Principles of Vaccination

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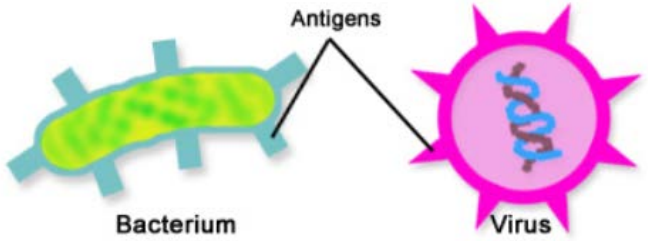
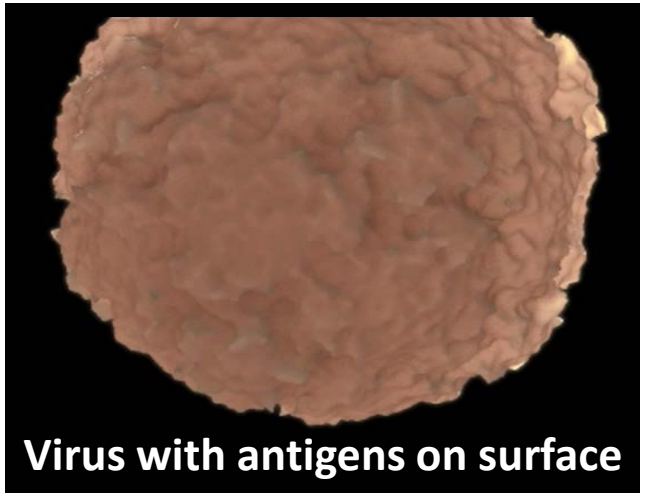
Immunity

- Self vs. “nonself”
- Protection from infectious diseases
- Usually indicated by the presence of antibody
- Generally specific to a single organism

Antigen

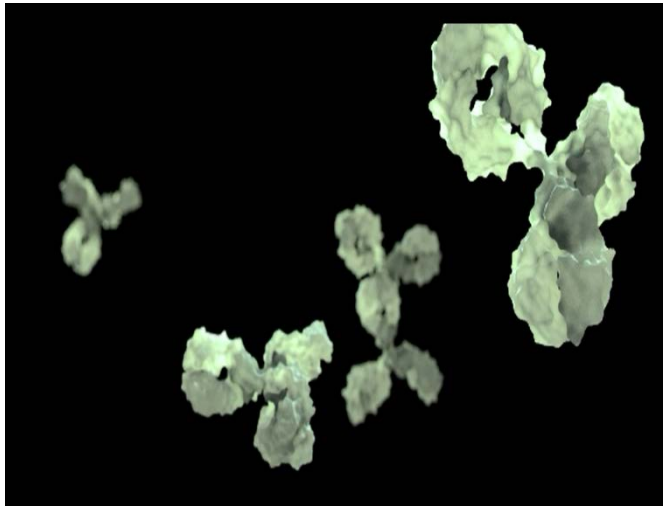
- Live or inactivated substances (e.g., viruses, bacteria, toxins)
  - Capable of stimulating an immune response
- Anti + gen = antibody generator

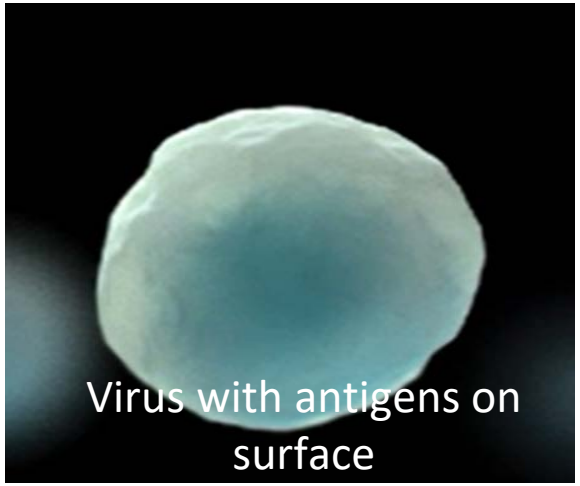




Antibody

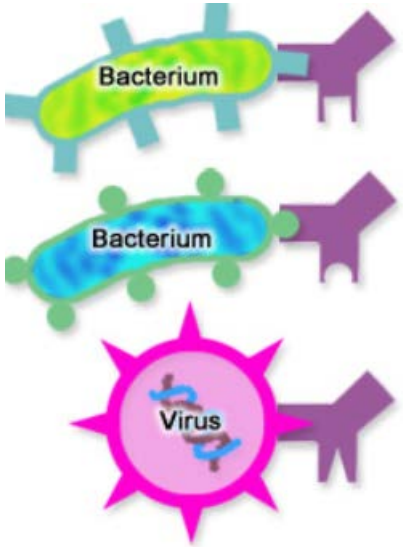
- Protein molecules (immunoglobulins)
  - Produced by B cells (lymphocytes) to bind to a corresponding antigen (lock and key mechanism)
  - Helps neutralize antigen and prepare it for destruction
  - B cells develop in the bone marrow



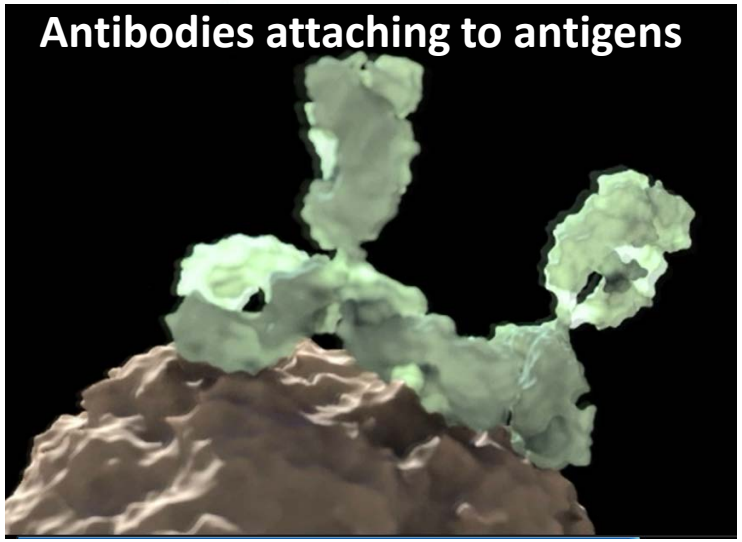


Arms of the Immune System

- Humoral
  - Production of antibodies that are specific to a certain antigen or group of antigens
  - Antibodies attach to invading organism and interfere with its ability to produce more invading organisms

