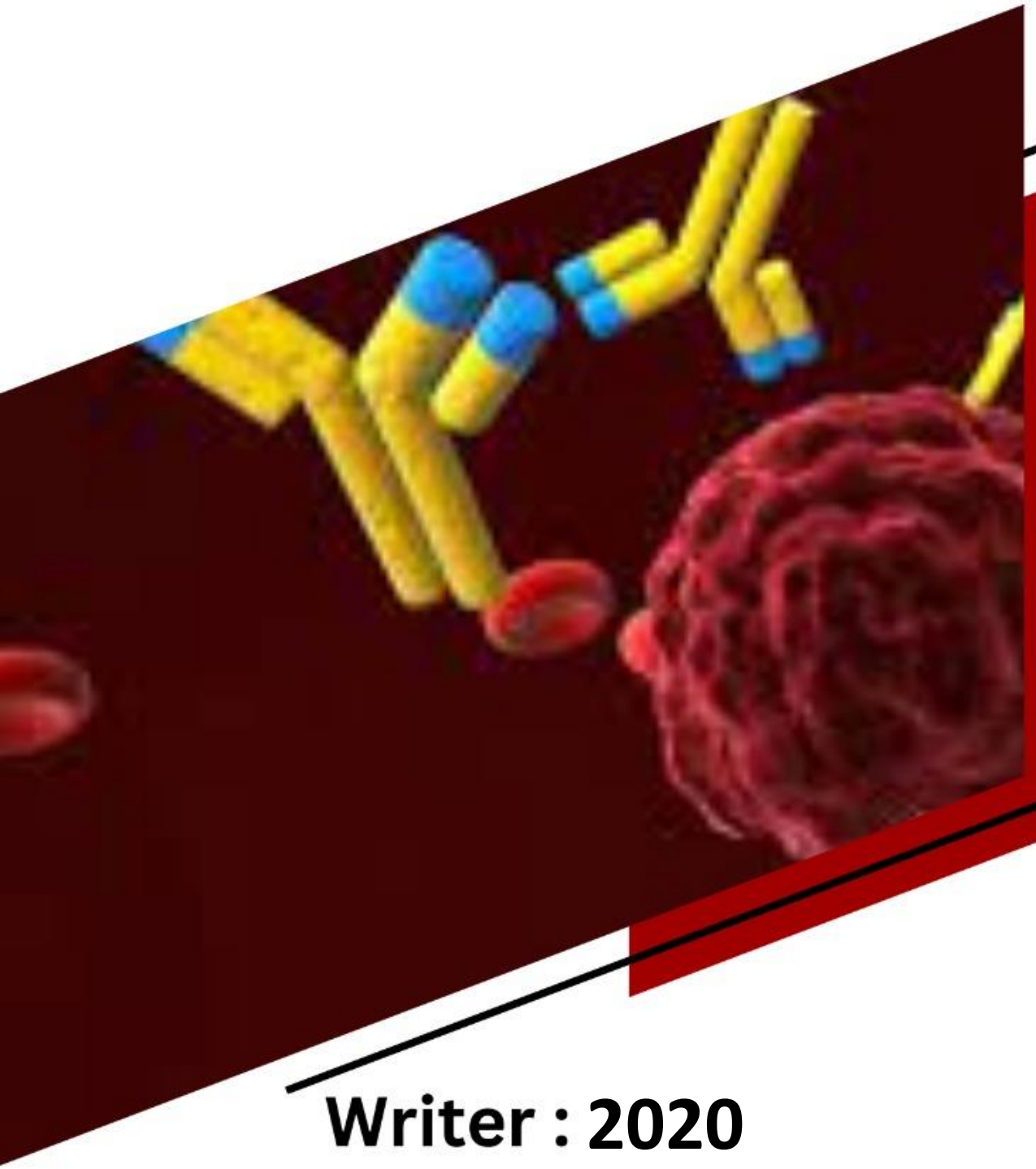
Doctor 021

IMMUNOLOGY

Sheet no. 15



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When you get an infection, you develop adaptive immunity.

