"Vaccination"

Vaccination is the administration of antigenic material (a vaccine) to stimulate an individual's immune system to develop adaptive immunity to a pathogen.

Objective: Prevention of viral disease.

The tradition of vaccination may have originated in India in the 10th century when vaccination with powdered scabs from people infected with smallpox was used to protect against the disease. Smallpox used to be a common disease through the world and 20-30% of infected persons died from the disease.

Types of vaccines:

Scientist takes many approaches to designing vaccines against a microbe. These choices are typically based on fundamental information about the microbe such as how it infects cells and how the immune system responds to it. The following vaccines are some of the options that researchers might pursue:

- Live attenuated vaccines
- Inactivated vaccines
- Subunit vaccines
- Toxoid vaccines
- DNA vaccines
- Recombinant vector vaccines.

Currently viable viral vaccines:

1. Attenuated live- virus vaccines
2. Killed- virus vaccines

Attenuated live- virus vaccines:

Antigenically identical to wild type but lack the virulence. It can be achieved by:

1- Serial passages in Embryonated eggs or in cell culture example: Measles, Mumps, Rubella vaccines.
2- Temperate sensitive mutants: grow at low temperature but not at high temperature. Virus will grow in the cooler upper airways ($33^{o}C$) where it cause few symptoms and induce antibodies, but it will not grow in the warmer ($37^{o}C$), lower airways where it can cause pneumonia. Example: Influenza virus vaccine.
3- Cold adaptation: the virus is encourages to grow at ($25^{o}C$) example: Influenza virus vaccine.
4- Recombinant vaccines (Genetic reassortment): this method only occurs between viruses with segmented genomes example: Influenza virus vaccine. Cells are co- infected with an attenuated laboratory donor virus and a virulent wild- type influenza virus isolate; the desired reassortment vaccine virus will contain the surface genes that confer attenuation from the attenuated donor virus.
5- Genetic manipulation: including deletion mutants like deletion of oncogene in which we delete part of the genome of the virus by restricted enzyme, (there is no risk of reversion to virulence).

Advantages of Attenuated- live vaccine:

- Produce immunity similar to the immunity produce by natural host
- Produce cell- mediated immunity
- Induce produce antibodies at entry of the virus

Disadvantages of Attenuated- live vaccine:

- Risk of reversion to greater virulence during multiplication within the host cell leading to subclinical infection
- Storage and limited half life
- Using of culture substrate like eggs to prepare vaccine may be lead to latently infection
- It may produce persistent infection in the host
- Interference by naturally occurring wild type virus leading to inhibition of replication of vaccine virus and reduce effectiveness.

Killed inactivated virus vaccines:

Using destroying virus which is antigenically remain intact but lack virulence consist of purified of whole viral virion but loose its infectivity by using either mild formalin, B-propiolactone or ethylenimines.

Killed viral vaccine is either as:

1- Whole virus vaccines
2- Subunit vaccines (purified component vaccine): subunit vaccines were separated from purified virus by detergent then centrifugation. This vaccine contains only those viral components needed to stimulate protective antibody.

Advantages of killed inactivated vaccines:

- No risk of reversion to virulence
- Use when there is no available of acceptable attenuated virus

Disadvantages of killed inactivated vaccines:

- Produce short duration of immunity
- Not stimulate of CMI
- Not stimulate production of local IgA but stimulate production circulating IgM and IgG.
- Required extreme care during preparation to avoid presence of residual live virulence virus.
- Some of them induce hypersensitivity to infected person.

Comparsion of characteristics of live and killed viral vaccines

Characteristics	Killed vaccine	live vaccine
Number of doses	Multiple	Single
Need to adjuvant	yes	No
Duration of immunity	shorter	longer
Effectiveness of protection	lower	greater
Immunoglobulins produced	IgG	IgG and IgA
Mucosal immunity produced	poor	yes
Cell mediated immunity	poor	yes
Residual virulent virus vaccine	Possible	No
Reversion	No	Possible
Interference by other viruses	No	possible
Stability at room temperature	high	low

New approaches to vaccine design:

Molecular biology and modern technologies are combining to devise novel approaches to vaccine development.

1. Synthetic peptides

Viral nucleic acid can be readily sequenced and the amino acid sequence of the gene products predicted. Also the technology for synthesis of peptides in vitro has been refined. It is now possible to synthesize short peptides that correspond to antigenic determinants on a viral protein.

The immune response induced by synthetic peptides is considerably weaker than that induced by intact protein.

2. Purified proteins produced using cloned genes:

Viral genes can be easily cloned into plasmids and this cloned DNA then expressed in:

a. Bacteria E. Coli

b. Yeast cells

c. Mammalian cells

Vectors: plasmid, or DNA mammalian virus.

Gene coding for immunizing proteins of the influenza virus, herpes simplex virus, and rabies virus have been synthesized in bacteria. A recombinant hepatitis B virus vaccine contains viral protein synthesized in yeast cells or mammalian cell lines.

3. Recombinant Vaccinia virus as vaccines:the concept is to use recombinant DNA techniques to insert the gene coding for the protein of interest into the genome of an avirulent virus that can be administered as the vaccine (the prototype vector is vaccinia virus).

4.Edible vaccines: Whereby transgenic plants synthesizing antigen from pathogenic viruses may provide new cost-effective ways of delivering vaccines.

5. Naked DNA vaccines: recombinant plasmids carrying the gene for the protein of interest are injected into hosts and the DNA produces the immunizing protein.

6. Administration of vaccine locally to stimulate antibody at the portal of entry (such as aerosol vaccines for respiratory disease).

Passive immunity

Immunity acquired by an individual by the transfer of preformed antibodies. These antibody preparations are often called immune globulins.

The main advantage of passive immunity is that it provides immediate protection. The main disadvantage is that it does not provide long-term protection i.e., it active only for a few weeks to a few months.

Immune globulin preparations against rabies virus, hepatitis A virus, hepatitis B virus and Varicella-zoster virus are in common use.

Passive-active immunity:

Consists of administering both immune globulins and a viral vaccine. This provides both immediate as well as long-term protection (e.g. Protection against rabies in an unimmunized person who has been bitten by a potentially rabid animal. Persons exposed to hepatitis B virus percutaneous or by contamination of mucosal surfaces.

Adjuvant:

Is a pharmacological or immunological agent that modifies the effect of other agents. Adjuvant may be added to a vaccine to modify the immune response by boosting it such as to give a higher amount of antibodies. Adjuvants give greater antibodies with less quantity of antigen with fewer doses.

Adjuvants also be used to enhance the efficacy of a vaccine by helping to modify the immune response to particular types of immune response cells. Example activating of T-cells instead of antibody secreting B- cells.

Types of adjuvants:

- Inorganic salt like (Aluminum hydroxide, Aluminum phosphate and calcium phosphate)
- Delivery system including liposome
- Bacterial product called freund's adjuvant including Mycobacterium bovis, oil and Muramyl dipeptide
- Cytokines including IL-12, interferon gamma.