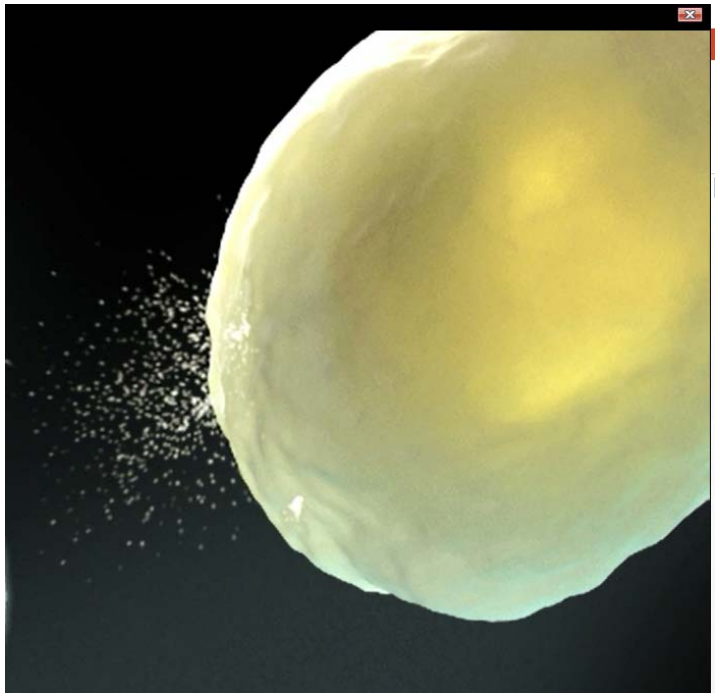


Antibodies specific to certain antigens



Arms of the Immune System

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



Types of Immunity: Active and Passive

Passive Immunity

- Transfer of antibody produced by one human or animal to another
- Temporary protection that wanes with time
- Transfer of antibody through placenta – important to protect infants

Passive Immunity Video

- The video will start shortly.

Sources of Passive Immunity

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

Sources of Passive Immunity

- Homologous human hyperimmune globulin (e.g., HBIG)
  - Taken from donors with high concentrations of a specific antibody
  - HBIG, RIG, TIG, VariZIG, VIG
- Heterologous hyperimmune serum
  - Antitoxin (e.g., diphtheria antitoxin)
  - Serum sickness

Sources of Passive Immunity

- Monoclonal antibodies
  - Derived from a single type, or clone, of antibody-producing cells (B cells)
    - Immune globulin from human sources is polyclonal (contains many different kinds of antibodies)
  - 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, as well as prevention of transplant rejection
  - Monoclonal-antibody-derived drugs end in –mab (i.e., Palivizumab)

Antibody for Prevention of RSV

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

Active Immunity

- Protection produced by a person's own immune system
- Lasts for many years, often lifetime

Active Immunity Video

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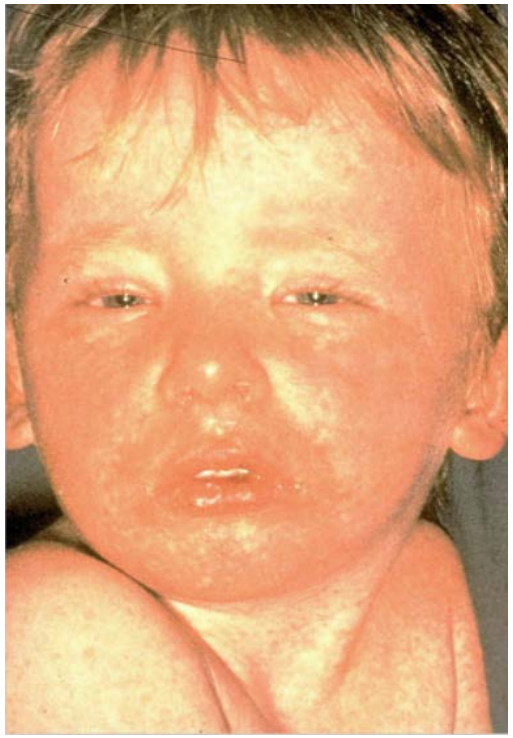
Sources of Active Immunity

- Infection with disease-causing form of organism



- Vaccination

Vaccination

- Active immunity produced by vaccine
  - Vaccine delivers a dead or attenuated (weakened, nonpathogenic) form of the pathogen
- Immunity and immunologic memory similar to natural infection but without risk of disease
  - Immunologic memory allows for an anamnestic response after the primary immune response, so that antibody reappears when the antigen is introduced

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
- Vaccinee
  - Age
  - Nutritional status
  - Genetics
  - Coexisting disease

Classification of Vaccines

Classification of Vaccines

- Live, attenuated (weakened form of the organism)
  - Viral
  - Bacterial
- Inactivated (non-live or fraction of the organism)
  - Viral
  - Bacterial

Principles of Vaccination

- General rule: The more similar a vaccine is to the natural disease, the better the immune response to the vaccine

