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# IMMUNOLOGY

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## Passive vs. active immunity

	Passive immunity	active immunity
The concept	refers to the transfer of <b>“ready-made” antibodies</b> , from one individual to another	refers to the process of exposing the body to an antigen to <b>generate an adaptive immune response</b>
Methods to getting each type of immunity	<p><b>naturally</b> by <b>transplacental transfer</b> of <b>maternal</b> antibodies to the <b>developing fetus</b>, or through <b>colostrum</b> and <b>breast milk</b> rich in IgA.</p> <p><b>artificially</b> by <b>injecting</b> a recipient with <b>exogenous antibodies</b> targeted to a specific pathogen or toxin.</p>	<p>Naturally through infection with a certain pathogen.</p> <p>Artificially through administration of vaccines.</p>
examples	<p><b>Natural:</b> Maternal antibodies protect against some diseases such as measles, rubella, and tetanus for the first few months of life.</p> <p><b>Artificial:</b> Pooled human immunoglobulins used intravenously (<b>IVIG</b>) can be used</p>	<p><b>Natural:</b> Wild infection with hepatitis A virus (HAV) and subsequent recovery gives rise to an active immune response usually leading to lifelong protection.</p> <p><b>Artificial:</b> In a similar manner, administration of two doses of hepatitis A vaccine generates an acquired active immune response leading to long-lasting (possibly lifelong) protection</p>

→ active immunity stay longer than passive because long lived plasma cells and memory cells.

→How we can get Passive immunity ?

1- maternal antibodies naturally

2- monoclonal antibodies artificial

→in which cases we use monoclonal antibodies ?

acute infection :

-in rabies Virus

-in corona virus

→How we can get active immunity ?

1- immunization artificial

2- infection natural

→to induce immune system against something we have this ways :

