VACCINE

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➢A preparation of either killed microorganisms; living, weakened (attenuated) microorganisms; or inactivated bacterial toxins (toxoids) administered to induce development of the immune response and protect the individual against a pathogen or a toxin.

➢A **vaccine** is a biological preparation that provides active acquired immunity to a particular infectious disease.

Table 12.2 Factors required for a successful vaccine.

Factor	Requirements
Efficacy	Must evoke protective levels of immunity: at the appropriate site of relevant nature (Ab, CD4 T-cell and CD8 T-cell) of adequate duration
Availability	Readily cultured in bulk or accessible source of subunit
Stability	Stable under extreme climatic conditions, preferably not requiring refrigeration
Affordability	Must be priced to allow use in developing countries
Safety	Eliminate any pathogenicity

➢The discipline of Immunology has its roots in the early vaccination trials of **Edward Jenner** and **Louis Pasteur.**

➢ **Edward Jenner** was to develop first vaccines against small pox.
➢ Calmette and Guerin developed B.C.G vaccines for TB
➢Salk made Polio vaccine (injectable)
➢Sabin also prepared polio vaccine (oral).

➢In may 1974, Global immunization was launched by WHO for Six disease

1. Diptheria
2. Measles
3. Tetanus
4. TB
5. Polio
6. Pertusis (Whooping cough)

IMMUNIZATION

Immunization is the process of eliciting a long-lived state of protective immunity against a disease-causing pathogen.

• Immunity to infectious microorganisms can be achieved by active or passive **immunization.**

• In each case, immunity can be acquired either by natural processes (usually by transfer from mother to fetus or by previous infection by the organism) or by artificial means such as injection of antibodies or vaccines

TABLE 18-1 Acquisition of passive and active immunity

Type	Acquired through
Passive immunity	Natural maternal antibody
	Immune globulin*
	Humanized monoclonal antibody
	Antitoxin†
Active immunity	Natural infection
	Vaccines‡
	Attenuated organisms
	Inactivated organisms
	Purified microbial macromolecules
	Cloned microbial antigens
	Expressed as recombinant protein
	As cloned DNA alone or in virus vectors
	Multivalent complexes
	Toxoid§

*An antibody-containing solution derived from human blood, obtained by cold ethanol fractionation of large pools of plasma; available in intramuscular and intravenous preparations.

†An antibody derived from the serum of animals that have been stimulated with specific antigens.

‡A suspension of attenuated live or killed microorganisms, or antigenic portions of them, presented to a potential host to induce immunity and prevent disease.

§A bacterial toxin that has been modified to be nontoxic but retains the capacity to stimulate the formation of antitoxin.

PASSIVE IMMUNIZATION

Passive immunization, in which preformed antibodies are transferred to a recipient, occurs naturally by transfer of maternal antibodies across the placenta to the developing fetus.

Maternal antibodies to diphtheria, tetanus, rubeola, rubella, mumps, and poliovirus all afford passively acquired protection to the developing fetus.

Passive immunization can provide immediate protection to travelers or health-care workers who will soon be exposed to an infectious organism and lack active immunity to it. Because passive immunization does not activate the immune system.

It generates no memory response and the protection provided is transient.

TABLE 18-2 Common agents used for passive immunization

Disease	Agent
Black widow spider bite	Horse antivenin
Botulism	Horse antitoxin
Diphtheria	Horse antitoxin
Hepatitis A and B	Pooled human immune gamma globulin
Measles	Pooled human immune gamma globulin
Rabies	Pooled human immune gamma globulin
Respiratory disease	Monoclonal anti-RSV*
Snake bite	Horse antivenin
Tetanus	Pooled human immune gamma globulin or horse antitoxin

*Respiratory syncytial virus

ACTIVE IMMUNIZATION

• Active Immunization to Induce Immunity and Memory

• In active immunization, as the name implies, the immune system plays an active role— proliferation of antigen-reactive T and B cells is induced and results in the formation of protective memory cells.

• Active immunization can be achieved by natural infection with a microorganism, or it can be acquired artificially by administration of a vaccine.