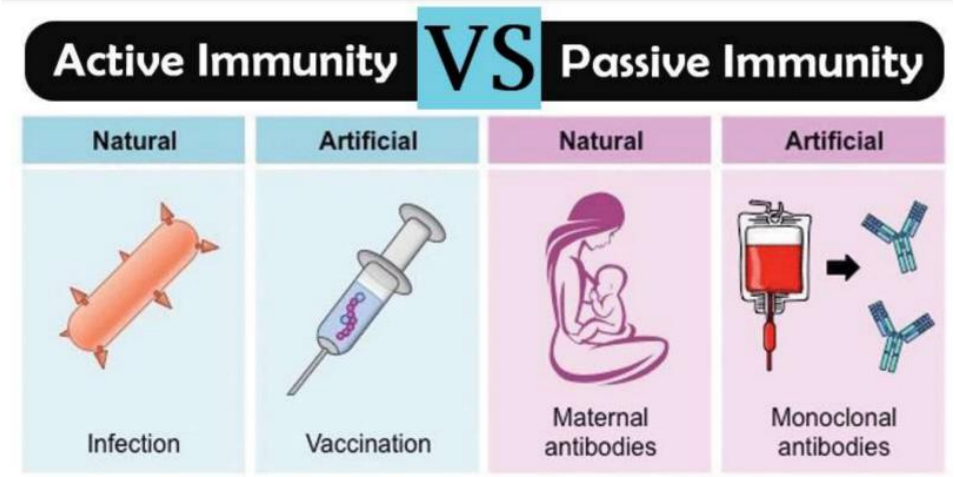
In other words, you generate memory T and B cells, so that if you encounter the same antigen again, they can quickly replicate and respond.

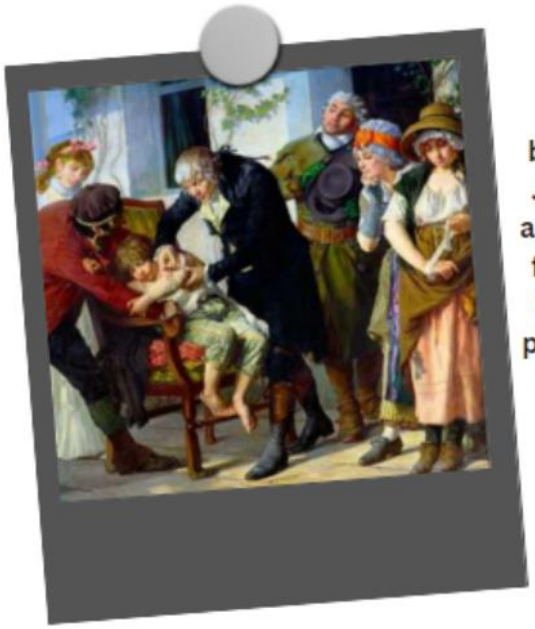
Most of the time we think of immunologic memory developing after natural infection. But memory T and B cells also develop after vaccination.

Vaccination is the process of generating a protective adaptive immune responses against microbes by exposure to nonpathogenic forms or components of microbes.

Acquired immunity is attained through either passive or active immunization.

	Passive immunity	active immunity
The concept	refers to the transfer of "ready-made" antibodies, from one individual to another	refers to the process of exposing the body to an antigen to generate an adaptive immune response
Methods to getting each type of immunity	naturally by transplacental transfer of maternal antibodies to the developing fetus, or through colostrum and breast milk rich in IgA. artificially by injecting a recipient with exogenous antibodies targeted to a specific pathogen or toxin.	Naturally through infection with a certain pathogen. Artificially through administration of vaccines.
examples	Natural: Maternal	Natural: Wild infection
	antibodies protect against some diseases such as measles, rubella, and tetanus for the first few months of life. Artificial: Pooled human immunoglobulins used intravenously (IVIG) can be used in the case of immunodeficiency diseases, or specific antibodies used in the treatment of several types of acute infections such as rabies	with hepatitis A virus (HAV) and subsequent recovery gives rise to an active immune response usually leading to lifelong protection. Artificial: 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





back to 1796, when Edward Jenner was about to inject an 8 year old with an extract from a milk maid's cowpox lesion, in order to provide protection from smallpox in a process known then as variolation

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

→How we can get Passive immunity ?

I- maternal antibodies naturally

2- monoclonal antibodies artificial

→in which cases we use monoclonal antibodies ? acute infection :

-in rapes 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 :

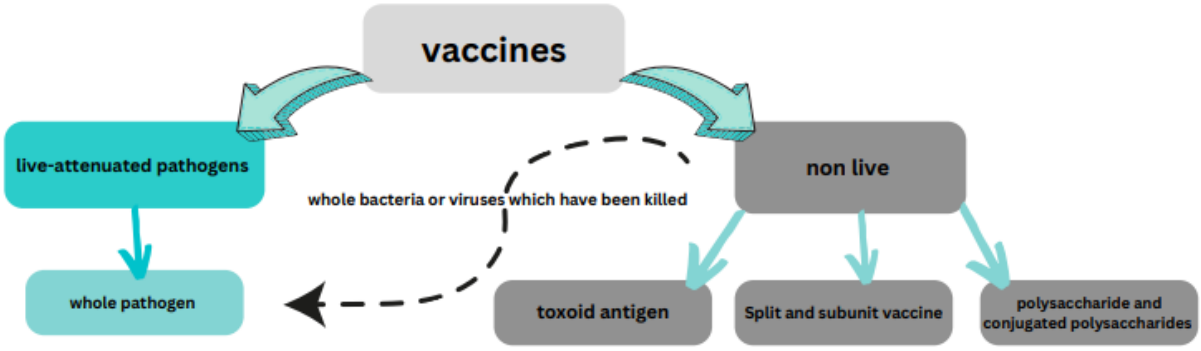
1. life Infection

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 .



