

# Recombinant vaccine



# Vaccine



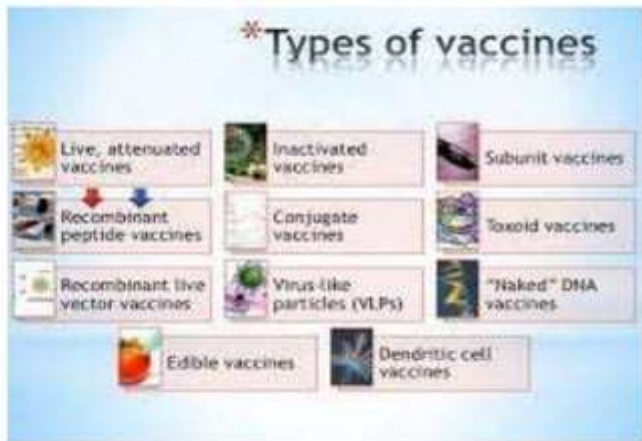
- A vaccine is a biological preparation that improves immunity to a particular disease.  
(<http://www.who.int/>)
- Injection of a killed microbe in order to stimulate the immune system against the microbe, thereby preventing disease.  
(<http://www.medicinenet.com/>)

# History

- The term "vaccine" was derived from the Edward Jenner's 1796 use of the term "cow pox" (Latin "*variola vaccinae*", adapted from the Latin "*vaccīn-us*", from "*vacca*" cow).
- He was the pioneer of using cow pox vaccines to prevent small pox infections.

# Vaccine types

- Live, attenuated vaccines
- Inactivated vaccine
- Subunit vaccine
- Toxoid vaccine
- Conjugated vaccine
- DNA vaccine
- Recombinant vector vaccines





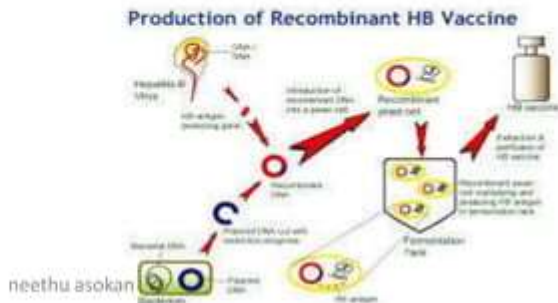
# RECOMBINANT VACINE

- Vaccine antigens may also be produced by genetic engineering technology. These products are sometimes referred to as recombinant vaccines.



# HISTORY

- The FDA licensed Merck's Recombivax HB. This hepatitis B vaccine was the first human vaccine produced by recombinant DNA methods in 1981.
- In 1986, research resulted in a second generation of genetically engineered (or DNA recombinant) hepatitis B vaccines.



# TYPES OF RECOMBINANT VACCINE

- **Subunit vaccines:**

These are the components of the pathogenic organisms. Subunit vaccines include protein , peptides and DNA.

- **Attenuated recombinant vaccines:**

These are the genetically modified pathogenic organisms that are made non-pathogenic and used as vaccines.

- **Vector recombinant vaccines:**

These are the genetically modified viral vectors that can be used as vaccines against certain pathogens.

# SUBUNIT VACCINE

- Subunit recombinant vaccine are the components (proteins, peptides, DNA) of the pathogenic organisms.

- **Advantages :**

This vaccines include their purity in preparation, stability and safe use.

- **Disadvantages:**

High cost factor and possible alteration in native conformation.

Eg: Hepatitis B, HSV, BCG.





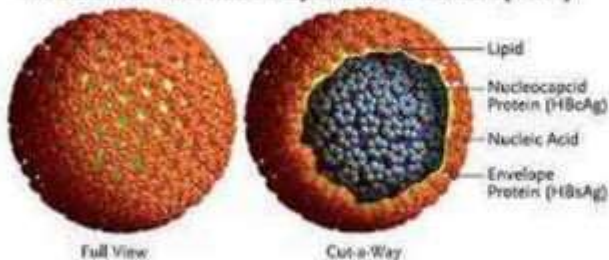
# SUBUNIT VACCINE

- **Subunit vaccines can be broadly grouped into two kinds:**
  - (i) **Recombinant protein vaccines:** This is based on production of recombinant DNA which is expressed to release the specific protein used in vaccine preparation
  - (ii) **DNA vaccines:** Here the gene encoding for immunogenic protein is isolated and used to produce recombinant DNA which acts as vaccine to be injected into the individual.