Live Attenuated Vaccine Video

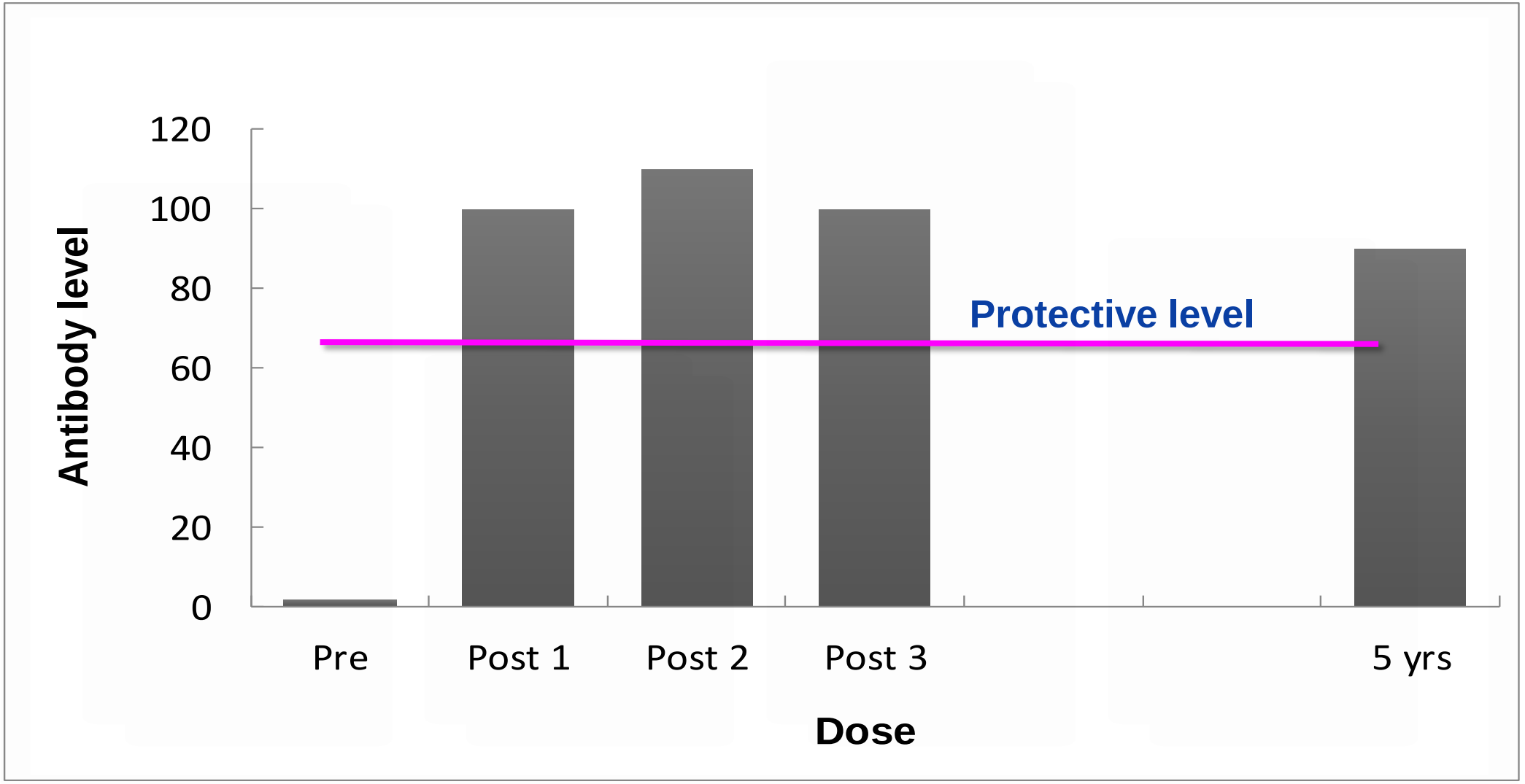
- The video will start shortly.

Live, Attenuated Vaccines

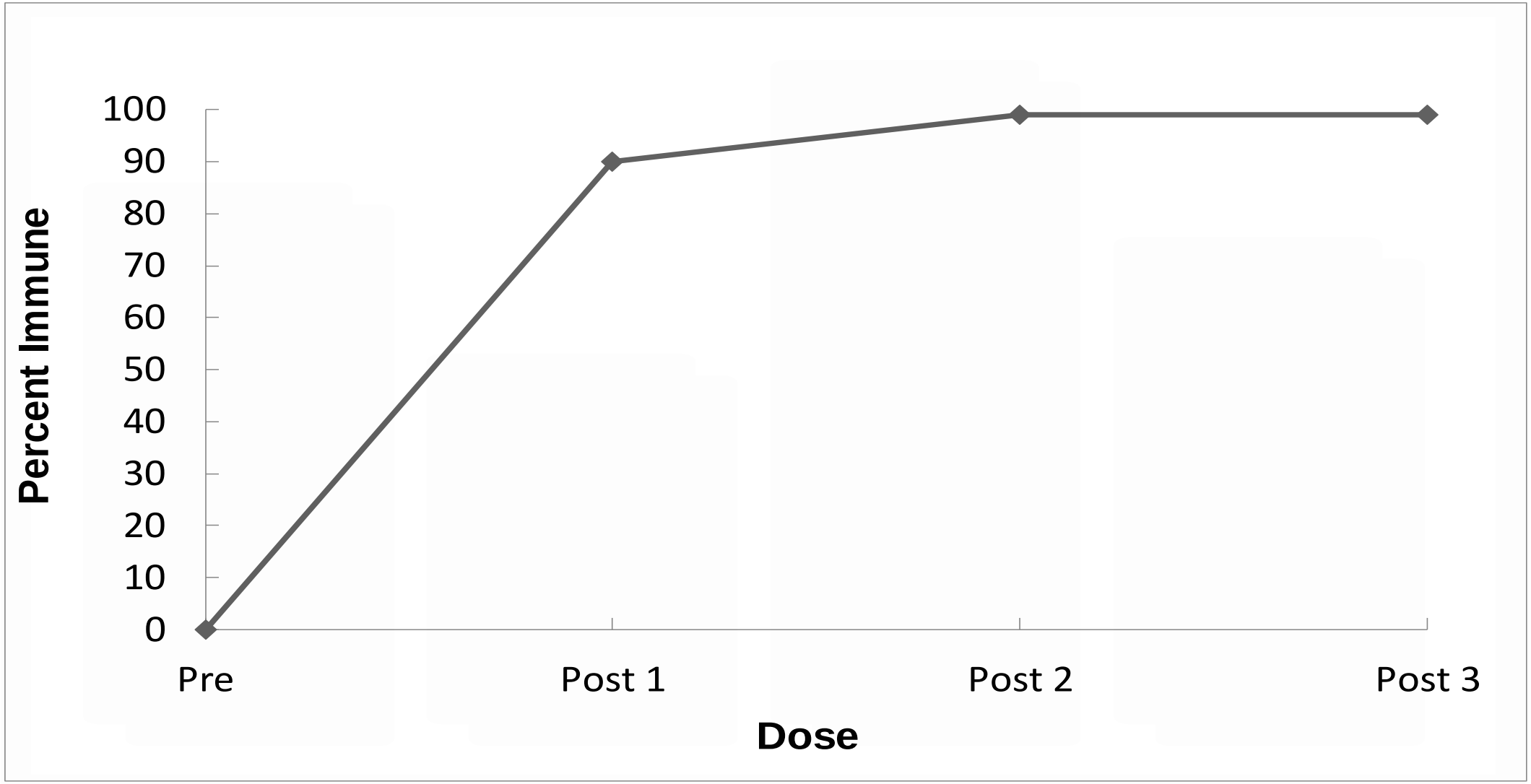
- Attenuated (weakened) form of the "wild" virus or bacterium
- Must replicate to produce an immune response
- Immune response virtually identical to natural infection
- Usually produce immunity with 1 dose*