TABLE 17-6 Recommended childhood immunization schedule in the United States, 2012

Vaccine	Birth	1 mo	2 mo	4 mo	6 mo	9 mo	12 mo	15 mo	18 mo	19–23 mo	2–3 yr	4–6 yr
	AGE											
Hepatitis B	Hep B	← Hep B →			←		Hep B		→			
Rotavirus			RV	RV	RV							
Diphtheria, tetanus, pertussis			DTaP	DTaP	DTaP			← DTaP →				DTaP
Haemophilus influenzae type b			Hib	Hib	Hib		← Hib →					
Pneumococcal			PCV	PCV	PCV		← PCV →				← PPSV →	
Inactivated poliovirus			IPV	IPV	←		IPV		→			IPV
Influenza					←			Influenza (yearly)				→
Measles, mumps, rubella							← MMR →					MMR
Varicella							← Varicella →					Varicella
Hepatitis A			(Two doses at least 6 months apart)				←	Dose 1	→		← HepA series →	
Meningococcal						←		MCV4		→		

Recommendations in effect as of 12/23/11. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. A combination vaccine is generally preferred over separate injections of equivalent component vaccines.

MCV4 and PPSV ranges are recommended for certain high risk groups. See website for further details.

Source: Modified version of 2012 American Academy of Pediatrics recommendations, found on CDC chart, www.cdc.gov/vaccines/schedules/index.html.

TYPES OF VACCINES

A. Whole-Organism Vaccines
    1. Live Vaccine (Attenuated)
    2. Killed Vaccine (Inactivated)
B. Purified Macromolecules/ Subunit vaccines
    1. Inactivated exotoxins (ex. Diphtheria, Tetanus, Cholera)
    2. Capsular polysacchrides (*Haemophilus*, *Neissera meningitidis)*
    3. Recombinant microbial antigen (Hepatitis B)
C. Recombinant-Vector Vaccines
D. DNA Vaccines
E. Multivalent Subunit Vaccines
F. Conjugate Vaccines

LIVE ATTENUATED VACCINE

Microorganisms can be attenuated so that they lose their ability to cause significant disease (pathogenicity) but retain their capacity for transient growth within an inoculated host.

- Attenuation can be achieved by growing a pathogenic bacterium or virus for prolonged period under abnormal culture conditions.

- For example, an attenuated strain of *Mycobacterium bovis called* ***Bacillus Calmette- Guérin (BCG) was developed by growing M. bovis*** on a medium containing increasing concentrations of bile.

- After 13 years, this strain had adapted to growth in strong bile and had become sufficiently attenuated that it was suitable as a vaccine for tuberculosis.

INACTIVATED OR KILLED VACCINES

Pathogens are inactivated by heat or chemicals means so that the pathogens raises an immune response but not capable of replication in the host.

- It is critically important to maintain the structure of epitopes on surface antigens during inactivation.

- Heat inactivation is often unsatisfactory because it causes extensive denaturation of proteins; thus, any epitopes that depend on higher orders of protein structure are likely to be altered significantly.

- Chemical inactivation with formaldehyde or various alkylating agents has been successful. The Salk polio vaccine is produced by formaldehyde inactivation of the poliovirus.

SUBUNIT VACCINE

Many of the risks associated with attenuated or killed whole organism vaccines can be avoided with a strategy that uses only specific, purified macromolecules derived from the pathogen.

➢A subunit vaccine is a fragment of a pathogen, typically a surface protein, that is used to trigger an immune response and stimulate acquired immunity against the pathogen from which it is derived.

1. Inactivated exotoxins or toxoids
2. Capsular polysaccharides or surface glycoproteins
3. Recombinant protein antigens

TOXOID

Toxoid vaccines are made by purifying the bacterial exotoxin and then inactivating it with formaldehyde.

➢Vaccination with the toxoid induces anti-toxoid antibodies, which are also capable of binding to the toxin and neutralizing its effects.

e.g. Tetanus, Diphtheria

BACTERIAL POLYSACCHARIDE CAPSULES

- **Bacterial Polysaccharide Capsules Are Used as Vaccines**
- The virulence of some pathogenic bacteria depends primarily on the antiphagocytic properties of their hydrophilic polysaccharide capsule.
- Coating of the capsule with antibodies and/or complement greatly increases the ability of macrophages and neutrophils to phagocytose such pathogens. These findings provide the rationale for vaccines consisting of purified capsular polysaccharides.
- The current vaccine for *Streptococcus pneumoniae*, *which* causes pneumococcal pneumonia, consists of 23 antigenically different capsular polysaccharides. The vaccine induces formation of opsonizing antibodies and is now on the list of vaccines recommended for all infants.

RECOMBINANT PROTEIN ANTIGENS

Proteins from Pathogens Are Produced by Recombinant Techniques

- A number of genes encoding surface antigens from viral, bacterial, and protozoan pathogens have been successfully cloned into bacterial, yeast, insect, or mammalian expression systems, and the expressed antigens used for vaccine development.

