General Best Practice Guidelines for Immunization, Part I

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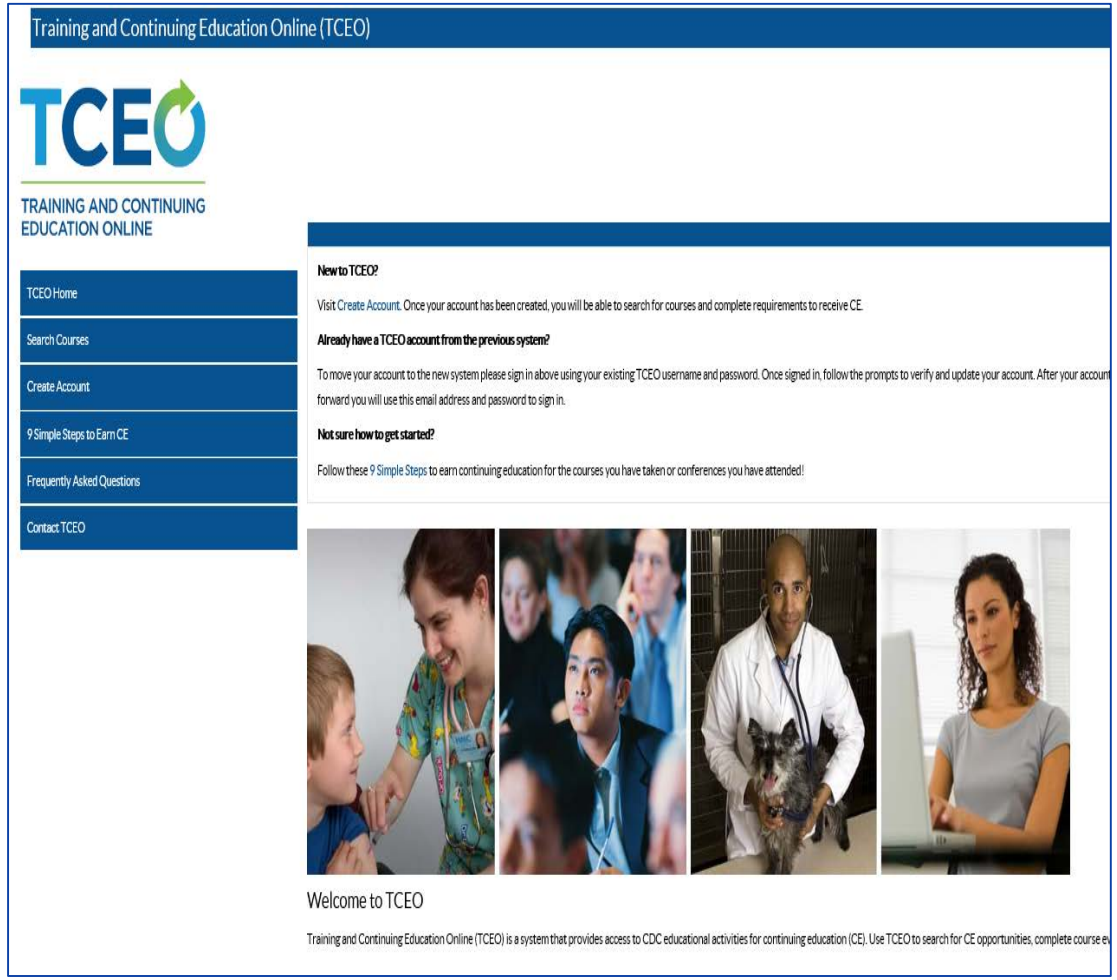
Learning Objectives

- Describe the Advisory Committee on Immunization Practices General Best Practice Guidelines on Immunization.
- 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.
- Implement disease detection and prevention health care services (e.g., smoking cessation, weight reduction, diabetes screening, blood pressure screening, immunization services) to prevent health problems and maintain health.

