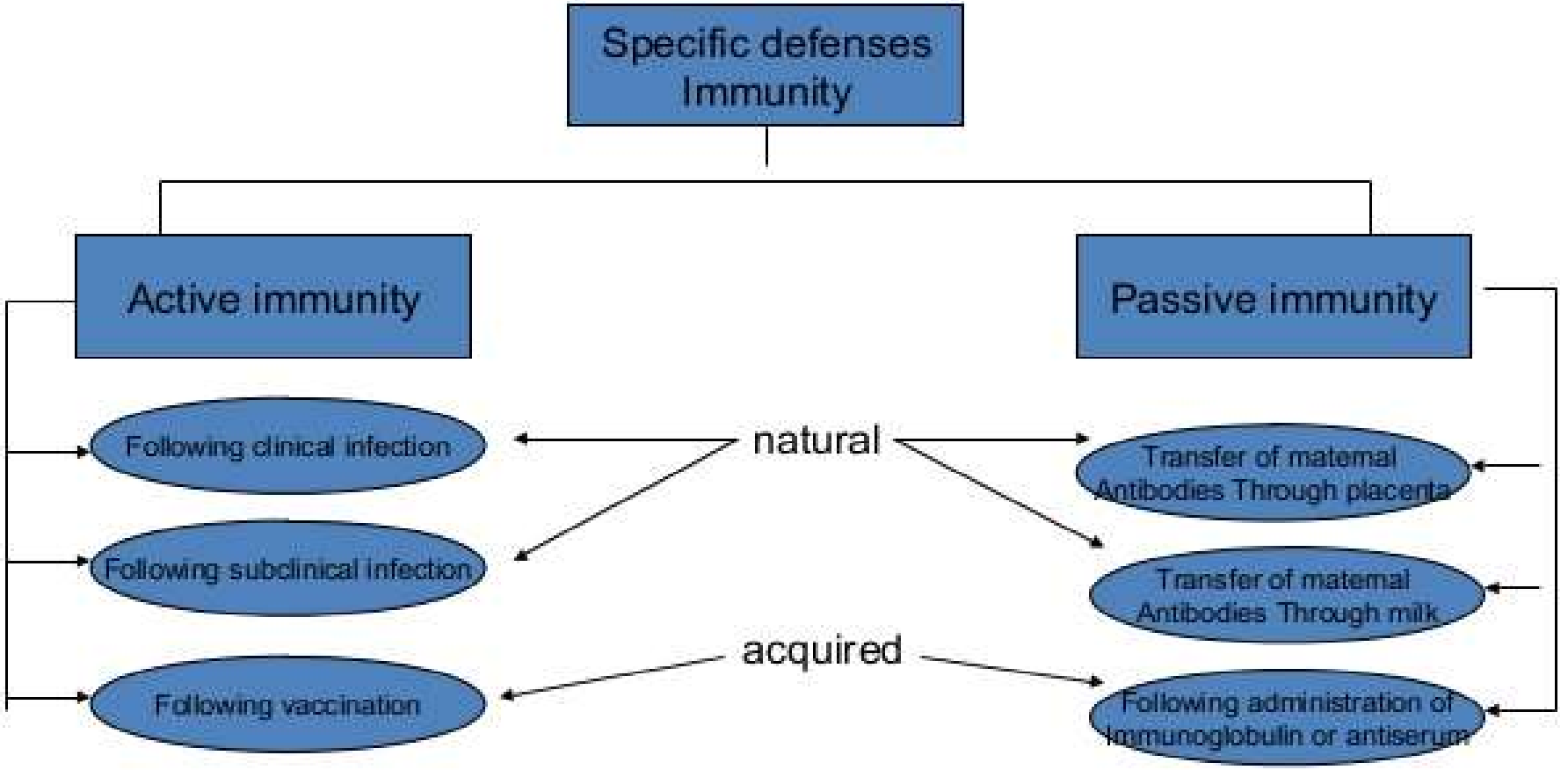
Vaccines

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 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).

