains only monoclonal RSV antibody
- Does not interfere with live virus vaccination

□ Red blood cells (RBCs), washed

- Negligible antibody content

Interval Between Doses of Different Vaccines

- **Simultaneous administration**
- **Non-simultaneous administration**

Simultaneous Administration

General Rule

- **All vaccines can be administered at the same visit as all other vaccines.**
- **Exceptions:**
 - PCV13 and PPSV23: Give PCV13 first
 - MCV4-D (Menactra only) and PCV13 in asplenic or HIV infected persons: Give PCV13 first

Non-simultaneous Administration: Live-vaccine Effectiveness

Combination

2 live injected OR
1 live injected and 1 intranasal
influenza vaccine

All other vaccines

One exception
Menactra and DTaP

Minimum interval

4 weeks

None

6 months

Spacing of Live Vaccines Not Given Simultaneously

- If 2 live parenteral or intranasal vaccines are given less than 28 days apart, the vaccine given second should be repeated.
- Antibody response from first vaccine interferes with replication of second vaccine.

Intervals Between Doses

General Rule

- Increasing the interval between doses of a multidose vaccine does not diminish the effectiveness of the vaccine.

Extended Interval Between Doses

- Not all variations among all schedules for all vaccines have been studied
- Available studies of extended intervals have shown no significant difference in final titer
- It is not necessary to restart the series or add doses because of an extended interval between doses

Intervals Between Doses

General Rule

- Increasing the interval between doses of a multidose vaccine does not diminish the effectiveness of the vaccine.
- Decreasing the interval between doses of a multidose vaccine may interfere with antibody response and protection.

Recommended and Minimum Ages and Intervals Between Doses of Routinely Recommended Vaccines ^{1,2,3,4}				
Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
Diphtheria-tetanus-acellular pertussis (DTaP)-1 ⁹	2 months	6 weeks	8 weeks	4 weeks
DTaP-2	4 months	10 weeks	8 weeks	4 weeks
DTaP-3	6 months	14 weeks	6-12 months ⁶	6 months ⁶
DTaP-4	15-18 months	15 months ⁶	3 years	6 months
DTaP-5 ⁷	4-6 years	4 years	—	—
<i>Haemophilus influenzae type b (Hib)-1⁸</i>	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3 ⁹	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	—	—
Hepatitis A (HepA)-1 ⁵	12-23 months	12 months	6-18 months	6 months
HepA-2	≥18 months	18 months	—	—
Hepatitis B (HepB)-1	Birth	Birth	4 weeks-4 months	4 weeks
HepB-2	1-2 months	4 weeks	8 weeks-17 months	8 weeks
HepB-3 ¹⁰	6-18 months	24 weeks	—	—
Herpes zoster (HZV) ¹¹	≥60 years	60 years	—	—
Human papillomavirus (HPV)-1 ¹²	11-12 years	9 years	8 weeks	4 weeks
HPV-2	11-12 years	9 years	4 months	12 weeks ¹²
HPV-3 ^{12,13}	11-12 years	9 years	—	—
Influenza, inactivated (IIV) ¹⁴	≥6 months	6 months ¹⁵	4 weeks	4 weeks
Influenza, live attenuated (LAIV) ¹⁴	2-49 years	2 years	4 weeks	4 weeks
Measles-mumps-rubella (MMR)-1 ¹⁶	12-15 months	12 months	3-5 years	4 weeks
MMR-2 ¹⁶	4-6 years	13 months	—	—
Meningococcal conjugate (MenACWY)-1 ¹⁷	11-12 years	6 weeks ¹⁸	4-5 years	8 weeks
MenACWY-2	16 years	11 years ¹⁹	—	—
Meningococcal polysaccharide (MPSV4)-1 ¹⁶	—	2 years	5 years	5 years
MPSV4-2	—	7 years	—	—
Pneumococcal conjugate (PCV13)-1 ⁸	2 months	6 weeks	8 weeks	4 weeks
PCV-2	4 months	10 weeks	8 weeks	4 weeks
PCV-3	6 months	14 weeks	6 months	8 weeks
PCV-4	12-15 months	12 months	—	—
Pneumococcal polysaccharide (PPSV)-1	—	2 years	5 years	3 years
PPSV-2 ²⁰	—	7 years	—	—
Poliovirus, Inactivated (IPV)-1 ⁵	2 months	6 weeks	8 weeks	4 weeks
IPV-2	4 months	10 weeks	8 weeks-14 months	4 weeks
IPV-3	6-18 months	14 weeks	3-5 years	6 months
IPV-4 ²¹	4-6 years	4 years	—	—
Rotavirus (RV)-1 ²²	2 months	6 weeks	8 weeks	4 weeks
RV-2	4 months	10 weeks	8 weeks	4 weeks
RV-3 ²²	6 months	14 weeks	—	—
Tetanus-diphtheria (Td)	11-12 years	7 years	10 years	5 years
Tetanus-diphtheria-acellular pertussis (Tdap) ²³	≥11 years	7 years	—	—
Varicella (Var)-1 ¹⁶	12-15 months	12 months	3-5 years	12 weeks ²⁴
Var-2 ¹⁶	4-6 years	15 months ²⁵	—	—

