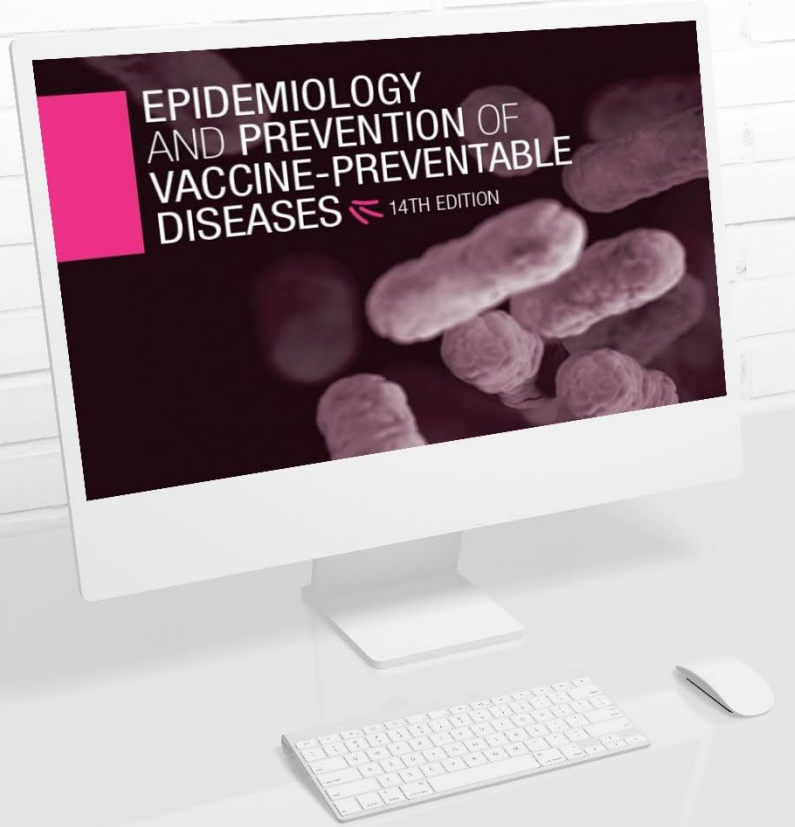
National Center for Immunization and Respiratory Diseases

General Best Practices for Immunization, Part 1



Pink Book Web-on-Demand Series

July 9, 2024

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Learning Objectives

- Describe the fundamental principles of the immune response.
- Describe immunization best practices.
- Describe an emerging immunization issue.
- For each vaccine-preventable disease, identify those for whom routine immunization is recommended.
- For each vaccine-preventable disease, describe characteristics of the vaccine used to prevent the disease.
- Locate current immunization resources to increase knowledge of team's role in program implementation for improved team performance.

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Introduction

General Best Practices 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

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

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Timing and Spacing

Timing and Spacing – Categories of Vaccine

Vaccine Category	Examples	
Live	Oral adenovirus vaccine*	
Live attenuated	ACAM2000 smallpox vaccine Bacille Calmette Guerin (BCG) vaccine Dengue vaccine Ebola vector vaccine Live attenuated influenza vaccine (LAIV) Live oral typhoid vaccine (Ty21a)	Measles-mumps-rubella – containing (MMR, MMRV) Oral cholera vaccine Rotavirus vaccines (RV1, RV5) Varicella (Var) vaccine Yellow Fever vaccine
Non-live	Anthrax vaccine COVID-19 vaccines (Pfizer, Moderna, Novavax) *Haemophilus influenzae* type b (Hib) vaccines Hepatitis A (HepA) vaccines Hepatitis B (HepB) vaccines Human papillomavirus (HPV) vaccines Inactivated poliovirus vaccine (IPV) Inactivated typhoid vaccine (Typhim Vi) Influenza vaccines (IIV4, RIV4)	Japanese Encephalitis Vaccine (JEV) Meningococcal conjugate (MenACWY) vaccine Pneumococcal conjugate vaccines (PCV20, PCV15) Pneumococcal polysaccharide vaccine (PPSV23) Rabies vaccine Recombinant zoster vaccine (RZV) Respiratory syncytial virus vaccine (RSV) Serogroup B meningococcal (MenB) vaccines (MenB-FHbp, MenB-4C) Tetanus-toxoid, diphtheria-toxoid, or pertussis-containing vaccines (DTaP, Tdap, DT, Td, DTaP-HepB-IPV, DTaP-IPV/Hib, DTaP-IPV, DTaP-IPV-Hib-HepB)†
Non-replicating§	Jynneos smallpox/mpox vaccine	