Vaccination

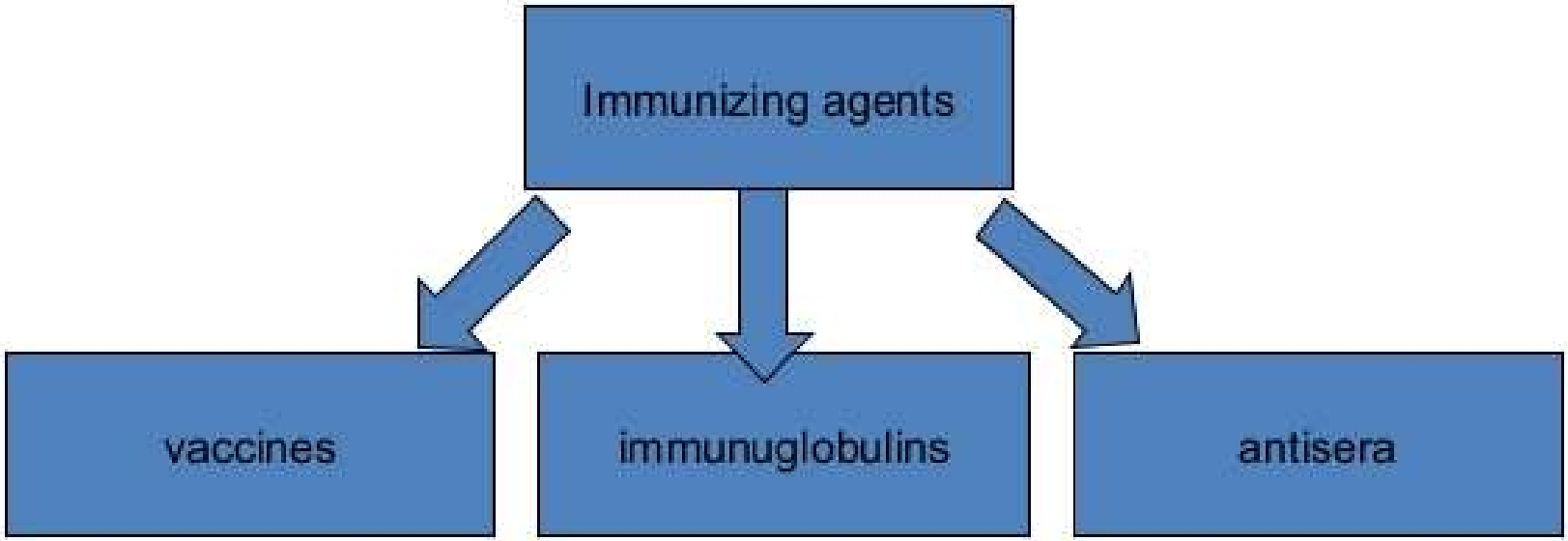
- Vaccination is a method of giving antigen to stimulate the immune response through active immunization.

- A vaccine is an immuno-biological substance designed to produce specific protection against a given disease.
- A vaccine is “antigenic” but not “pathogenic”.

- *Immunization* is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine.
Immunising agents may be classified as vaccines , immunoglobulins & antisera

Vaccines stimulate the body's own immune system to protect the person against subsequent infection or disease.

Immunizing agents



❖ What is the difference between vaccination and immunisation:

Vaccination is when a vaccine is administered to you (usually by injection).

Immunisation is what happens in your body after you have the vaccination. The vaccine stimulates your immune system so that it can recognise the disease and protect you from future infection (i.e. you become immune to the infection).

'Vaccination' and 'immunisation' are often used interchangeably but their meanings are not exactly the same.

Types of vaccines

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

Live vaccines

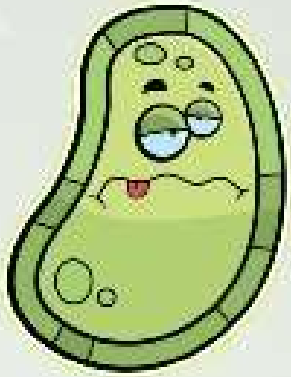
- Live vaccines are made from live infectious agents without any amendment.
- The only live vaccine is “Variola” small pox vaccine, made of live vaccinia cow-pox virus (not variola virus) which is not pathogenic but antigenic, giving cross immunity for variola.