*Except those administered orally

Individual Response to Live Vaccine

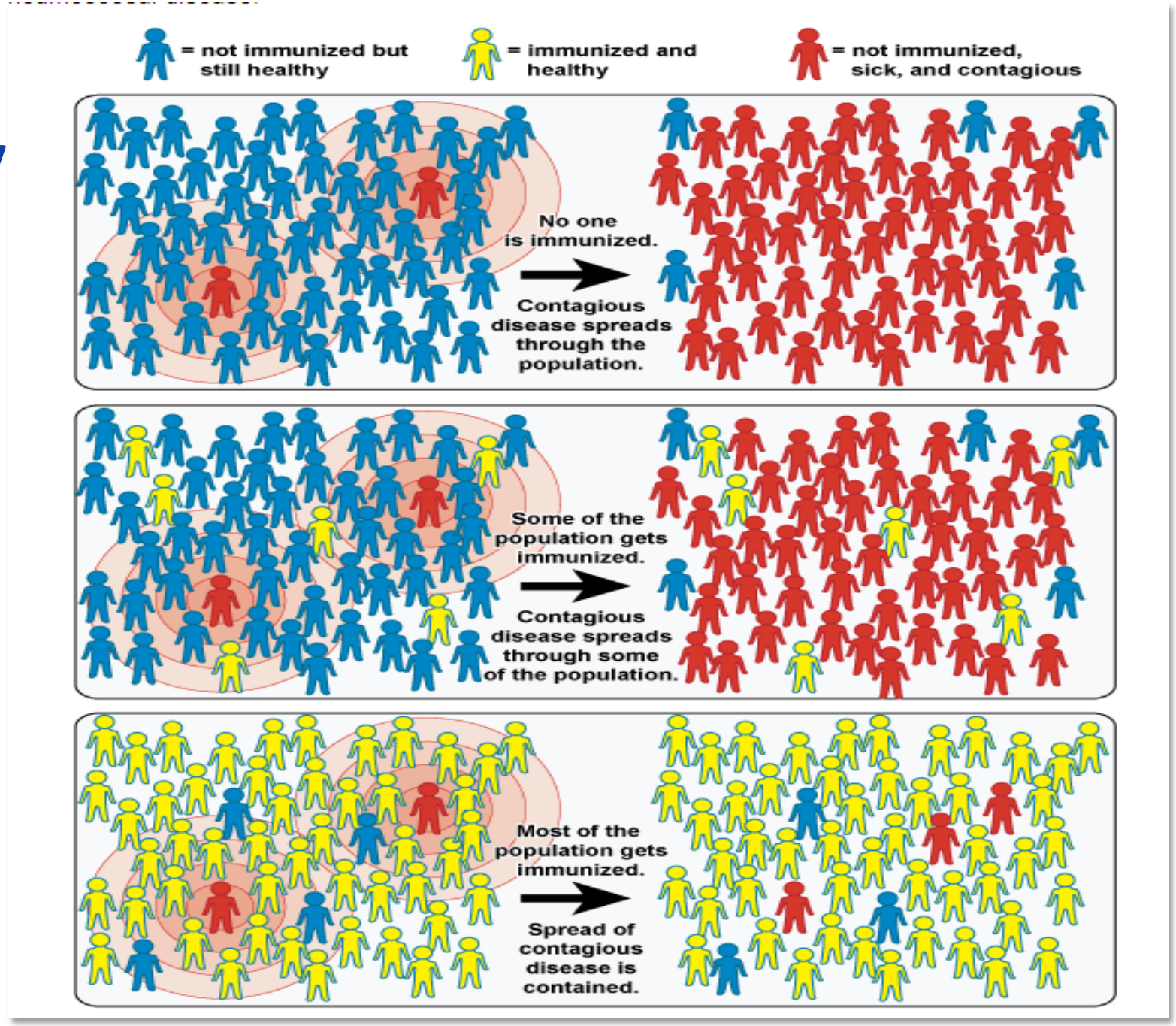


Population Response to Live Vaccine



Herd Immunity/ Community Immunity

- When a significant portion of the population is immune and provides protection for individuals who are not immune



Live, Attenuated Vaccines

- Severe reactions possible
- Interference from circulating antibody
- Fragile – must be stored and handled carefully

Live, Attenuated Vaccines

- Viral

MMR, varicella, zoster vaccine live (ZVL), yellow fever, rotavirus, LAIV (intranasal influenza), smallpox (vaccinia), oral adenovirus, oral polio*

- Bacterial

BCG**, oral typhoid, oral cholera

* Not used in the United States

**Not used in the United States for routine TB protection

Inactivated Vaccines

- Whole
  - Viruses
  - Bacteria
- Fractional
  - Protein-based
    - Toxoid
    - Subunit
  - Polysaccharide-based
    - Pure
    - Conjugate

