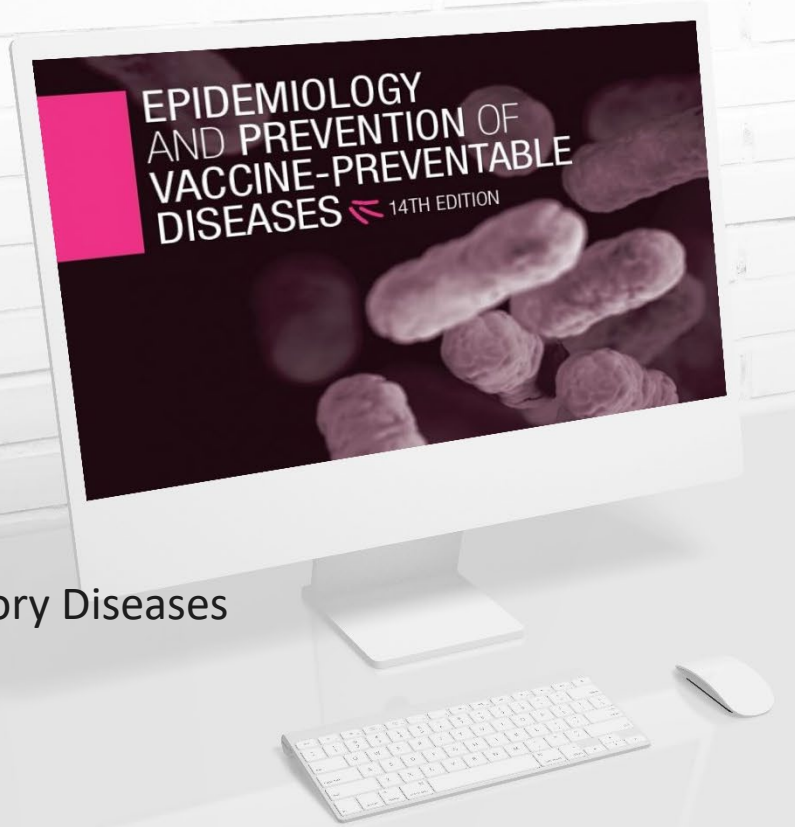
Principles of Vaccination



Pink Book Web-on-Demand Series

July 2, 2024

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Centers for Disease Control and Prevention

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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Disclosure Statements

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1

Immunity

Human Immune System

- Complex network of interacting cells and proteins whose purpose is to identify, and eliminate, foreign substances

American Academy of Pediatrics. Active and passive immunization. In: Kimberlin D, Brady M, Jackson M, et al., eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed. Itasca, IL: American Academy of Pediatrics;2018:13–64

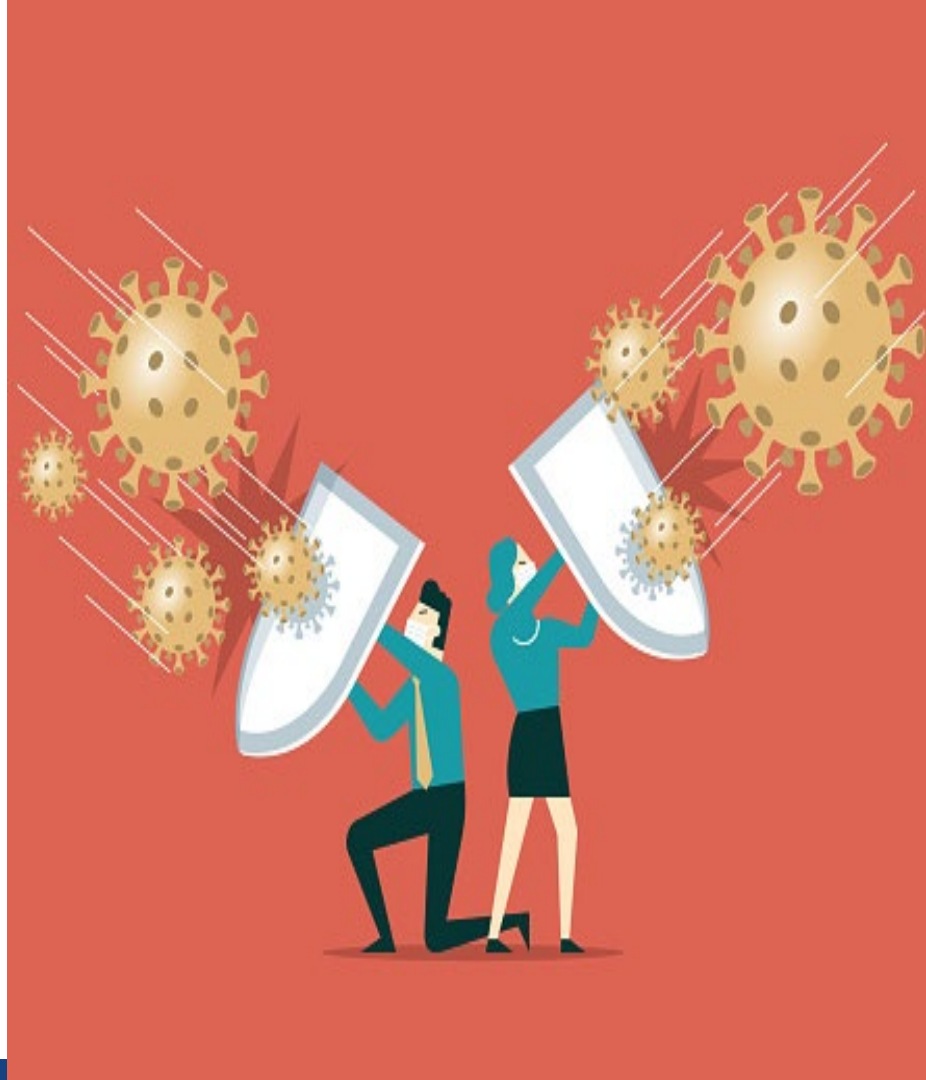
Pinkbook | Principles of Vaccination | Epidemiology of VPDs | CDC

Plotkin S. Vaccines, vaccination, and vaccinology. J Infect Dis 2003;187:1347–59.

Siegrist C. Vaccine immunology. In: Plotkin S, Orenstein W, Offit P, et al., eds. Plotkin's Vaccines. 7th ed. Elsevier;2018:16–34

Immunity

- The ability of the human body to:
  - Tolerate the presence of material indigenous to the body
  - Eliminate foreign substances
- Self vs. “non-self”



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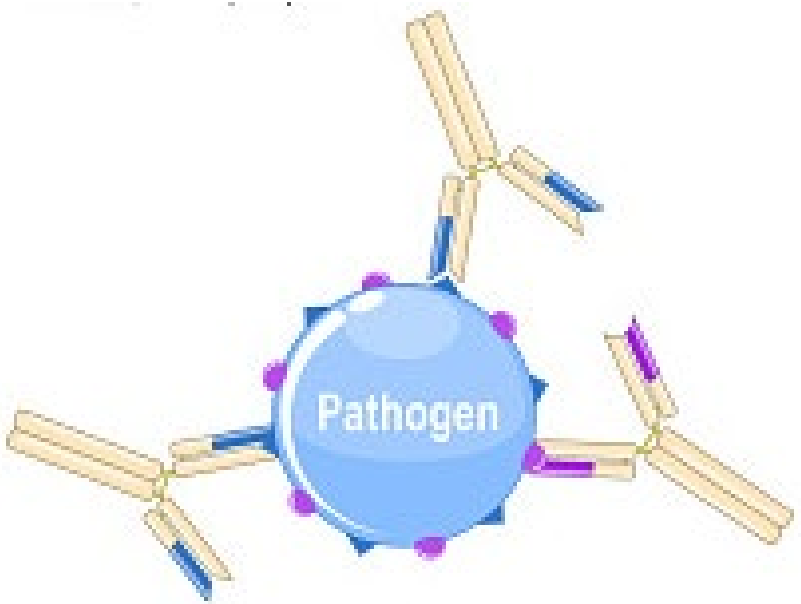
Immunity, cont.

- Most organisms recognized as foreign.
  - Virus, bacteria, fungi
  - Immune system provides protection from infectious diseases.
- Immunity is generally specific to a single organism.
  - E.g., immunity against a specific bacteria will not protect against a specific virus.



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Pinkbook | Principles of Vaccination | Epidemiology of VPDs | CDC

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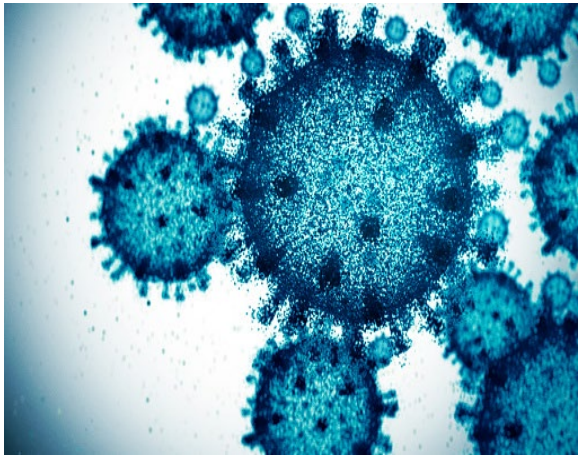
Siegrist C. Vaccine immunology. In: Plotkin S, Orenstein W, Offit P, et al., eds. Plotkin's Vaccines. 7th ed. Elsevier;2018:16–34.

