Immunization

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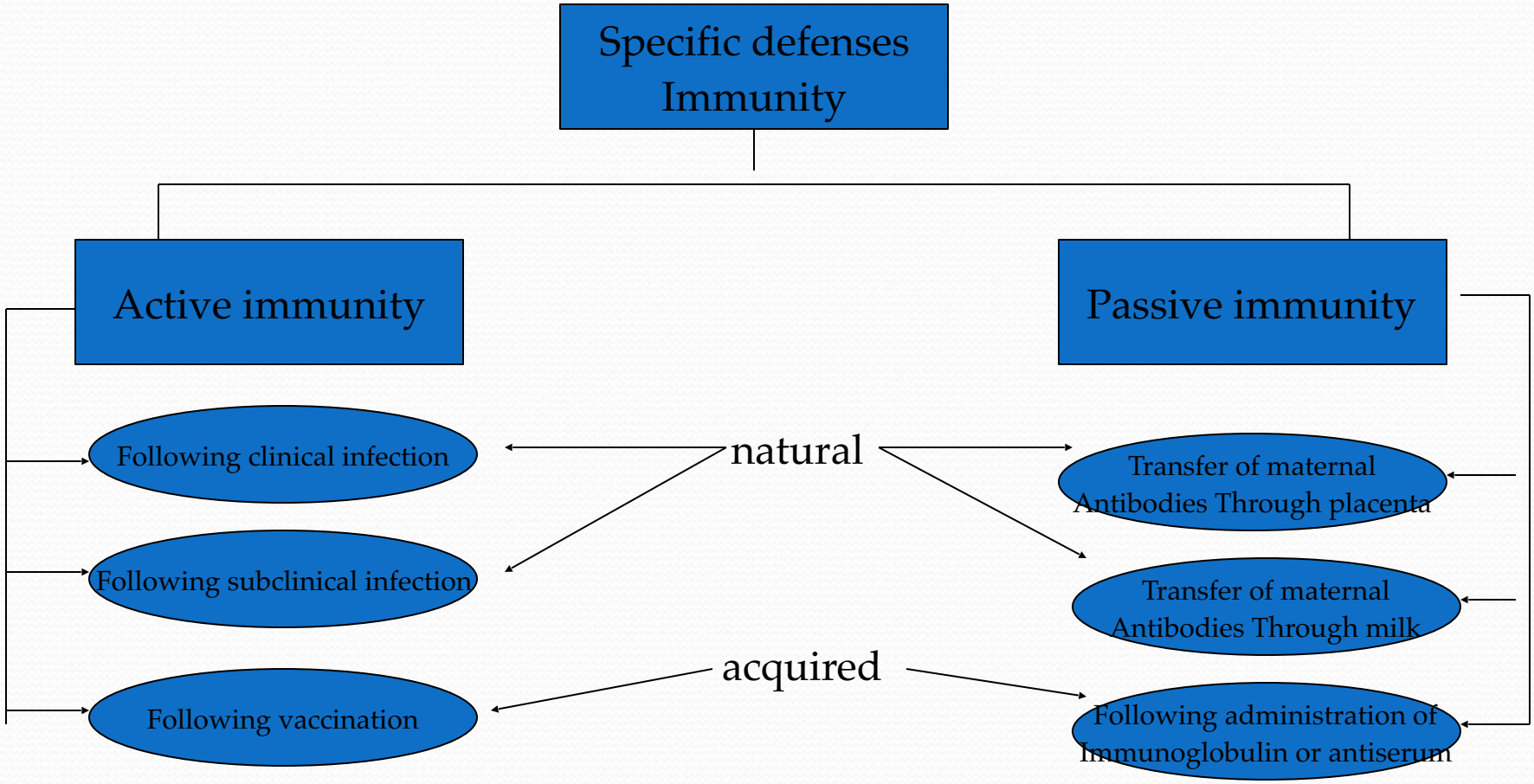
Objectives