Centers for Disease Control and Prevention
Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th Edition

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**Recommended and Minimum Ages and Intervals
Between Doses of Routinely Recommended Vaccines^{1,2,3,4}**

Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
Diphtheria-tetanus-acellular pertussis (DTaP)-1 ⁵	2 months	6 weeks	8 weeks	4 weeks
DTaP-2	4 months	10 weeks	8 weeks	4 weeks
DTaP-3	6 months	14 weeks	6-12 months	6 months ⁶
DTaP-4 ⁶	15-18 months	12 months ⁶	3 years	6 months
DTaP-5	4-6 years	4 years	—	—
<i>Haemophilus influenzae type b (Hib)-1^{b,7}</i>	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3 ⁸	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	—	—
Hepatitis A (HepA)-1 ⁵	12-23 months	12 months	6-18 months	6 months
HepA-2	≥18 months	18 months	—	—
Hepatitis B (HepB)-1 ^b	Birth	Birth	4 weeks-4 months	4 weeks
HepB-2	1-2 months	4 weeks	8 weeks-17 months	8 weeks
HepB-3 ⁹	6-18 months	24 weeks	—	—

Minimum Intervals and Ages

- Vaccine doses should not be administered at intervals less than the minimum intervals or earlier than the minimum age.

When Can Minimum Intervals Be Used?

- Catch-up for a lapsed vaccination schedule**
- Impending international travel**
- NOT to be used routinely**

The “Grace Period”

- ACIP recommends that vaccine doses given up to four days before the minimum interval or age be counted as valid
- Should not be used for scheduling future vaccination visits
- Use for reviewing vaccination records

Use of the “Grace Period”

- To schedule a future appointment **NO!**
- When evaluating a vaccination record **Yes**
- Client is in the office or clinic early **Maybe**

Use of the “Grace Period”

Client is in the office or clinic

- Client/parent is known and dependable Reschedule
- Client/parent is unknown or undependable Vaccinate

Use of the “Grace Period”

- **Basic principles**
 - The recommended interval or age is preferred
 - The minimum interval can be used to catch up
 - The grace period is last resort

Violations of Minimum Intervals and Minimum Ages

- Grace period may conflict with some state school entry requirements
- Immunization programs and/or school entry requirements may not accept some or all doses given earlier than the minimum age or interval, particularly varicella and/or MMR vaccines
- Providers should comply with local and/or state immunization requirements

Violations of Minimum Intervals and Minimum Ages

- Minimum interval/age has been violated**
 - Dose invalid**
- The repeat dose should be administered at least a minimum interval from the invalid dose**

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Contraindications & Precautions

Vaccine Adverse Reaction

- **Adverse reaction**

- Extraneous effect caused by vaccine
- “Side effect”

Vaccine Adverse Reaction

- **Adverse reaction**
- **Adverse event**
 - Any medical event following vaccination
 - May be true adverse reaction
 - May be only coincidental

Vaccine Adverse Reactions

- Local
 - Pain, swelling, redness at site of injection
 - Common with inactivated vaccines
 - Usually mild and self-limited

Vaccine Adverse Reactions

- Local
- Systemic
 - Fever, malaise, headache
 - Nonspecific
 - May be unrelated to vaccine

Live, Attenuated Vaccines

- Must replicate to produce immunity
- Symptoms usually mild
- Occur after an incubation period
(usually 3-21 days)

Vaccine Adverse Reactions

- Local
- Systemic
- Allergic
 - Due to vaccine or vaccine component
 - Rare
 - Risk minimized by screening

Contraindication

- A condition in a recipient that greatly increases the chance of a serious adverse event

Precaution

- A condition in a recipient that may increase the chance or severity of an adverse event
- May compromise the ability of the vaccine to produce immunity
- Might cause diagnostic confusion

Permanent Contraindications

- Severe allergic reaction to a prior dose of vaccine or to a vaccine component

Permanent Contraindications

- **Rotavirus vaccines only**
 - Severe Combined Immunodeficiency disease (SCID)
 - History of intussusception

- **Pertussis vaccines only**
 - Encephalopathy not due to another identifiable cause occurring within 7 days of pertussis vaccination

Contraindications and Precautions

<u>Condition</u>	<u>Live</u>	<u>Inactivated</u>
Allergy to component	C	C
Encephalopathy	---	C
Pregnancy	C	V*
Immunosuppression	C	V
Moderate/severe illness	P	P
Recent blood product	P**	V