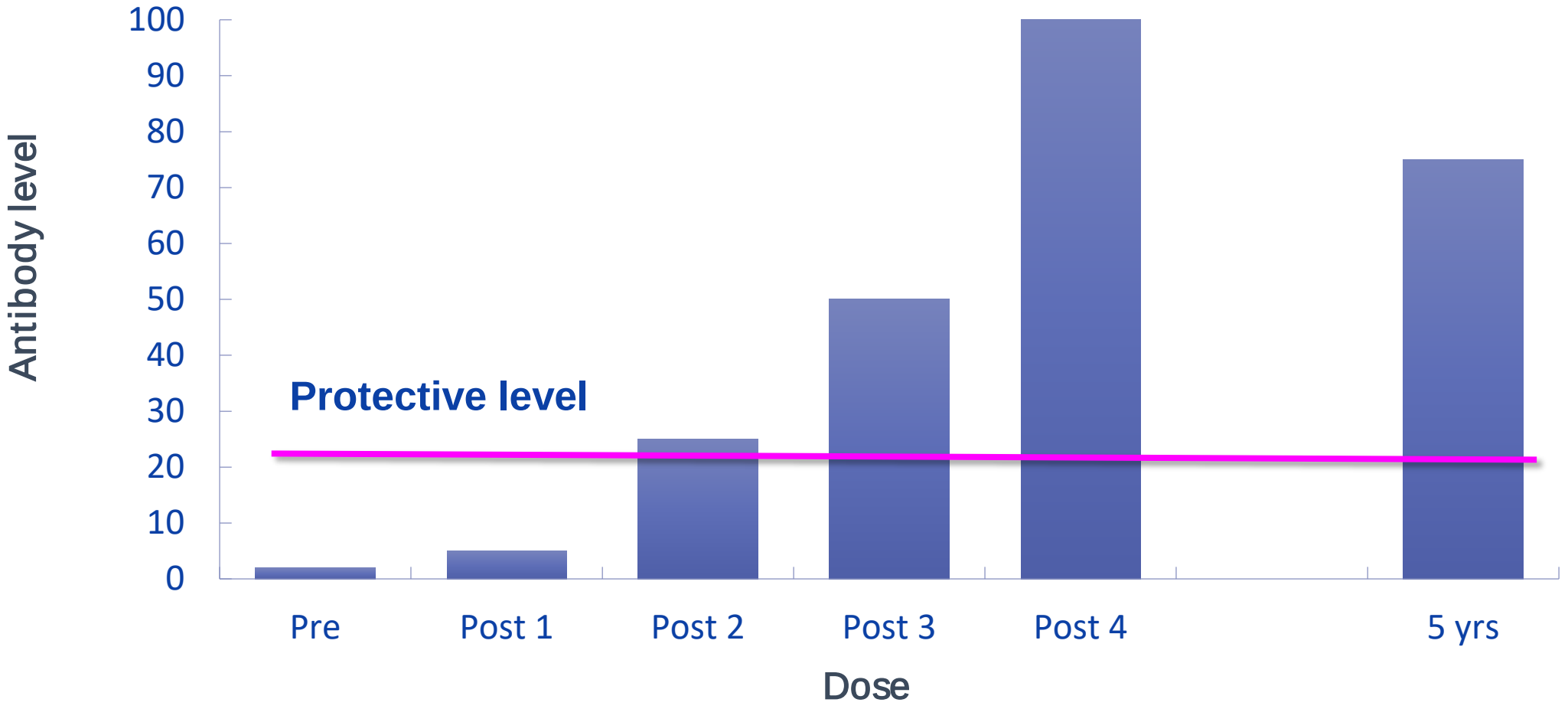
Inactivated Vaccine Vaccine Video

- The video will start shortly.

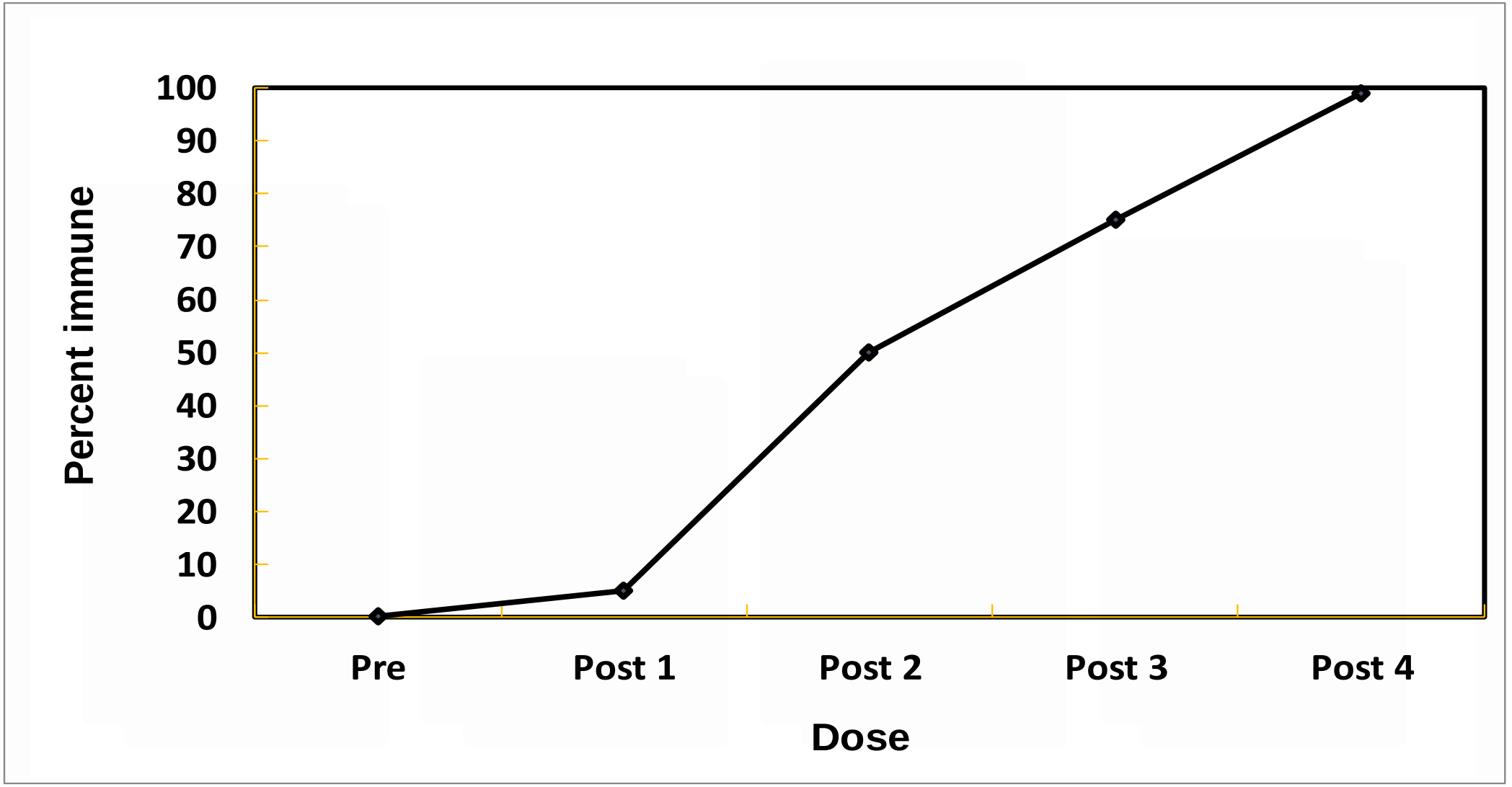
Inactivated Vaccines

- Cannot replicate
- Less affected by circulating antibody than live vaccines
  - Example: HepB vaccine and HBIG for perinatal hepatitis B PEP
- Always require multiple doses
- Immune response mostly humoral
- Antibody titer diminishes with time
- May require periodic supplemental doses