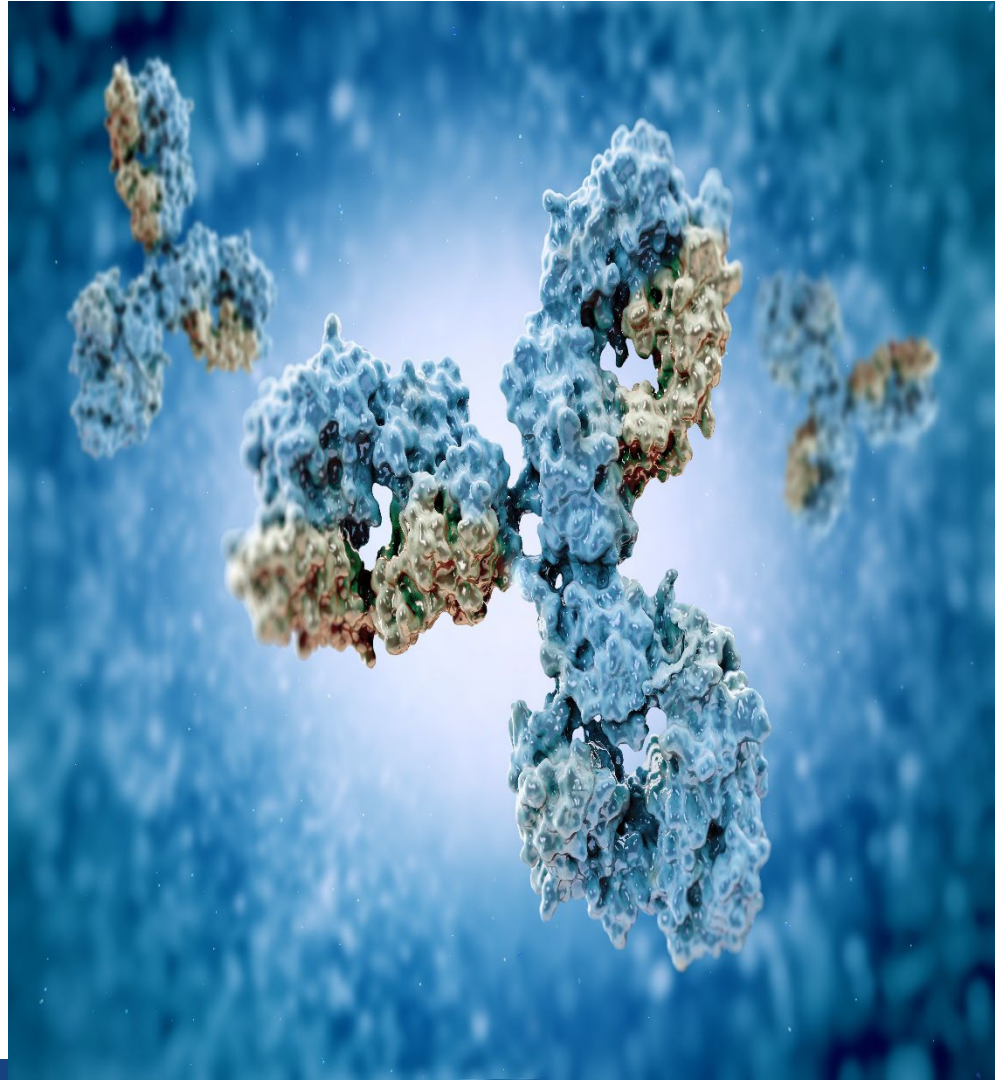
Antigen

- Live or inactivated substances (e.g., viruses, bacteria, toxins)
  - Capable of stimulating an immune response
- Antigen = antibody generator



Antibody

- Protein molecules (immunoglobulins)
- Help infection-fighting cells recognize and kill foreign organisms, including viruses
- Antibodies are produced by the body

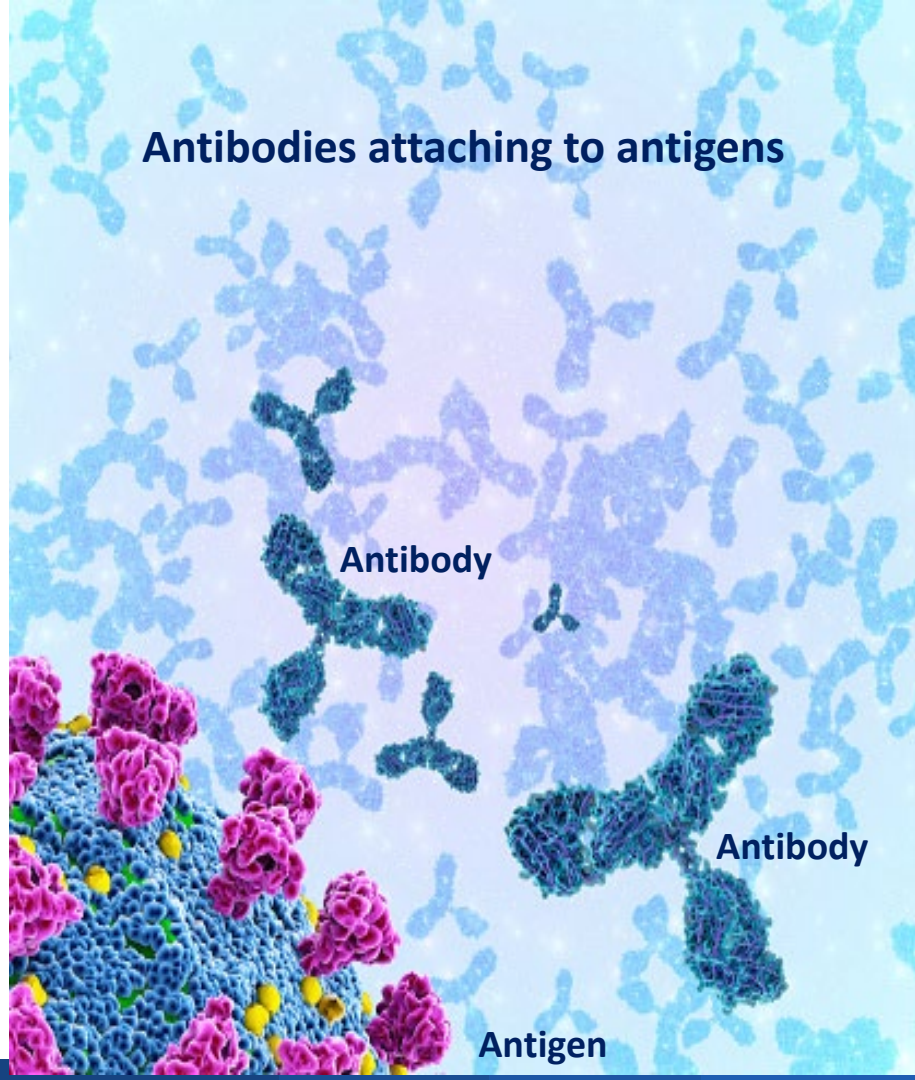


Arms of the Immune System

- Humoral
- Cell-mediated

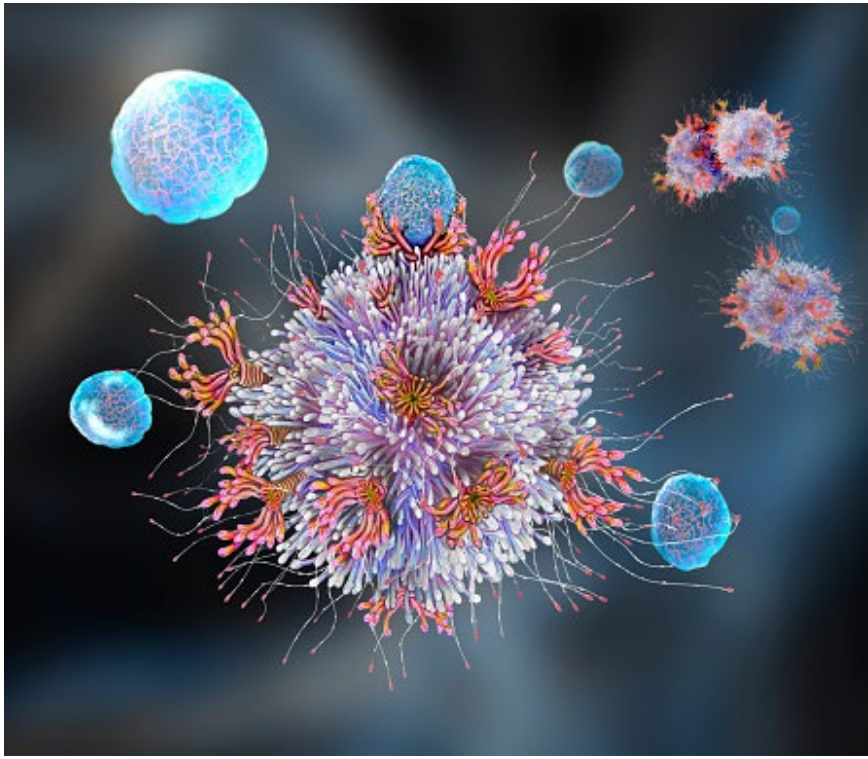
Arms of the Immune System, cont.

- Humoral
  - Antibodies attach to invading organisms and interfere with its ability to produce more invading organisms.
  - Antibodies are produced by B-cells (lymphocytes) to bind to a corresponding antigen, such as a virus (lock and key mechanism).