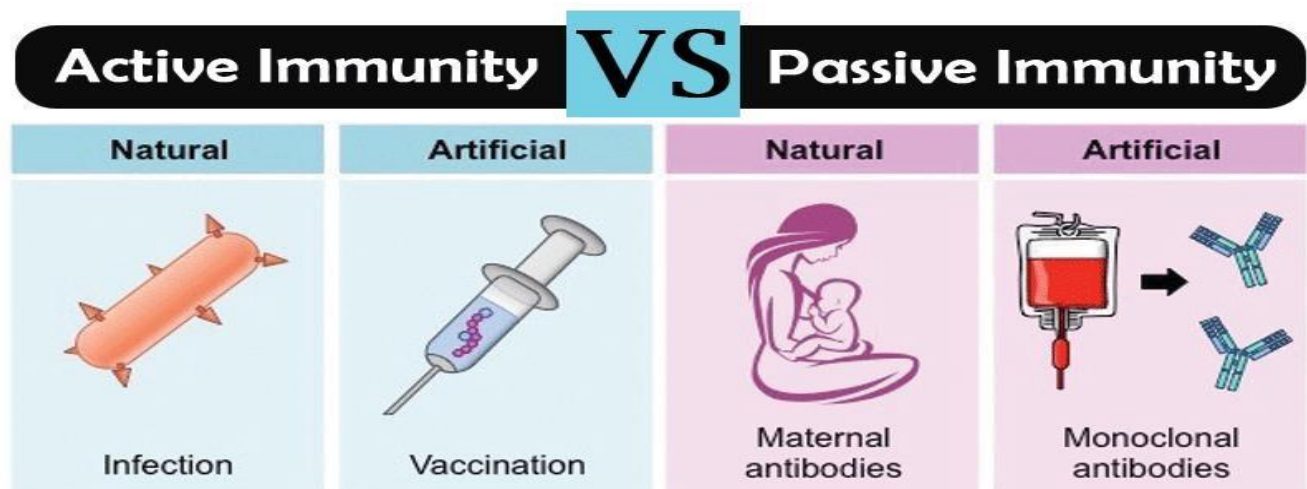
1. life Infection

2. immunization

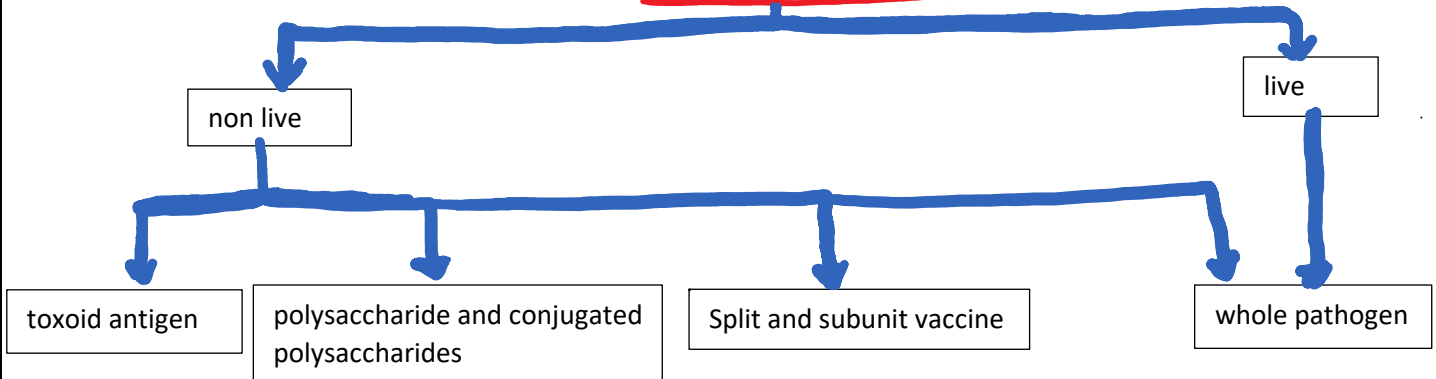
- live attenuated pathogen ( weakened the pathogen)

- Non-live pathogen (dead pathogen)

→ live vaccines more effective than non live vaccines and non live vaccines more effective than split and subunit vaccines .