(*) Oral adenovirus vaccine is used primarily in the military for prevention of adenovirus infection.
(†) The tetanus-toxoid components of these vaccines are toxoids, not vaccines.
(§) These vaccines do not replicate and therefore behave like non-live vaccines.

https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html

Timing and Spacing Issues

- **Interval between**
  - Receipt of antibody-containing blood products and live vaccines
  - Doses of different vaccines not administered simultaneously
  - 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**
  - Non-live 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

Product given first		**Interval**
Vaccine	→	Wait 2 weeks before giving antibody

Antibody Products and Measles- and Varicella-Containing Vaccines

Product given first		**Interval**
Vaccine	→	Wait 2 weeks before giving antibody

Action if interval violated

Test for immunity, or repeat dose. If dose is repeated, administer after the recommended interval.

Antibody Products and Measles- and Varicella-Containing Vaccines

Product given first		**Interval**
Antibody	→	Wait at least 3 months before giving vaccine

Antibody Products and Measles- and Varicella-Containing Vaccines

Product given first		**Interval**
Antibody	→	Wait at least 3 months before giving vaccine

Action if interval violated

Repeat dose; administer at the interval indicated for the antibody-containing product.

Spacing of Antibody-Containing Products and MMR and Varicella Vaccines

Product	Interval
Washed red blood cells	0 months
Hepatitis A (IG)	3 months
Measles prophylaxis (IG) (immunocompetent recipient)	6 months
Plasma/platelet products	7 months
Immune globulin intravenous (IGIV)	7 through 11 months

Examples of Products Containing Type-Specific or Negligible Antibody

- **Nirsevimab (Beyfortus)**
  - Contains only monoclonal RSV antibody
  - Does not interfere with live-virus vaccination
- **Red blood cells (RBCs), washed**
  - Negligible antibody content

Exceptions to the General Rule

Antibody-vaccine spacing recommendations apply to:

- MMR-containing vaccines
- Varicella-containing vaccines
- Dengue vaccine

These recommendations Do NOT apply to:

- Yellow fever vaccine (negligible antibody in the U.S. blood supply)
- Oral typhoid vaccines (negligible antibody in the U.S. blood supply)
- LAIV (viruses change annually)
- Rotavirus (replication in GI tract)

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Knowledge Check

Which type of vaccine is affected by antibody?

A. Live vaccines
B. Non-live vaccines

Answer

Which type of vaccine is affected by antibody?

A. Live vaccines ⟵

B. Non-live vaccines

Interval Between Doses of Different Vaccines

- **Simultaneous administration: same clinic day**
- **Non-simultaneous administration: different clinic day**

Simultaneous Administration

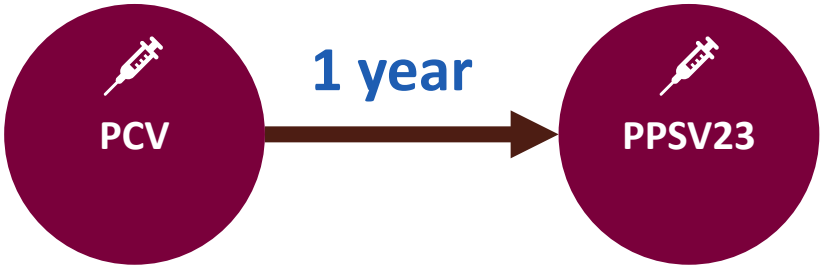
- **General Rule**
  - Most vaccines can be administered at the same visit as all other vaccines.