- Differentiates active and passive immunity
- To understand the types of currently used vaccines, the differences, and the mechanisms of protection
- Vaccination scheme, routes of administration, and common side effects
- To understand how to develop a vaccine and the general requirements for vaccine development and adjvuants
- To understand the new concept of vaccines against non-microbes such as self or tumor molecules

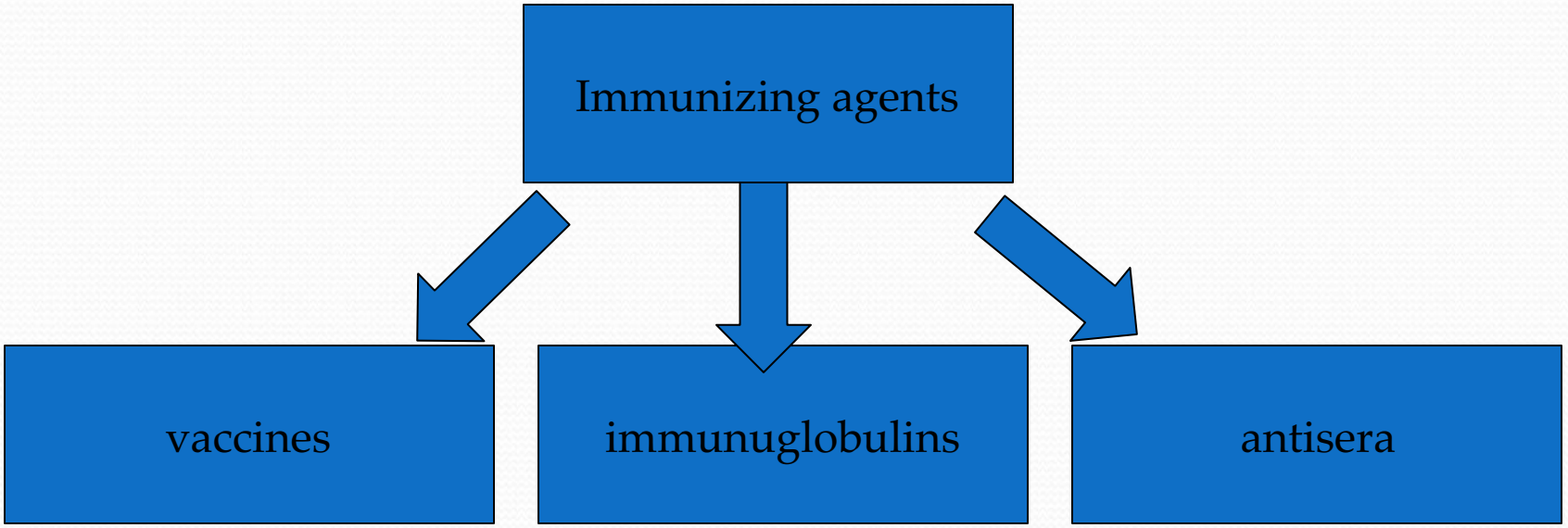
Immunity


Specific defenses
Immunity
Active immunity
Passive immunity
Following clinical infection
Following subclinical infection
Following vaccination
natural
acquired
Transfer of maternal
Antibodies Through placenta
Transfer of maternal
Antibodies Through milk
Following administration of
Immunoglobulin or antiserum

Active and passive immunity

- Active immunity: Resistance developed in response to stimulus by an antigen (infecting agent or vaccine) and is characterized by the production of antibodies by the host.
- Passive immunity: Immunity conferred by an antibody produced in another host. It may be acquired naturally or artificially (through an antibody-containing preparation).

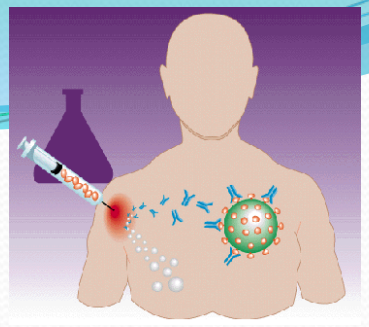
Immunizing agents



Immunoglobulins

- Immunoglobulins: Two types of immunoglobulin preparations are available for passive immunization:
  - Normal human immunoglobulin
  - Specific (hyper-immune) human immunoglobulin
- Antisera or antitoxins: These are materials prepared in animals or non human sources such as horses.