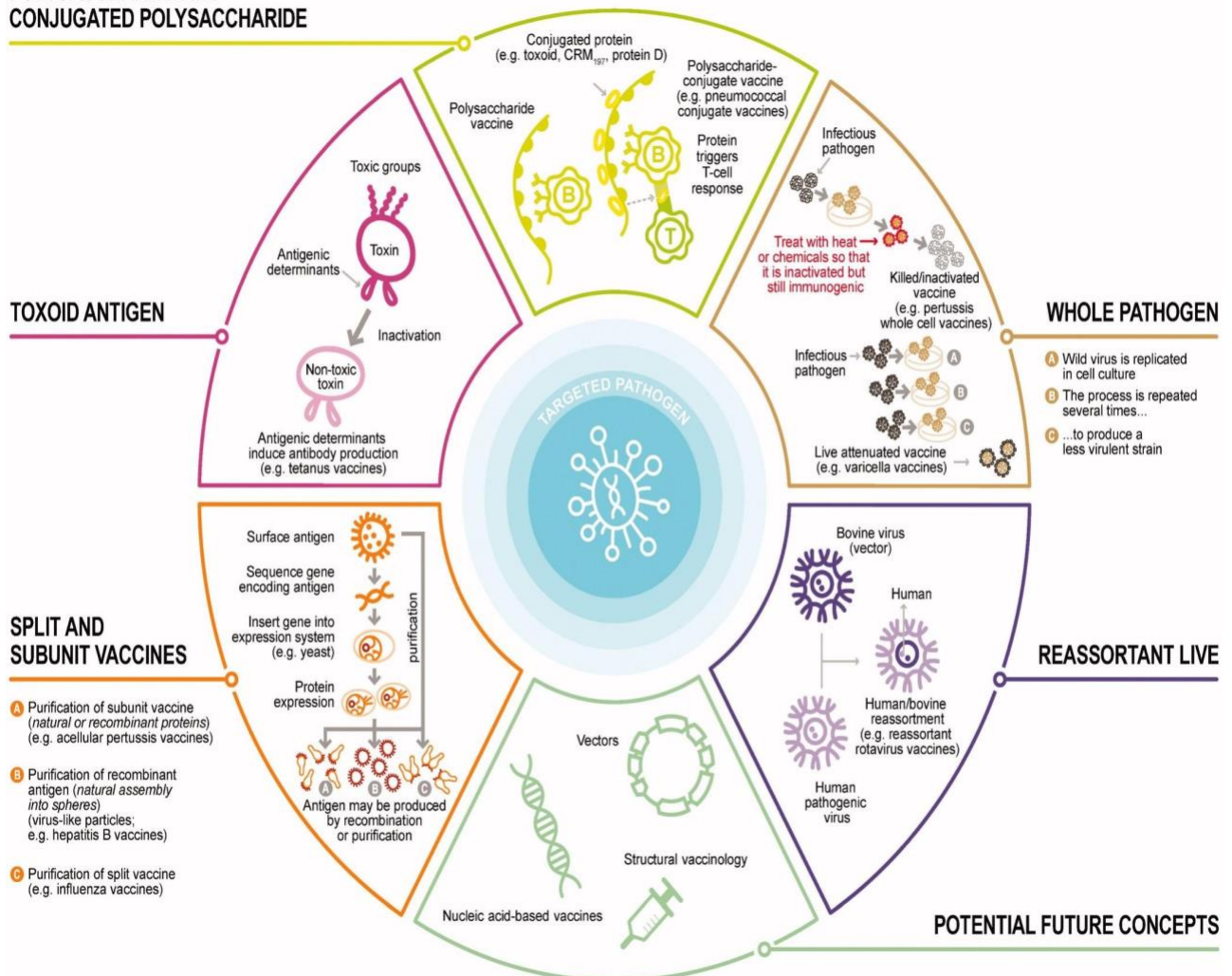


## → vaccines ←



→ here another two types of vaccines ( reassortant live & nucleic acid vaccines) but doctor doesn't talk about it much just he say that nucleic acid vaccines we use it in corona virus vaccines

### POLYSACCHARIDE AND CONJUGATED POLYSACCHARIDE



## A-Live attenuated vaccines →

**1-whole pathogen** : contain pathogens that have been **weakened, altered** or **selected** to be less virulent than their wild-type counterparts. In their altered form, they cannot cause the actual disease or only mimic the disease in a very mild way. They are generally produced **from viruses rather than bacteria** because viruses contain fewer genes and attenuation can be obtained and controlled more reliably. The most **common method** to obtain live attenuated vaccines is to **pass the virus** through a series of in vitro cell cultures (e.g. in chick embryo cells). At each “passage”, the selected viruses **become better at infecting and replicating in cell cultures** but progressively **lose their ability to infect** and replicate in their **original human host**.