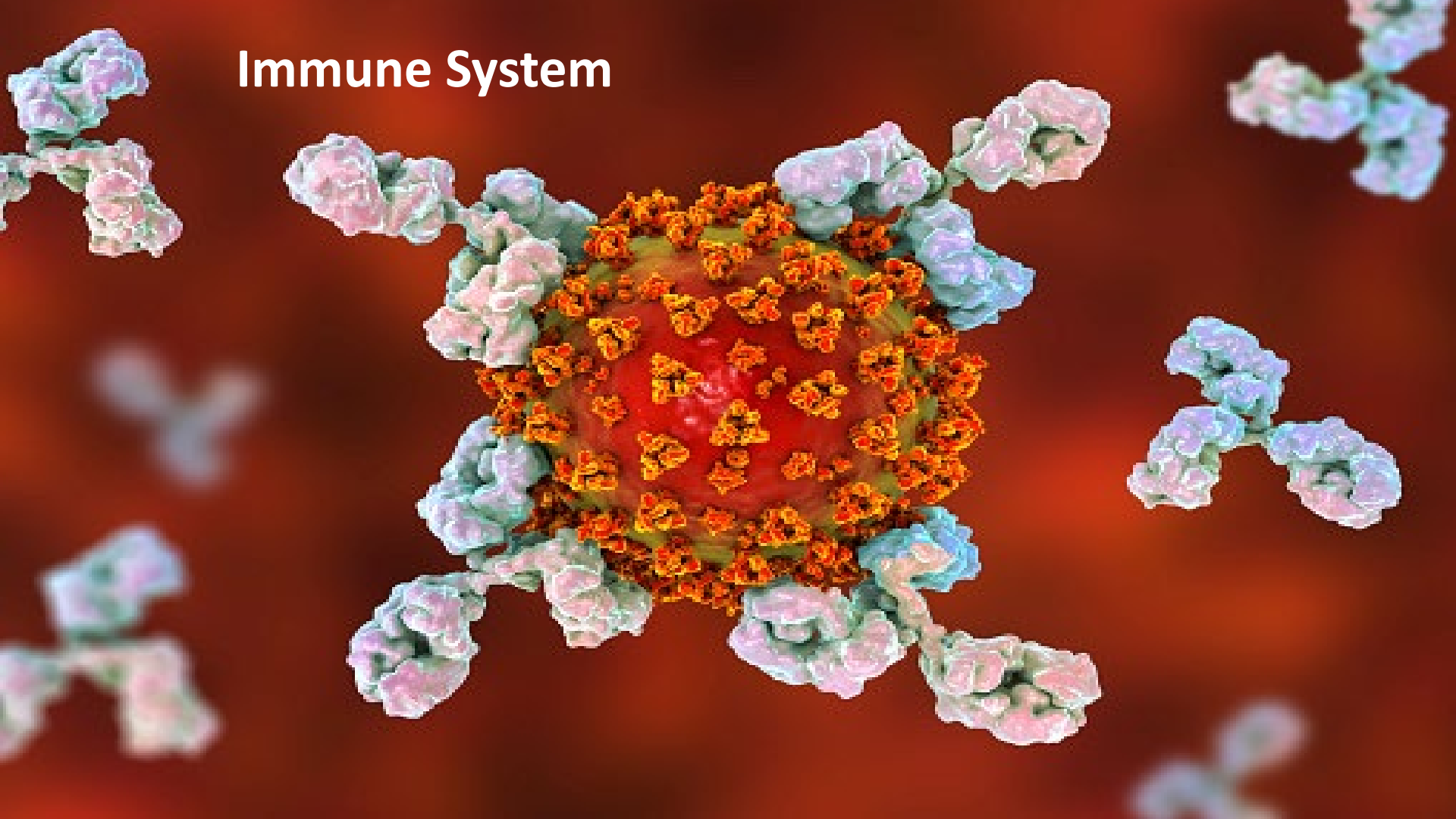


Arms of the Immune System, cont.

- Cell-mediated
  - Involves the activation of T-cells, macrophages, and other substances that eliminate the antigen.
  - T-cells mature in the thymus gland.



Immune System



Knowledge Check

Which of the following helps infection-fighting cells recognize and kill a microorganism?

A. Antigen

B. Antibody

Answer

Which of the following helps infection-fighting cells recognize and kill a microorganism?

A. Antigen

B. Antibody

2

Types of Immunity: Passive and Active

Types of Immunity

- Passive immunity
- Active immunity

Passive Immunity

- Passive immunity is the transfer of antibody produced by one human, animal, or recombinant technology, to another.
- It is temporary protection that wanes with time.
- There are different sources.

Sources of Passive Immunity (1)

- Transfer of antibody from the mother through placenta to the infant.
- These antibodies can help protect the baby from some diseases during the first few months of life.

Sources of Passive Immunity (2)

- Many types of blood or blood products
- Homologous pooled human antibody (immune globulin or IG)
  - IgG antibody from the blood of thousands of adult donors
  - Hepatitis A and measles post-exposure prophylaxis (PEP)

Sources of Passive Immunity (3)

- Homologous human hyperimmune globulin
- From donors with high concentrations of a specific antibody
  - Hepatitis B Immune Globulin (HBIG), Human Rabies Immune Globulin (HRIG), Tetanus Immune globulin (TIG), Varicella Zoster Immune Globulin (Human) (VariZIG), Vaccinia Immune Globulin Intravenous (Human) (VIGIV)
- Heterologous hyperimmune serum
  - Antitoxin (e.g., diphtheria antitoxin)
  - Serum sickness

Sources of Passive Immunity (4)

- Monoclonal antibodies are derived from a single type, or clone, of antibody-producing cells (B-cells) or through recombinant technology.
  - Immune globulin from human sources is polyclonal (contains many kinds of antibodies).
  - Monoclonal antibody is specific to a single antigen or closely related group of antigens.
  - Used for diagnosis of and therapy for certain cancers and autoimmune and infectious diseases (e.g., COVID-19)
  - Used for prevention of certain infectious diseases and transplant rejection.
  - Monoclonal-antibody-derived drugs end in –mab.

Antibody for Prevention of RSV

- Nirsevimab (Beyfortus)
  - Monoclonal
  - Contains only RSV antibody
  - Will not interfere with the response to a live-virus vaccine

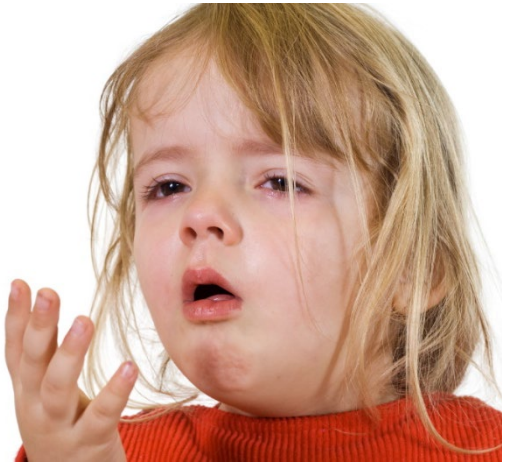
Use of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease Among Infants and Young Children: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023 | MMWR (cdc.gov)

Active Immunity

- Protection produced by a person's own immune system
- The process of developing antibodies takes time.
  - It can take up to a few weeks.
- Lasts for many years, often lifetime

Sources of Active Immunity

- Infection with disease-causing form of organism



- Vaccination

Vaccination

- Active immunity produced by vaccine
  - Vaccine delivers an attenuated (weakened, nonpathogenic) or non-live (dead or disrupted) form of the pathogen.
- Vaccination primes the body to make antibodies when exposed to the specific organism the vaccine was designed to protect against.
  - Immunologic memory allows for an anamnestic response after the primary immune response so that antibody reappears when the antigen is introduced.

Knowledge Check

Which type of immunity lasts longer?

A. Passive immunity

B. Active immunity

Answer

Which type of immunity lasts longer?

A. Passive immunity

B. Active Immunity

3

Principles of Vaccination

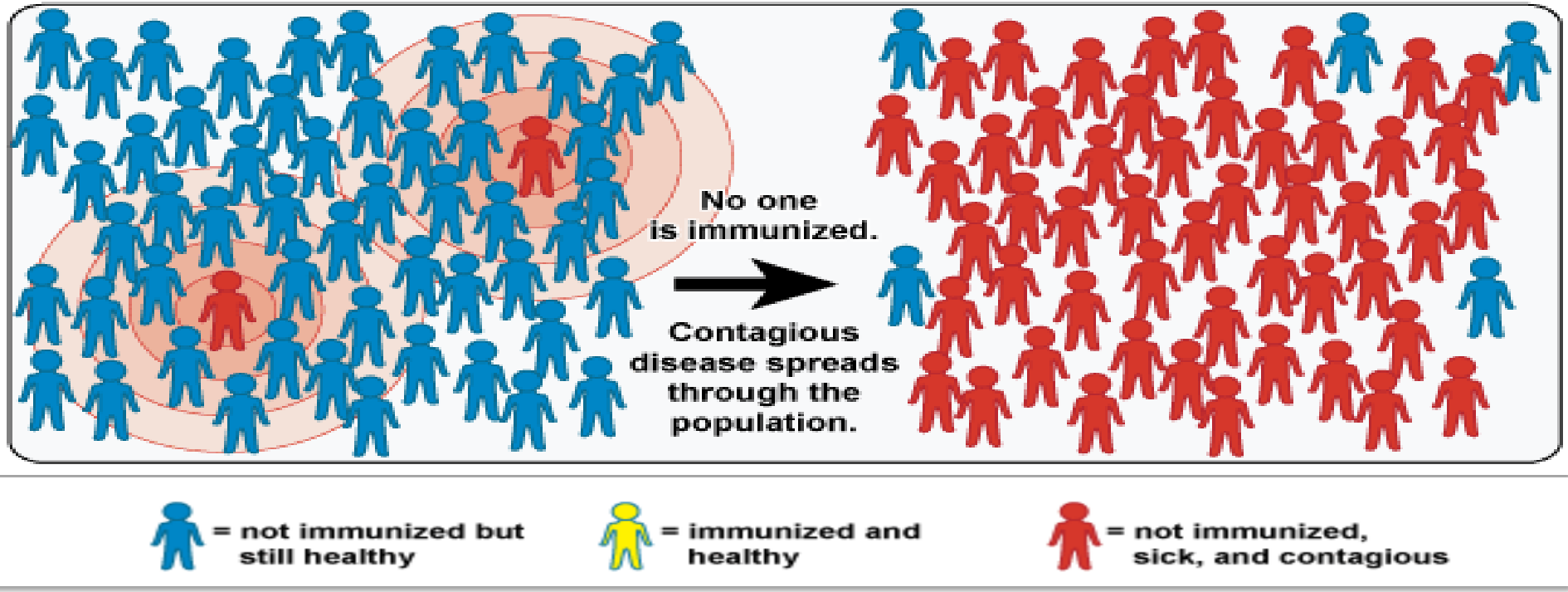
Principles of Vaccination

- The more similar the antibody [or immune response] produced by vaccination is to antibody produced by natural disease (infection), the better the protection provided by the vaccine.