# HEPATITIS B

- Hepatitis B is a widespread disease in man.
- It primarily affects liver causing chronic hepatitis, cirrhosis and liver cancer.

**Model of Human Hepatitis B Virus (HBV)**

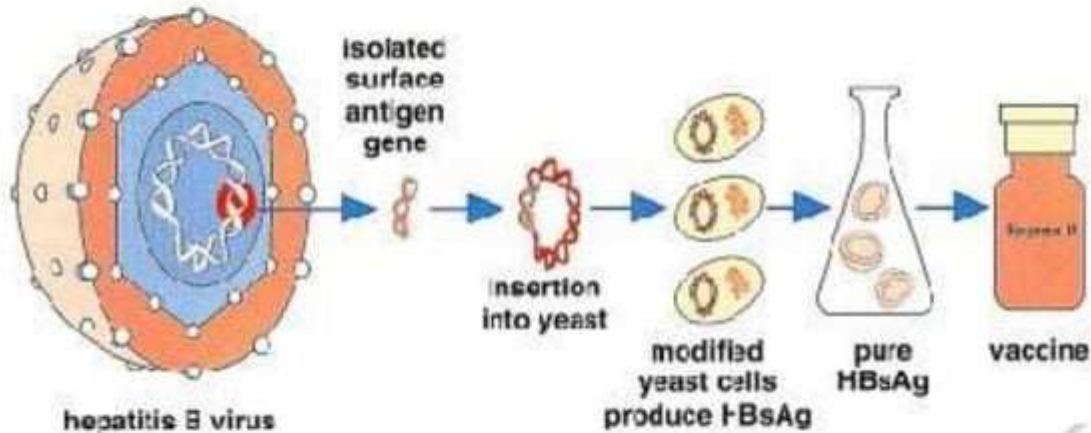


# HEPATITIS B VACCINE



- The gene encoding for hepatitis B surface antigen (HBsAg) has been identified.
- The HBsAg vaccine as a subunit vaccine, is produced by cloning HBsAg gene in yeast cells (*Sacchromyces cerevisiae*).

# HEPATITIS B VACCINE



Preparation of a genetically engineered vaccine



# DNA VACCINES



- The immune response of the body is stimulated by a DNA molecule.
- The DNA vaccine, gene encoding an antigenic protein.
- Inserted onto a plasmid and incorporated to the target animal cell of the host.
- Antigenic proteins are developed the humoral immunity or cellular immunity

# DNA vaccine and its mechanism

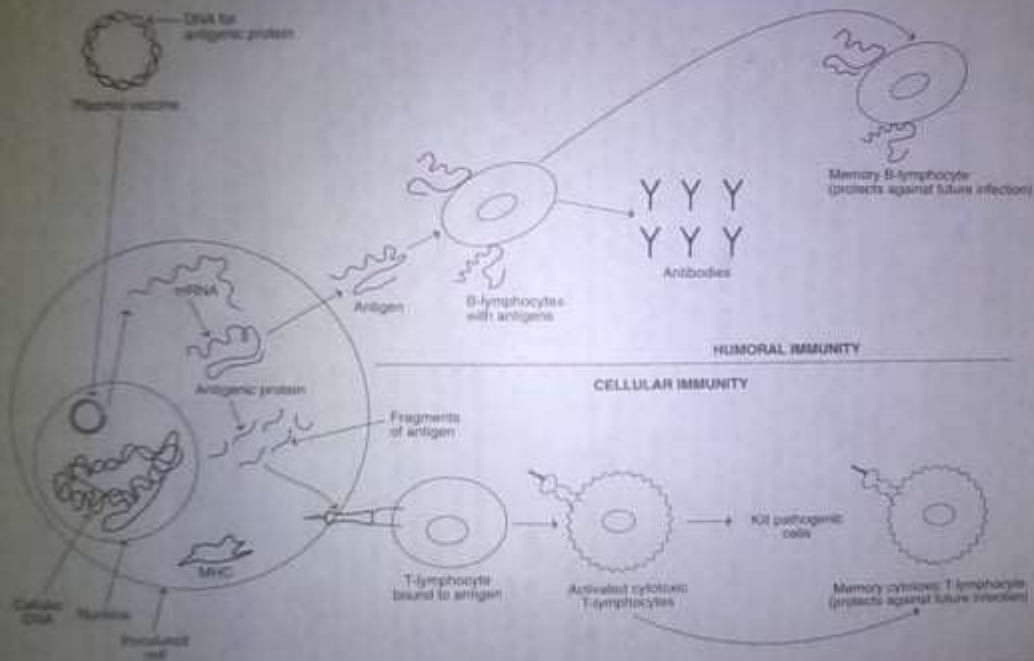


Fig. 18.3 DNA vaccine and mechanism of its action in developing immunity (APC: Antigen Presenting Cell; mRNA: Messenger RNA; APC: Antigen Presenting Complex; MHC: Major Histocompatibility Complex)

## Advantages:

- DNA vaccine are very specific in producing target protein.
- Higher immune responds.
- more stable in various temperature.

