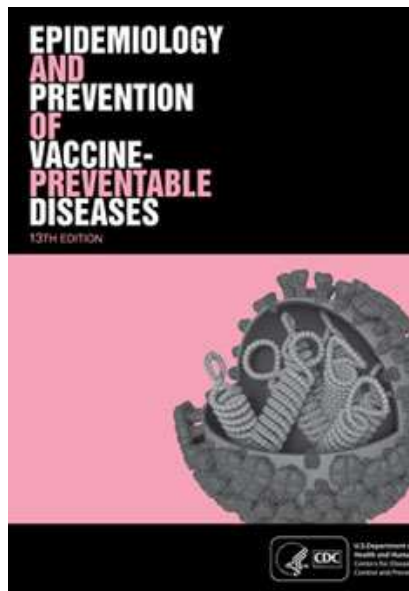




## The Ground Rules of Immunizations

Todd Mahr, MD



<https://www.cdc.gov/vaccines/pubs/pinkbook/index.html>

Please note: An update and an erratum have been published for this report. To view the update, [click here](#). To view the erratum, [click here](#).

Centers for Disease Control and Prevention  
**MMWR** Morbidity and Mortality Weekly Report  
Recommendations and Reports / Vol. 60 / No. 2  
January 28, 2011

### General Recommendations on Immunization Recommendations of the Advisory Committee on Immunization Practices (ACIP)



Continuing Education Examination available at <http://www.cdc.gov/mmwr/rr/rr6002.html>

 U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention

<https://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf>

<http://www.immunize.org/>



## Impact of Vaccines in the 20<sup>th</sup> & 21<sup>st</sup> Centuries

### Comparison of 20<sup>th</sup> Century Annual Morbidity & Current Morbidity: Vaccine-Preventable Diseases

Disease	20 <sup>th</sup> Century Annual Morbidity <sup>*</sup>	2017 Reported Cases <sup>†</sup>	% Decrease
Smallpox	29,005	0	100%
Diphtheria	21,053	0	100%
Pertussis	200,752	18,975	91%
Tetanus	580	33	94%
Polio (paralytic)	16,316	0	100%
Measles	530,217	120	>99%
Mumps	162,344	6,109	96%
Rubella	47,745	7	>99%
CRS	152	5	97%
<i>Haemophilus influenzae</i>	20,000 (est.)	33 <sup>§</sup>	>99%

<sup>\*</sup> JAMA. 2007;298(18):2155-2163

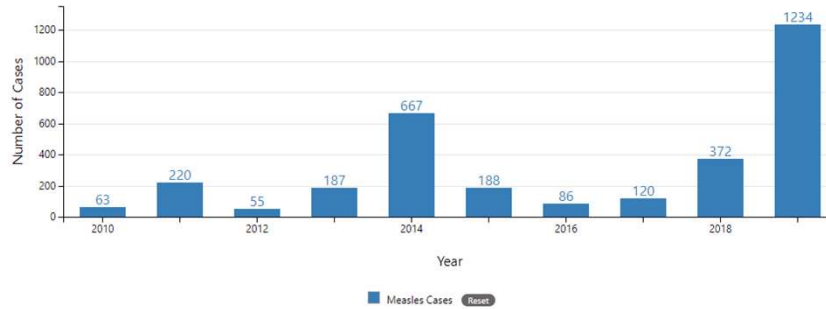
<sup>†</sup> CDC. National Notifiable Diseases Surveillance System, 2017 Annual Tables of Infectious Disease Data. Atlanta, GA. CDC Division of Health Informatics and Surveillance, 2018. Available at: [www.cdc.gov/nndss/infectious-tables.html](http://www.cdc.gov/nndss/infectious-tables.html). Accessed on December 3, 2018. NNDSS finalized annual data as of November 28, 2018.

<sup>§</sup> *Haemophilus influenzae* type b (Hib) <5 years of age. An additional 10 cases of Hib are estimated to have occurred among the 203 notifications of Hi (<5 years of age) with unknown serotype.

<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/e/impact.pdf>

## Number of Measles Cases Reported by Year

2010-2019\*\* (as of August 29, 2019)



Data Table

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Measles Cases	63	220	55	187	667	188	86	120	372	1234