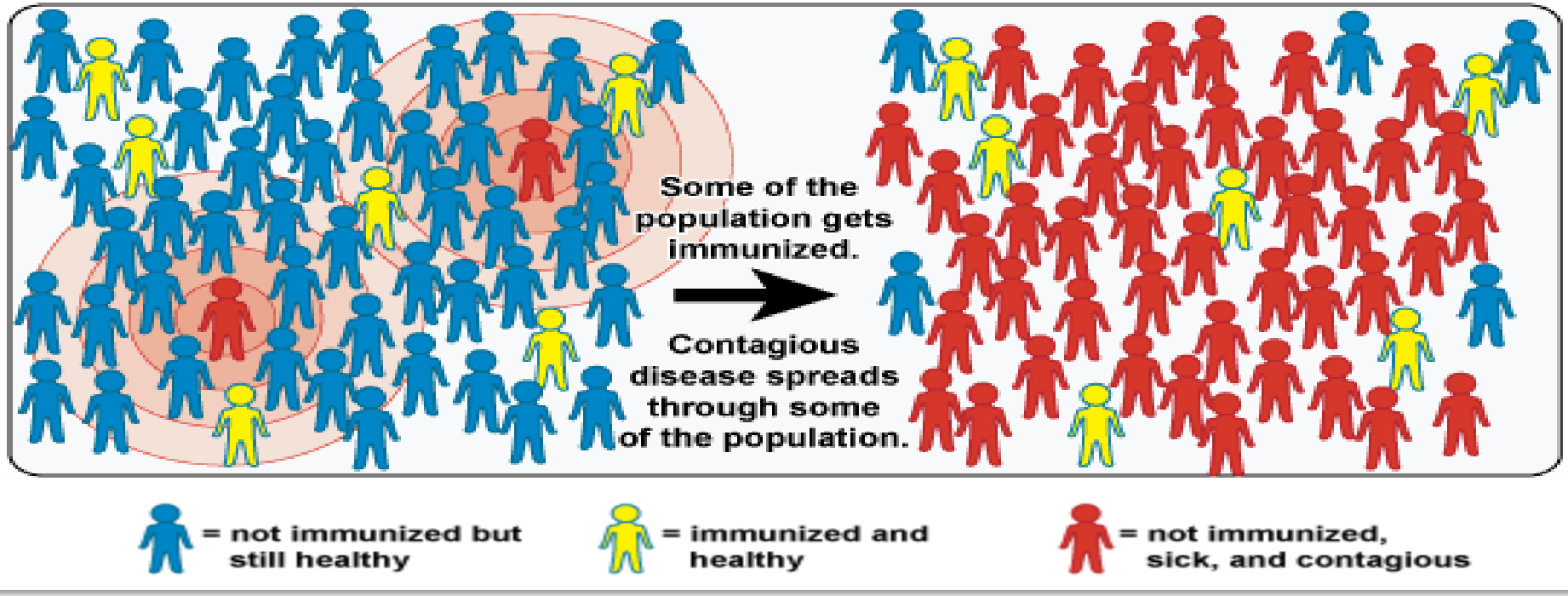
Factors that Affect Immune Response to Vaccines

- Presence of maternal antibodies
- Nature and amount of antigen in vaccine
- Route of administration
- Presence of an adjuvant (ingredient that promotes a stronger immune response)
- Storage and handling of vaccine
- Vaccine recipient
  - Age
  - Nutritional status
  - Genetics
  - Coexisting disease
  - Immune suppression

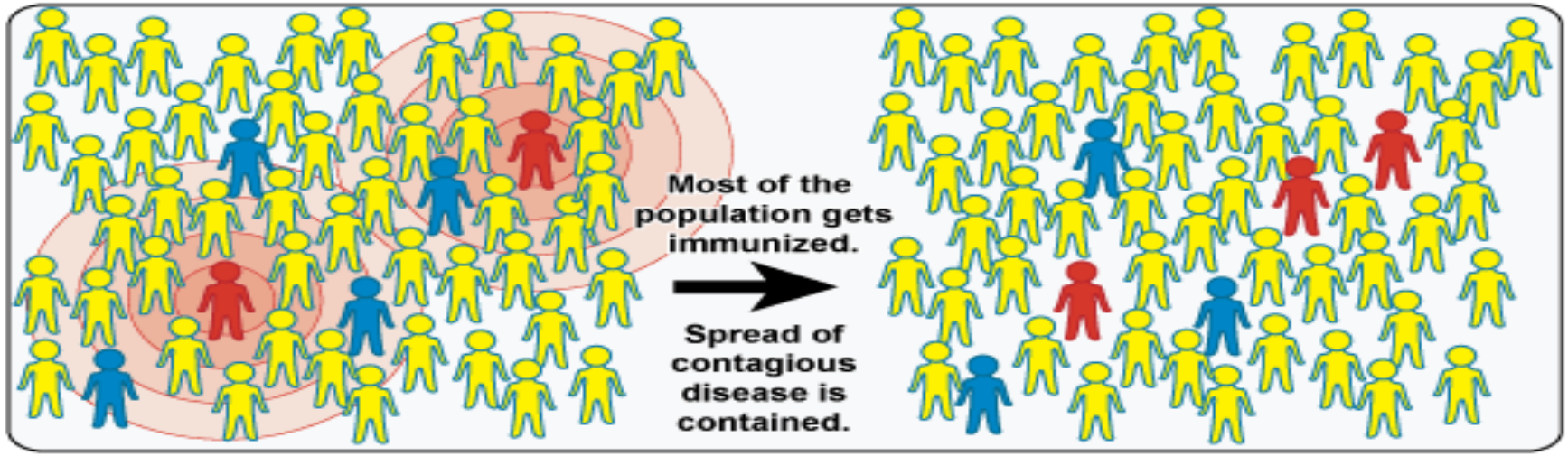
Community Immunity



Community Immunity, cont.



Community Immunity, cont.



4

Classification of Vaccines

Classification of Vaccines

- Live
  - Most live vaccines used in the United States are “live, attenuated,” meaning that the microbe in the vaccine is alive but has been weakened (attenuated).

- Non-live
  - A non-live vaccine contains inactivated or dead virus or bacterium, or a fraction of the organism.
  - Non-live vaccines are sometimes referred to as inactivated vaccines.

Classification of Vaccines (2)

- Live
  - Viral or bacterial
- Non-live
  - Viral or bacterial

Classification of Vaccines (3)

- Live, attenuated

- Non-live
  - Whole-cell
  - Subunit
  - Toxoid
  - Recombinant
  - mRNA

Live, Attenuated Vaccines

- “Wild” virus or bacterium weakened by repeated passage in culture media
- Must replicate to produce an immune response
- Immune response similar to natural infection
- Usually produce long-lasting immunity with 1-2 doses
  - Except those administered orally or intranasally

Live, Attenuated Vaccines (2)

- Severe reactions possible in persons with immune compromise.

- Interference from circulating antibody, including:
  - Maternal antibody
  - Other sources of passive immunity, i.e., blood products

- Fragile – must be stored and handled carefully

Live, Attenuated Vaccines

- Viral
  - Live Attenuated Influenza Vaccine (LAIV), Measles Mumps Rubella (MMR), Measles Mumps Rubella Varicella (MMRV), Mpox (Mpox)‡, Varicella (VAR), Rotavirus (RV1,RV5), Dengue (DEN4CYD), Chikungunya, Yellow fever (YF), oral adenovirus*, oral polio†, Ebola
- Bacterial
  - Bacille Calmette-Guérin (BCG)§, oral typhoid, oral cholera

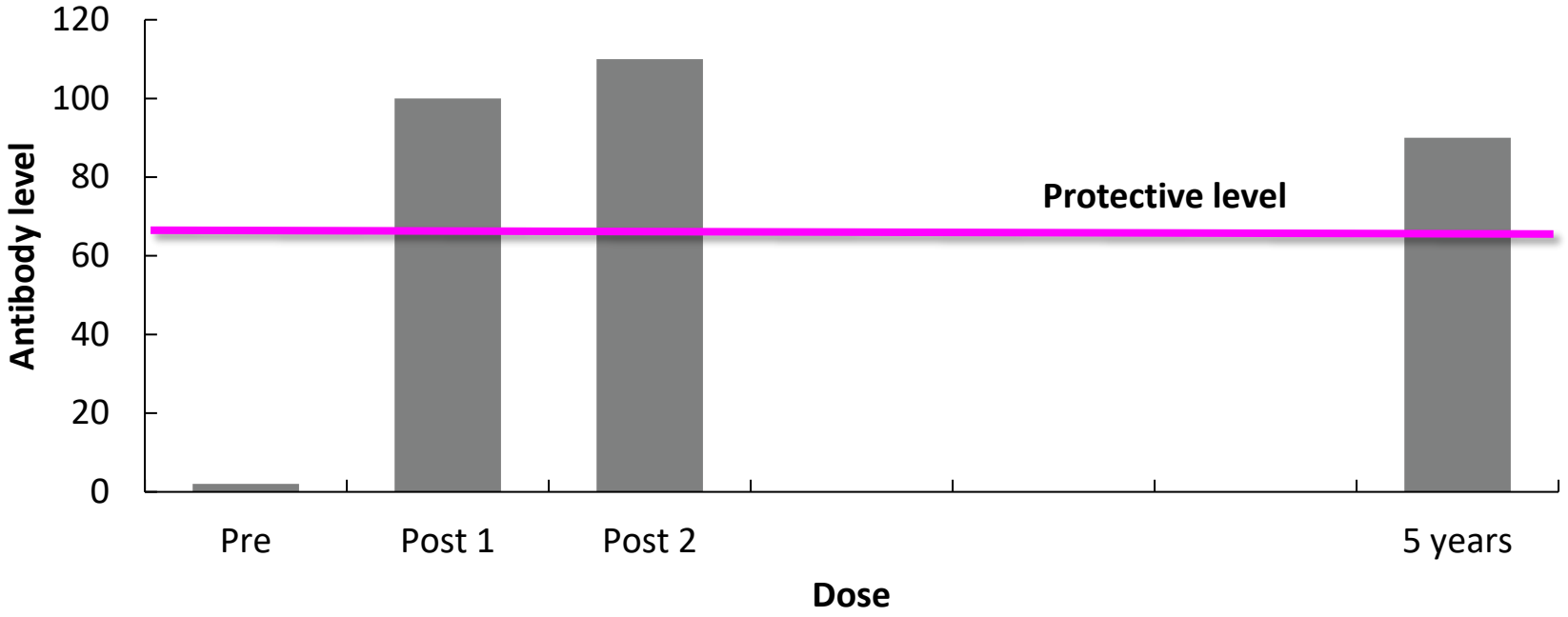
*Live, but not attenuated. Limited use in the United States