live-attenuated vaccines :

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.

vaccines live-attenuated pathogens non live toxoid antigen Split and subunit vaccine polysaccharide and conjugated polysaccharides whole pathogen whole bacteria or viruses which have been killed 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

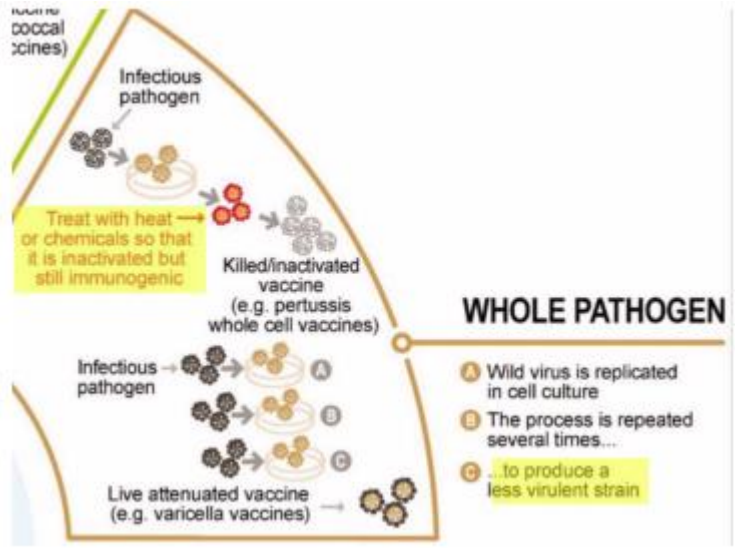
• **Classical examples of live attenuated vaccines** produced by serial passage are those against measles, mumps, rubella and varicella, which are usually combined into trivalent or tetravalent vaccines

• 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 poliovirustransmission 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.



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 primeboost 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.

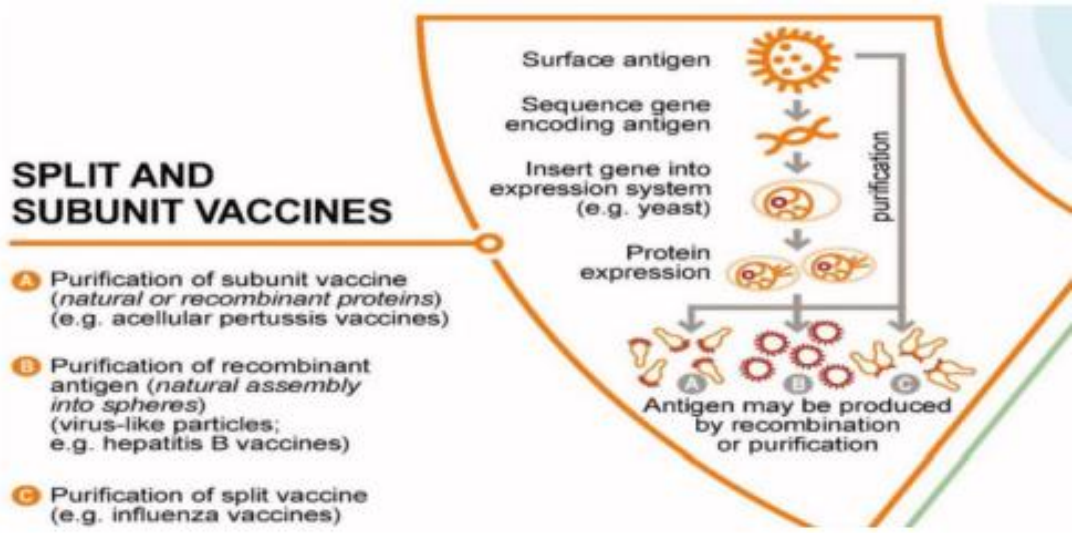
• Antigenic proteins can be purified from preparations of the whole pathogen, as for the acellular pertussis vaccines, or can be produced by recombinant genetic engineering.

• 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 choosen ? to know which subunite is Immunogenic we need to test that in lab by mice.