<https://www.cdc.gov/measles/cases-outbreaks.html>

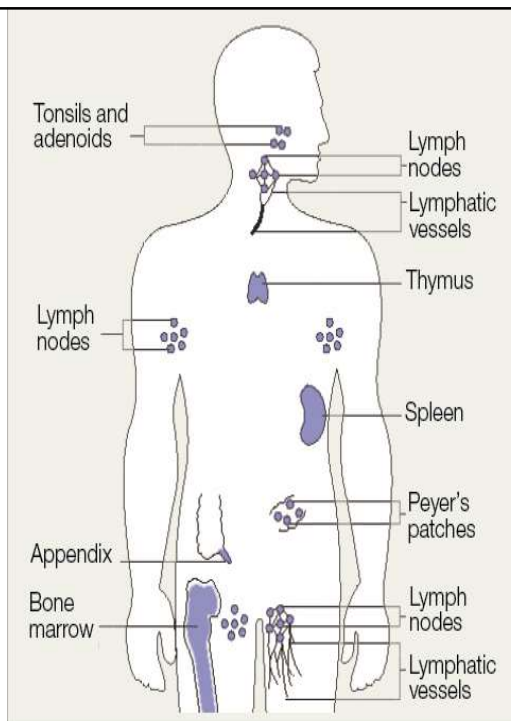
## Three Lines of Defense

**Nonspecific** - not specialized for specific pathogens

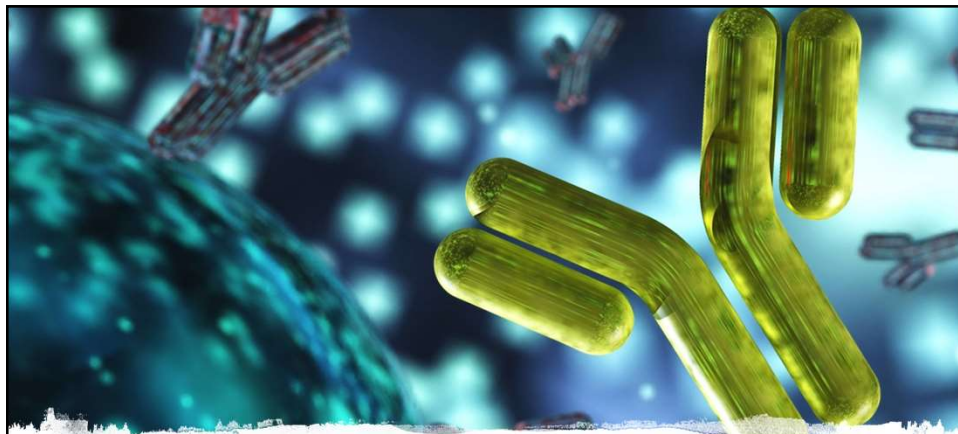
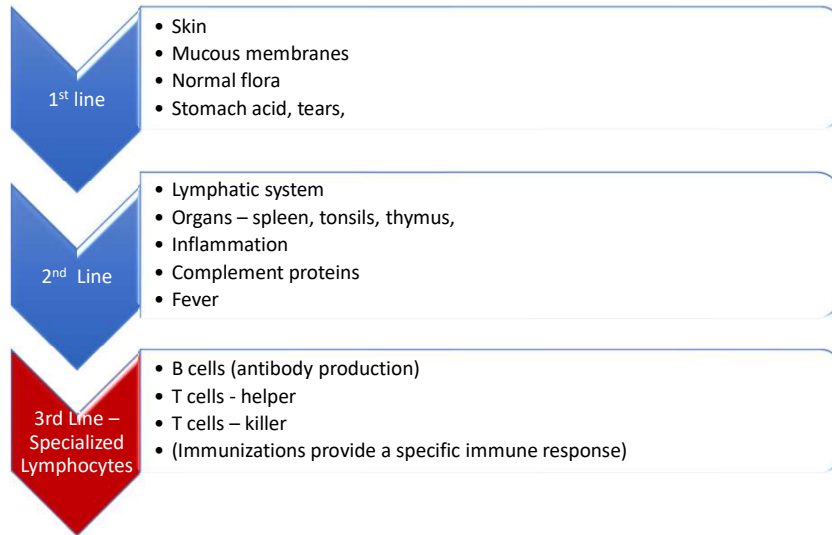
- Outside protection
- Inside protection
  - Fast response

**Specific**

- Adaptive immunity
  - Specific immune response
  - Targeted response
  - Delayed response
  - Remembers



## Immune Defense System



## Immunology of Vaccine-Preventable Diseases

- Antigen – a live (e.g. viruses and bacteria) or inactivated substance capable of producing an immune response.
- Antibody – protein molecules (immunoglobins) produced by B lymphocytes to help eliminate an antigen

## Immunity



- Self vs non self
- Protection from infectious diseases
- Usually indicated by the presence of an antibody
- Generally specific to a single antigen
- Active/Natural Immunity
  - Protection by the persons own immune system – usually lifetime
- Passive immunity
  - Protection transferred from another - wanes

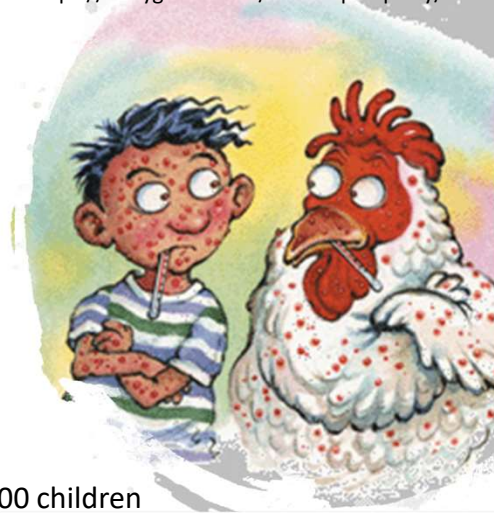


<https://rotary5790.org/stories/an-introduction-to-poliomyelitis>

## Is Natural Immunity Better?

## Chicken Pox and Natural Immunity

(The Chicken Pox Party)



- Risk for shingles later in life.
- Missed work and school.
- Risk to others.
- Chicken pox killed almost 7,000 children in the United States every year before the vaccine was available.