†Not used in the United States

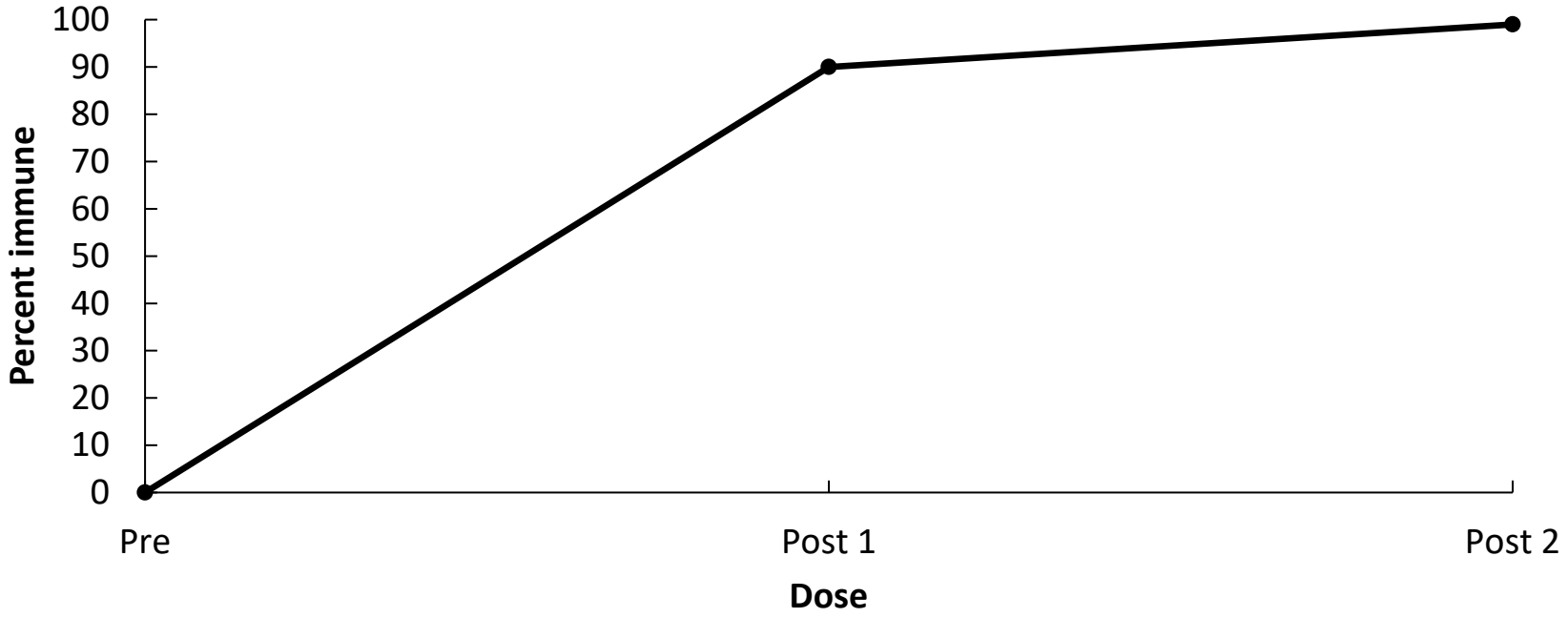
‡Jynneos vaccine does not replicate and behaves like non-live vaccines

§Not used in the United States for routine TB protection

Individual Response to a Hypothetical Live, Attenuated Vaccine



Population Response to a Hypothetical Live, Attenuated Vaccine



Non-live Vaccines

- Cannot replicate
- May be less affected by circulating antibody than live vaccines.
- May require multiple doses
- Antibody titer diminishes with time
- May include an adjuvant

Non-live Vaccines

- Whole-cell, inactivated
  - Polio, hepatitis A, rabies
- Subunit
  - Antigens can be protein, polysaccharide, or combination of polysaccharide and protein molecule (i.e., conjugate vaccine)
- Toxoid
  - Diphtheria, tetanus
- Recombinant
  - Hepatitis B, HPV
- mRNA
  - COVID-19

Adjuvants

- An adjuvant is an ingredient used in some vaccines that helps create a stronger immune response.
- Adjuvants have been used safely in vaccines for decades.

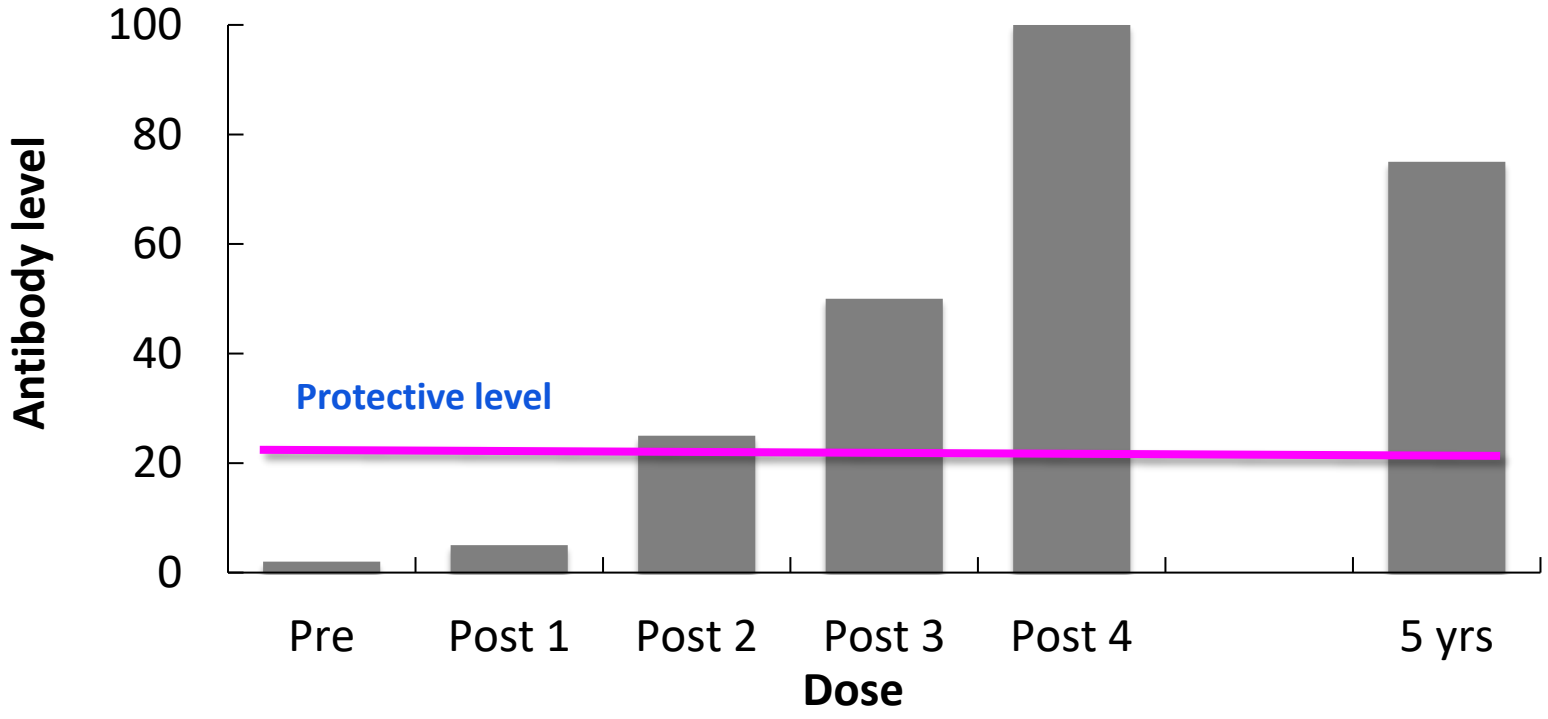
Adjuvants and Vaccines | Vaccine Safety | CDC

Several Different Adjuvants are Used in U.S. Vaccines

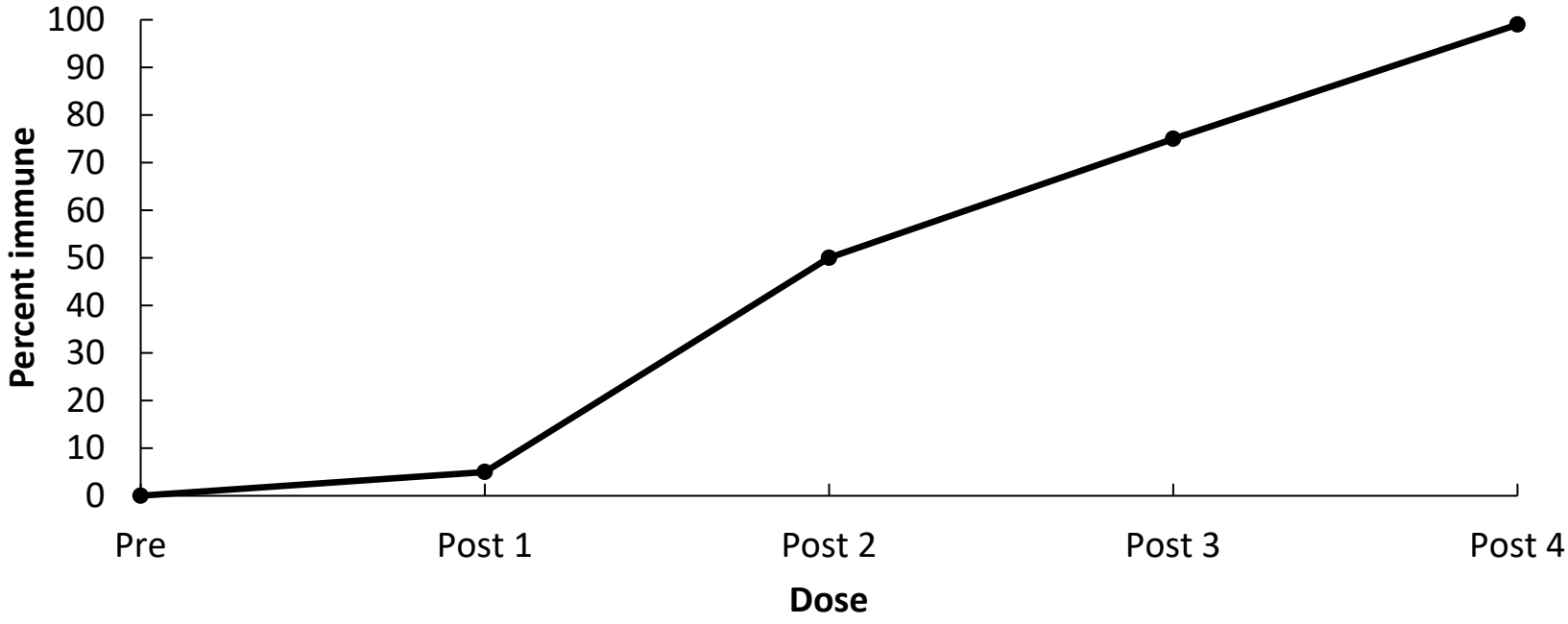
Adjuvant	Vaccines
Aluminum	DTaP (Daptacel, Infanrix), DTaP-HepB-IPV (Pediarix), DTaP-IPV (Kinrix, Quadracel), DTaP-IPV/Hib (Pentacel), DTaP-IPV-Hib-HepB (VAXELIS), HepA (Havrix, Vaqta), HepB (Engerix-B, PREHEVBRIO, Recombivax), HepA/HepB (Twinrix), HIB (PedvaxHIB), HPV (Gardasil 9), MenB (Bexsero, Trumenba), Pneumococcal (Prevnar 20, VAXNEUVANCE), Td (Tenivac, no trade name), Tdap (Adacel, Boostrix),
$AS01_B$	RZV (Shingrix)
CpG1018	HepB (Heplisav-B)
Matrix-M™	COVID-19 (Novavax)
MF59	Influenza (Fluad and Fluad Quadrivalent)

Adjuvants and Vaccines | Vaccine Safety | CDC

Individual Response to Hypothetical Non-live Vaccine



Population Response to Hypothetical Non-live Vaccine



Knowledge Check

Which type of vaccine must replicate to generate an immune response?