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

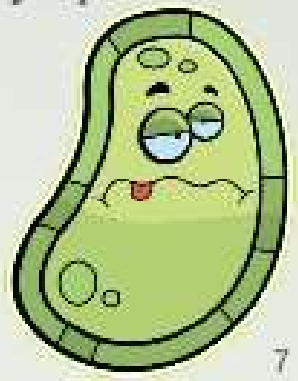
Attenuated Vaccines

- Advantages
  - Closely simulate natural infection
  - Stimulate humoral and cell mediated immunity
    - Important for intracellular organisms such as viruses
  - Adjuvants not as necessary
  - Generally cheaper (Valley Vet On-Line 12-09-13)
    - Pyramid 5 (MLV) 10 ds = $11.99
    - Triangle (killed) 10 ds = $15.65



Attenuated Vaccines

- Disadvantages
  - Potential to cause pathology
    - Replicating organism can cause mild signs - Brucellosis
    - Intact virulence - BVDV, IBR
    - Potential for reversion to virulence – low, low risk
  - Contamination
    - Jencine(4-way live vaccine) contaminated with non-cytopathic BVDV
  - Stability



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.

Killed Vaccines

- Advantages
  - Generally safer
    - No disease due to virulent organism
    - No contamination
  - Greater stability
- Disadvantages
  - Hypersensitivity reactions (adjuvants, toxins or large antigen loads)
  - Endotoxins
  - More costly
    - Pyramid 5 (MLV) 10 ds = $11.99
    - Triangle (killed) 10 ds = $15.65

COMPARISON OF KILLED &LIVE VACCINES

characterstic	*killed vaccine*	*Live vaccine*
No of dose	Multiple	Single
Need for adjuvant	Yes	No
Duration of immunity	Shorter	Longer
Immunoglobulins produsced	IgG	IgA &IgG
Stability at room temperature	High	Low

Toxoids

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

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

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.

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.

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

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).

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.

VACCINE	POSSIBLE MINOR ADVERSE REACTION
BCG	Local reaction (pain , swelling , redness)
CHOLERA	Oral presentation - none
DTP	Local reaction (pain ,swelling , redness) Fever
HEPATITIS A	Local reaction (pain ,swelling ,redness)
TETANUS	Local reaction (pain swelling , redness) Malaise & non specific symptoms

DNA Vaccine production

What is DNA vaccine?

- DNA vaccines are the vaccines which contain DNA that codes for specific proteins (antigens) from a pathogen.
- The DNA is injected into cells
- uses the DNA to synthesize the proteins
- Because these proteins are recognized as foreign, when they are processed by the host cells and displayed on their surface, the immune system is alerted,
- which then triggers immune responses.

Why DNA vaccines?

This approach offers a number of potential advantages over traditional approaches