## Passive Immunity

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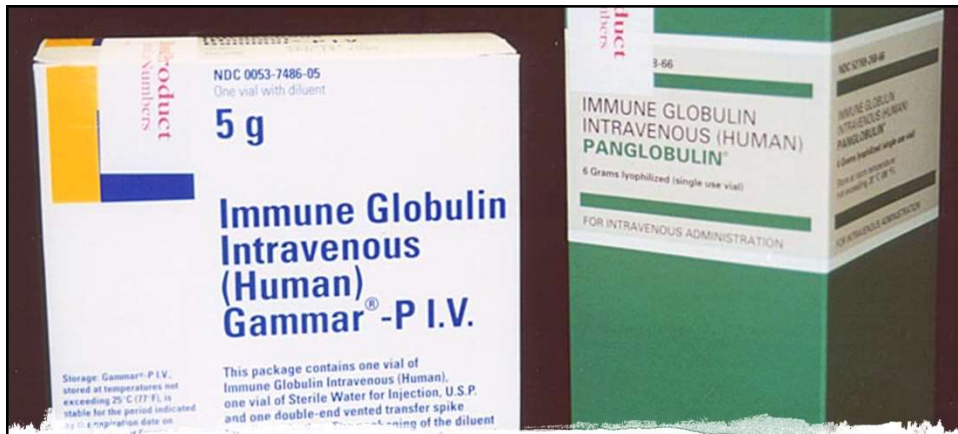
- Transfer of exogenously produced antibody
- Transplacental most important source in infancy
- Temporary protection





## Passive Immunity

- Antitoxin or Heterologous hyperimmune serum
  - Produced in animals
  - Used for diphtheria and botulism
  - Problem: serum sickness



## Passive Immunity

- Immune globulin
  - Pooled IgG from adult U.S. donors
  - Used for measles and Hepatitis A
  - All blood products contain antibodies

## Passive Immunity

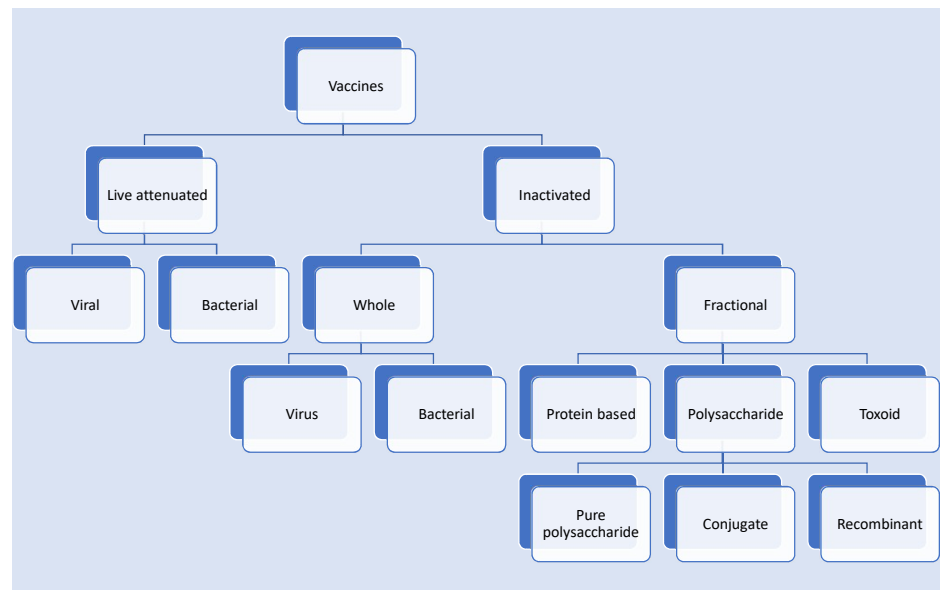


FIGURE 1. Finger that has just been injected with 1.0 mL of immunoglobulin. Note that no blanching is seen.