C=contraindication

P=precaution

V=vaccinate if indicated

*Except HPV

**MMR and varicella-containing (except zoster vaccine and LAIV)

<https://www.cdc.gov/vaccines/hcp/acip-recommendations/general-recommendations/contraindications.html>

Hepatitis A	(39)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
Hepatitis B	(40)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Hypersensitivity to yeast	Moderate or severe acute illness with or without fever
Hib	(41)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Age <6 weeks	Moderate or severe acute illness with or without fever
HPV	(42)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Pregnancy Moderate or severe acute illness with or without fever
IIV	(43)	Severe allergic reaction (e.g., anaphylaxis) after previous dose of influenza vaccine or to vaccine component.	GBS <6 weeks after a previous dose of influenza vaccine Moderate or severe acute illness with or without fever Egg allergy other than hives, e.g., angioedema, respiratory distress, lightheadedness, recurrent emesis; or required epinephrine or another emergency medical intervention (IIV may be administered in an inpatient or outpatient medical setting and under the supervision of a health care provider who is able to recognize and manage severe allergic conditions).
IPV	(44)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Pregnancy Moderate or severe acute illness with or without fever

Vaccination During Pregnancy

- Live vaccines should not be administered to women known to be pregnant.
- In general, inactivated vaccines may be administered to pregnant women for whom they are indicated.
- HPV vaccine should be deferred during pregnancy.

Vaccination during Pregnancy

- Inactivated vaccines – influenza and Tdap
- Other vaccines
- In general, inactivated vaccines can be administered
 - NO CONTRAINDICATIONS
 - Precautions (risk-benefit decision) – MenB, IPV
 - Special considerations: <https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html> and <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-indications.html>
 - RZV, HPV-delay
 - Hib, PCV13-no recommendations language at all
 - HepA, HepB, MenACWY, PPSV23 – give if another risk factor is present

Vaccination of Immunosuppressed Persons

- Live vaccines should not be administered to severely immunosuppressed persons.
- Persons with isolated B-cell deficiency (i.e. deficiency in humoral immunity) may receive varicella and zoster vaccine.
- Inactivated vaccines are safe to use in immunosuppressed persons, but the response to the vaccine may be decreased.

Immunosuppression

- **Disease**

- Congenital immunodeficiency
- Leukemia or lymphoma
- Generalized malignancy

- **Cancer Therapy**

- Alkylating agents
- Antimetabolites
- Radiation

Immunosuppressive Drugs

- Immune mediators**
- Immune modulators**
- Iso-antibodies (therapeutic monoclonal antibodies)**
 - Antitumor necrosis factor agents
 - B-lymphocyte depleting agent
- Transplant rejection suppression**
- Checkpoint inhibition**

Corticosteroids and Immunosuppression

- The amount or duration of corticosteroid therapy needed to increase adverse event risk is not well-defined.
- Dose generally believed to be a concern:
 - 20 mg or more/day of prednisone for 2 weeks or longer
 - 2 mg/kg per day or more of prednisone for 2 weeks or longer

Corticosteroids and Immunosuppression

- Does NOT apply to aerosols, topical, alternate-day, short courses (less than 2 weeks), physiologic replacement schedules
- Delay live vaccines for at least 1 month after discontinuation of high-dose therapy

Vaccination of Immunosuppressed Persons

Safety:

- Immunocompromised persons are at increased risk of adverse events following live vaccines.
- Live vaccines may be administered at least 3 months following termination of chemotherapy (at least 1 month after high -dose steroid use of 2 weeks or more).
- LAIV, MMR, varicella, and rotavirus vaccines may be administered to susceptible household and other close contacts.

Vaccination of Immunosuppressed Persons

- **Safety and efficacy**
- **Anti-tumor necrosis factor inhibitors**
 - Wait 3 months after stopping medication before administering live vaccines
 - Do not initiate medication until 1 month after the live vaccine
- **Other iso-antibodies (e.g., anti-B cell antibodies aka lymphocyte depleting agents, checkpoint inhibition)**
 - Some experts recommend up to 6 months

Persons with HIV Infection

- Persons with HIV/AIDS are at increased risk for complications of measles, varicella, influenza, and pneumococcal disease.

Live, Attenuated Vaccines for Persons with HIV/AIDS*

<u>Vaccine</u>	<u>Asymptomatic</u>	<u>Symptomatic*</u>
Varicella	Yes	No
Zoster	No	No
MMR	Yes	No
MMRV	No	No
LAIV	No	No
Rotavirus	Consider	Consider
Yellow Fever	Consider	No

Yes=vaccinate No=do not vaccinate

*See specific ACIP recommendations for details.