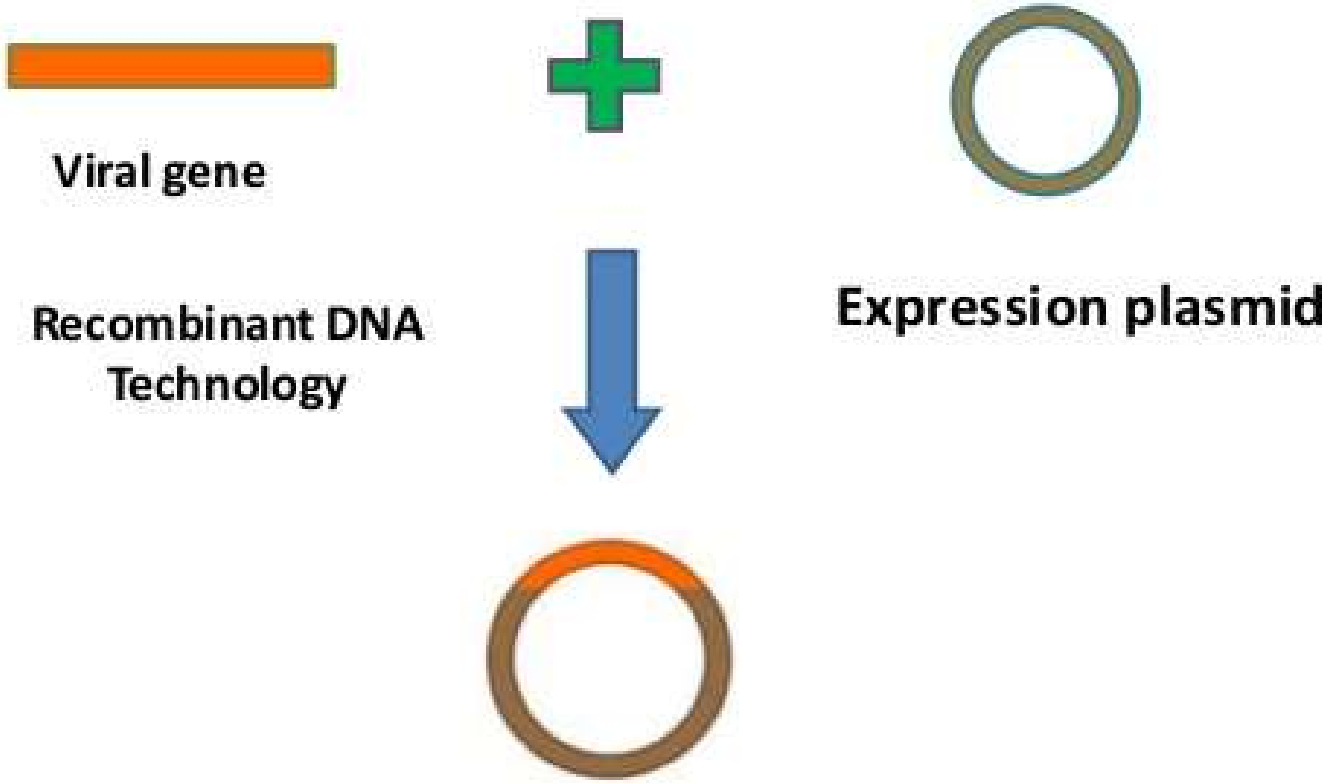
DNA vaccines

- Uses only the DNA from infectious organisms.
- Avoid the risk of using actual infectious organism.
- Provide both Humoral & Cell mediated immunity
- Refrigeration is not required

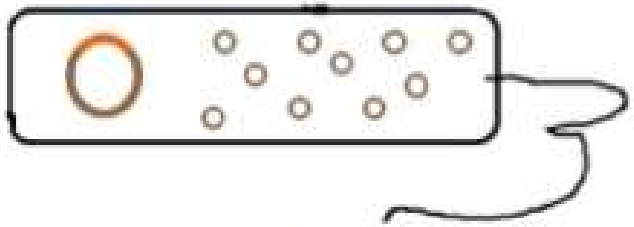
Traditional vaccines

- Uses weakened or killed form of infectious organism.
- Create possible risk of the vaccine being fatal.
- Provide primarily Humoral immunity
- Usually requires Refrigeration.

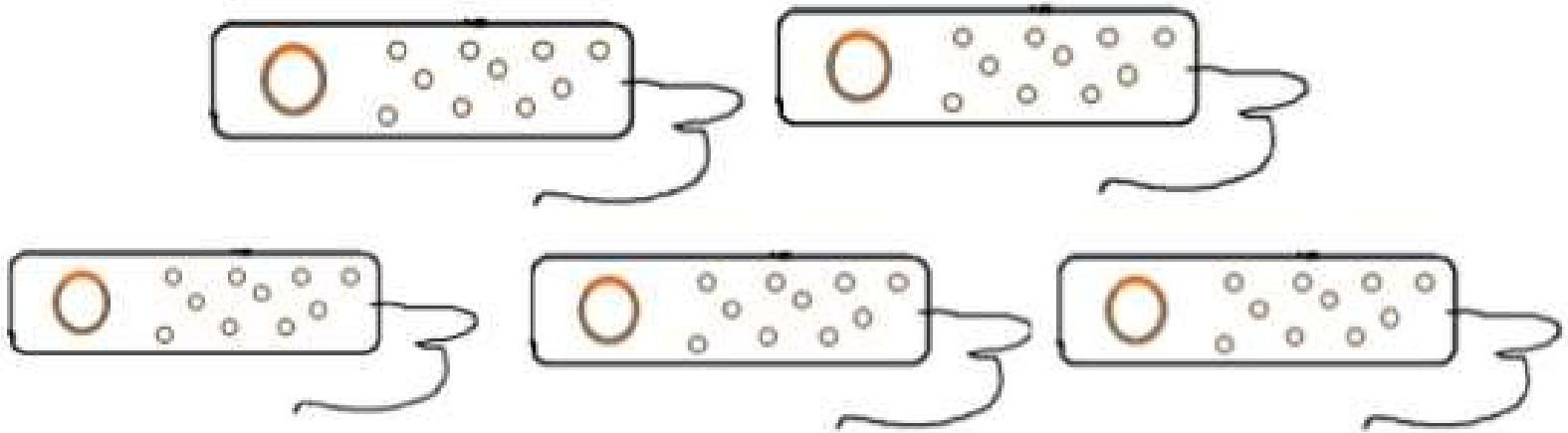
Principal of DNA Vaccine?