Continuing Education Information

- **CE credit, go to**: https://tceols.cdc.gov/
- **Search course number: WD4564-071222**
- **CE credit expires: July 1, 2024**
- **CE instructions are available on the Pink Book Web-on-Demand Series web page**
- **Questions and additional help with the online CE system, e-mail CE@cdc.gov**



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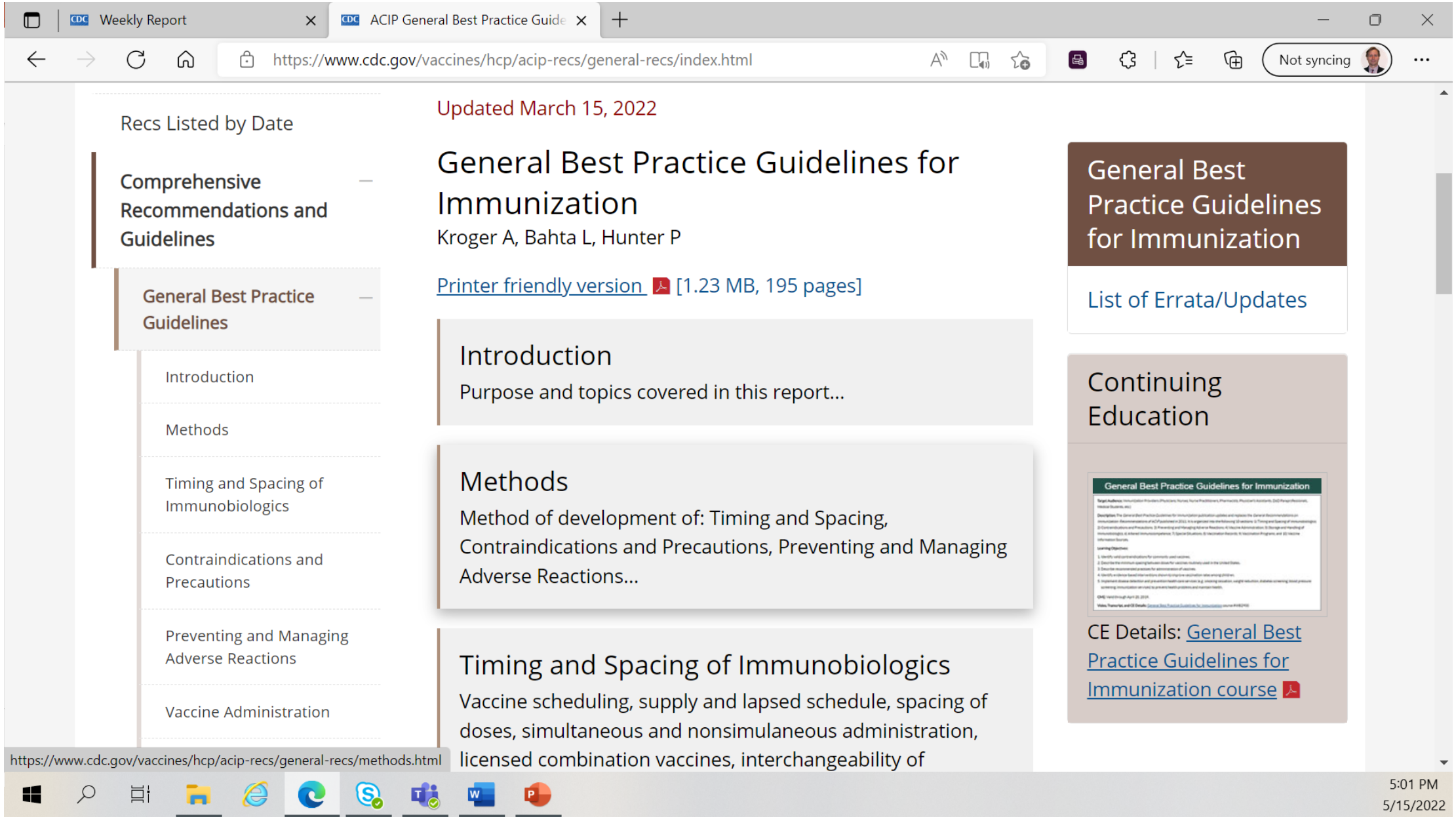
Introduction



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

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

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Timing and Spacing

Timing and Spacing – Categories of Vaccine

TABLE 3-1 Types of Vaccines

Vaccine Category	Examples
Live	Oral adenovirus vaccine*
Live attenuated	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) *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 (PCV13, PCV20, PCV15) Pneumococcal polysaccharide vaccine (PPSV23) Rabies vaccine Recombinant zoster vaccine (RZV) 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§	COVID-19 vaccine (Janssen) Jynneos smallpox/monkeypox vaccine

* Oral adenovirus vaccine is used primarily in the military for prevention of adenovirus infection. It should not be confused with Janssen COVID-19 vaccine which is used for the prevention of SARS-CoV-2 infection

† The tetanus-toxoid components of these vaccines are toxoids, not vaccines.