Individual Response to Inactivated Vaccine



Population Response to Inactivated Vaccine



Inactivated Vaccines

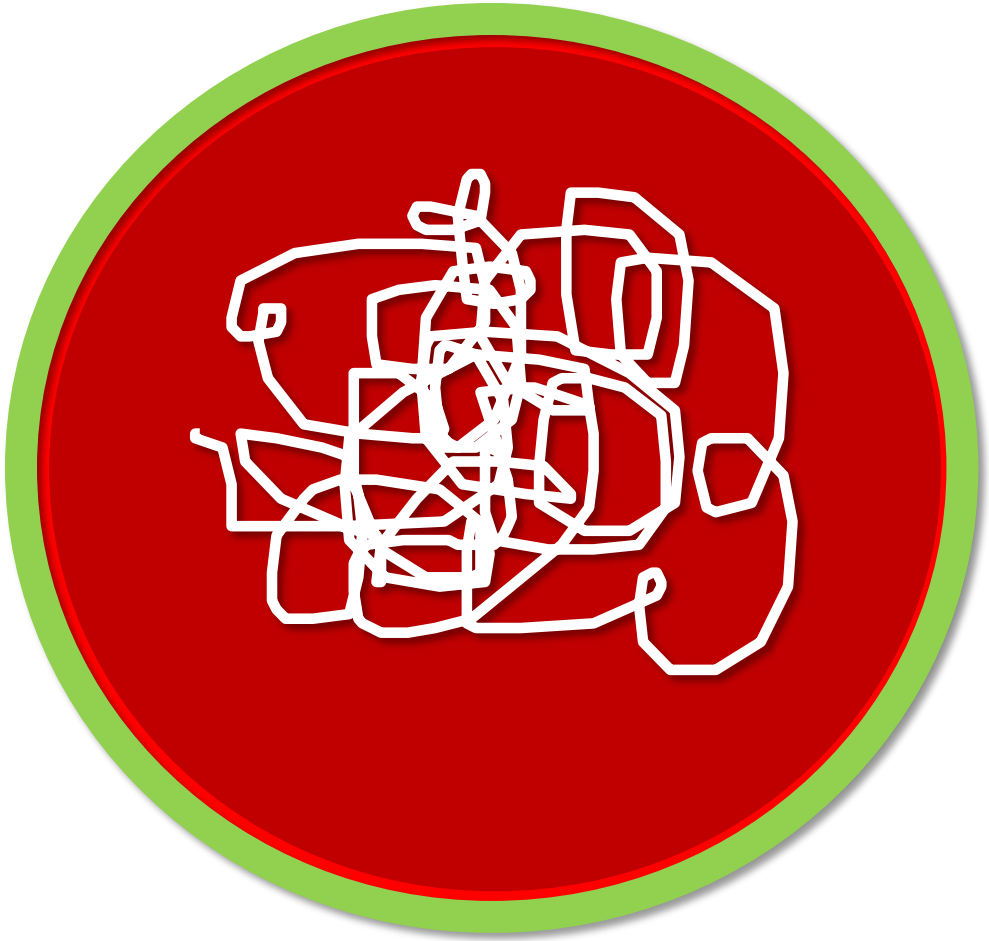
- Whole
  - Viral
    - Polio, hepatitis A, rabies, Japanese encephalitis, and influenza*
  - Bacterial
    - Pertussis*, typhoid*, cholera*, plague*

*Not available in the United States

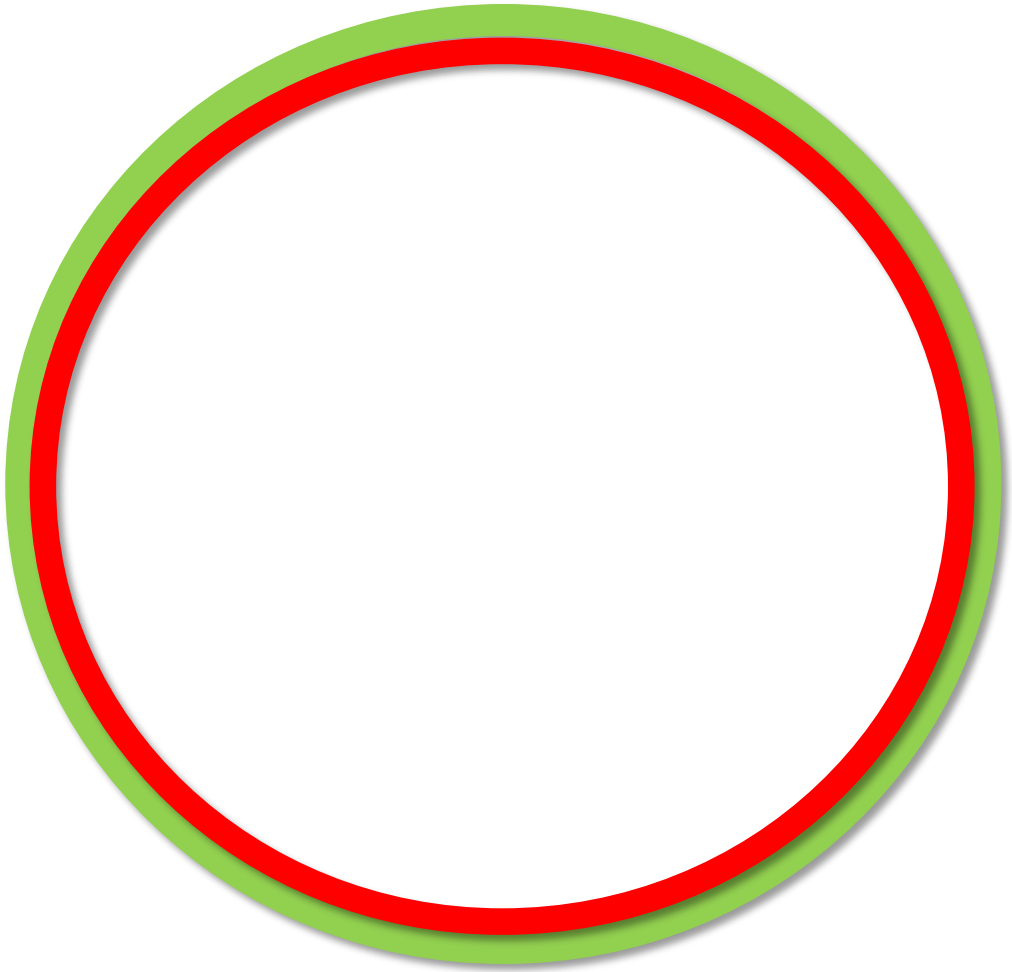
Inactivated Vaccines

- Fractional
  - Subunit
    - Hepatitis B, influenza, acellular pertussis, human papillomavirus, and anthrax
    - Polysaccharide vaccines
  - Toxoid
    - Diphtheria, tetanus

Capsular Polysaccharide



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

Polysaccharide Vaccines

- Pure polysaccharide
  - Pneumococcal (PPSV23)
  - *Salmonella* Typhi (Vi)
- Conjugate polysaccharide
  - *Haemophilus influenzae* type b (Hib)
  - Pneumococcal (PCV13)
  - Meningococcal