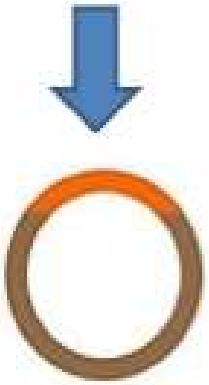
Transform in to bacteria



Plasmid DNA get Amplified



Plasmid DNA isolated

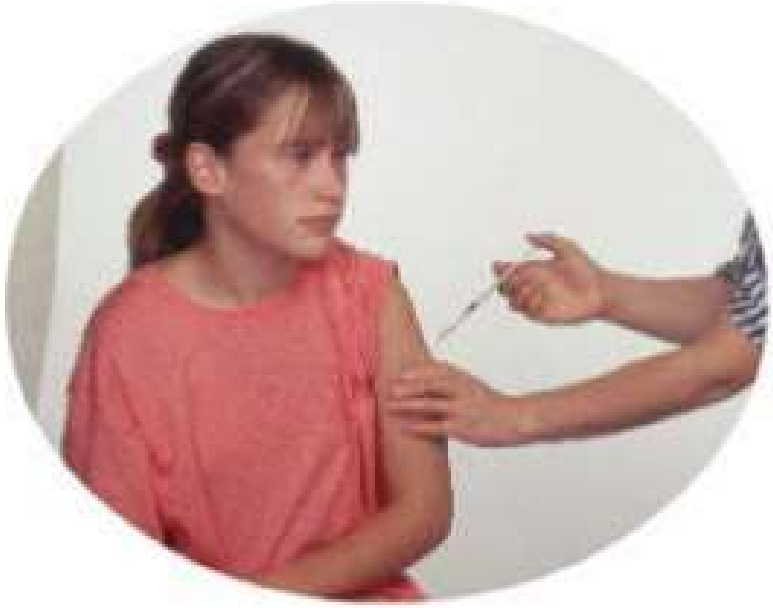


Stored in vials

Ready for Apply

METHODS OF DELIVERY

- **Syringe delivery:-**



Either intramuscularly

or

Intradermally

❑ Gene gun delivery:-

- ❑ Adsorbed plasmid DNA into gold particles
- ❑ Ballastically accelerated into body with gene gun.

Pneumatic Jet Injection: Very high amount of vaccine applied to the abdominal skin.

6. MECHANISMS OF ACTION

- A **plasmid vector** that expresses the protein of interest (e.g. viral protein) under the control of an appropriate *promoter* is
  - ✓ injected into the skin or muscle of the the host.
- After uptake of the plasmid,
  - ✓ protein is produced endogenously (Antigenic Protein is presented by cell in which it is produced)and
  - ✓ intracellularly processed into small antigenic peptides by the host proteases.

Con'd

- The **peptides** then enter in to
  - lumen of the endoplasmic reticulum (E.R.) by transporters.
- In the E.R., peptides bind to MHC class I molecules.
- Subsequent CD8+ cytotoxic T cells (**CTL**) are
  - stimulated and
  - evoke cell-mediated immunity.
- CTLs inhibit viruses through both
  - cytolysis of infected cells and
  - non cytolysis mechanisms such as cytokine production.