Vaccination

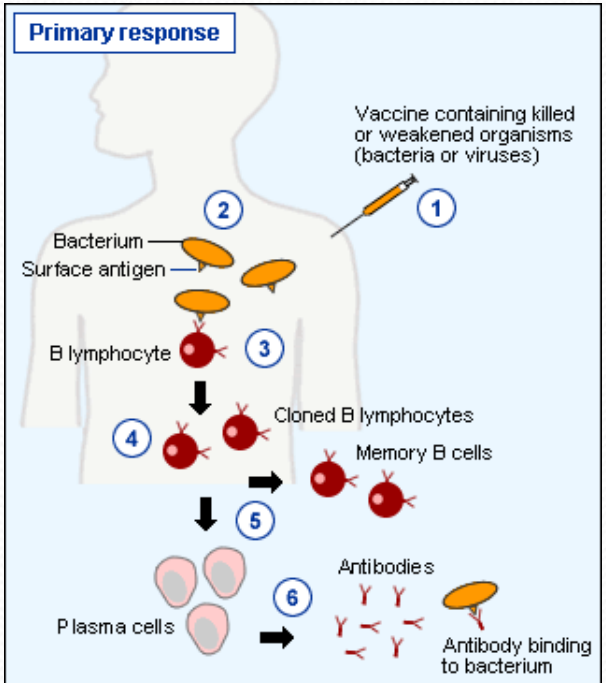


- Vaccination is a method of giving antigen to stimulate the immune response through active immunization.
- A vaccine is an immuno-biological substance designed to produce specific protection against a given disease.
- A vaccine is “antigenic” but not “pathogenic”.

Importance of Vaccination

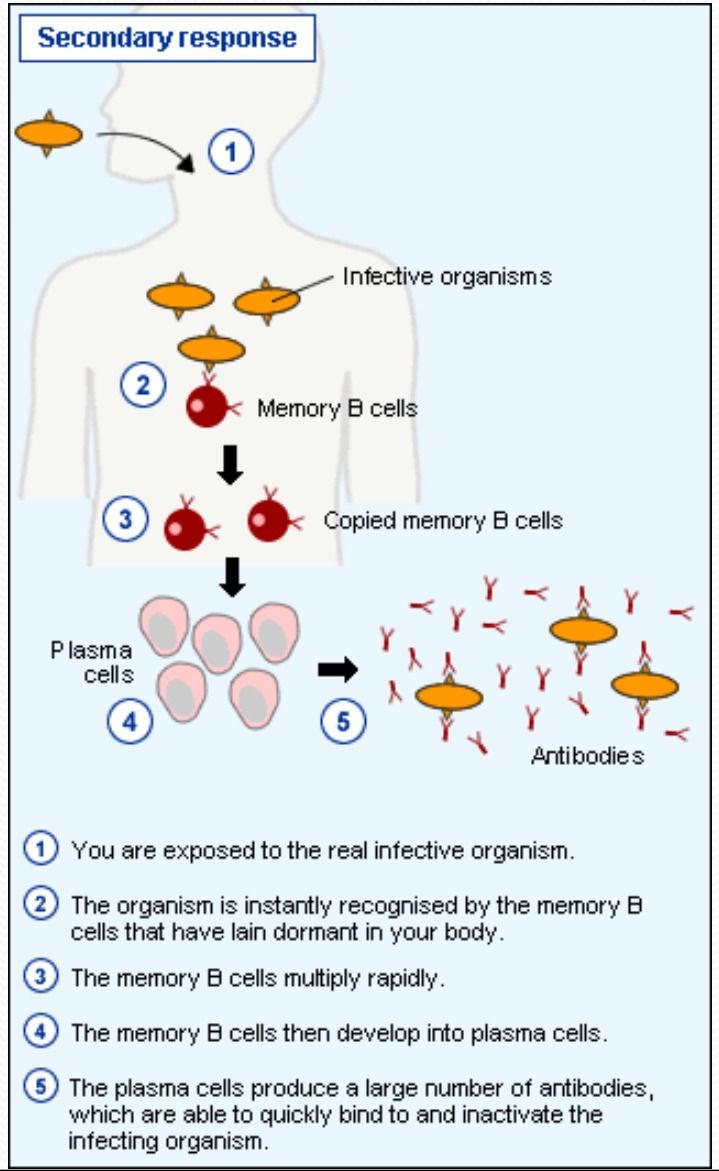
- The most effective and safe methods of preventing deadly infections including viral and bacterial diseases
- Childhood immunization became part of routine health care almost in all countries
- As a results of vaccination: Poliomyelitis, Diphtheria, Tetanus have disappeared in developed countries. Measles, Rubella and Pertussis become rare. While smallpox has been eradicated.