Genetically Engineered Vaccines

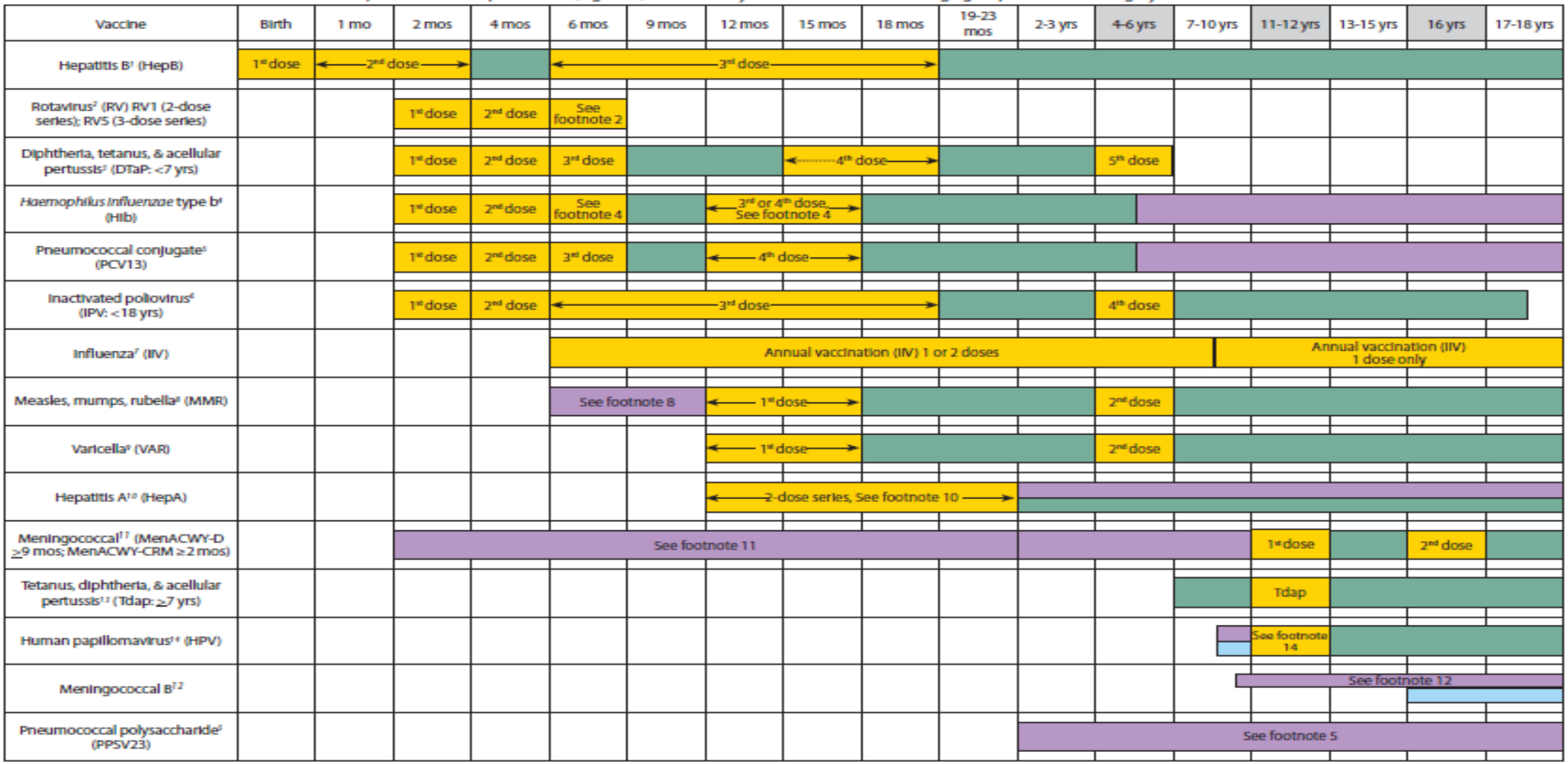
- Viral: hepatitis B, human papillomavirus, influenza (RIV), influenza (LAIV), and rotavirus (RV5)

- Bacterial: meningococcal B

Figure 1. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2018.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded in gray.



NOTE: The above recommendations must be read along with the footnotes of this schedule.

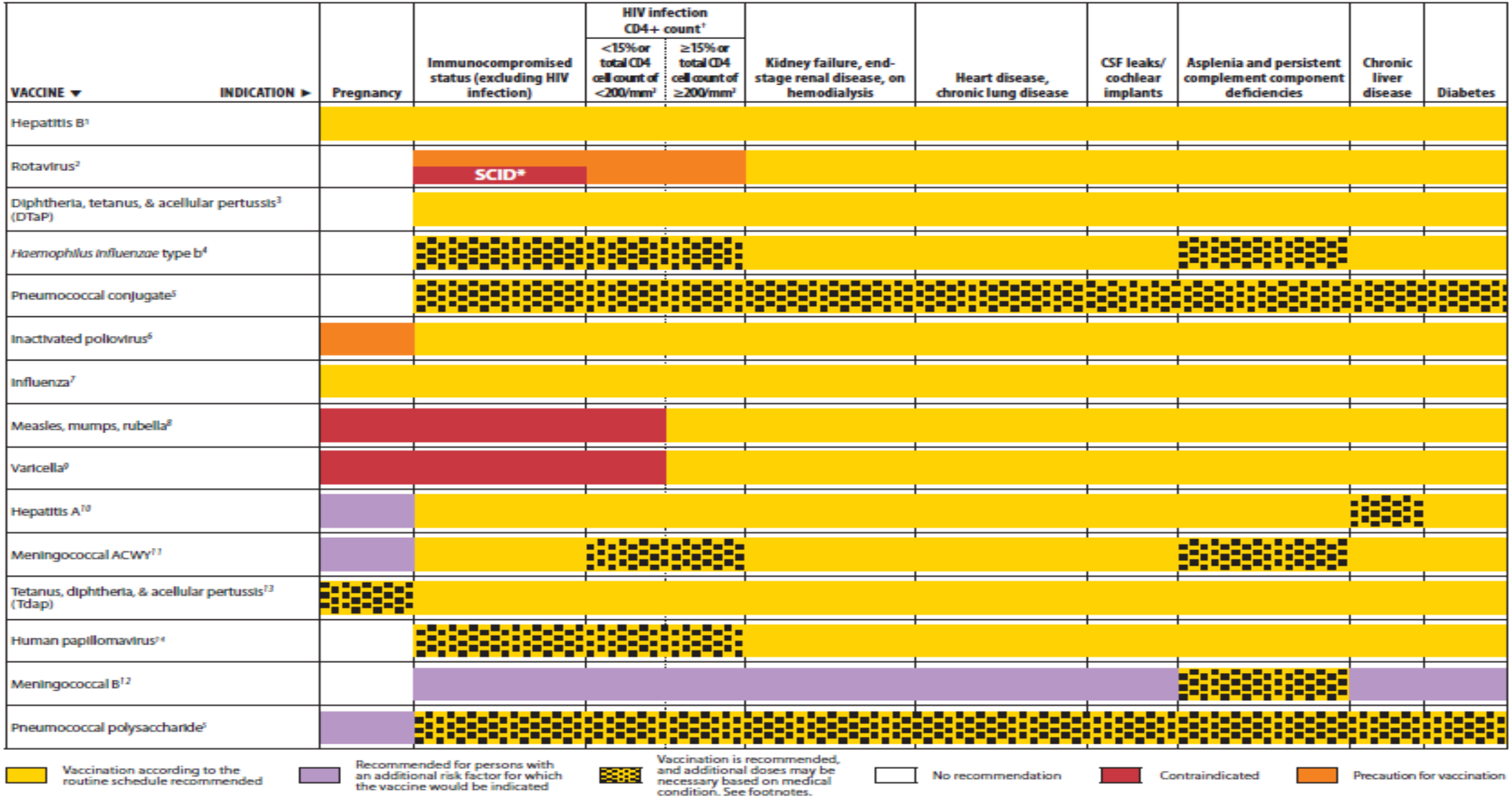
FIGURE 2. Catch-up immunization schedule for persons aged 4 months–18 years who start late or who are more than 1 month behind—United States, 2018.