- **Exceptions**
  - PCV and PPSV23: Give PCV first
  - Jynneos or ACAM2000, and COVID-19 vaccine: consider separating 4 weeks

Pneumococcal Vaccine Recommendations | CDC, Interim Clinical Considerations for Use of JYNNEOS Vaccine for Mpox Prevention in the United States | Mpox | Poxvirus | CDC

Simultaneous Administration

- **PCV and PPSV23: Give PCV first**



Pneumococcal Vaccine Recommendations | CDC

Simultaneous Administration

- **Jynneos or ACAM2000, and COVID-19 vaccines**
  - Risk of myocarditis, particularly with ACAM2000 and mRNA COVID-19 vaccines
  - Risk of myocarditis, particularly in adolescent males
  - Consider 4 weeks between the two vaccines
  - Need to weigh risk and benefits, particularly in outbreak settings

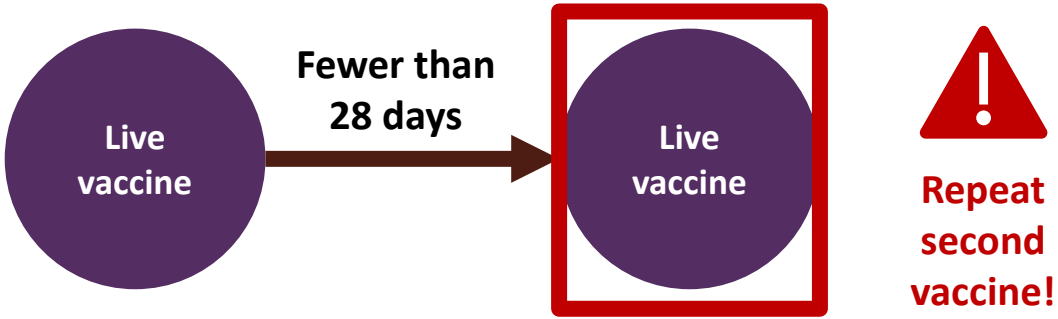
Interim Clinical Considerations for Use of JYNNEOS Vaccine for Mpox Prevention in the United States | Mpox | Poxvirus | CDC

Non-Simultaneous Administration: Live-Vaccine Effectiveness

Combination	Minimum interval
2 live injected ***or*** 1 live injected and 1 intranasal influenza vaccine	4 weeks
All other vaccines	None

Spacing of Live Vaccines Not Given Simultaneously

- If 2 live parenteral or intranasal vaccines are given fewer 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 Vaccine Doses

Vaccine dose and number	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
DEN4CYD-1	9-16 years	9 years	6 months	5 months after age at 1st dose
DEN4CYD-2	9-16 years	9 years + 5 months	6 months	5 months after age at second dose
DEN4CYD-3	9-16 years	9 years + 10 months	---	---
DTaP-1(e)	2 months	6 weeks	8 weeks	4 weeks
DTaP-2	2 months	10 weeks	8 weeks	4 weeks
DTaP-3	6 months	14 weeks	6-12 months(f)	6 months(f)
DTaP-4	15-18 months	15 months(f)	3 years	6 months
DTaP-5(g)	4-6 years	4 years	---	---
HepA-1(e)	12-23 months	12 months	6-18 months	6 months
HepA-2	≥18 months	18 months	---	---

See Table 3-2 at https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html#t-02 for full table and footnotes

Minimum Intervals and Ages

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

Special Circumstances for use of Intervals Shorter than Recommended Intervals

- **Catch-up for a lapsed vaccination schedule**
- **Impending international travel**

- **Not be used routinely**

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- Catch-up for a lapsed vaccination schedule
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The “Grace Period”

- **Recommended that vaccine doses given up to 4 days before the minimum interval or age be counted as valid**

Dose 1 given 1/01/2023

January 2023						
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Grace period in which dose counts

Minimum interval for dose 2 = 4 weeks

When to Use the “Grace Period”

Use of Grace Period	Recommendation
To schedule a future appointment	✗ No
When evaluating a vaccination record	✓ Yes
Patient is in the office or clinic early	? Maybe

Use of the “Grace Period”: Patient is in the Office/Clinic Early

Patient Characteristic	Recommended Action
Patient/parent is known and dependable	Reschedule
Patient/parent is unknown or not dependable	Vaccinate today

Use of the “Grace Period”