- Hyperimmune globulin
  - High titer specific human antibody
  - Used for Hepatitis B, rabies, tetanus and others
  - Not a vaccine

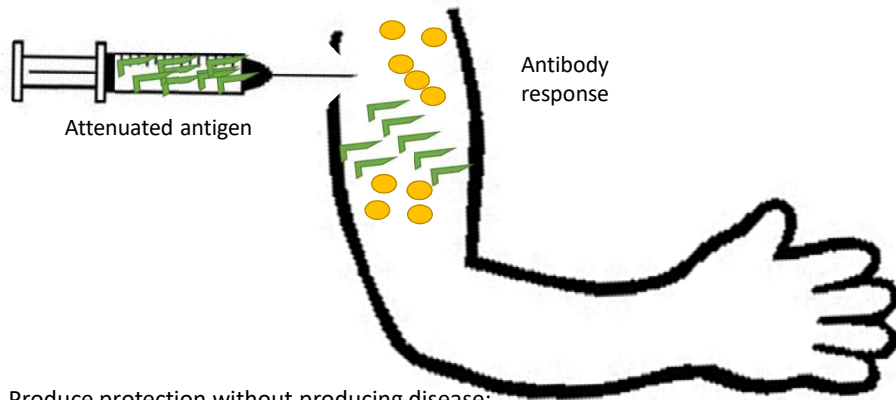
*Am. J. Trop. Med. Hyg.*, 75(2), 2006, pp. 363–364

## Classification of Vaccines



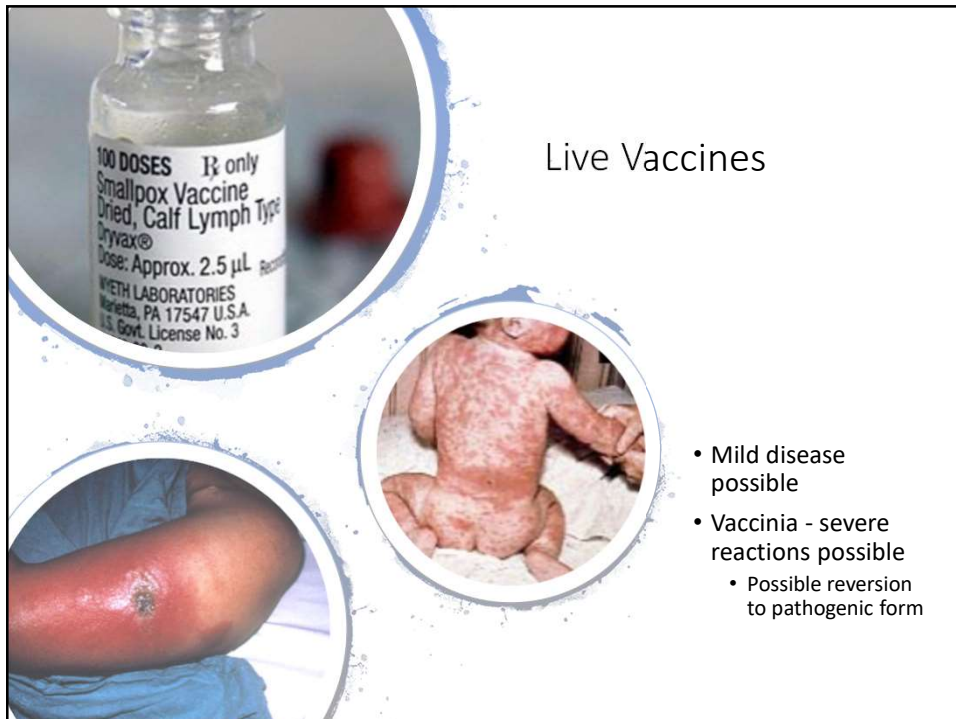


## Live Vaccines



- Produce protection without producing disease; derived from wild agent
- Attenuated (weakened)
- Must replicate to be effective
- Immune response like natural infection
- Effective with 1-2 doses

## Live Vaccines



- Mild disease possible
- Vaccinia - severe reactions possible
  - Possible reversion to pathogenic form



ELVIS Concert

## General Principle #1

The more similar a vaccine is to the natural diseases, the better the response.

## Live Vaccines

- Interference from circulating antibody
- Unstable
  - Temperature sensitive
  - Light sensitive



## Antibody for Prevention of RSV

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



<http://www.rtmagazine.com/2014/07/rsv-research-infected-children/>

## Live Attenuated Vaccines

Viral      MMR  
              Rotavirus  
              Oral polio  
              Yellow fever  
              Vaccinia  
              Varicella  
              Nasal influenza

Bacterial    BCG  
               Oral typhoid



<https://www.thesun.co.uk>

*Infant with measles*

- *Conjunctivitis*
- *Coryza*
- *Cough*



## Inactivated Vaccines

- Can not replicate
- Minimal interference from circulating antibody
- Generally require 3-5 doses
- Immune response mostly humoral
- Antibody titer falls over time – booster doses
- Principal antigen may not be defined

Inactivated  
Vaccines –  
Whole cell

<b>Viral</b>	Influenza Polio Rabies Hepatitis B
<b>Bacterial</b>	Pertussis Typhoid Cholera Plague

Inactivated Vaccines	<b>Subunit</b>	Hepatitis B Influenza Acellular pertussis Anthrax
	<b>Toxoid</b>	Diphtheria Tetanus
	<b>Recombinant</b>	Hepatitis B HPV



**Polysaccharide Vaccines**

- Age-related immune response
- Not consistently immunogenic in children <2 years of age
- No booster response
- Antibody with less functional activity
- Immunogenicity improved by conjugation

