VACCINES & ITS TYPES

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Immunization is the process of eliciting a long-lived state of protective immunity against a disease-causing pathogen. Exposure to the live pathogen followed by recovery is one route to immunization.

Passive immunization	Active immunization
• In Passive immunization, the preformed antibodies are transferred to a recipient, occurs naturally when maternal IgG crosses the placenta to the developing fetus. • Passive immunization can also be achieved by injecting a recipient with preformed antibodies, called antiserum, from immune individuals.	• Active immunization can be achieved by natural infection with a microorganism, or it can be acquired artificially by administration of a vaccine. • In active immunization, 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.

- Vaccines are biological preparations, produced from living organisms, that enhance immunity against disease and either prevent (prophylactic vaccines) or, in some cases, treat disease (therapeutic vaccines).

Type of vaccine	Examples
Live-attenuated	Measles, Mumps, Rubella, Varicella zoster
Inactivated	Hepatitis A, Influenza, Pneumococcal polysaccharide
Recombinant sub-unit	Hepatitis B
Toxoid	Tetanus, Diphtheria
Conjugate polysaccharide-protein	Pneumococcal, meningococcal, Haemophlius influenzea type b (Hib)

Live, Attenuated Vaccines

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

- The first vaccine used by Jenner is of this type.

Inoculation of humans with vaccinia (cowpox) virus confers immunity to smallpox (without causing smallpox).

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

- This helps to select mutants that are better suited for growth in the abnormal culture conditions than in the natural host.

- 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 became sufficiently attenuated that it was suitable as a vaccine for tuberculosis.

- The attenuated vaccines can replicate within host cells and particularly suitable for inducing cell-mediated responses.

- It requires only a single immunization.

Inactivated or "Killed" Vaccines

- The pathogen is treated with heat or chemicals, killed making it incapable of replication, but allows it to induce an immune response to at least some of the antigens contained within the organism.

- It is important to maintain the structure of epitopes on the surface antigens during inactivation. Heat inactivation is often unsatisfactory because it causes extensive denaturation of proteins.

- Chemical inactivation with formaldehyde or various alkylating agents has been successful.

- The Salk polio vaccine is produced by formaldehyde inactivation of the poliovirus.

- Killed vaccines often require repeated boosters to achieve a protective immune status as they do not replicate in the host.

- Killed vaccines typically induce a predominantly humoral antibody response and are less effective than attenuated vaccines in inducing cell-mediated immunity.

- The safety of inactivated vaccines is greater than that of live attenuated vaccines.

Subunit Vaccines

- Subunit Vaccines contains only specific, purified macromolecules derived from the pathogen.

- It contains only the antigenic parts of the pathogen which are necessary to elicit a protective immune response.

- The three most common available subunit vaccines are
  - inactivated exotoxins or toxoids
  - capsular polysaccharides or surface glycoproteins
  - key recombinant protein antigens.

Toxoid Vaccines

- Some bacteria produce disease in their host by producing exotoxins.
- Toxoid Vaccines are inactivated exotoxins.
- The exotoxins are treated with heat/ chemicals to inactivate it.
- This makes them unable to cause the disease but can stimulate the body to produce antitoxoid antibodies which are capable of binding to the toxins and neutralizing their effects.
- **Example**: Tetanus, Diphtheria bacterial vaccines

Capsular polysaccharides

- The virulence of some pathogenic bacteria depends primarily on the antiphagocytic properties of their polysaccharide capsule.

- Coating the capsule with antibodies and/or complement greatly increases the ability of macrophages and neutrophils to phagocytose such pathogens.

- The current vaccine for *Streptococcus pneumoniae* consists of 13 antigenically distinct capsular polysaccharides (PCV13). The vaccine induces formation of opsonizing antibodies and it is on the list of vaccines recommended for all infants.

- The vaccine for *Neisseria meningitidis*, a common cause of bacterial meningitis, also consists of purified capsular polysaccharides.

Recombinant Vector Vaccines

- Live attenuated vaccines prolong antigen delivery and encourage cell-mediated responses, but have the disadvantage of reverting to pathogenic forms rarely.

- Recombinant vectors maintain the advantages of live attenuated vaccines while avoiding this major disadvantage.

- Individual genes that encode key antigens of especially virulent pathogens can be introduced into attenuated viruses or bacteria.

- The attenuated organism serves as a vector, replicating within the vaccinated host and expressing the gene product of the pathogen.

- Since most of the genome of the pathogen is missing, reversion potential is virtually eliminated.

- Recombinant vector vaccines have been prepared utilizing existing licensed live, attenuated vaccines and adding to them genes encoding antigens present on newly emerging pathogens.

- Such chimeric virus vaccines can be more quickly tested and approved than an entirely new product.

- Example: yellow fever vaccine that was engineered to express antigens of WNV. A number of organisms have been used as the vector in such preparations, such as vaccinia virus, canarypox virus, attenuated poliovirus, adenoviruses, attenuated strains of *Salmonella*, BCG strain of *Mycobacterium bovis* , and certain strains of *Streptococcus* that normally exist in the oral cavity.

DNA Vaccines

- A DNA vaccine, utilizes plasmid DNA encoding antigenic proteins that are injected directly into the muscle of the recipient.

- This strategy relies on the host cells to take up the DNA and produce the immunogenic protein in vivo, thus directing the antigen through endogenous MHC class I presentation pathways, helping to activate better CTL responses.

- The DNA appears either to integrate into the chromosomal DNA or to be maintained for long periods in an episomal form, and is often taken up by dendritic cells or muscle cells in the injection area.

- Tests in animal models have shown that DNA vaccines are able to induce protective immunity against a number of pathogens, including influenza and rabies viruses.

- The addition of a follow-up booster shot with protein antigen or inclusion of supplementary DNA sequences in the vector, may enhance the immune response.

- Advantages of DNA vaccines: Since the encoded protein is expressed in the host in its natural form, there is no denaturation or modification.

- The immune response is directed to the antigen exactly as it is expressed by the pathogen, inducing both humoral and cell-mediated immunity.

- No refrigeration of the plasmid DNA is required, eliminating longterm storage challenges. In addition, the same plasmid vector can be custom tailored to insert DNA encoding a variety of proteins, which allows the simultaneous manufacture of a variety of DNA vaccines for different pathogens, saving time and money.

- Human trials are underway with several different DNA vaccines, for malaria, HIV, influenza, Ebola, and herpes virus, along with several vaccines aimed at cancer therapy.

- Although there are currently no licensed human DNA vaccines, three such vaccines have been licensed for veterinary use, including a WNV vaccine that is protective in horses.

Reference:

- Kuby Immunology, Seventh Edition
- http://www.phrmajp.org/wordpress/wpcontent/uploads/old/library/vaccinefactbook_e/1_Basic_Concept_of_Vaccination.pdf

THANK YOU