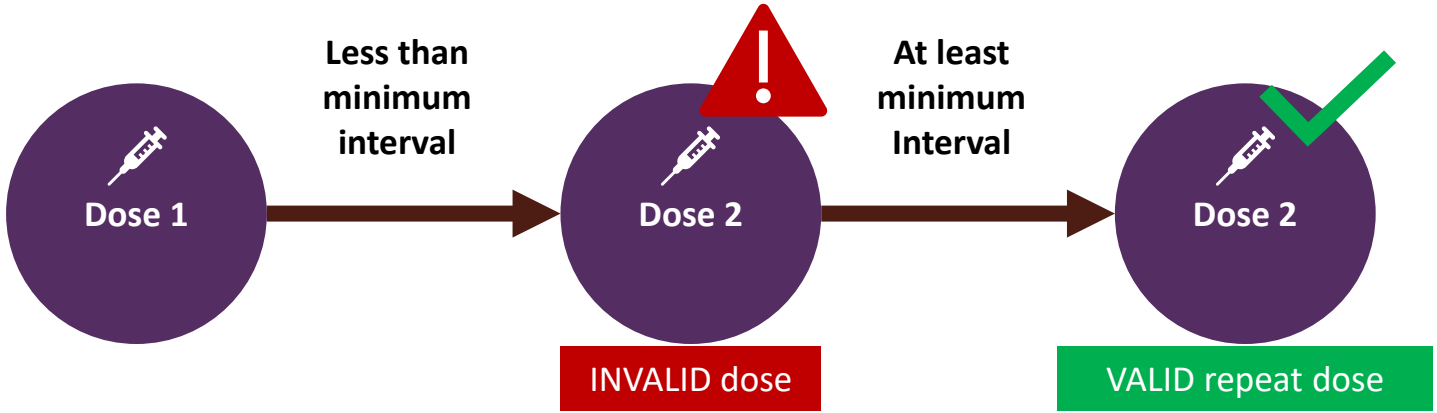
- **Basic principles**
  - The recommended interval or age is preferred.
  - The minimum interval can be used to catch up.
  - The grace period is last resort.

Violations of Minimum Intervals and Minimum Ages

- **Grace period may conflict with some state school entry requirements.**
- **Some doses given earlier than the minimum age or interval might violate immunization program or school entry requirements, 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 Event

- **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 non-live vaccines
  - Usually mild and self-limited

Vaccine Adverse Reactions

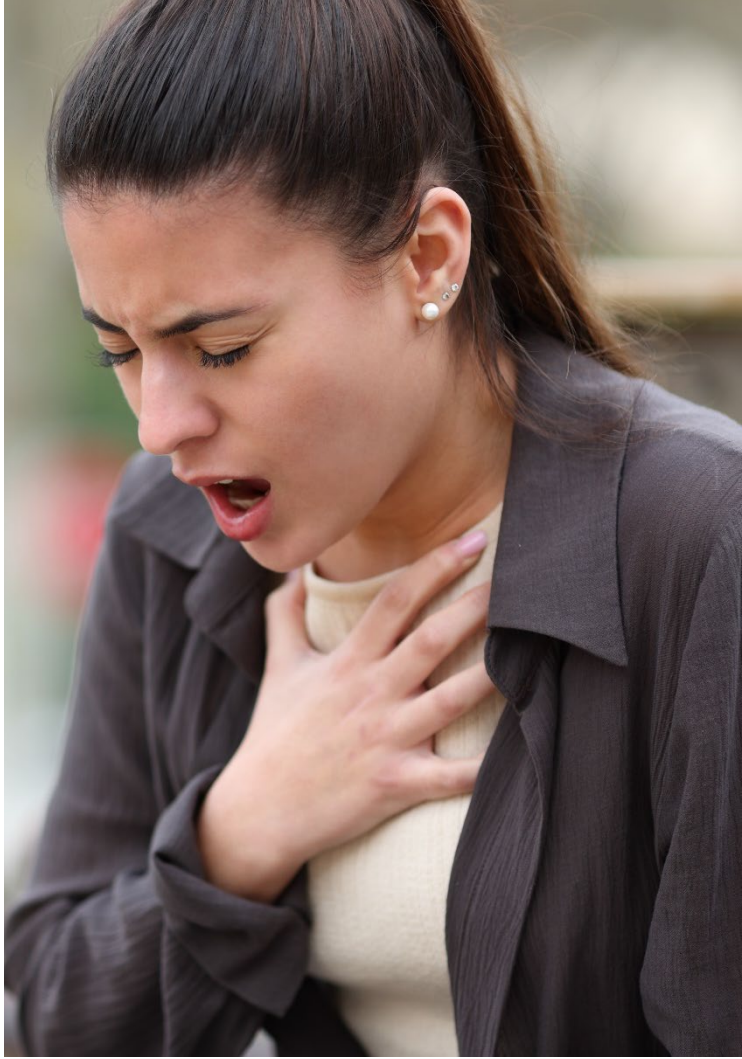
- **Systemic**
  - Fever, malaise, headache
  - Nonspecific
  - May be unrelated to vaccine