## Polysaccharide Vaccines

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

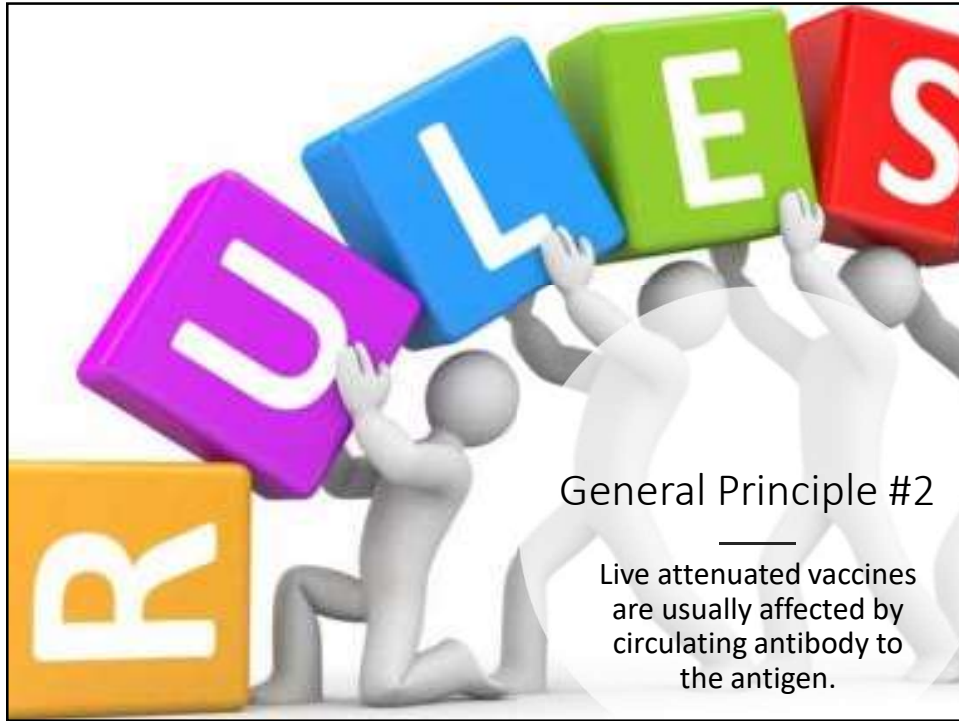


## SUMMARY



### Summary of Principles

- Active immunity is most desirable
- Two types of vaccines – live attenuated and inactivated
- Schedule, contraindications, and adverse events can generally be predicted based on type of vaccine



### General Principle #2

Live attenuated vaccines are usually affected by circulating antibody to the antigen.



### General Principle #3

Inactivated vaccines are generally not affected by circulating antibody to the antigen.

## Antibody and Measles or Varicella Containing\* Vaccines

Product Given First	Action
Vaccine	Wait two weeks before giving antibody
Antibody	Wait 3 months or longer before giving vaccine

\*except zoster vaccine

## General Principle #4

All vaccines can be administered at the same the same visit as other vaccines.\*

\*Exceptions

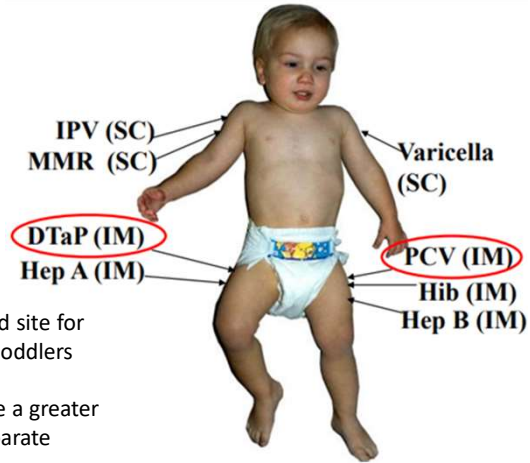
- MCV4 and PCV 13
- PCV13 & PPSV 23
- except cholera and yellow fever



<https://www.nytimes.com/2014/11/18/science/taking-more-than-one-vaccine-at-a-time-doesnt-hurt.html>



## Multiple injections during one visit



- Anterolateral thigh is the preferred site for multiple IM injections and for all toddlers aged 12 months-2 years
- Administer vaccines likely to cause a greater local reaction (DTaP, PCV) into separate limbs
- Inject the most painful injections last (i.e., MMR, PCV)
- Separate injection sites by 1-2 inches

## General Principle #5

- Increasing the interval between doses of a multi-dose vaccine does not diminish the effectiveness of the vaccine.
  - Commonly asked with HPV, Hepatitis B & DTaP