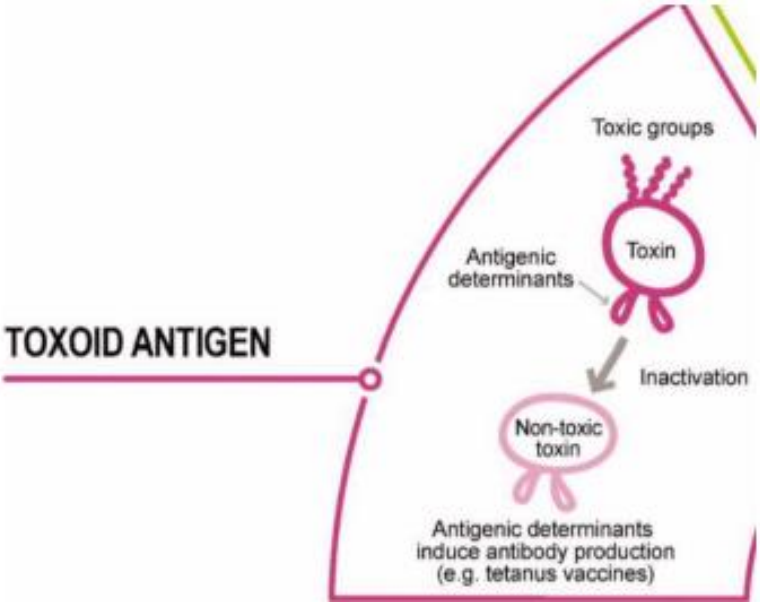
Toxoid vaccines :

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 hear 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 inter host cell

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.

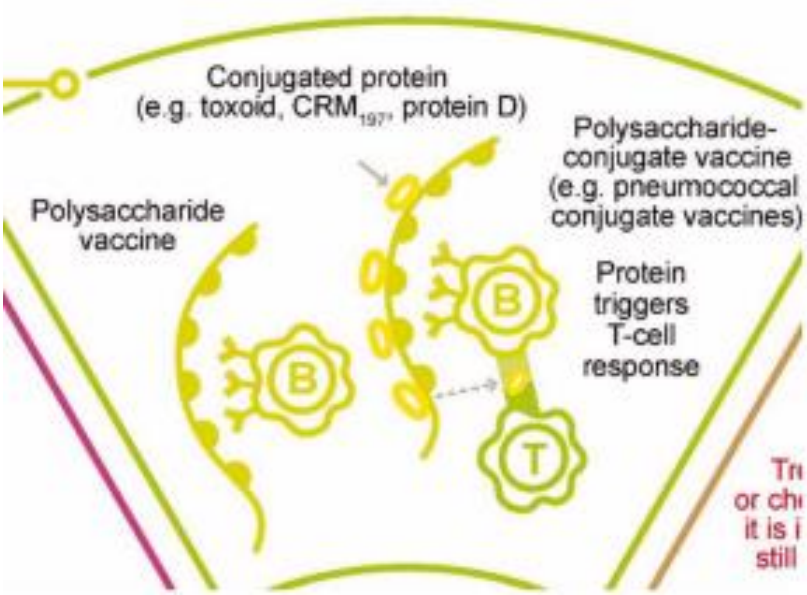
• Immunogenicity of purified polysaccharides could be enhanced by coupling (i.e. conjugating) them to a protein.