Live, Attenuated Vaccines

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

Vaccine Adverse Reactions

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



Contraindication

- **A condition in a recipient that increases the risk for a serious adverse reaction**

ACIP Contraindications Guidelines for Immunization | CDC

Precaution

- **A condition in a recipient that….**
  - Might increase the risk of an adverse reaction

  Or

  - Might compromise the ability of the vaccine to produce immunity

  Or

  - Might cause diagnostic confusion

ACIP Contraindications Guidelines for Immunization | CDC

Contraindications and Precautions

Condition	Live	Non-live
Allergy to component	Contraindication	Contraindication
Encephalopathy	---	Contraindication*
Pregnancy	Contraindication	Vaccinate, if indicated**
Immunosuppression	Contraindication	Vaccinate, if indicated
Moderate/severe illness	Precaution	Precaution
Recent blood product	Precaution***	Vaccinate, if indicated

*Applies only to pertussis-containing vaccines
**Except HPV, HepB (Heplisav, Prehevbrio), and consider RZV
***MMR and varicella-containing

Knowledge Check

A 3-year-old child is due for vaccines today, but she is taking antibiotics for an ear infection. Can she be vaccinated with:

A. Live, attenuated vaccines

B. Non-live vaccines

C. Both live, attenuated and non-live vaccines

Answer

A 3-year-old child is due for vaccines today, but she is taking antibiotics for an ear infection. Can she be vaccinated with:

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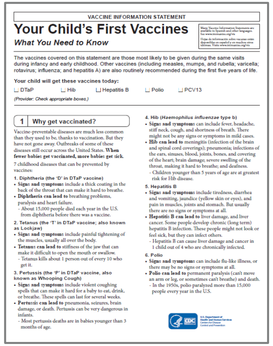
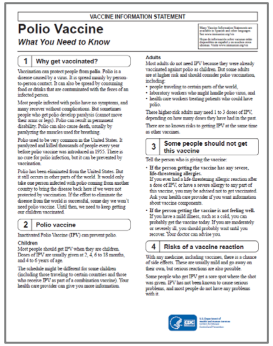
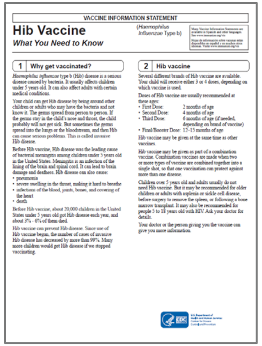
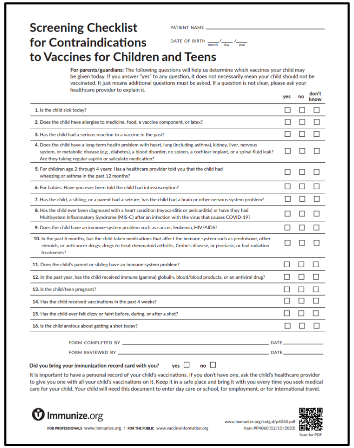
C. Both live, attenuated and non-live vaccines ⟵

Vaccine Information Statement (VIS) and Screening Checklist









[Vaccine Information Statement | Current VISs | CDC](https://www.immunize.org/catg.d/p4060.pdf), https://www.immunize.org/catg.d/p4060.pdf

Vaccination During Pregnancy

- **Live vaccines should *not* be administered to persons known to be pregnant.**

- **In general, non-live vaccines may be administered to pregnant persons for whom they are indicated.**
  - **Exceptions:** HepB (Heplisav, Prehevbrio), HPV; RZV – consider deferring during pregnancy

Vaccination During Pregnancy

- **Recommended non-live vaccines – influenza, Tdap, RSV, COVID-19**
- **In general, inactivated vaccines can be administered**
  - No contraindications
  - Precautions (risk-benefit decision) – MenB, IPV
  - Special considerations:
    - HPV, HepB (Prehevbrio, Heplisav) – delay, RZV consider delay
    - Hib, PCV – no recommendations language at all
    - HepA, HepB (Engerix-B, Recombivax HB), MenACWY, PPSV23 – give if another risk factor is present

https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html and https://www.cdc.gov/vaccines/schedules/hcp/imz/child-indications.html