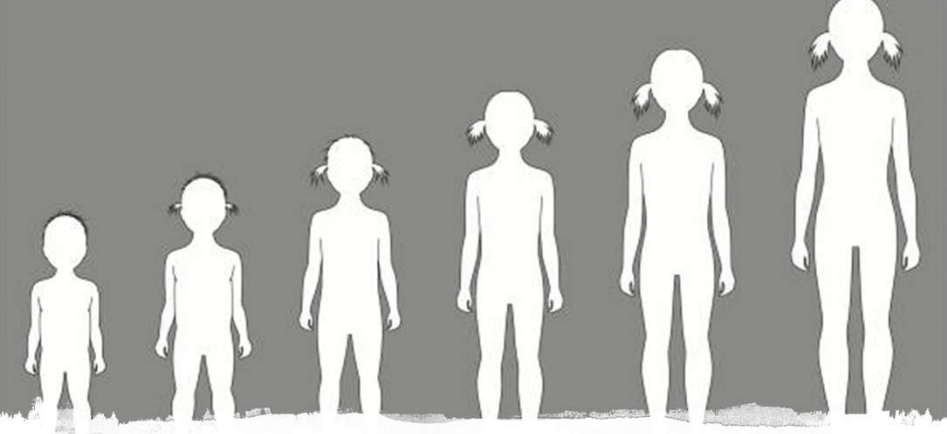
## General Principle #6

- Decreasing the interval between doses of a multi-dose vaccine may interfere with antibody response and protection.



Recommended and Minimum Ages and Intervals Between Doses of Routinely Recommended Vaccines <sup>1,2,3,4</sup>				
Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
Diphtheria-tetanus-acellular pertussis (DTaP)-1 <sup>5</sup>	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 <sup>6</sup>	6 months <sup>6</sup>
DTaP-4	15-18 months	15 months <sup>6</sup>	3 years	6 months
DTaP-5 <sup>7</sup>	4-6 years	4 years	—	—
<i>Haemophilus influenzae</i> type b (Hib)-1 <sup>8</sup>	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3 <sup>9</sup>	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	—	—
Hepatitis A (HepA)-1 <sup>5</sup>	12-23 months	12 months	6-18 months	6 months
HepA-2	≥18 months	18 months	—	—
Hepatitis B (HepB)-1 <sup>10</sup>	Birth	Birth	4 weeks-4 months	4 weeks
HepB-2	1-2 months	4 weeks	8 weeks-17 months	8 weeks
HepB-3 <sup>11</sup>	6-18 months	24 weeks	—	—
Herpes zoster Live (ZVL) <sup>12</sup>	≥60 years	60 years <sup>13</sup>	—	—
Herpes zoster Recombinant (RZV)-1	≥50 years	50 years <sup>14</sup>	2-6 months	4 weeks
RZV-2	≥50 years (+2-6 months)	50 years	—	—
Human papillomavirus (HPV) – Two-Dose Series <sup>15</sup>				
HPV-1	11-12 years	9 years	6 months	5 months
HPV-2	11-12 years (+ 6 months)	9 years (+ 5 months) <sup>16</sup>	—	—
Human papillomavirus (HPV) – Three-Dose Series				
HPV-1 <sup>17</sup>	11-12 years	9 years	1-2 months	4 weeks


<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/a/age-interval-table.pdf>



Grace Period

- 4-day grace period
- Know your state immunization laws.
- Know the minimum intervals

The image shows a series of six white silhouettes of a child growing into an adult, arranged from left to right against a dark grey background. The silhouettes increase in size and detail, with the final one showing pigtails and a more developed body.



General Principle #7

Live attenuated vaccines generally produce long-lasting immunity with a single dose.

The image shows a series of black silhouettes representing the life cycle of a woman, from left to right: a baby in a stroller, a toddler, a young girl, a pregnant woman, a woman holding a baby, a woman with a shopping bag, a woman with a shopping bag, a woman with a cane, and a gravestone. The silhouettes are reflected on a white surface below them.



## General Principle #8

Inactivated vaccines require multiple doses and often require periodic boosting to maintain immunity.



## General Principle #9

Adverse events following live attenuated vaccines are similar to a mild form of the natural illness.

<https://www.sciencedirect.com/topics/neuroscience/progressive-vaccinia>

# YOU CALL THE SHOTS

Shoulder injuries related to vaccine administration  
Improper vaccine administration could result in shoulder injuries such as shoulder bursitis and tendinitis.

Make sure vaccination is safe.

## KNOW THE SITE. GET IT RIGHT!

When administering vaccine by an intramuscular (IM) injection to an adult:



### Use the correct syringe and needle

- » Vaccine may be administered using either a 1-mL or 3-mL syringe
- » Use a 22 to 25 gauge needle
- » Use the correct needle size based on your patient's size

Injection site: Deltoid muscle of upper arm



\*Some experts recommend a 5/8-inch needle for men and women who weigh less than 60 kg (130 lbs).