A. Live, attenuated vaccines

B. Non-live vaccines

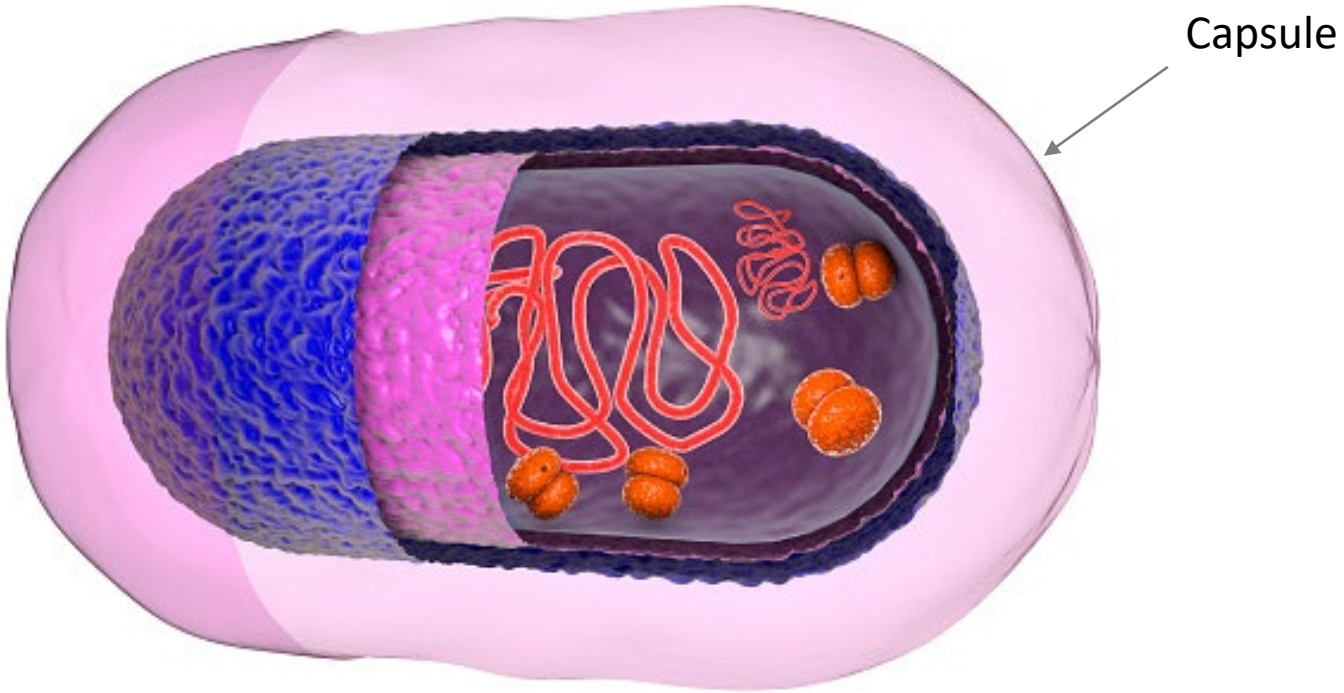
Answer

Which type of vaccine must replicate to generate an immune response?

A. Live, attenuated vaccines

B. Non-live vaccines

Capsular Polysaccharide



Pure Polysaccharide Vaccines

- Immune response typically T-cell-independent
- Not consistently immunogenic in children younger than 2 years of age
- No booster response
- Antibody with less functional activity (IgM rather than IgG)
- Immunogenicity improved by conjugation
  - i.e., combined with a protein

Polysaccharide Vaccines

- **Pure polysaccharide**
  - Pneumococcal (PPSV23)
  - *Salmonella typhi* (Vi)
- **Conjugate polysaccharide**
  - *Haemophilus influenzae* type b (Hib)
  - Pneumococcal (PCV13, PCV15, PCV20)
  - Meningococcal ACWY

Knowledge Check

Which type of polysaccharide vaccine has improved immunogenicity?

A. Pure polysaccharide vaccine

B. Conjugated polysaccharide vaccine

Answer

Which type of polysaccharide vaccine has improved immunogenicity?

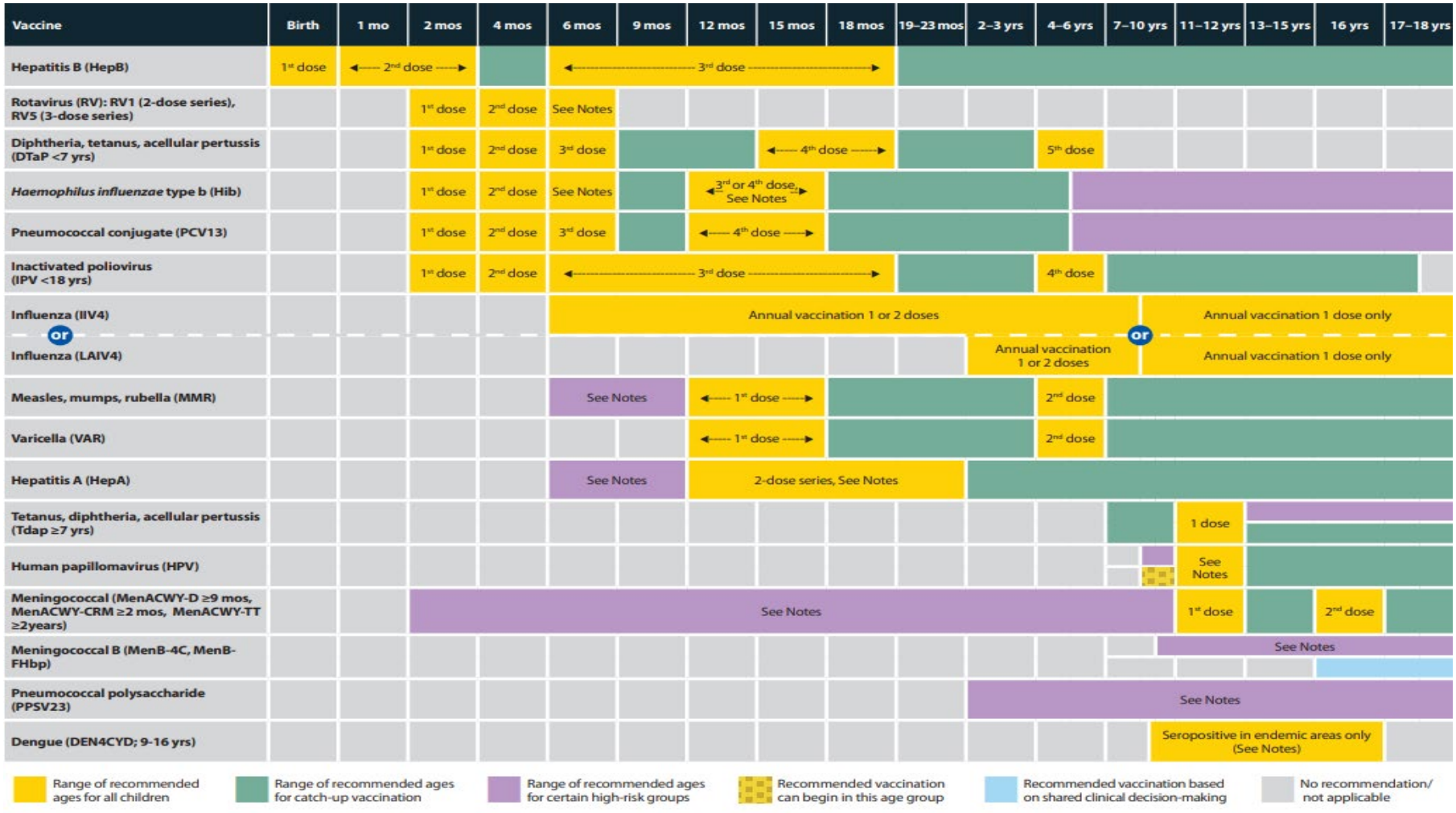
A. Pure polysaccharide vaccine

B. Conjugated polysaccharide vaccine

5

ACIP Immunization Schedules

Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger, United States, 2024



Child and Adolescent Immunization Schedule – Healthcare Providers | CDC

Recommended Catch-up Immunization Schedule for Children and Adolescents Who Start Late or Who Are More than 1 Month Behind, United States, 2024

Table 2 Recommended Catch-up Immunization Schedule for Children and Adolescents Who Start Late or Who Are More than 1 Month Behind, United States, 2024

The table below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. **Always use this table in conjunction with Table 1 and the Notes that follow.**

Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
Children age 4 months through 6 years					
Hepatitis B	Birth	**4 weeks**	**8 weeks *and* at least 16 weeks after first dose** minimum age for the final dose is 24 weeks		
Rotavirus	6 weeks Maximum age for first dose is 14 weeks, 6 days.	**4 weeks**	**4 weeks** maximum age for final dose is 8 months, 0 days		
Diphtheria, tetanus, and acellular pertussis	6 weeks	**4 weeks**	**4 weeks**	**6 months**	**6 months** A fifth dose is not necessary if the fourth dose was administered at age 4 years or older ***and*** at least 6 months after dose 3
Haemophilus influenzae type b	6 weeks	**No further doses needed** if first dose was administered at age 15 months or older. **4 weeks** if first dose was administered before the 1st birthday. **8 weeks (as final dose)** if first dose was administered at age 12 through 14 months.	**No further doses needed** if previous dose was administered at age 15 months or older **4 weeks** if current age is younger than 12 months ***and*** first dose was administered at younger than age 7 months ***and*** at least 1 previous dose was PRP-T (ActHib®, Pentacel®, Hiberix®), Vaxelis® or unknown **8 weeks *and* age 12 through 59 months (as final dose)** if current age is younger than 12 months ***and*** first dose was administered at age 7 through 11 months; **OR** if current age is 12 through 59 months ***and*** first dose was administered before the 1st birthday ***and*** second dose was administered at younger than 15 months; **OR** if both doses were PedvaxHIB® and were administered before the 1st birthday	**8 weeks (as final dose)** This dose only necessary for children age 12 through 59 months who received 3 doses before the 1st birthday.	
Pneumococcal conjugate	6 weeks	**No further doses needed** for healthy children if first dose was administered at age 24 months or older **4 weeks** if first dose was administered before the 1st birthday **8 weeks (as final dose for healthy children)** if first dose was administered at the 1st birthday or after	**No further doses needed** for healthy children if previous dose was administered at age 24 months or older **4 weeks** if current age is younger than 12 months ***and*** previous dose was administered at <7 months old **8 weeks (as final dose for healthy children)** if previous dose was administered between 7–11 months (wait until at least 12 months old); **OR** if current age is 12 months or older ***and*** at least 1 dose was administered before age 12 months	**8 weeks (as final dose)** This dose is only necessary for children age 12 through 59 months regardless of risk, or age 60 through 71 months with any risk, who received 3 doses before age 12 months.	
Inactivated poliovirus	6 weeks	**4 weeks**	**4 weeks** if current age is <4 years **6 months (as final dose)** if current age is 4 years or older	**6 months (minimum age 4 years for final dose)**	
Measles, mumps, rubella	12 months	**4 weeks**			
Varicella	12 months	**3 months**			
Hepatitis A	12 months	**6 months**			
Meningococcal ACWY	2 months MenACWY-CRM 2 years MenACWY-TT	**8 weeks**	See Notes	See Notes	
Children and adolescents age 7 through 18 years					
Meningococcal ACWY	Not applicable (N/A)	**8 weeks**			
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis	7 years	**4 weeks**	**4 weeks** if first dose of DTaP/DT was administered before the 1st birthday **6 months (as final dose)** if first dose of DTaP/DT or Tdap/Td was administered at or after the 1st birthday	**6 months** if first dose of DTaP/DT was administered before the 1st birthday	
Human papillomavirus	9 years	**Routine dosing intervals are recommended.**			
Hepatitis A	N/A	**6 months**			
Hepatitis B	N/A	**4 weeks**	**8 weeks *and* at least 16 weeks after first dose**		
Inactivated poliovirus	N/A	**4 weeks**	**6 months** A fourth dose is not necessary if the third dose was administered at age 4 years or older ***and*** at least 6 months after the previous dose.	A fourth dose of IPV is indicated if all previous doses were administered at <4 years **OR** if the third dose was administered <6 months after the second dose.	
Measles, mumps, rubella	N/A	**4 weeks**			
Varicella	N/A	**3 months** if younger than age 13 years. **4 weeks** if age 13 years or older			
Dengue	9 years	**6 months**	6 months		

Child and Adolescent Immunization Schedule – Healthcare Providers | CDC

Table 3 Recommended Child and Adolescent Immunization Schedule by Medical Indication, United States, 2024

Always use this table in conjunction with Table 1 and the Notes that follow. Medical conditions are often not mutually exclusive. If multiple conditions are present, refer to guidance in all relevant columns. See Notes for medical conditions not listed.

Vaccine and other immunizing agents	Pregnancy	Immunocompromised (excluding HIV infection)	HIV infection CD4 percentage and count[a]		CSF leak or cochlear implant	Asplenia or persistent complement component deficiencies	Heart disease or chronic lung disease	Kidney failure, End-stage renal disease or on Dialysis	Chronic liver disease	Diabetes
			<15% or <200mm	≥15% and ≥200mm						
RSV-mAb (nirsevimab)		2nd RSV season		1 dose depending on maternal RSV vaccination status, See Notes			2nd RSV season for chronic lung disease (See Notes)	1 dose depending on maternal RSV vaccination status, See Notes		
Hepatitis B										
Rotavirus		SCID[b]								
DTaP/Tdap	DTaP Tdap: 1 dose each pregnancy									
Hib		HSCT: 3 doses	See Notes			See Notes				
Pneumococcal										
IPV										
COVID-19		See Notes								
IIV4										
LAIV4							Asthma, wheezing: 2–4 years[c]			
MMR	*									
VAR	*									
Hepatitis A										
HPV	*	3 dose series. See Notes								
MenACWY										
MenB										
RSV (Abrysvo)	Seasonal administration, See Notes									
Dengue										
Mpox	See Notes									

Recommended for all age-eligible children who lack documentation of a complete vaccination series

Not recommended for all children, but is recommended for some children based on increased risk for or severe outcomes from disease

Recommended for all age-eligible children, and additional doses may be necessary based on medical condition or other indications. See Notes.

Precaution: Might be indicated if benefit of protection outweighs risk of adverse reaction

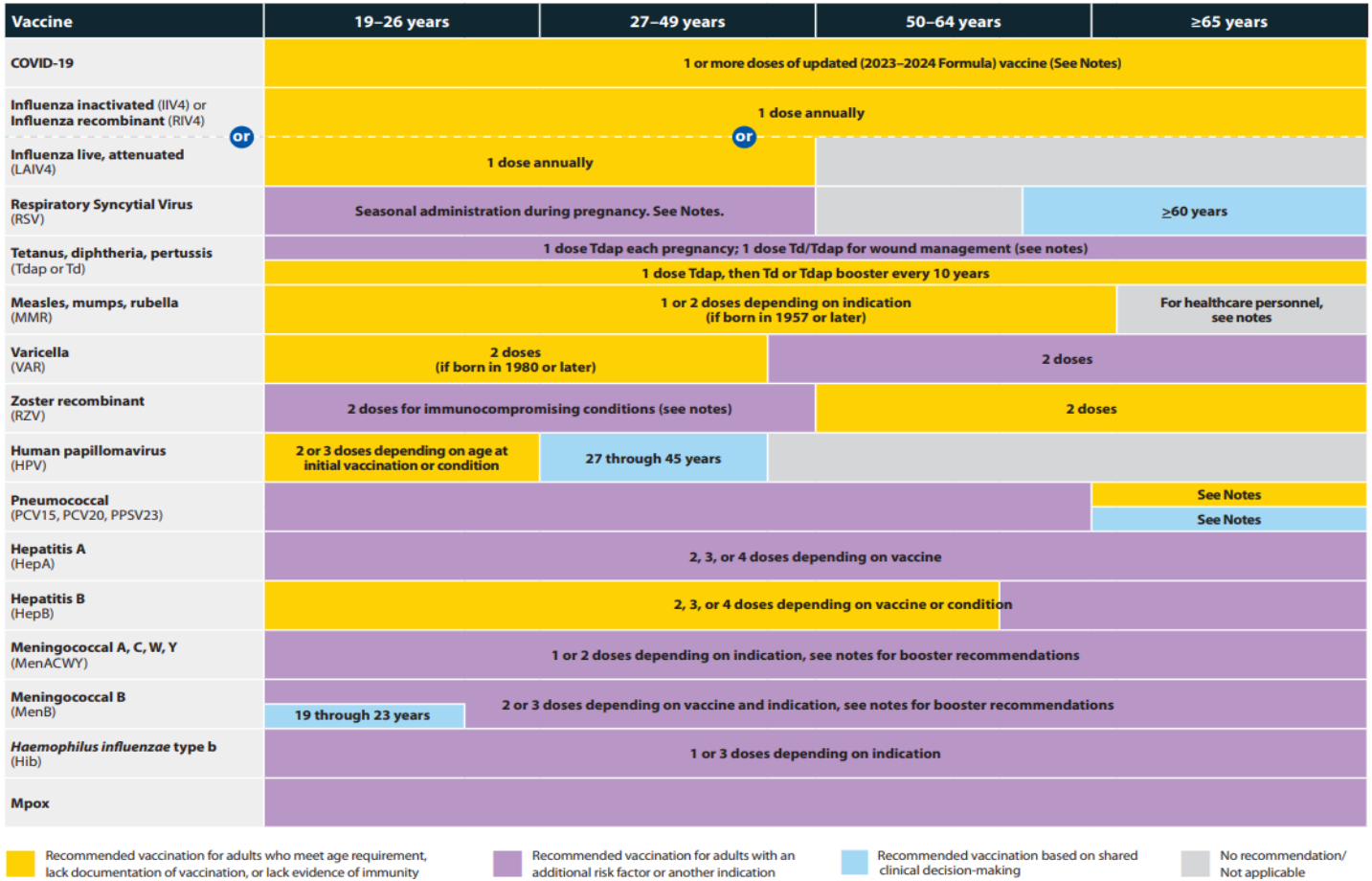
Contraindicated or not recommended
*Vaccinate after pregnancy, if indicated

No Guidance/ Not Applicable

Child and Adolescent Immunization Schedule – Healthcare Providers | CDC

Recommended Adult Immunization Schedule by Age Group, United States, 2024

Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2024



Adult Immunization Schedule by Age | CDC

Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2024

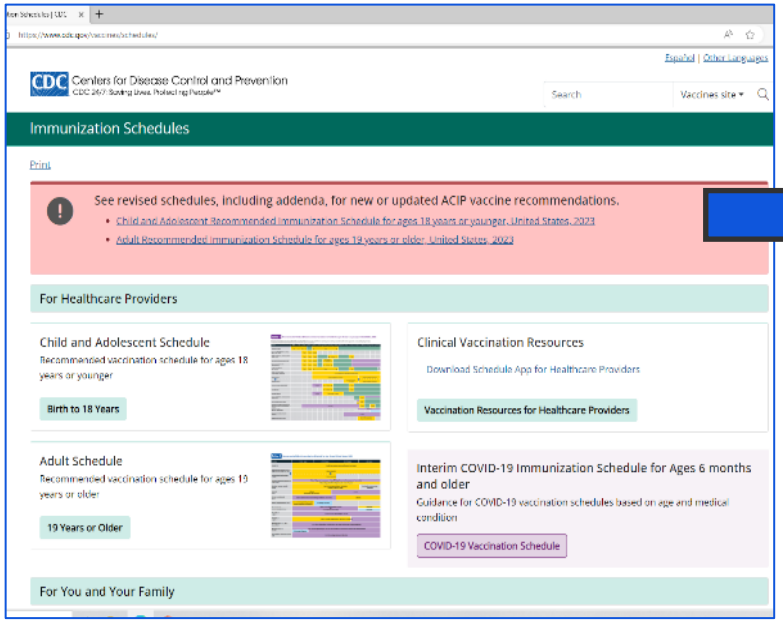
Always use this table in conjunction with Table 1 and the Notes that follow. Medical conditions or indications are often not mutually exclusive. If multiple medical conditions or indications are present, refer to guidance in all relevant columns. See Notes for medical conditions or indications not listed.