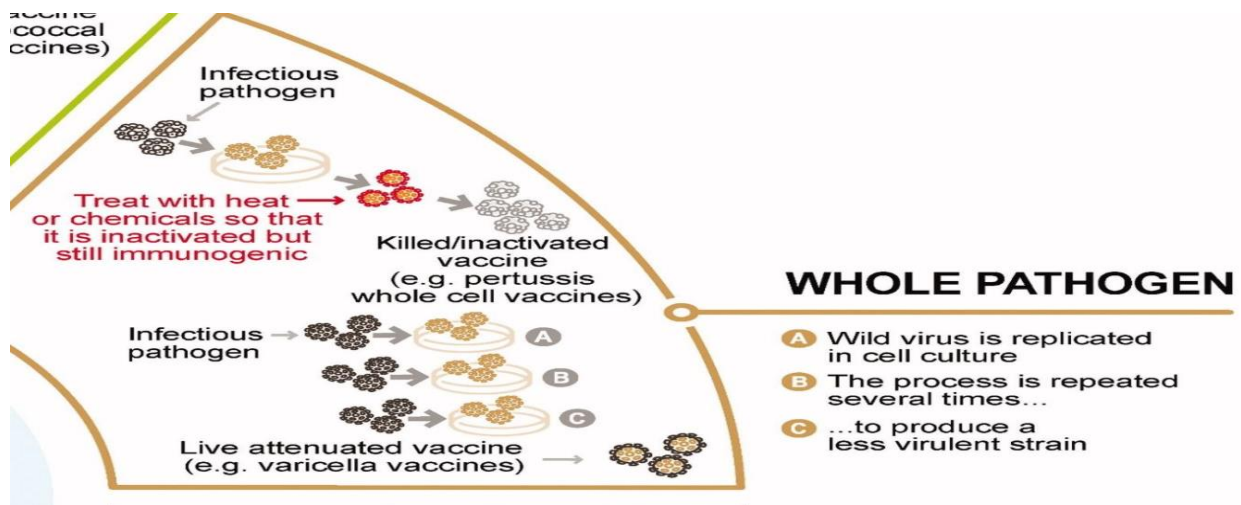
- These vaccines induce robust cell-mediated and antibody responses and **often confer longterm immunity** after only one or two doses. Although rare, clinical disease can occur after vaccination, but vaccine-induced symptoms are typically much milder than after natural infection. However, live attenuated vaccines **are often contraindicated** in **immunocompromised** individuals
- Classical examples of live attenuated vaccines produced by serial passage are those against **measles, mumps, rubella** and **varicella**, which are usually combined into trivalent or tetravalent vaccines
- The **only live attenuated bacterial** vaccine currently in use is the bacillus Calmette-Guérin (**BCG**) **vaccine**, which was developed almost a century ago

- attenuated doesn't work on Bacterial pathogen except for (BCG) vaccine

• **Oral polio vaccine (OPV)** is a live attenuated vaccine that was obtained through serial passages in non-human cells, OPV is easily administered through oral drops, inexpensive, and effective at inducing intestinal mucosal immunity.

However, in very rare cases (one case per million doses), OPV can mutate into a virulent form and induce very rare cases of vaccine-associated paralytic poliomyelitis.

- **OPV** should be stopped after wild poliovirus transmission has been controlled. For this reason and to maintain population immunity, OPV has been replaced by an **inactivated polio vaccine (IPV)** in an increasing number of countries worldwide.



**B-Non-live vaccines**→do not contain any living or infectious particles, so they cannot cause disease and cannot reactivate. Therefore, they generally have a good safety profile, even in immunocompromised individuals