- The first recombinant antigen vaccine approved for human use eg. hepatitis B vaccine.

RECOMBINANT VECTOR VACCINES

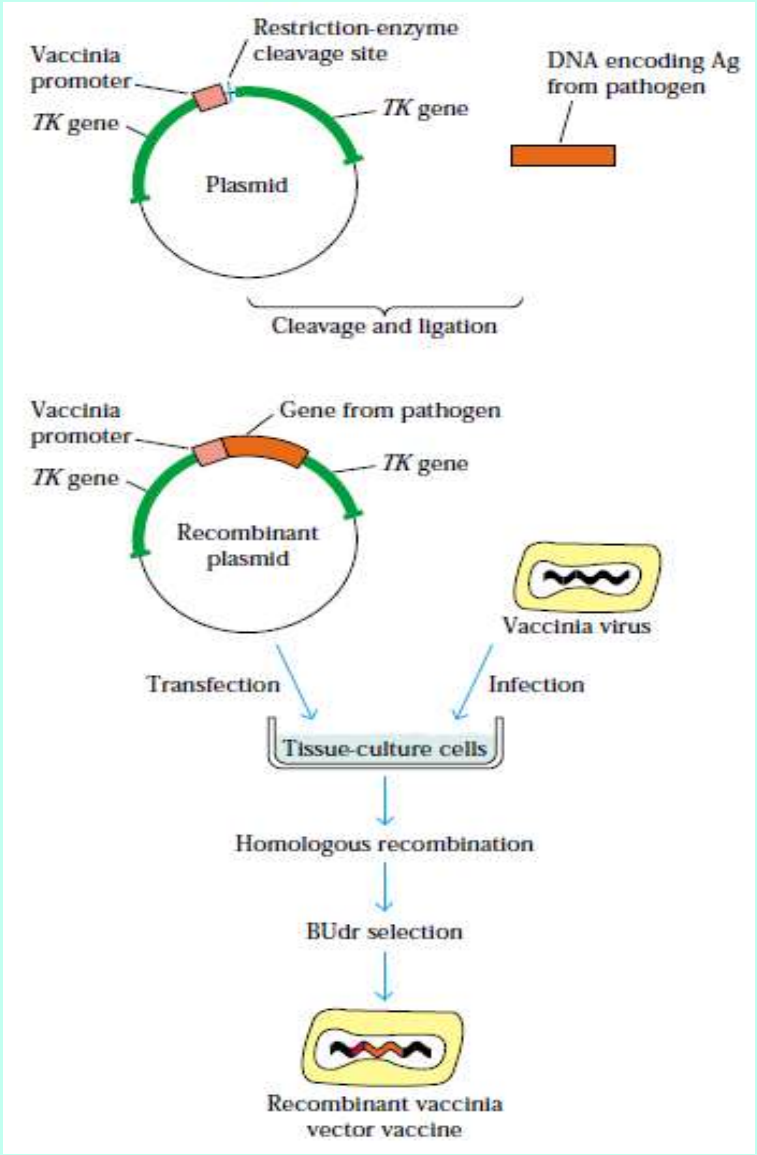


FIGURE 18-5 Production of vaccinia vector vaccine. The gene that encodes the desired antigen (orange) is inserted into a plasmid vector adjacent to a vaccinia promoter (pink) and flanked on either side by the vaccinia thymidine kinase (*TK*) gene (green). When tissue-culture cells are incubated simultaneously with vaccinia virus and the recombinant plasmid, the antigen gene and promoter are inserted into the vaccinia virus genome by homologous recombination at the site of the nonessential *TK* gene, resulting in a TK^{-} recombinant virus. Cells containing the recombinant vaccinia virus are selected by addition of bromodeoxyuridine (BUdr), which kills TK^{+} cells. *[Adapted from B. Moss, 1985,* Immunol. Today **6**:243.*]*