Primary response to a vaccine



1. You are vaccinated against a specific disease, for example, tetanus or influenza. The vaccine contains dead or weakened forms of the organism you are being immunised against.
2. Although the organisms are 'inactivated' like this so that they can't produce disease, they still retain the characteristic antigens that stimulate your body to produce antibodies against that organism.
3. One of your B lymphocytes detects the antigens on the surface of the organisms in the vaccine.
4. The B lymphocyte starts to multiply and forms a clone of identical cells.
5. These cloned B lymphocytes become either plasma cells or memory B cells.
6. Plasma cells secrete antibodies, which are trained to bind to and disable the bacterium or virus you are being immunised against.

Secondary response to an infection primed by vaccine



Types of vaccines

- Live vaccines
- Attenuated live vaccines
- Inactivated (killed vaccines)
- Toxoids
- Polysaccharide and polypeptide (cellular fraction) vaccines
- Surface antigen (recombinant) vaccines.

1. Live vaccines

- Live vaccines are made from live infectious agents without any amendment.
- The only live vaccine is “Variola” small pox vaccine, made of live vaccinia cow-pox virus (not variola virus) which is not pathogenic but antigenic, giving cross immunity for variola.

2. Live attenuated (avirulent) vaccines

- Virulent pathogenic organisms are treated to become attenuated and avirulent but antigenic. They have lost their capacity to induce full-blown disease but retain their immunogenicity.
- Live attenuated vaccines should not be administered to persons with suppressed immune response due to:
  - Leukemia and lymphoma
  - Other malignancies
  - Receiving corticosteroids and anti-metabolic agents
  - Radiation
  - Pregnancy

3. Inactivated (killed) vaccines

- Organisms are killed or inactivated by heat or chemicals but remain antigenic. They are usually safe but less effective than live attenuated vaccines. The only absolute contraindication to their administration is a severe local or general reaction to a previous dose.

4. Toxoids

- They are prepared by detoxifying the exotoxins of some bacteria rendering them antigenic but not pathogenic. Adjuvant (e.g. aluminum precipitation) is used to increase the potency of vaccine.

- The antibodies produces in the body as a consequence of toxoid administration neutralize the toxic materials produced during infection rather than act upon the organism itself. In general toxoids are highly efficacious and safe immunizing agents.

5. Polysaccharide and polypeptide (cellular fraction) vaccines

- They are prepared from extracted cellular fractions e.g. meningococcal vaccine from the polysaccharide antigen of the cell wall, the pneumococcal vaccine from the polysaccharide contained in the capsule of the organism, and hepatitis B polypeptide vaccine.

- Their efficacy and safety appear to be high.