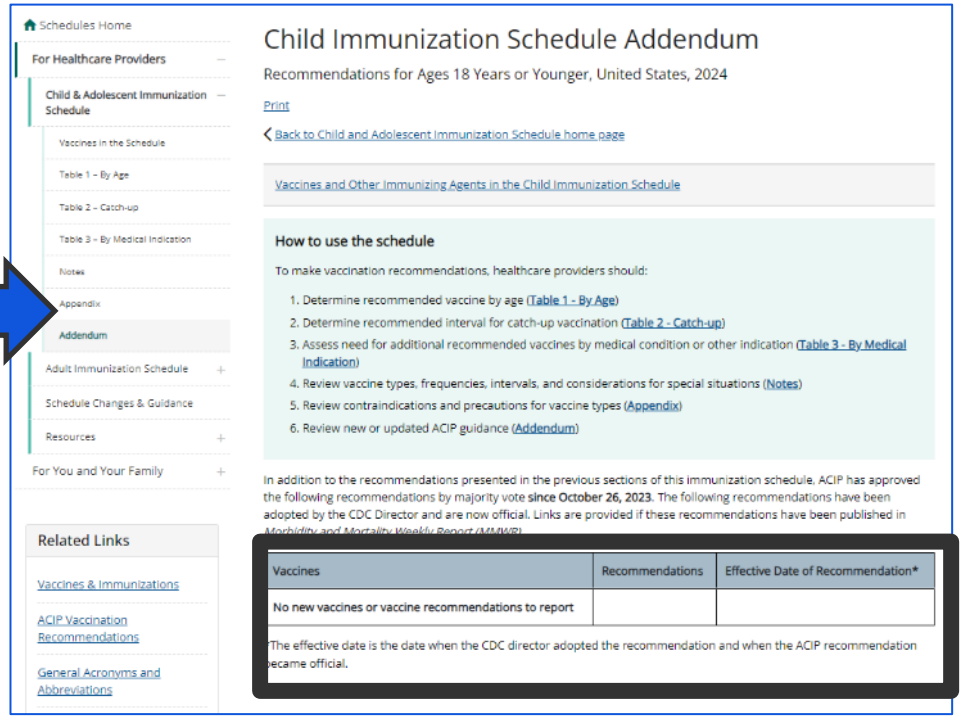
VACCINE	Pregnancy	Immunocompromised (excluding HIV infection)	HIV infection CD4 percentage and count		Men who have sex with men	Asplenia, complement deficiency	Heart or lung disease	Kidney failure, End-stage renal disease or on dialysis	Chronic liver disease; alcoholism[a]	Diabetes	Healthcare Personnel[b]
			<15% or <200mm³	≥15% and ≥200mm³							
COVID-19		See Notes									
IIV4 or RIV4	1 dose annually										
LAIV4					1 dose annually if age 19–49 years		1 dose annually if age 19–49 years				
RSV	Seasonal administration. See Notes	See Notes				See Notes					
Tdap or Td	Tdap: 1 dose each pregnancy	1 dose Tdap, then Td or Tdap booster every 10 years									
MMR	*										
VAR	*			See Notes							
RZV		See Notes									
HPV	*	3 dose series if indicated									
Pneumococcal											
HepA											
Hep B	See Notes									Age ≥ 60 years	
MenACWY											
MenB											
Hib		HSCT: 3 doses[c]				Asplenia: 1 dose					
Mpox	See Notes				See Notes						See Notes

- Recommended for all adults who lack documentation of vaccination, **OR** lack evidence of immunity
- Not recommended for all adults, but recommended for some adults based on either age **OR** increased risk for or severe outcomes from disease
- Recommended based on shared clinical decision-making
- Recommended for all adults, and additional doses may be necessary based on medical condition or other indications. See Notes.
- Precaution: Might be indicated if benefit of protection outweighs risk of adverse reaction
- Contraindicated or not recommended *Vaccinate after pregnancy, if indicated
- No Guidance/ Not Applicable

Adult Immunization Schedule by Age | CDC

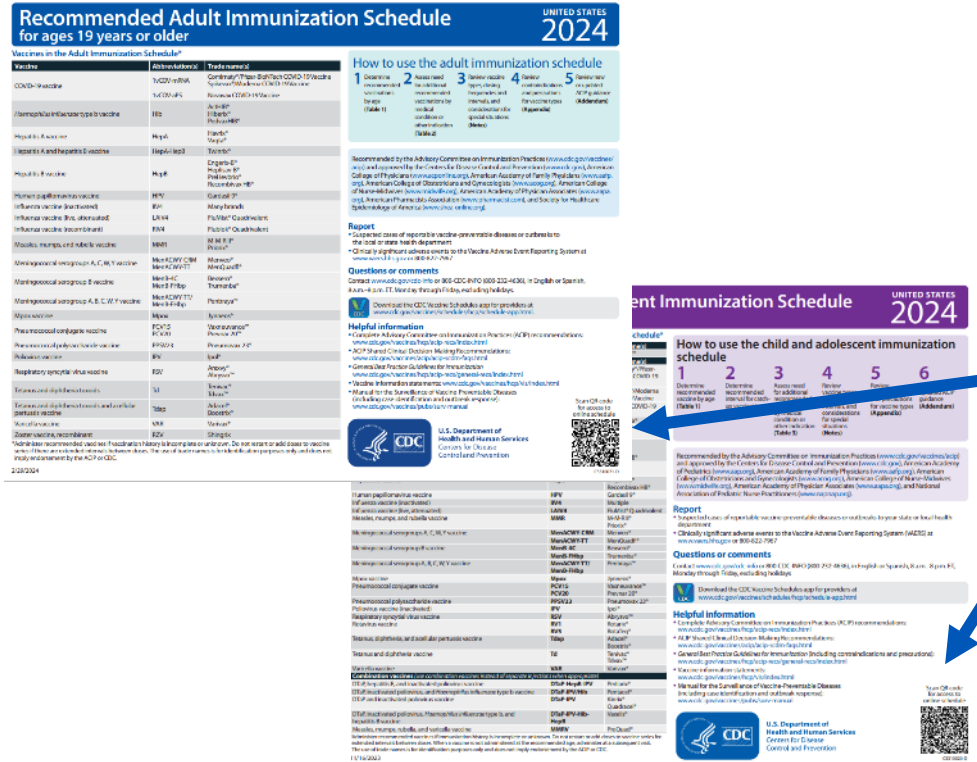
Schedule Addendums





[Immunization Schedules | CDC]

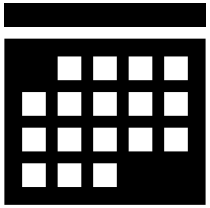
Best Practice: Immunization Schedules



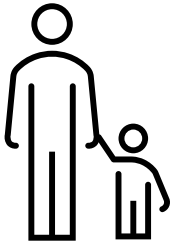
Use the QR code located on the first page to access the online schedule to check for updates!

[Immunization Schedules | CDC]

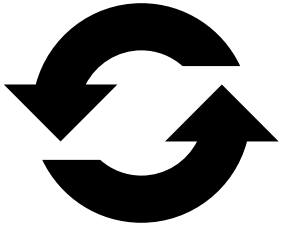
Immunization Schedule Best Practices



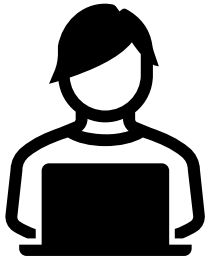
Follow the current schedule



Use the schedule for the patient's age

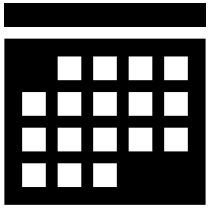


Check for updates



Know your patient's complete immunization history

Immunization Schedule Best Practices



Follow the current schedule

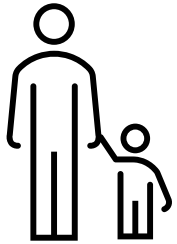
Use the schedule for the patient's age

Check for updates

Know your patient's complete immunization history

Immunization Schedule Best Practices

Follow the current schedule



Use the schedule for the patient's age

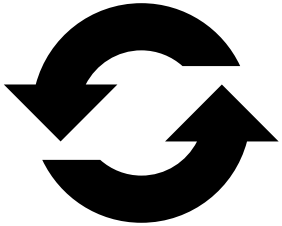
Check for updates

Know your patient's complete immunization history

Immunization Schedule Best Practices

Follow the current schedule

Use the schedule for the patient's age



Check for updates

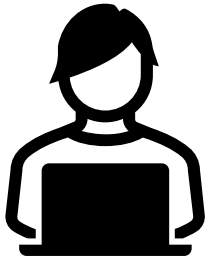
Know your patient's complete immunization history

Immunization Schedule Best Practices

Follow the current schedule

Use the schedule for the patient's age

Check for updates



Know your patient's complete immunization history

Immunization Information Systems (IIS) | CDC
Basics of Immunization Information Systems (IISs) (cdc.gov)

Continuing Education Information

- To claim continuing education (CE) for this course, please follow the steps below by July 2, 2026.
- Search and register for course WD4810-070224 in CDC TRAIN.
- Pass the post-assessment at 80%.
- Complete the evaluation.

- Visit “Your Learning” to access your certificates and transcript.
- If you have any questions, contact CDC TRAIN at train@cdc.gov or NCIRD’s CE Coordinator, Melissa Barnett, at MBarnett2@cdc.gov

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

E-mail Your Immunization Questions to Us

NIPINFO@cdc.gov

Thank You from Atlanta!

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.