• 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

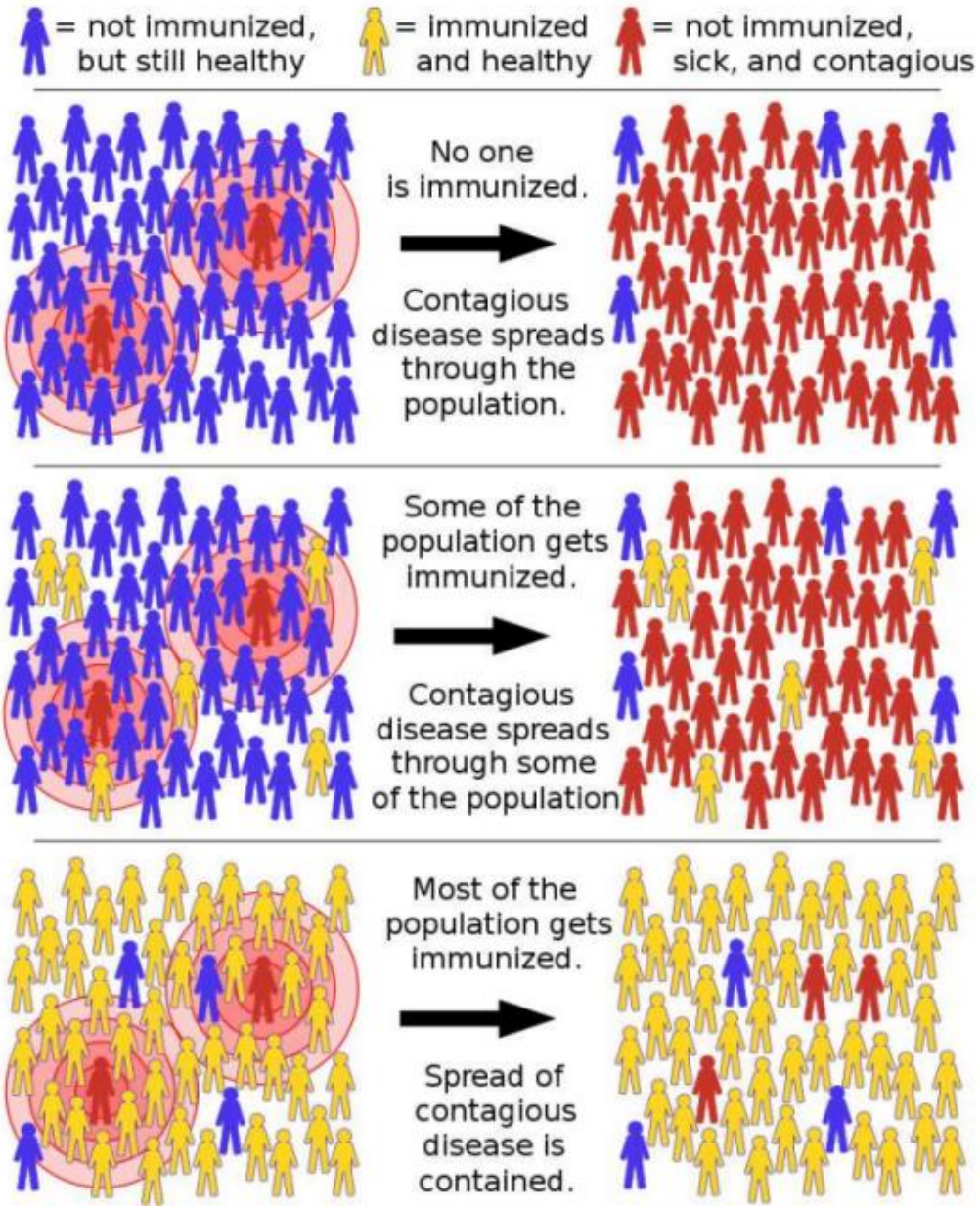


Vaccination also helps up to establish herd immunity.

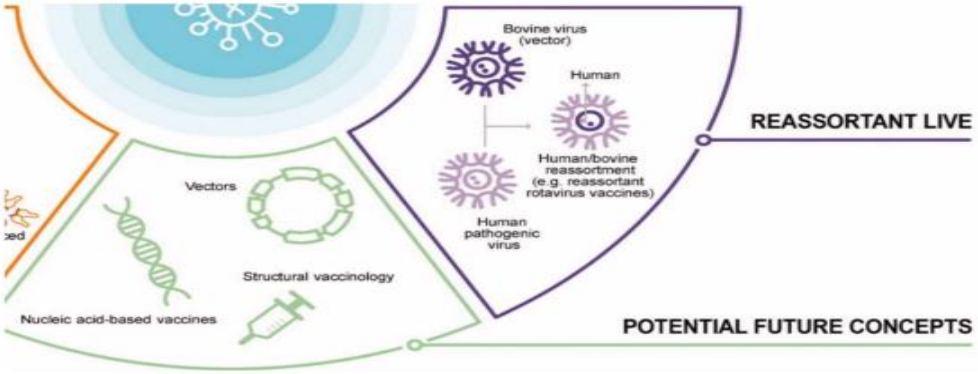
→Herd immunity:

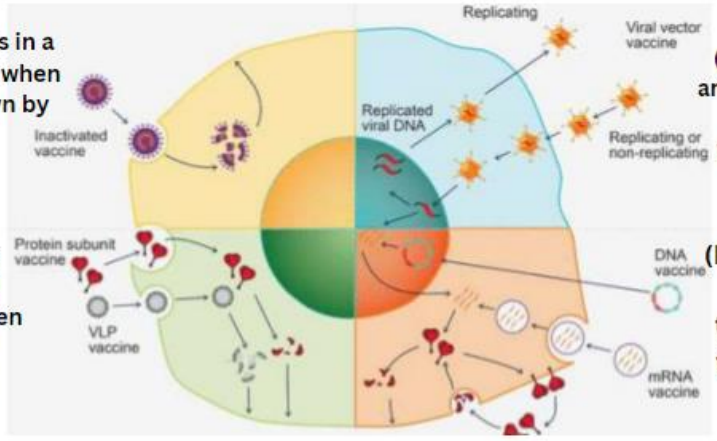
is a form of indirect protection from infectious disease that occurs when a large percentage of a population has become immune to an infection, thereby providing a measure of protection for individuals who are not immune.