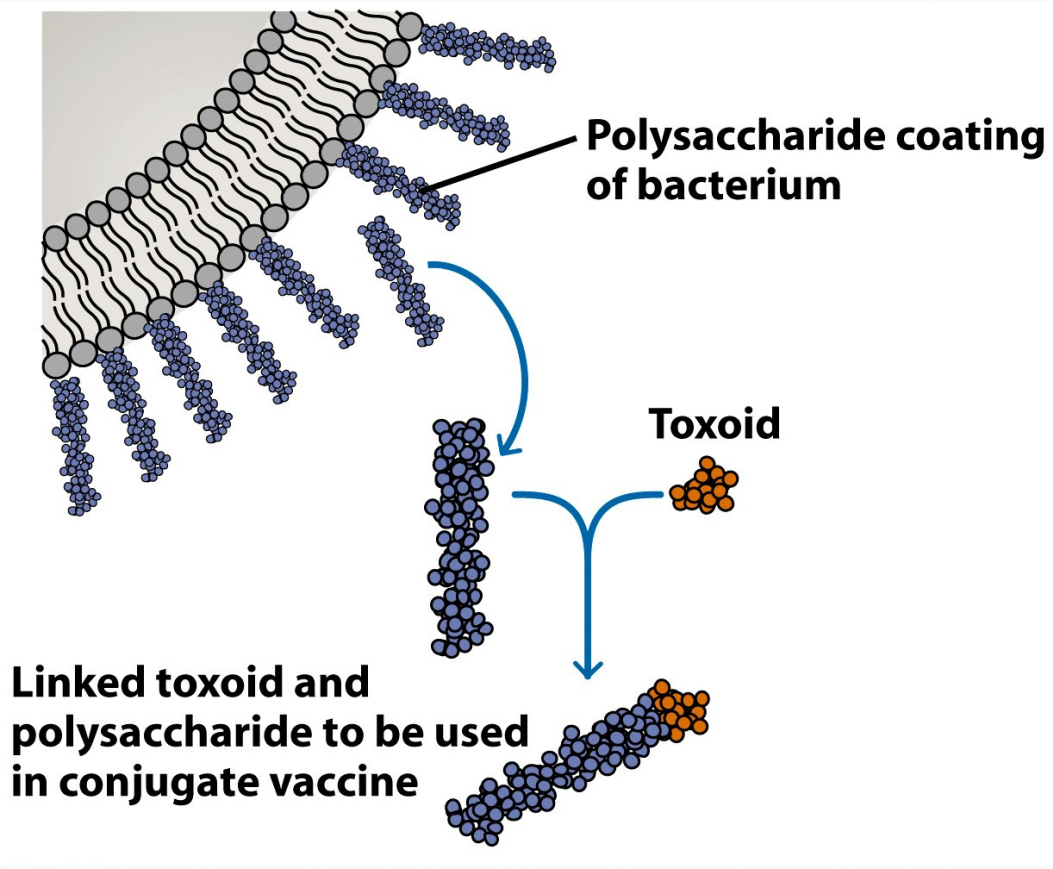
6. Surface antigen (recombinant) vaccines.

- It is prepared by cloning HBsAg gene in yeast cells where it is expressed. HBsAg produced is then used for vaccine preparations.

- Their efficacy and safety also appear to be high.

Conjugate vaccines

A **conjugate vaccine** is created by covalently attaching a (polysaccharide organism) antigen to a carrier protein (preferably from the same microorganism), thereby conferring the immunological attributes of the carrier on the attached antigen.
This technique for the creation of an effective immunogen is most often applied to bacterialpolysaccharides



Types of vaccines

Live vaccines	Live Attenuated vaccines	Killed Inactivated vaccines	Toxoids	Cellular fraction vaccines	Recombinant vaccines
• Small pox variola vaccine	• BCG • Typhoid oral • Plague • Oral polio • Yellow fever • Measles • Mumps • Rubella • Intranasal Influenza • Typhus	• Typhoid • Cholera • Pertussis • Plague • Rabies • Salk polio • Intra-muscular influenza • Japanise encephalitis	• Diphtheria • Tetanus	• Meningococcal polysaccharide vaccine • Pneumococcal polysaccharide vaccine • Hepatitis B polypeptide vaccine	• Hepatitis B vaccine