Vaccination of Immunosuppressed Persons

- **Live vaccines should *not* be administered to severely immunosuppressed persons – due to safety concerns.**
- **Persons with isolated deficiency in humoral immunity may receive varicella vaccines.**
- **Non-live 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
  - HIV
  - Immunosuppressive drugs

Persons with HIV Infection

- **Persons with HIV/AIDS are at increased risk for complications of measles, varicella, influenza, meningococcal, and pneumococcal disease.**
- **ACIP recommends vaccination with non-live vaccines.**
- **ACIP qualifies its vaccination recommendation with live, attenuated vaccines.**

Live, Attenuated Vaccines for Persons with HIV/AIDS*

Vaccine	Asymptomatic	Symptomatic*
Varicella	Yes	Consider
MMR	Yes	Consider
MMRV	No	No
LAIV	No	No
Rotavirus	Consider	Consider
Yellow fever	Consider	Consider
Dengue	Consider	No

Yes=vaccinate No=do not vaccinate

*See specific ACIP recommendations for details

Immunosuppressive Drugs

- **Corticosteroids**
- **Cancer therapy**
- **Biologic response modifiers**
  - Isoantibodies
  - Chimeric Antigen Receptor T-Cell (CAR-T) agents
  - Checkpoint inhibition therapies
  - Transplant rejection therapies
  - Lymphocyte depleting agents

Corticosteroids and Immunosuppression

- **The amount or duration of corticosteroid therapy needed to increase the adverse event risk is not well-defined.**
- **Dose generally believed to be a concern**
  - 20 mg or more per 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

- **Delay live vaccines for at least 1 month after discontinuation of high-dose therapy.**
- **Does *not* apply to aerosols, topical, alternate-day, short courses (less than 2 weeks), physiologic replacement schedules**
- **No interval required after non-live vaccination prior to initiation of corticosteroids**
  - 2 week interval required after live vaccination prior to initiation of corticosteroids

Cancer Therapy and Immunosuppression

- **Treatments: antimetabolites, methylating agents, mitotic spindle inhibitors, radiation therapy**
- **Safety considerations: Delay live vaccines until 3 months following conclusion of therapy, and patient is deemed immunocompetent.**
- **Effectiveness considerations: Consider delaying non-live vaccines 3 months following conclusion of therapy; a partial response is better than no response (doses may need to be repeated).**

Biologic Response Modifiers and Immunosuppression

- **Isoantibodies**
  - Tumor necrosis factor inhibitors
  - Janus kinase inhibitors
  - Cytokine inhibitors
- **Chimeric antigen receptor T-Cell (CAR-T) agents**
  - CD19 directed
  - B-cell maturation antigen directed
- **Checkpoint inhibition**
  - PD-1 Agonists
- **Other transplant rejection therapies**
  - Mycophenolate mofetil
  - Calcineurin agents
- **Lymphocyte depleting agents**
  - Thymoglobulin
  - B-cell depleting (CD20) inhibitors
  - General lymphocyte depleting (CD52) inhibitors

Biologic Response Modifiers and Immunosuppression

- **Safety Considerations**
  - If prior to therapy initiation, delay initiation for 1 month following a live vaccine.
  - If currently on therapies, delay re-initiation for 2 weeks following a live vaccine.
  - Delay live vaccines for 3 months following cessation of isoantibodies.
  - Delay live vaccines for 3-6 months for following cessation of transplant rejection therapy, CAR-T cells and checkpoint inhibition.
  - Delay live vaccines for 6 months for lymphocyte depleting agents following cessation of medication.

Biologic Response Modifiers and Immunosuppression

- **Effectiveness Considerations**
  - Live vaccines and non-live vaccines may be delayed following these therapies, per provider discretion.

Immunosuppressive Drugs and Vaccines

- **The determination of immunosuppression (and by extension, the duration of withholding of therapy) is the discretion of the treating provider.**

Other General Vaccination Principles: Altered Immunocompetence

- **Altered Immunocompetence is also an opportunity to screen for specific vaccine indications (not only contraindications and precautions).**

- **Household contacts of persons with altered immunocompetence should be vaccinated with either live or non-live vaccines.**

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https://www.train.org/cdctrain/welcome

E-mail Your Immunization Questions to us

NIPINFO@cdc.gov

Thank You From Atlanta!

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