• 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



what was a potential future concept , become our present due to COVID-19





(A) Inactivated vaccine results in a broader spectrum of antigens when it is taken up and broken down by cells.

(B) Protein-based vaccine produces a more focused response to a targeted antigen when it is taken up and processed into multiple epitopes by cells.

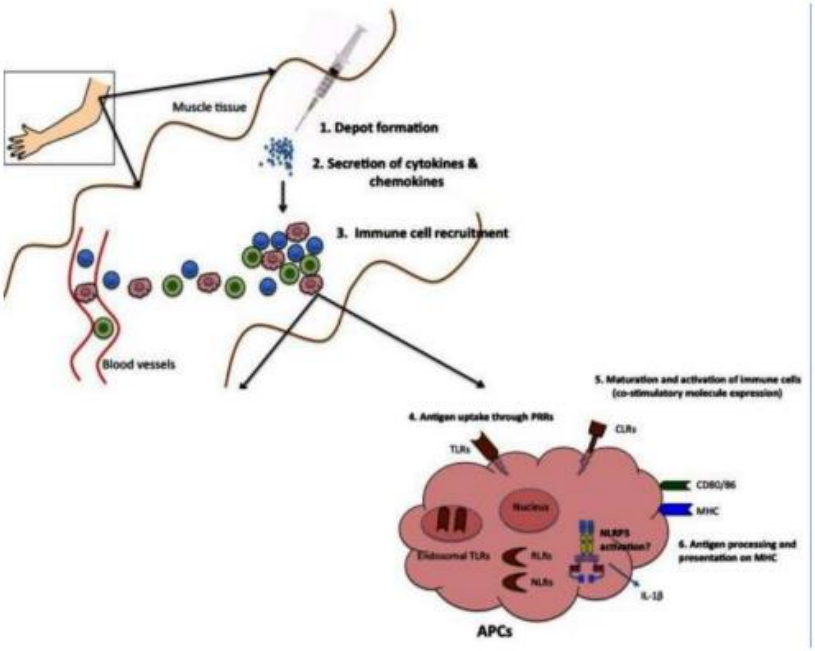
(C) Viral vector vaccine delivers antigen-encoding DNA to cells and enhances the inflammatory response and immunity

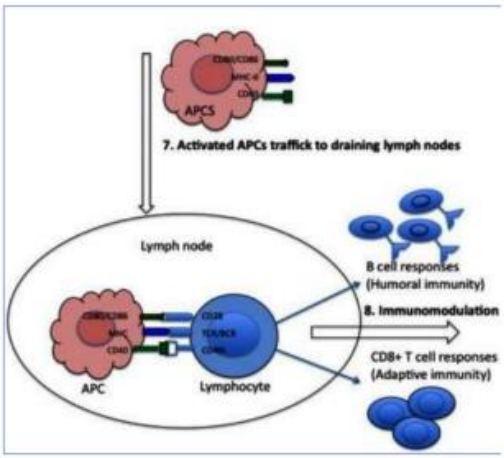
(D) Nucleic acid vaccine enters cells and serves as the transcriptional/translational template for protein antigen synthesis

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 (A) Inactivated vaccine results in a broader spectrum of antigens when it is taken up and broken down by cells. (B) Protein-based vaccine produces a more focused response to a targeted antigen when it is taken up and processed into multiple (C) Viral vector vaccine delivers antigen-encoding DNA to cells and enhances the inflammatory response and immunity (D) Nucleic acid vaccine enters cells and serves as the transcriptional/translational template for protein antigen synthesis 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.





Our improved understanding of the immune system and host-pathogen interactions has allowed transition from an empirical to a more rational vaccine design, but progress is still needed to address unmet needs and improve protection induced by current vaccines.

• Like all medicines, vaccines can have adverse events. However, because vaccines are given as preventive measures mostly to healthy individuals, especially infants and children, a highly positive benefit–risk profile is essential. Vaccine safety is evaluated in the preclinical and clinical phases of development but is also continuously monitored after licensure.