Con'd

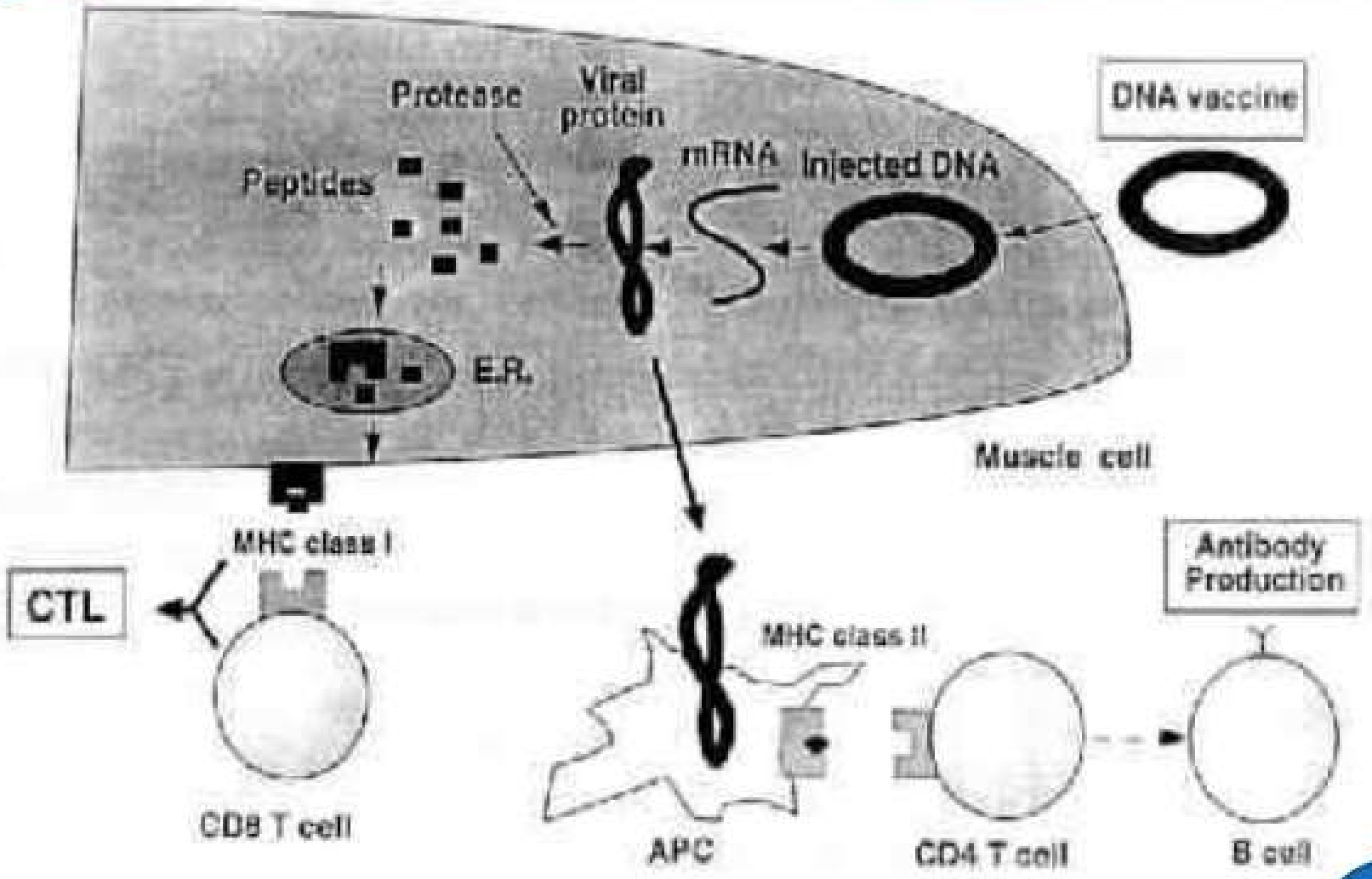
- The ***foreign protein*** can also be presented by
  - MHC class II pathway by APCs
- These **CD4+ cells** are able to
  - recognize the peptides formed from exogenous proteins
  - degraded to peptide fragments and loaded onto MHC class II molecules.
- Depending on the type of **CD4+ cell** that binds to the complex,
  - B cells are stimulated and
  - antibody production is stimulated.

⊕ This is the same manner in which traditional vaccines work

Con'd

- So in addition to mounting an attack against
  - the free-floating proteins,
  - the immune system attacks and
  - eliminates cells that have been colonized by a pathogen.
- The vaccine, then, works like a live vaccine, but without the risk. (With a live vaccine, the pathogen can continue to replicate and destroy cells as it does so.)

Con'd



Source; Faham *et al.*, 2011

7. ADVANTAGES

- Subunit vaccination with no risk for infection
- Antigen presentation by both MHC class I and class II molecules
- Able to polarise T-cell help toward type 1 or type 2
- Immune response focused only on antigen of interest
- Ease of development and production
- Stability of vaccine for storage and shipping
- Cost-effectiveness
- Obviates need for peptide synthesis, expression and purification of recombinant proteins and the use of toxic adjuvants
- Long-term persistence of immunogen
- In vivo expression ensures protein more closely resembles normal eukaryotic structure, with accompanying post-translational modifications

8. Disadvantages

- Limited to protein immunogens (not useful for non-protein based antigens such as bacterial polysaccharides)
- Risk of affecting genes controlling cell growth
- Possibility of inducing antibody production against DNA
- Possibility of tolerance to the antigen (protein) produced
- Potential for atypical processing of bacterial and parasite proteins