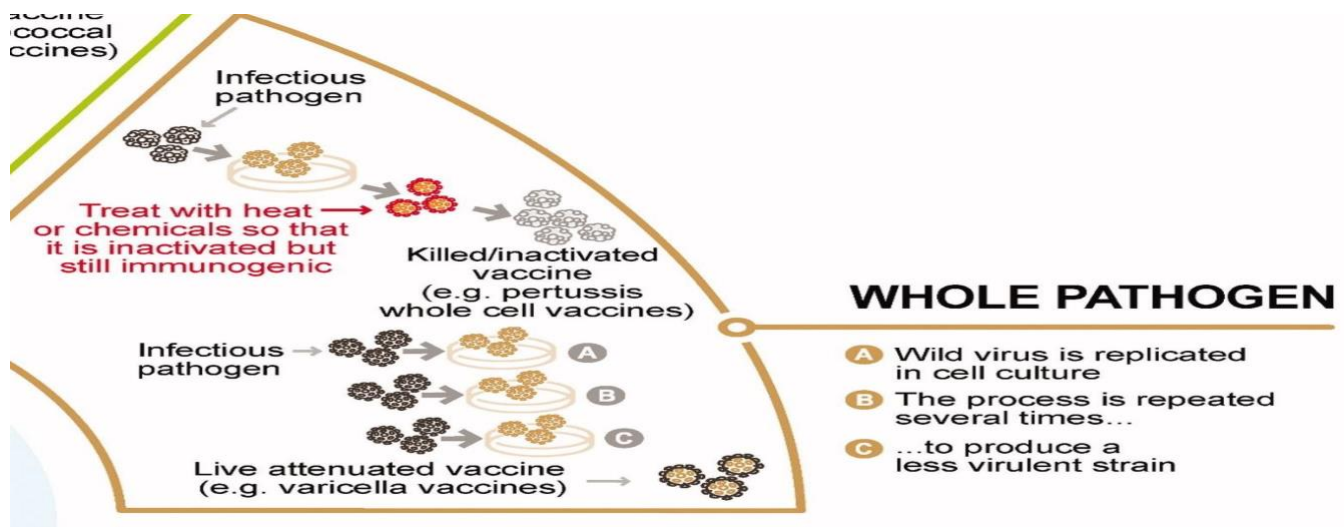
However, a **drawback** of these vaccines is that **immunogenicity** and **duration of protection** tend to be less than for live vaccines, and they may require several doses or adjuvants to improve immunogenicity.

- Therefore, these vaccines are usually given repeatedly based on the prime-boost principle to induce long-term immunity.
- Non-live vaccines can contain inactivated **whole pathogens** or **only parts of them** such as **proteins** or **polysaccharides (subunit vaccines)**.

**1-whole pathogen:** Vaccines based on inactivated pathogens are produced by inactivating preparations of whole pathogens by **heat, radiation, or chemicals** such as formalin or formaldehyde.

Current examples of inactivated vaccines include the previously mentioned **IPV, whole-cell pertussis, rabies and hepatitis A vaccines**.





**2-Subunit vaccines:** contain selected fragments of the pathogen as antigens instead of the whole pathogen. These fragments can be **proteins, polysaccharides**, or parts of a virus that may form **virus-like particles (VLPs)**.

- Subunit vaccines generally cause less adverse reactions than live or inactivated whole organism vaccines, but they may be less immunogenic because they contain fewer antigens and the purification process often eliminates components that trigger innate immunity.
- Examples of subunit vaccines include **tetanus toxoid**, inactivated split and subunit seasonal **influenza**, **acellular pertussis** and **pneumococcal polysaccharide vaccines**.
- Antigenic proteins can be **purified** from preparations of the whole pathogen, as for the acellular pertussis vaccines, or can be **produced by recombinant genetic engineering**.
- **Acellular pertussis vaccines** are other examples of **purified antigenic proteins**. These vaccines contain between one and five highly purified pertussis antigens, compared to more than 3000 antigens for whole-cell inactivated pertussis vaccines.

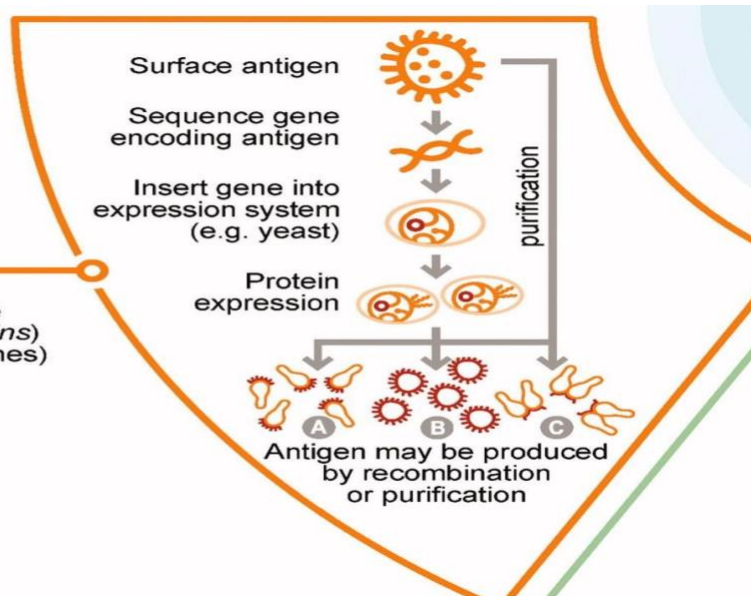
- An example of **recombinant protein vaccine** is provided by the widely used hepatitis B vaccine in which the gene of the **hepatitis B surface antigen (HBsAg)** has been inserted into appropriate vectors for production in yeast.
- The concept of combining recombinant proteins helped to develop the first malaria vaccine. In this vaccine, the gene of a **surface protein** of the infectious form of **Plasmodium falciparum** is fused to the **HBsAg gene**, and the resulting recombinant fusion protein is expressed in yeast with free recombinant HBsAg