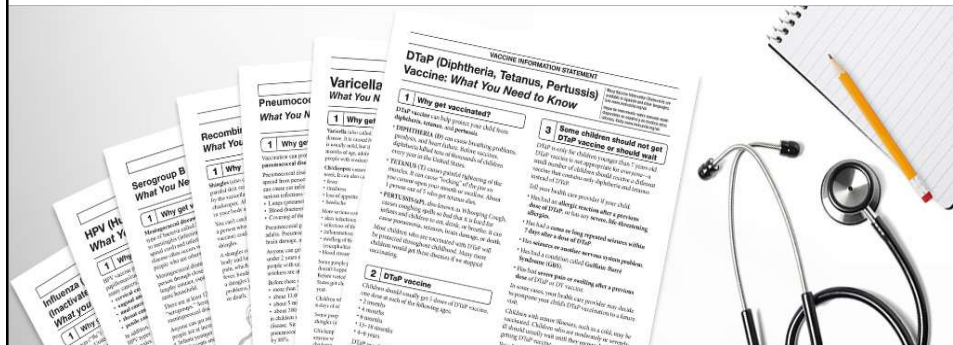
## General Principle #10

Select the appropriate injection site and needle

Adverse events following inactivated vaccines are mostly local with or without fever.

## General Principle #11 - VISs are required by law

- **Prior** to the vaccination,
- Must be given prior to **each dose** of a multi-dose series.
- Must be provided **regardless of the age**





# CAUTION

## General Principle #12

### Screen for Contraindications and Precautions

- Precautions are not contraindications
- Confer with provider regarding precautions



## Precautions

- A condition in recipient which may result in a life-threatening problem if vaccine is administered OR
- May compromise the ability of the vaccine to produce immunity.
- Examples include:
  - GBS – ascending paralysis 6 weeks following previous dose of influenza vaccine
  - Temperature  $\geq 105^{\circ}\text{F}$ , inconsolable crying lasting more than 3 hours, or collapse w/in 48 hrs. or convulsions w/out fever within 3 days after receiving DTaP
  - Acute or moderate severe gastroenteritis before receiving Rotavirus vaccine

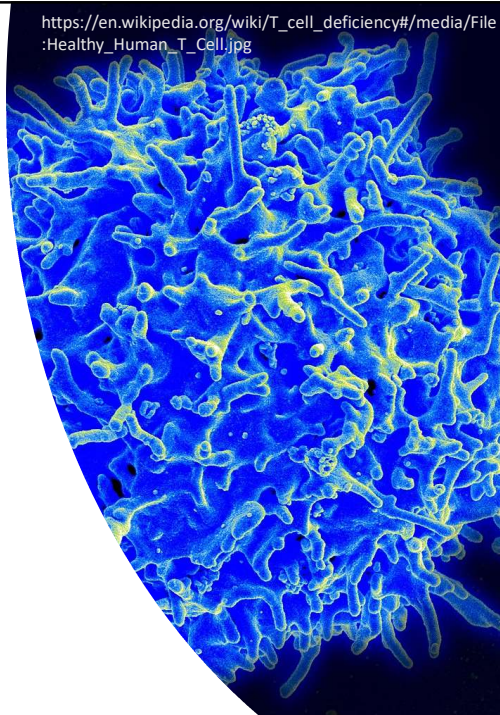
## Contraindications and Precautions

- A likely recipient which is likely to result in a life-threatening problem if vaccine is administered.
- Most contraindications and precautions are temporary, and the vaccine may be given at a later time.
- 2 Permanent contraindications:
  - severe allergy to vaccine component
  - encephalopathy w/in 7 of pertussis vaccination
- 4 temporary contraindications
  - Pregnancy (live)
  - Immunosuppression (live)
  - Severe illness (live and inactivated)
  - Blood products (live)



## Immunosuppression

- Live vaccines should not be administered to severely immunosuppressed persons
- Persons with isolated B-cell deficiency may receive varicella vaccine
- Inactivated vaccines are safe to use but may yield sub-optimal response
- Immunosuppressed
  - Chemotherapy
  - Radiation
  - Steroids
    - $\geq 20$  mg prednisone daily
    - $\geq 2$  mg/kg daily
    - Not aerosols, alternate day, short courses, topical





<https://phil.cdc.gov/Details.aspx?pid=22161>

## Allergy to Vaccine Component

- Egg – no longer an issue for MMR or influenza
- Thimerosal- most vaccines are preservative free except the MDV of influenza vaccine
- Latex – read package insert

## What's in a vaccine?

- Some excipients are added to a vaccine for a specific purpose. These include:
- Preservatives, to prevent contamination. For example, thimerosal.
- Adjuvants, to help stimulate a stronger immune response. For example, aluminum salts.
- Stabilizers, to keep the vaccine potent during transportation and storage. For example, sugars or gelatin.
- Others are residual trace amounts of materials that were used during the manufacturing process and removed. These can include:
- Cell culture materials, used to grow the vaccine antigens. For example, egg protein, various culture media.
- Inactivating ingredients, used to kill viruses or inactivate toxins. For example, formaldehyde.
- Antibiotics, used to prevent contamination by bacteria (e.g. neomycin).

<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf>



## Vaccine Excipient & Media Summary

### Excipients Included in U.S. Vaccines, by Vaccine

In addition to weakened or killed disease antigens (viruses or bacteria), vaccines contain very small amounts of other ingredients – excipients or media.