DNA VACCINES

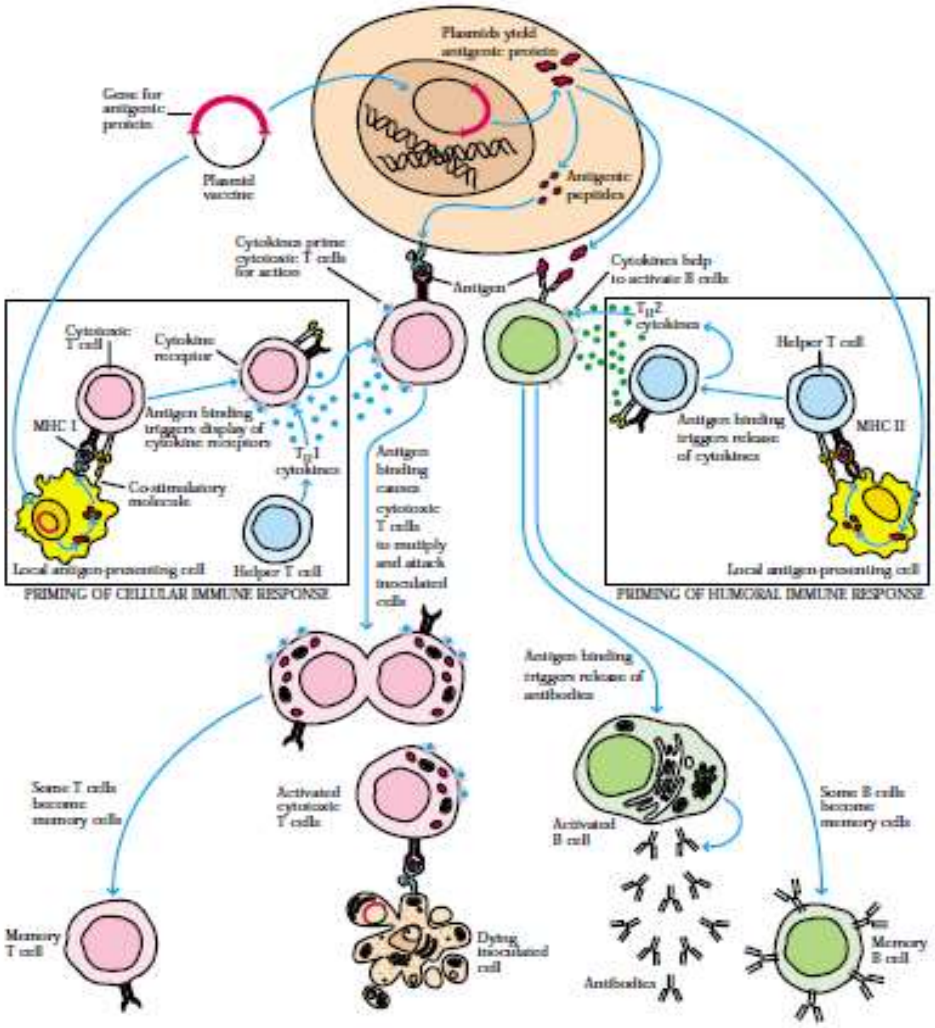


FIGURE 18-6 Use of DNA vaccines raises both humoral and cellular immunity. The injected gene is expressed in the injected muscle cell and in nearby APCs. The peptides from the protein encoded by the DNA are expressed on the surface of both cell types after processing as an endogenous antigen by the MHC class I pathway. Cells that present the antigen in the context of class I MHC molecules stimulate development of cytotoxic T cells. The protein encoded by the injected DNA is also expressed as a soluble, secreted protein, which is taken up, processed, and presented in the context of class II MHC molecules. This pathway stimulates B-cell immunity and generates antibodies and B-cell memory against the protein. *(Adapted from D. B. Weiner and R. C. Kennedy, 1999, Sci. Am. 281:50.)*

CONJUGATE VACCINE

- A conjugate vaccine is a substance that is composed of a polysaccharide antigen fused (conjugated) to a carrier molecule.
- This enhances the stability and the effectiveness of the vaccine.

Conjugate vaccines are replacing pure polysaccharides.