The figure 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 Figure 1 and the footnotes 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[7]	Birth	4 weeks	8 weeks ***and*** at least 16 weeks after first dose. Minimum age for the final dose is 24 weeks.		
Rotavirus[2]	6 weeks Maximum age for first dose is 14 weeks, 6 days	4 weeks	4 weeks[2] Maximum age for final dose is 8 months, 0 days.		
Diphtheria, tetanus, and acellular pertussis[3]	6 weeks	4 weeks	4 weeks	6 months	6 months[3]
Haemophilus influenzae type b[4]	6 weeks	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 first dose was administered at age 15 months or older.	4 weeks[4] 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) or unknown. 8 weeks ***and*** age 12 through 59 months (as final dose)[4] • 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 administered at younger than 15 months; OR • if both doses were PRP-OMP (PedvaxHIB; Comvax) **and** were administered before the 1st birthday. No further doses needed if previous dose was administered at age 15 months or older.	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[5]	6 weeks	4 weeks if first dose 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 first dose was administered at age 24 months or older.	4 weeks if current age is younger than 12 months and previous dose given at <7 months old. 8 weeks (as final dose for healthy children) if previous dose given 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 given before age 12 months. No further doses needed for healthy children if previous dose administered at age 24 months or older.	8 weeks (as final dose) This dose only necessary for children aged 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age.	
Inactivated poliovirus[6]	6 weeks	4 weeks[6]	4 weeks[6] if current age is < 4 years 6 months (as final dose) if current age is 4 years or older	6 months[6] (minimum age 4 years for final dose).	
Measles, mumps, rubella[8]	12 months	4 weeks			
Varicella[9]	12 months	3 months			
Hepatitis A[10]	12 months	6 months			
Meningococcal[17] (MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)	6 weeks	8 weeks[11]	See footnote 11	See footnote 11	
Children and adolescents age 7 through 18 years					
Meningococcal[17] (MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)	Not Applicable (N/A)	8 weeks[11]			
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis[13]	7 years[13]	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[14]	9 years	Routine dosing intervals are recommended.[14]			
Hepatitis A[10]	N/A	6 months			
Hepatitis B[7]	N/A	4 weeks	8 weeks **and** at least 16 weeks after first dose.		
Inactivated poliovirus[6]	N/A	4 weeks	6 months[6] 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[8]	N/A	4 weeks			
Varicella[9]	N/A	3 months if younger than age 13 years. 4 weeks if age 13 years or older.			

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Figure 3. Vaccines that might be indicated for children and adolescents aged 18 years or younger based on medical indications



*Severe Combined Immunodeficiency
†For additional information regarding HIV laboratory parameters and use of live vaccines; see the General Best Practice Guidelines for Immunization "Altered Immunocompetence" at: www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html; and Table 4-1 (footnote D) at: www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html.

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Figure 1. Recommended immunization schedule for adults aged 19 years or older by age group, United States, 2018

This figure should be reviewed with the accompanying footnotes. This figure and the footnotes describe indications for which vaccines, if not previously administered, should be administered unless noted otherwise.

Vaccine	19–21 years	22–26 years	27–49 years	50–64 years	≥65 years
Influenza[1]	1 dose annually				
Tdap[2] or Td[2]	1 dose Tdap, then Td booster every 10 yrs				
MMR[3]	1 or 2 doses depending on indication (if born in 1957 or later)				
VAR[4]	2 doses				
RZV[5] (preferred)				2 doses RZV (preferred)	
or				or	
ZVL[5]					1 dose ZVL
HPV–Female[6]	2 or 3 doses depending on age at series initiation				
HPV–Male[6]	2 or 3 doses depending on age at series initiation				
PCV13[7]	1 dose				
PPSV23[7]	1 or 2 doses depending on indication				1 dose
HepA[8]	2 or 3 doses depending on vaccine				
HepB[9]	3 doses				
MenACWY[10]	1 or 2 doses depending on indication, then booster every 5 yrs if risk remains				
MenB[10]	2 or 3 doses depending on vaccine				
Hib[11]	1 or 3 doses depending on indication				

Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended for adults with other indications

No recommendation

Figure 2. Recommended immunization schedule for adults aged 19 years or older by medical condition and other indications, United States, 2018

This figure should be reviewed with the accompanying footnotes. This figure and the footnotes describe indications for which vaccines, if not previously administered, should be administered unless noted otherwise.

Vaccine	Pregnancy[1-6]	Immuno-compromised (excluding HIV infection)[3-7,11]	HIV infection CD4+ count (cells/µL)[3-7,9-10]		Asplenia, complement deficiencies[7,10,11]	End-stage renal disease, on hemodialysis[7,9]	Heart or lung disease, alcoholism[7]	Chronic liver disease[7-9]	Diabetes[7,9]	Health care personnel[3,4,9]	Men who have sex with men[6,8,9]
			<200	≥200							
Influenza[1]	1 dose annually										
Tdap[2] or Td[2]	1 dose Tdap each pregnancy	1 dose Tdap, then Td booster every 10 yrs									
MMR[3]	contraindicated	1 or 2 doses depending on indication									
VAR[4]	contraindicated	2 doses									
RZV[5] (preferred)					2 doses RZV at age ≥50 yrs (preferred)						
or					or						
ZVL[5]	contraindicated				1 dose ZVL at age ≥60 yrs						
HPV–Female[6]		3 doses through age 26 yrs			2 or 3 doses through age 26 yrs						
HPV–Male[6]		3 doses through age 26 yrs			2 or 3 doses through age 21 yrs						2 or 3 doses through age 26 yrs
PCV13[7]		1 dose									
PPSV23[7]		1, 2, or 3 doses depending on indication									
HepA[8]	2 or 3 doses depending on vaccine										
HepB[9]	3 doses										
MenACWY[10]	1 or 2 doses depending on indication , then booster every 5 yrs if risk remains										
MenB[10]	2 or 3 doses depending on vaccine										
Hib[11]	3 doses HSCT recipients only	1 dose									

Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended for adults with other indications

Contraindicated

No recommendation

What Do You Think?

- Because pure polysaccharide vaccines (e.g., PPSV23) are T-cell-independent, they provide good booster responses with subsequent doses.
  - True
  - False