## Disadvantages:

- The fact of the DNA vaccine in the host cells is not yet clear.
- There also exists a danger of cancer due to DNA vaccine
- The post translational modified gene produced the antigen may not be the same as the native antigen.

# ATTENUATED RECOMBINANT VACCINES

- Genetically engineer the organism and use them as live vaccines.



## The production of vaccine based on the two types:

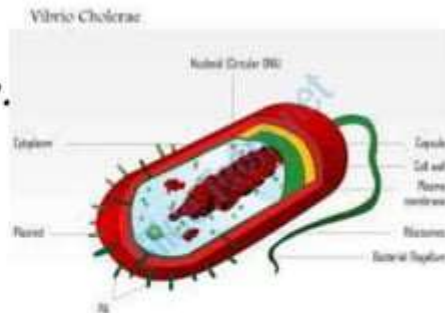
- Detection or modification of the virulence genes of the pathogenic organisms.
- Genetically manipulated non pathogenic organisms to carry and express antigen determinates from pathogenic organisms.

Eg: *Cholera*, *Salmonella spp*, *Leishmania spp*



# CHOLERA

- Cholera is an intestinal disease.
- It is characterized by diarrhea, dehydration, abdominal pain and fever.
- It is caused by a *vibrio cholerae*.





# CHOLERA VACCINE



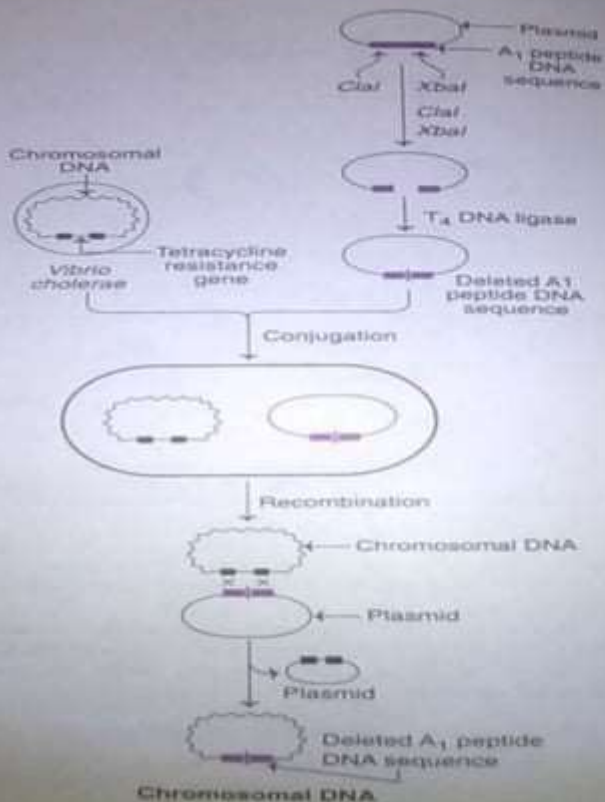
- The genetically engineered *V. cholerae* is a good attenuated vaccine.
- Cholera vaccine is composed of phenol killed *V. cholera*.
- The genetically engineered *V. cholerae* cells with deleted A1 peptide DNA sequence are quite stable. So they can not produce enterotoxin.

### Advantages:

- This type of vaccines is that the native conformation of the immunogenic determination is preserved, hence the immune response is substantially high.

### Disadvantages:

- There are caused some side effects.



Development of new strain of *V. cholerae* as a attenuated recombinant vaccine.

Fig. 16.7 - Development of a new strain of *V. cholerae* as an attenuated recombinant vaccine. (*Cla*I and *Xba*I are restriction endonucleases)

# VECTOR RECOMBINANT VACCINE

- Vectors can be genetically modified and employed as vaccines against pathogens.
- *Vaccinia virus* is used to the vector vaccine.
- The *vaccinia virus* is the possibility of vaccinating individuals against different diseases simultaneously.
- The advantage with vector vaccine is that it stimulates B-lymphocytes and T-lymphocytes.