TABLE 19-4 Classification of common vaccines for humans

Vaccine type	Diseases	Advantages	Disadvantages
Live attenuated	Measles Mumps Polio (Sabin vaccine) Rotavirus Rubella Tuberculosis Varicella Yellow fever	Strong immune response; often lifelong immunity with few doses	Requires refrigerated storage; may mutate to virulent form
Inactivated or killed	Cholera Influenza Hepatitis A Plague Polio (Salk vaccine) Rabies	Stable; safer than live vaccines; refrigerated storage not required	Weaker immune response than live vaccines; booster shots usually required
Toxoid	Diphtheria Tetanus	Immune system becomes primed to recognize bacterial toxins	
Subunit (inactivated exotoxin)	Hepatitis B Pertussis Streptococcal pneumonia	Specific antigens lower the chance of adverse reactions	Difficult to develop
Conjugate	*Haemophilus influenzae* type B Streptococcal pneumonia	Primes infant immune systems to recognize certain bacteria	
DNA	In clinical testing	Strong humoral and cellular immune response; relatively inexpensive to manufacture	Not yet available
Recombinant vector	In clinical testing	Mimics natural infection, resulting in strong immune response	Not yet available

Routes of administration

- Deep subcutaneous or intramuscular route (most vaccines)
- Oral route (sabine vaccine, oral BCG vaccine)
- Intradermal route (BCG vaccine)
- Scarification (small pox vaccine)
- Intranasal route (live attenuated influenza vaccine)

Scheme of immunization

- Primary vaccination
  - One dose vaccines (BCG, variola, measles, mumps, rubella, yellow fever)
  - Multiple dose vaccines (polio, DPT, hepatitis B)
- Booster vaccination

  To maintain immunity level after it declines after some time has elapsed (DT, MMR).