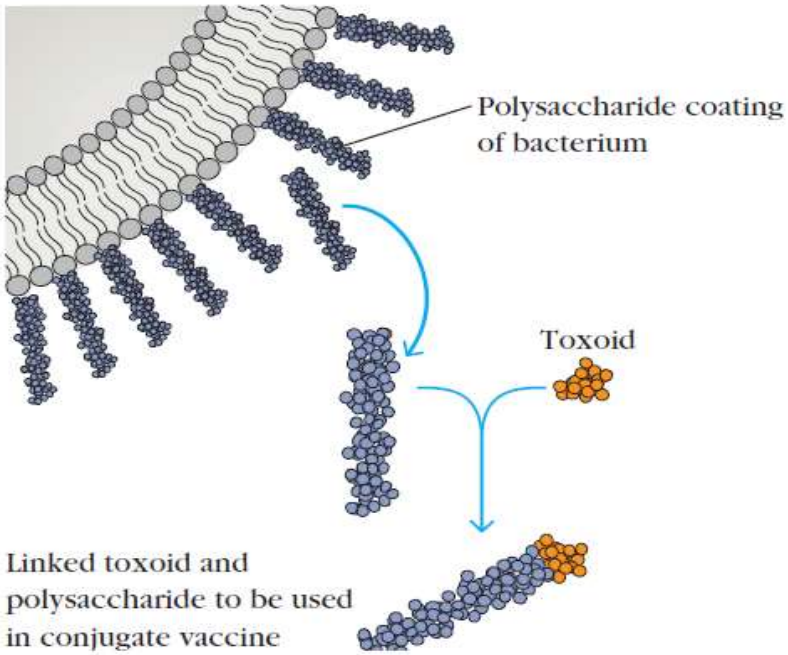
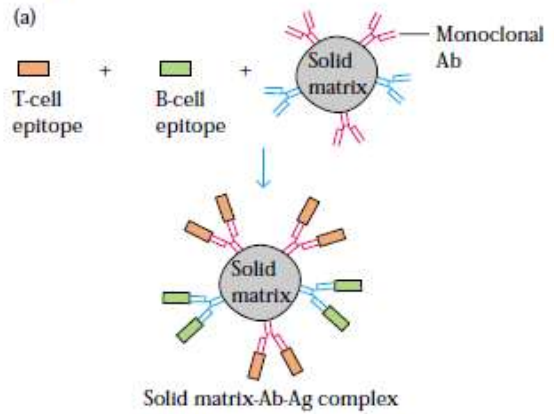


FIGURE 17-16 A conjugate vaccine protects against *Haemophilus influenzae* type b (Hib). The vaccine is prepared by conjugating the surface polysaccharide of Hib to a protein molecule, making the vaccine more immunogenic than either alone.

MULTIVALANT VACCINE

VISUALIZING CONCEPTS



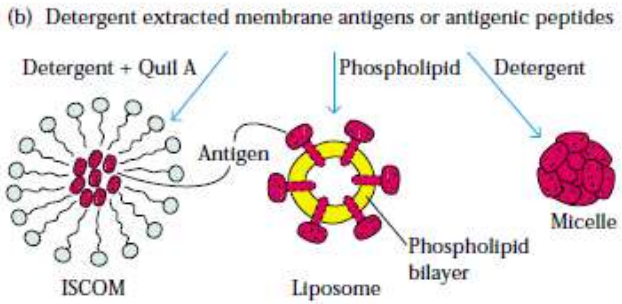


FIGURE 18-7 Multivalent subunit vaccines. (a) Solid matrix-antibody-antigen complexes can be designed to contain synthetic peptides representing both T-cell epitopes and B-cell epitopes. (b) Protein micelles, liposomes, and immunostimulating complexes (ISCOMs) can all be prepared with extracted antigens or antigenic peptides. In micelles and liposomes, the hydrophilic residues of the antigen molecules are oriented outward. In ISCOMs, the long fatty-acid tails of the external detergent layer are adjacent to the hydrophobic residues of the centrally located antigen molecules. (c) ISCOMs and liposomes can deliver antigens inside cells, so they mimic endogenous antigens. Subsequent processing by the cytosolic pathway and presentation with class I MHC molecules induces a cell-mediated response.

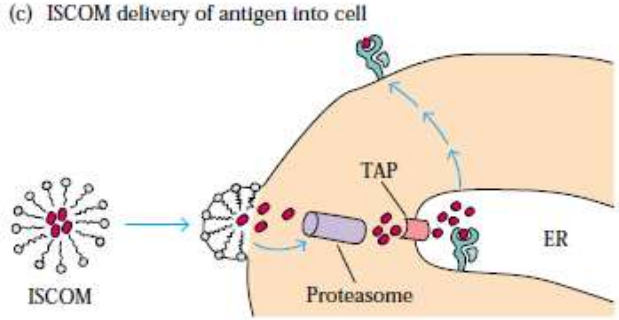


TABLE 17-7 Classification of common vaccines for humans

Vaccine type	Diseases	Advantages	Disadvantages
		WHOLE ORGANISMS	
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
		PURIFIED MACROMOLECULES	
Toxoid (inactivated exotoxin)	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	
		OTHER	
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

THANKS