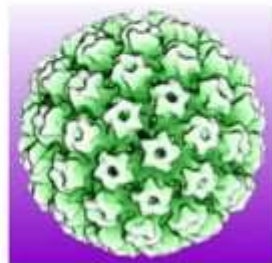




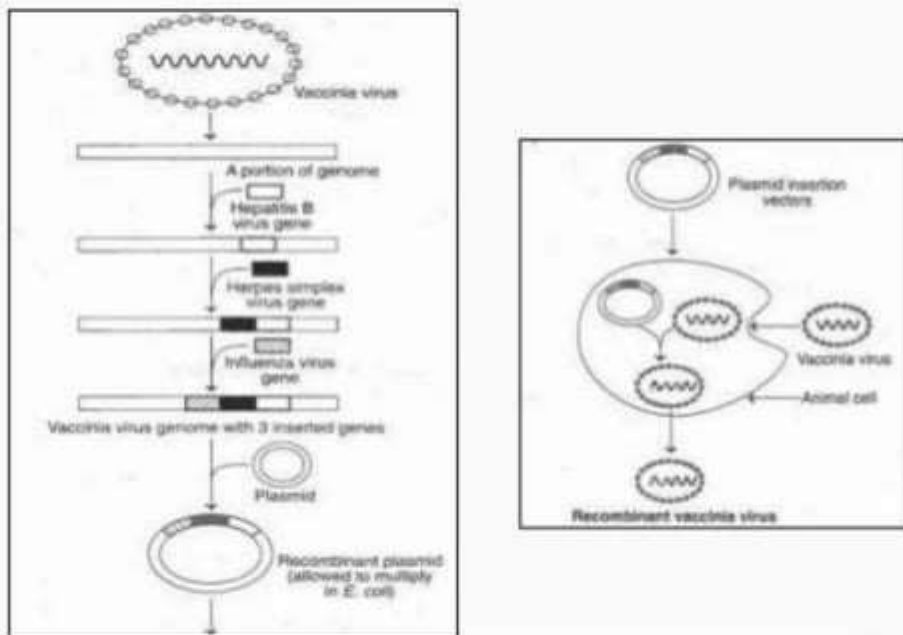
# VACCINIA VIRUS

- *Vaccinia virus* processed to release their DNAs.
- Then genes from *hepatitis B virus*, *herpes simplex virus* and *influenza virus* are inserted into *vaccinia virus* genome.
- This injected to *E.coli* and increasing their number and produce plasmid insertion vectors.

- The plasmid and *vaccinia virus* injected into the animal cell.
- The plasmid insertion vector incorporates its genes into *vaccinia virus* genome at a place encodes for the enzyme thymidine kinase (TK).
- This replicate the vector recombinant vaccine and purified the vaccine to use.



# Recombinant Vaccines:



**Fig: Production of vaccinia vector vaccine.**



# VECTOR RECOMBINANT VACCINE

## Advantages:

- Antigens that closely resemble natural antigen can be produced.
- Stimulate the T- lymphocytes and B- lymphocytes.

## Disadvantages:

- Important limitation is the unknown risk of using in humans.
- Using this, may be serious complication in immuno suppressed individuals as AIDS patients.

# OTHER RECOMBINANT VACCINE

- **FanC subunit** of *E. coli* expressed in soybeans as possible oral vaccine for *E. coli* induced diarrhea in **cattle, sheep and goats**.
- **Capripox vaccine** used as vector to protect against rinderpest and peste-des-petits ruminants.
- **Human adenovirus** used as vector to deliver hemagglutinin and nucleoproteins from **swine influenza virus**.
- **Fowlpox virus vectored vaccines** for avian *influenza*, *Newcastle disease*, *avian encephalomyelitis*, *laryngotracheitis*, and *Mycoplasma gallisepticum*.
- Canada licensed first **DNA vaccine** for infectious haemopoetic necrosis virus in **salmon**.
- **Canarypox-vectored feline vaccines** for leukemia and feline **rabies**.

# Recent recombinant vaccines

- Classical swine fever virus (CSFV) is a live attenuated vaccine.
- Bacterial vaccines - Bacille Calmette-Guérin (BCG), *Listeria monocytogenes*, *salmonellae* and *shigellae* vaccine vectors.
- Flu vaccine for influenza viruses.

# Reference

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