-which subunit should be chosen ?

to know which subunit is Immunogenic we need to test that in lab by mice

## SPLIT AND SUBUNIT VACCINES

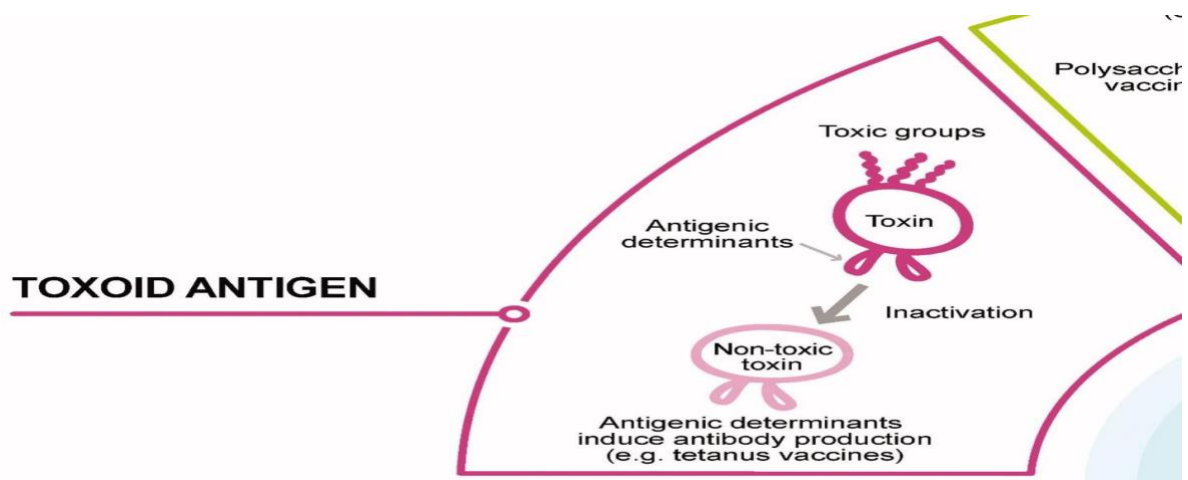
- A** Purification of subunit vaccine (*natural or recombinant proteins*) (e.g. acellular pertussis vaccines)
- B** Purification of recombinant antigen (*natural assembly into spheres*) (virus-like particles; e.g. hepatitis B vaccines)
- C** Purification of split vaccine (e.g. influenza vaccines)