• New vaccine designs and concepts are needed to improve existing vaccines or address unmet needs notably for pathogens with multiple serotypes (e.g. dengue, S. pneumoniae), antigenic hypervariability (e.g. human immunodeficiency virus) or an intracellular phase that are predominantly controlled by T-cell responses (e.g. tuberculosis, malaria)

برنامج التطعيم للأطفال / الأردن

Motherhood & More

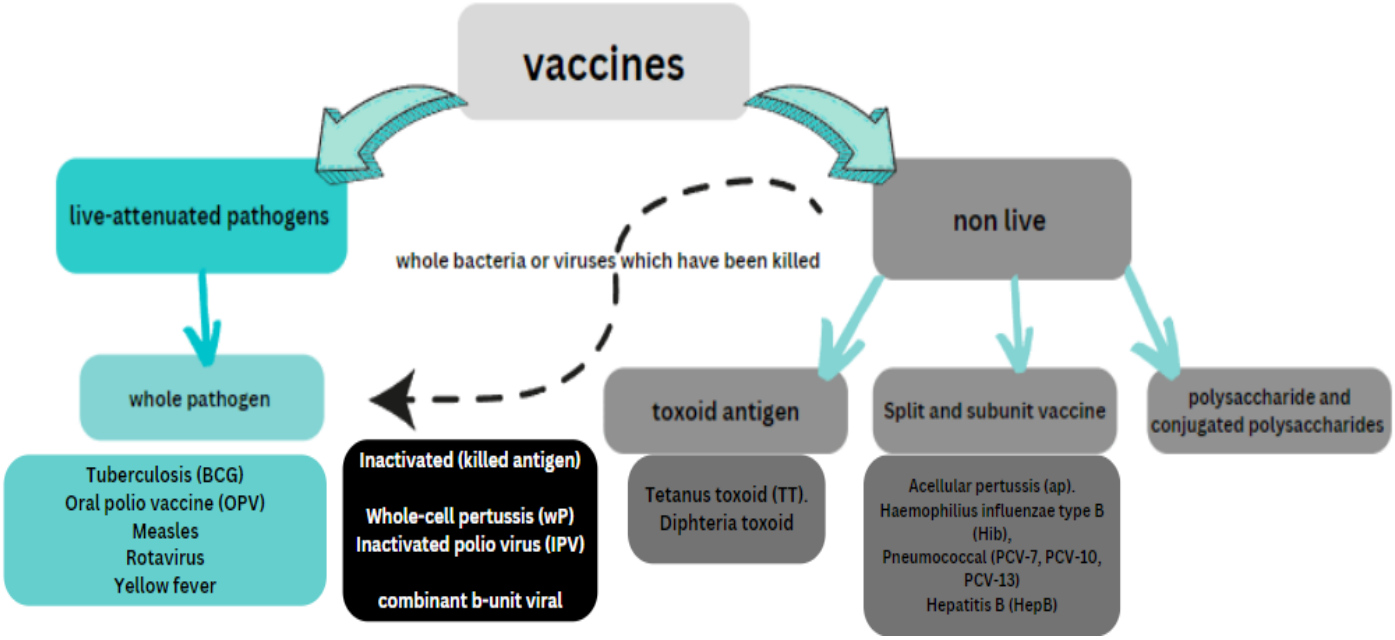
ألقرب وقت بعد الولادة: يُعطى مطعوم السل (BCG)	
على عمر شهرين (٦١ يوم) يُعطى الطفل الجرعة الأولى من مطعوم شلل الأطفال IPV والمطعوم الخماسي الذي يتكون من : المطعوم الثلاثي DPT (الدفتيريا والسعال الديكي والكزاز) +مطعوم المستديمة النزلية نوع (ب) + مطعوم التهاب الكبد نوع (ب)+ الجرعة الأولى من مطعوم الروتافيروس .	
على عمر ٣ اشهر (٩١ يوم) يُعطى الطفل الجرعة الثانية ـ مطعوم شلل الأطفال OPV+IPV +المطعوم الخماسي الذي يتكون من: المطعوم الثلاثي DPT (الدفتيريا والسعال الديكي والكزاز) +مطعوم المستديمة النزلية نوع (ب) + مطعوم التهاب الكبد نوع (ب) + الجرعة الثانية من مطعوم الروتافيروس .	
على عمر ٤ شهور (١٢١ يوم) يُعطى الطفل مطعوم شلل الاطفال الفموي OPV + المطعوم الثلاثي DPT (الدفتيريا والسعال الديكي والكزاز)+مطعوم المستديمة النزلية نوع (ب)+ مطعوم التهاب الكبد نوع (ب)على شكل رباعي أو خماسي + الجرعة الثالثة من مطعوم الروتافيروس .	
على عمر ٩ شهور (بداية الشهر العاشر) يُعطى الطفل مطعوم الحصبة Measles + مطعوم شلل الأطفال الفموي OPV + فيتامين أ (١٠٠ الف وحدة دولية).	
عند بلوغ الطفل عامه الأول يُعطى الطفل الجرعة الأولى من المطعوم الثلاثي الفيروسي MMR (الحصبة والحصبة الألمانية والنكاف)	
على عمر ١٨ شهر يُعطى الطفل الجرعة المدعمة من مطعوم شلل الأطفال الفموي OPV والمطعوم الثلاثي البكتيري DPT + الجرعة الثانية من مطعوم الثلاثي الفيروسي MMR + فيتامين أ (٢٠٠ الف وحدة دولية).	