Age of vaccination

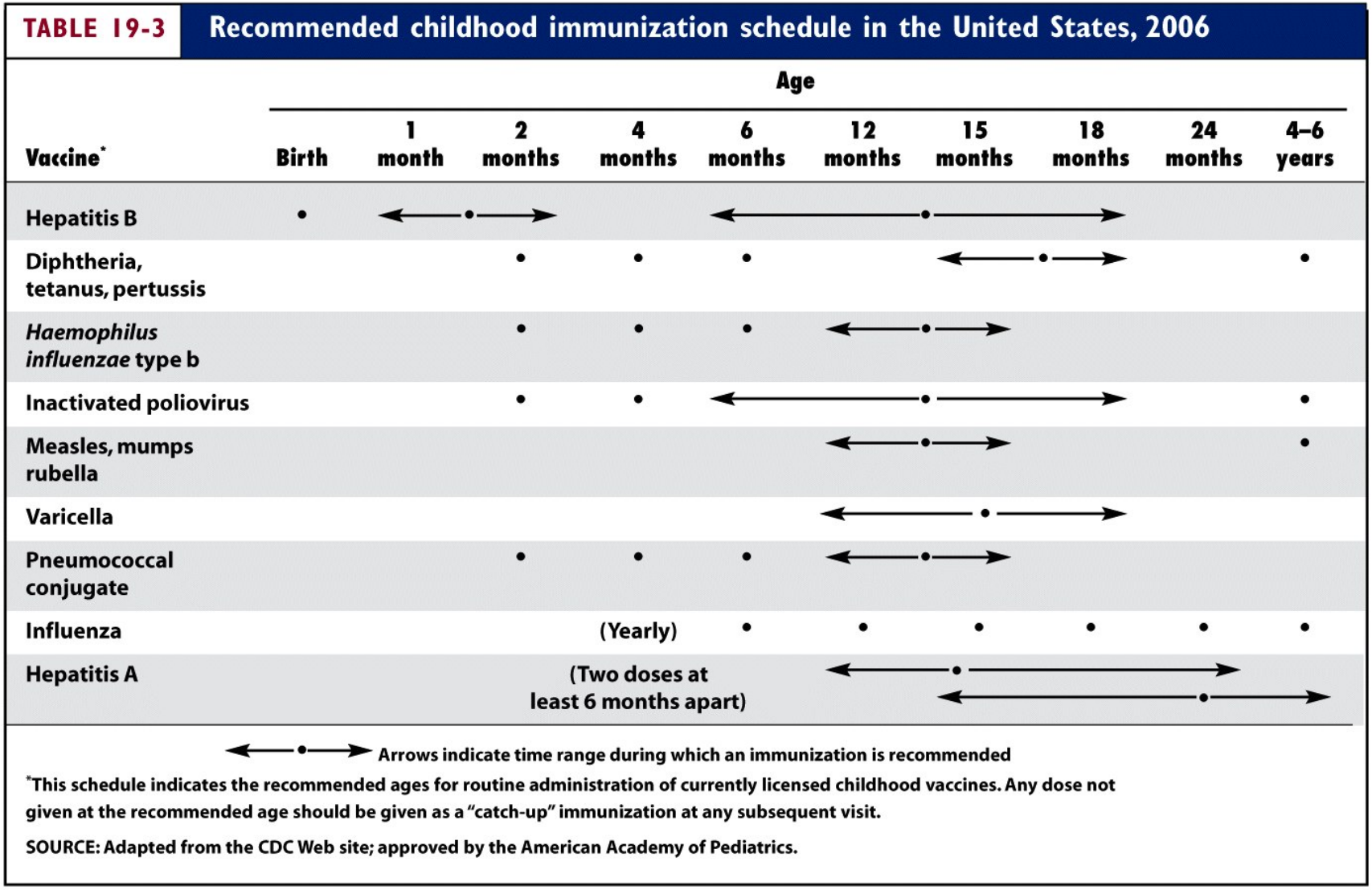


TABLE 19-3 Recommended childhood immunization schedule in the United States, 2006

Vaccine*	Age: Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	24 months	4–6 years
Hepatitis B	•	←•→			←———•———→					
Diphtheria, tetanus, pertussis			•	•	•		←•→			•
Haemophilus influenzae type b			•	•	•	←•→				
Inactivated poliovirus			•	•	←———•———→					•
Measles, mumps rubella						←•→				•
Varicella						←———•———→				
Pneumococcal conjugate			•	•	•	←•→				
Influenza				(Yearly)	•	•	•	•	•	•
Hepatitis A				(Two doses at least 6 months apart)		←———•———→				
							←———•———→			

←•→ Arrows indicate time range during which an immunization is recommended

*This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines. Any dose not given at the recommended age should be given as a "catch-up" immunization at any subsequent visit.

SOURCE: Adapted from the CDC Web site; approved by the American Academy of Pediatrics.

Periods of maintained immunity due to vaccines

- Short period (months): cholera vaccine
- Two years: TAB vaccine
- Three to five years: DPT vaccine
- Five or more years: BCG vaccine
- Ten years: yellow fever vaccine
- Solid immunity: measles, mumps, and rubella vaccines.

Levels of effectiveness

- Absolutely protective(100%): yellow fever vaccine
- Almost absolutely protective (99%): Variola, measles, mumps, rubella vaccines, and diphtheria and tetanus toxoids.
- Highly protective (80-95%): polio, BCG, Hepatitis B, and pertussis vaccines.
- Moderately protective (40-60%) TAB, cholera vaccine, and influenza killed vaccine.

Antibody Titer

- A test to measures the presence and amount of antibodies in blood against a particular type of tissue, cell, or substance
- Titer determines if you have adequate protection against a disease
- May need to give booster if titer too low
- E.g., happens with HepB vaccine

Hazards of Immunization

- The adverse reactions that may occur include:

1. Reactions inherent to inoculation: local and general
2. Reactions due to faulty techniques: during manufacturing or giving of vaccine
3. Reactions due to hypersensitivity
4. Neurological involvement: GuillainBarre syndrome in association with the swine influenza vaccine
5. Provocative reactions: occurrence of new disease not connected to the vaccine