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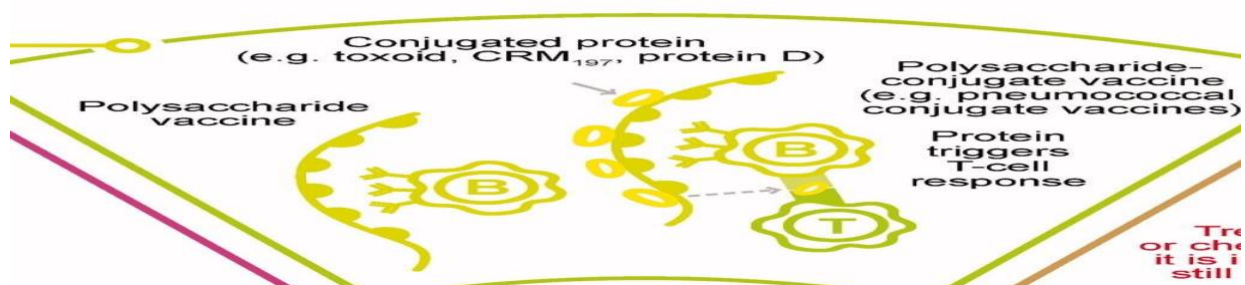
- **3-Toxoid vaccines** : Some bacteria such as **Clostridium tetani**, *Clostridium difficile* or **Corynebacterium diphtheriae** cause disease by releasing **pathogenic toxins**. Vaccines against these diseases are produced by **detoxifying the toxin** using heat, chemicals (e.g. formaldehyde) or both.
- The inactivated toxins, called **toxoids**, are no longer pathogenic but retain their ability to induce toxin-neutralizing antibodies. Classical examples of toxoid vaccines are those against diphtheria and tetanus, which have been used since their discovery in the 1920s
- However, toxoids **protect** only against disease pathogenesis in **vaccinated individuals** but **do not prevent infection or transmission**.
- Therefore, high vaccination coverage does not provide **herd protection** and unvaccinated or individuals not receiving regular booster doses are potentially at risk
- - toxoid vaccine (toxoids is a inactive form of toxins )  
toxins have two groups of subunits :  
- toxic subunits  
- antigenic subunits ( subunit that bind to host cell )  
we inactivate it by heat (exotoxins are heat labile but endotoxins (LPS) heat stable ) because it is exotoxins and inject them into host and the host form antibodies against antigenic subunit so the toxin can't enter host cell



- **4- polysaccharide and conjugated polysaccharides :**
- If the antigen is polysaccharide We need to conjugate it with protein because Polysaccharide vaccines are poorly immunogenic, provide only short term protection.
- **Streptococcus pneumoniae, Haemophilus influenzae type b and N. meningitidis** are three **encapsulated bacteria** that cause severe invasive disease. They possess **polysaccharide capsules** that **facilitate bacteria's survival** when carried in the **nasopharynx** and in the **blood** during disease pathogenesis.
- **Polysaccharide vaccines** are **poorly immunogenic**, provide only **short term protection**.
- **Immunogenicity** of purified polysaccharides **could be enhanced by coupling** (i.e. conjugating) them **to a protein**.
- **Conjugation transforms** the **T-cell-independent** response induced by polysaccharides into a **T-cell-dependent** response that induces high-affinity antibodies and immune memory

→How we can purified antigens ?