§ These vaccines do not replicate and therefore behave like non-live vaccines.

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**
  - 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	Action
Vaccine	Wait 2 weeks before giving antibody
Antibody	Wait at least 3 months before giving vaccine

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
Intravenous immune globulin (IGIV)	7–11 months

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

Exceptions to the General Rule

- **Antibody-vaccine spacing recommendations apply specifically to MMR and varicella-containing vaccines, and dengue vaccine.**

- **Do NOT apply to:**
  - yellow fever, oral typhoid vaccines (negligible antibody in the U.S. blood supply)
  - LAIV (viruses change annually)
  - rotavirus (replication in GI tract)

Antibody-Containing Blood Products – Dengue Vaccine

- All potential vaccinees need to have laboratory diagnostic screening prior to vaccination.
- Antibody-containing blood products may generate false-positive screening results.
- 12 months between antibody-containing blood products and dengue screening
- Default timing and spacing issue between antibody-containing blood products and dengue vaccine

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**

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:**
  - PCV and PPSV23: Give PCV13 first
  - MenACWY-D (Menactra only) and PCV in asplenic or HIV-infected persons: Give PCV first

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
One exception Menactra and DTaP	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.

TABLE 3-2. Recommended and minimum ages and intervals between vaccine doses[a],[b],[c],[d]

Known as the "grace period", 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

"3 calendar months" (or fewer) can be converted into weeks per the formula "1 month = 4 weeks"

Vaccine and dose 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	4 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	—	—
HepB-1[h]	Birth	Birth	4 weeks-4 months	4 weeks
HepB-2	1-2 months	4 weeks	8 weeks-17 months	8 weeks
HepB-3[i]	6-18 months	24 weeks	—	—
Hib-1[j]	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3[k]	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	—	—
HPV Two Dose Series[l]				

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

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* 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”

- **Patient is in the office or clinic**

  - patient/parent is known and dependable — *Reschedule*
  - patient/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 <u>event</u>**
  - 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

- **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 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

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

- **COVID-19 vaccine only**
  - History of a severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a component of the COVID-19 vaccine
  - History of a known diagnosed allergy to a component of the COVID-19 vaccine
  - Thrombosis with thrombocytopenia syndrome (TTS) following receipt of a previous Janssen COVID-19 vaccine (or other COVID-19 vaccines not currently authorized in the United States that are based on adenovirus vectors [e.g., AstraZeneca]) – Janssen Vaccine only

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

Contraindications and Precautions

Condition	Live	Non-live
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 LAIV)

Knowledge Check

- **A 1-year-old is due for vaccines today, but she is on antibiotics for an ear infection. Can she be vaccinated?**

- A. Live vaccines
- B. Non-live vaccines

Answer

- A 1-year-old is due for vaccines today, but she is on antibiotics for an ear infection. Can she be vaccinated?

- A. Yes
- B. Yes

Vaccination During Pregnancy

- **Live vaccines should not be administered to women known to be pregnant**
  - exception: pregnancy is a precaution to dengue vaccine

- **In general, non-live vaccines may be administered to pregnant women for whom they are indicated.**
  - exception: HPV vaccine, HepB (Heplisav, Prehevbrio) – these should be deferred during pregnancy

Vaccination During Pregnancy

- **Non-live – 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, PCV–no recommendations language at all
    - HepA, HepB [Engerix-B, Recombivax HB], MenACWY, PPSV23 – give if another risk factor is present

Vaccination of Immunosuppressed Persons

- Live vaccines should not be administered to severely immunosuppressed persons – 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

- **Corticosteroids**
- **Cancer Therapy**
- **Biologic response modifiers**
  - isoantibodies
  - Chimeric Antigen Receptor T-Cell (CAR-T) agents
  - checkpoint inhibition
  - other transplant rejection therapies
  - lymphocyte depleting agents

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

- 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 delay for non-live vaccines
- No interval required prior to initiation of corticosteroids