HAZARDS OF IMMUNIZATION

- No immune response is entirely free from the risk of adverse reactions or remote squeal. The adverse reactions that may occur may be grouped under the following heads:

1. *Reactions inherent to inoculation*
2. *Reactions due to faulty techniques*
3. *Reactions due to hypersensitivity*
4. *Neurological involvement*
5. *Provocative reactions*
6. Others

- *1.* ***Reactions inherent to inoculation:***

  These may be local general reactions. The local reactions may be pain, swelling, redness, tenderness and development of a small nodule or sterile abscess at the site of injection.
- The general reactions may be fever, malaise, headache and other constitutional symptoms. Most killed bacterial vaccines (e.g., typhoid) cause some local and general reactions. Diphtheria and tetanus toxoids and live polio vaccine cause little reaction.

- ***2. Reactions due to faulty techniques:***

Faulty techniques may relate to

- faulty production of vaccine (e.g. inadequate inactivation of the microbe, inadequate detoxication),
- too much vaccine given in one dose,
- improper immunization site or route,
- vaccine reconstituted with incorrect diluents,
- wrong amount of diluent used,
- drug substituted for vaccine or diluent,
- vaccine prepared incorrectly for use (e.g., an adsorbed vaccine not shaken properly before use),
- vaccine or dliluent contaminated,
- vaccine stored incorrectly,
- contraindications ignored (e.g. a child who experienced a severe reaction after a previous dose of DPT vaccine is immunized with he same vaccine),
- reconstituted vaccine of one session of immunization used again at the subsequent session.

- ***3. Reactions due to hypersensitivity:***

- Administration of antisera (e.g., ATS) may occasionally give rise to anaphylactic shock and serum sickness. Many viral vaccines contain traces of various antibiotics used in their preparation and some individuals may be sensitive to the antibiotic which it contains. Anaphylactic shock is a rare but dangerous complication of injection of antiserum. There is bronchospasm, dyspnoea, pallor, hypotension and collapse.

- The symptoms may appear within a few minutes of injection or may be delayed up to 2 hours. Some viral vaccines prepared from embryonated eggs (e.g., influenza) may bring about generalized anaphylactic reactions. *Serum sickness* is characterized by symptoms such as fever, rash, oedema and joint pains occurring 7 -12 days of injection of antiserum.

- ***4. Neurological involvement:***
- Neuritic manifestations may be seen after the administration of serum or vaccine. The well-known examples are the post-vaccinial encephalitis and encephalopathy following administration of anti -rabies and smallpox vaccines.
- Guillain-Barre syndrome in association with the swine influenza vaccine is another example.

- **5. Provocative reactions:**
- Occasionally following immunization there may occur a disease totally unconnected with the immunizing agent (e.g., provocative polio after DPT or DT administration against diphtheria).
- The mechanism seems to be that the individual is harboring the infectious agent and the administration of the vaccine shortens the incubation period and produces the disease or what may have been otherwise only a latent infection is converted into a clinical attack.

- **6. *Others:***
- These may comprise damage to the fetus (e.g., with rubella vaccination); displacement in the age-distribution of a disease (e.g., a potential problem in mass vaccination against measles, rubella and mumps).

PRECAUTIONS TO BE TAKEN

- Before administration of the antiserum or antitoxin, it is necessary to test for sensitivity reaction. This can be done in 2 ways:

(a) instilling a drop of the preparation into the conjunctival sac. A sensitized person will develop pricking of the conjunctiva.

(b) a more reliable way of testing is by intradermal injection of 0.2 ml of antiserum diluted 1 : 10 with saline. A sensitized patient will develop a wheal and flare within 10 minutes at the site of injection. It should be borne in mind that these tests are not infallible.

- Adrenaline (1: 1000 solution) should be kept ready when giving foreign serum. In the event of anaphylaxis, for an adult, 0.5 ml of adrenaline solution should be injected intramuscularly immediately, followed by 0.5 ml every 20 minutes if the systolic blood pressure is below 100 mm of mercury.
- An injection of antihistaminic drug should also be given, e.g., 10-20 mg of chlorpheniramine maleate by the intramuscular route, to minimise the after-effects such as urticaria or oedema. The patient should be observed for 30 minutes after any serum injection.

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THANK YOU