Some excipients are added to a vaccine for a specific purpose. These include:

**Preservatives**, to prevent contamination. For example, thimerosal.

**Adjuvants**, to help stimulate a stronger immune response. For example, aluminum salts.

**Stabilizers**, to keep the vaccine potent during transportation and storage. For example, sugars or gelatin.

Others are residual trace amounts of materials that were used during the manufacturing process and removed. These include:

**Cell culture materials**, used to grow the vaccine antigens. For example, egg protein, various culture media.

**Inactivating ingredients**, used to kill viruses or inactivate toxins. For example, formaldehyde.

**Antibiotics**, used to prevent contamination by bacteria. For example, neomycin.

The following table lists all components, other than antigens, shown in the manufacturers' package insert (PI) for each vaccine. Each of these PIs, which can be found on the FDA's website (see below) contains a description of that vaccine's manufacturing process, including the amount and purpose of each substance. In most PIs, this information is found in Section 11: "Description."

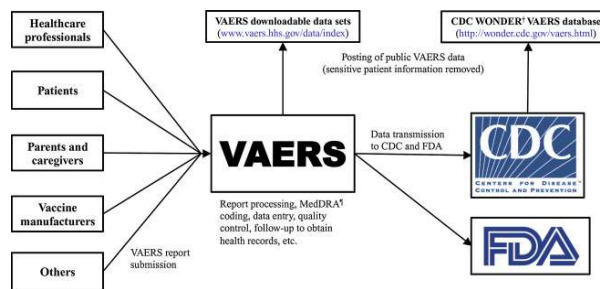
All information was extracted from manufacturers' package inserts.

If in doubt about whether a PI has been updated since this table was prepared, check the FDA's website at:  
<http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm>

Vaccine	Contains
Adenovirus	human-diploid fibroblast cell cultures (strain WI-38), Dulbecco's Modified Eagle's Medium, fetal bovine serum, sodium bicarbonate, monosodium glutamate, sucrose, D-mannose, D-fructose, dextrose, human serum albumin, potassium phosphate, plasdone C, anhydrous lactose, microcrystalline cellulose, polacrillin potassium, magnesium stearate, cellulose acetate phthalate, alcohol, acetone, castor oil, FD&C Yellow #6 aluminum lake dye
Anthrax (Biothrax)	amino acids, vitamins, inorganic salts, sugars, aluminum hydroxide, sodium chloride, benzethonium chloride, formaldehyde
BCG (Tice)	glycerin, asparagine, citric acid, potassium phosphate, magnesium sulfate, iron ammonium citrate, lactose
Cholera (Shanchol)	casamino acids, yeast extract, mineral salts, anti-foaming agent, ascorbic acid, hydrolyzed

<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf>

## General Principle #13



<https://doi.org/10.1016/j.vaccine.2015.07.035>

## Report adverse events following a vaccine

- Vaccine Adverse Event Reporting (VAERS)
- Vaccine Injury Compensation Program

**National Childhood Vaccine Injury Act  
Vaccine Injury Table<sup>a</sup>**

Vaccine	Adverse Event	Time Interval
I. Tetanus toxoid-containing vaccines (e.g., DTaP, Tdap, DTP-Hib, DT, Td, TT)	A. Anaphylaxis or anaphylactic shock	0-4 hours
	B. Brachial neuritis	2-28 days
	C. Any acute complication or sequela (including death) of above events	Not applicable
II. Pertussis antigen-containing vaccines (e.g., DTaP, Tdap, DTP, P, DTP-Hib)	A. Anaphylaxis or anaphylactic shock	0-4 hours
	B. Encephalopathy (or encephalitis)	0-72 hours
	C. Any acute complication or sequela (including death) of above events	Not applicable
III. Measles, mumps and rubella virus-containing vaccines in any combination (e.g., MMR, MR, M, R)	A. Anaphylaxis or anaphylactic shock	0-4 hours
	B. Encephalopathy (or encephalitis)	5-15 days
	C. Any acute complication or sequela (including death) of above events	Not applicable
IV. Rubella virus-containing vaccines (e.g., MMR, MR, R)	A. Chronic arthritis	7-42 days
	B. Any acute complication or sequela (including death) of above event	Not applicable
V. Measles virus-containing vaccines (e.g., MMR, MR, M)	A. Thrombocytopenic purpura	7-30 days
	B. Vaccine-Strain Measles Viral Infection in an immunodeficient recipient	0-6 months



Invalid Contraindications to Vaccinations – Minor Illness

- Low grade fever
  - Upper respiratory infection
  - Otitis media
  - Mild diarrhea
- No evidence of increased adverse events
- Decreased efficacy is doubtful in children with URIs
- Contributes to a missed opportunity



General Principle  
#13  
Avoid missed opportunities

**What is a missed opportunity?**

A child in need of immunization seeks health care but does not receive immunizations or all needed immunizations.

## Questions