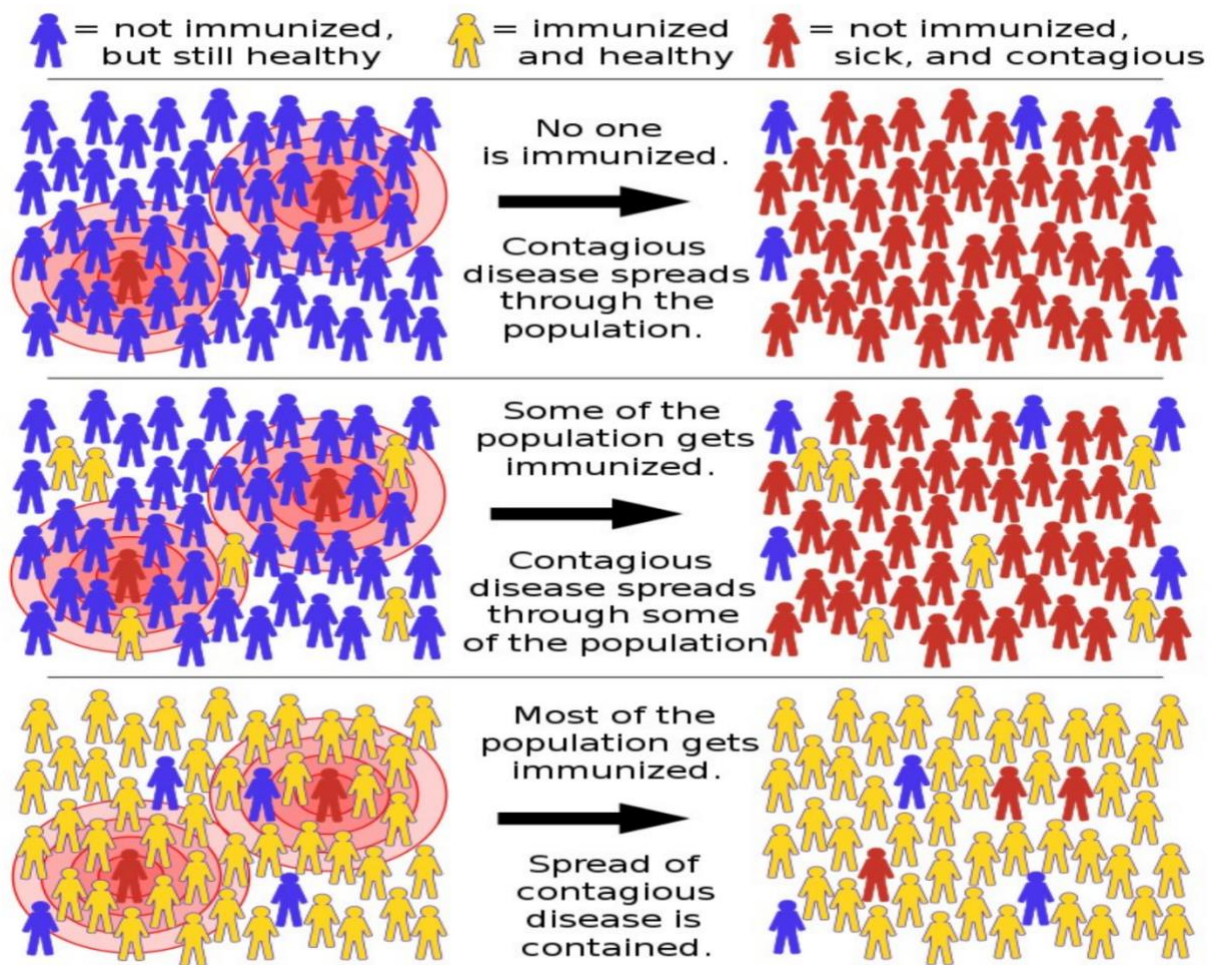
- lysis the pathogen and extract it's proteins in biochemical methods and use them in vaccines
- extract the genetic material for pathogen and put it in expression system ( in bacteria or yeast ) to synthesize protein's pathogen



## 8→Herd immunity:

is a form of **indirect protection from infectious disease** that occurs when a **large percentage** of a population has become immune to an infection, **thereby providing a measure of protection for individuals who are not immune**.

- The greater the proportion of individuals in a community who are immune, the smaller the probability that those who are not immune will come into contact with an infectious individual.



Why there are people not immunize ?

- immunocompromised people
- people can't access to vaccine

## Adjuvants :

are substances that can **enhance and modulate the immunogenicity of the antigen**. Adjuvants are usually not needed for live attenuated vaccines because these vaccines actively replicate and self-enhance the immune response.

- Due to their capacity to **activate innate immune responses**, adjuvants can **broaden or extend responses** and improve memory responses
- For almost a century, aluminium salts (also known as alum) were the only adjuvant approved worldwide and they still remain the most widely used.

تم بحمد الله

ملاحظة

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