Cancer Therapy and Immunosuppression

- Treatments: antimetabolites, methylating agents, mitotic spindle inhibitors, radiation therapy
- Safety considerations: delay live vaccines until three months following conclusion of therapy, and patient is deemed immunocompetent
- Effectiveness considerations: consider delaying non-live vaccines three months following conclusion of therapy, keeping in mind that 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**
  - CD-19 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**
  - prior to initiation of these therapies, delay initiation for 1 month following a live vaccine
  - if currently on therapies, delay re-initiation for two weeks following a live vaccine
  - delay live vaccines for three 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

- **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.*

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 the 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	No
Dengue	Consider	No

Yes=vaccinate No=do not vaccinate

*See specific ACIP recommendations for details

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.**

Additional General Best Practice Guidelines on Immunization

- **Screening for indications, contraindications, and precautions, and**

- **A discussion of vaccine safety, including**
  - vaccine safety monitoring
  - vaccine safety concerns

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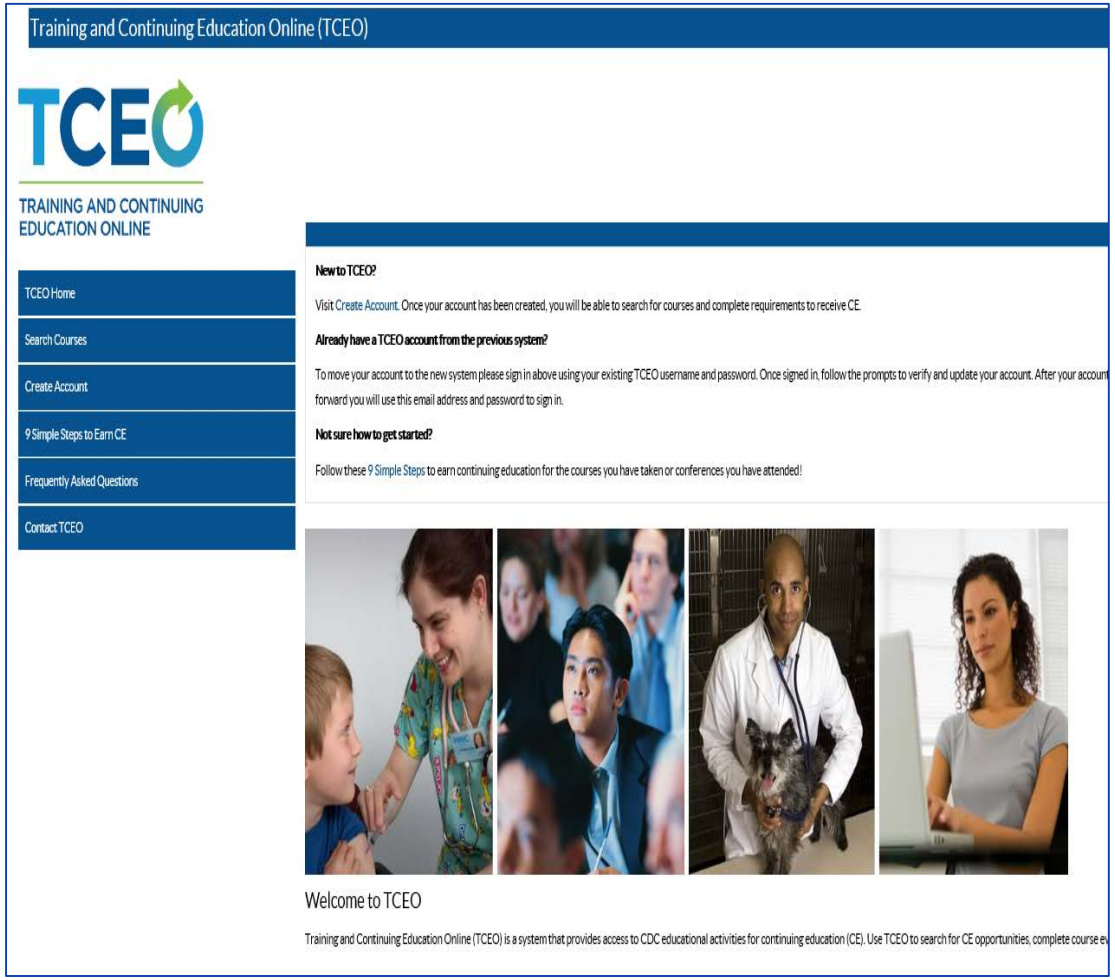

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- NIPINFO@cdc.gov

Thank You From Atlanta!