Motherhood & More

Vaccination Schedule جدول المطاعيم

اسم المطعوم	تاريخ أخذ الجرعات: الجرعة الأولى I	الجرعة الثانية II	الجرعة الثالثة III	الجرعة الرابعة IV	الجرعة المدعمة	ملاحظات
الفدرن BCG	٢٠١٨/٦/٢٨					
شلل الأطفال المقتول IPV						
شلل الأطفال الفموي OPV		٢٠١٨/٨/٦	٢٠١٨/١٠/٨	٢٠١٩/١/١٠	٢٠١٩/٧/٩	
الثلاثي البكتيري DPT						
الخماسي المحسن DPT IPV +HiB	٢٠١٨/٩/٥	٢٠١٩/١/٦	٢٠١٩/٣/١٠			
الخماسي العادي DPT-IPV -HiB						
التهاب الكبد الوبائي HBV	٢٠١٨/٩/٥	٢٠١٨/٩/٦	٢٠١٨/١١/٨			
المستديمة النزلية HiB						
الحصبة Measles	٢٠١٩/٣/١١					
الثلاثي الفيروسي MMR	٢٠١٩/٦/٥	٢٠١٩/٩/١٧				
مطعوم الروتافيروس *						
أخـــــرى Others						
هل تم أخذ عينة المسح الحلبي للتحري عن الأمراض الوراثية	نعم ☐ لا ☐					

* ملاحظة: عند الجرعات يعتمد على الشركة الصانعة للمطعوم



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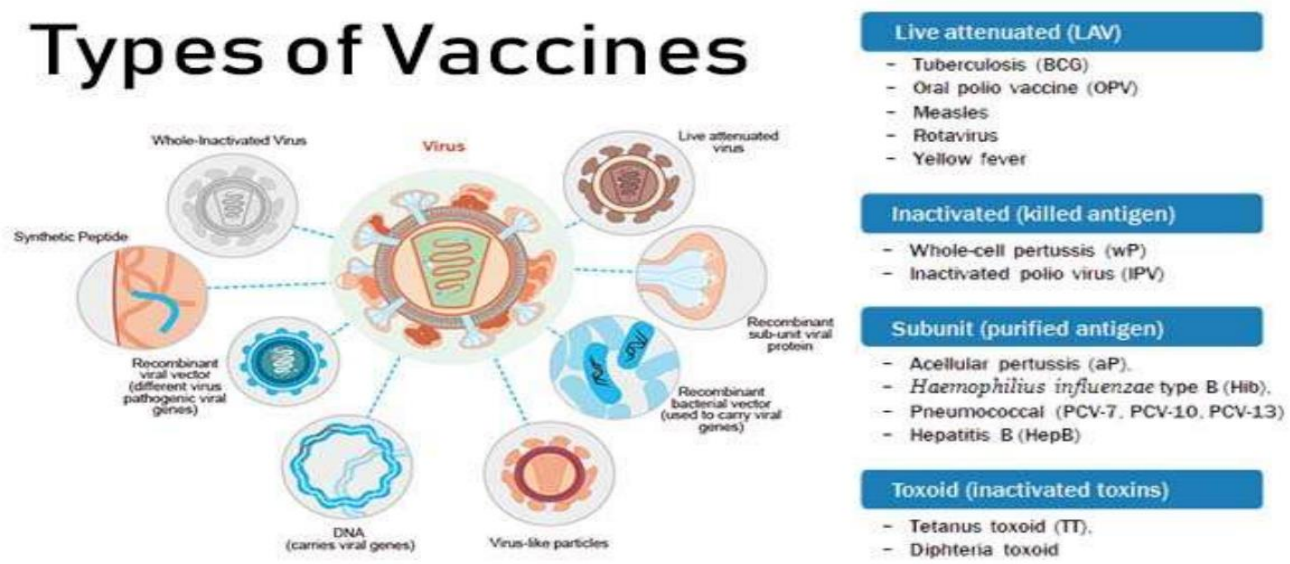

(Live/Inactivated) _____ vaccines have the advantage of inducing both humoral and cell-mediated immunity.

Inactivated vaccines are (more/less) _____ effective at inducing cell-mediated immunity because they do not replicate in the host.

The substances that are added to vaccines to enhance the response are referred to as _____.

Inactivated vaccines elicit a (weaker/stronger) _____ immune response than live attenuated vaccines.

Source: osmosis === ANS : live – less - Adjuvants - weaker