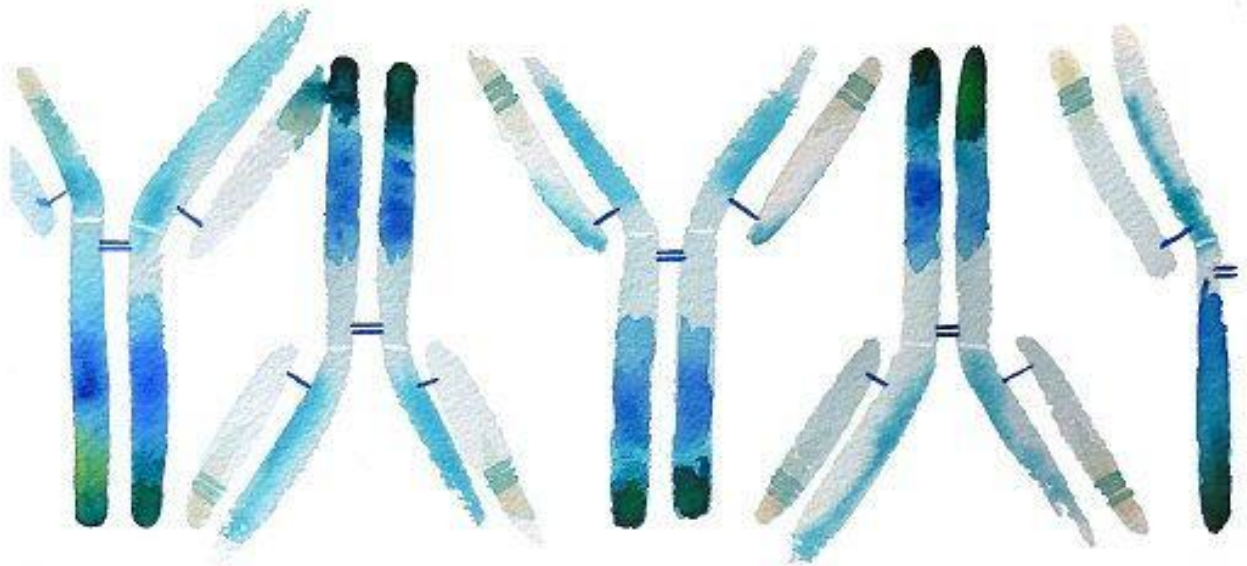
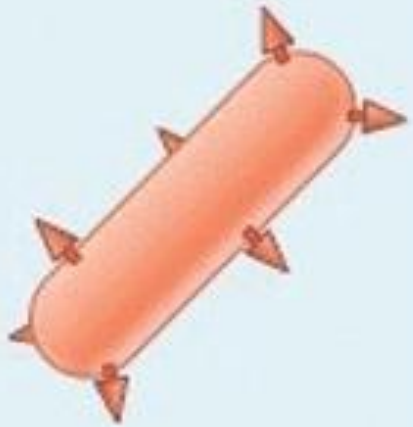
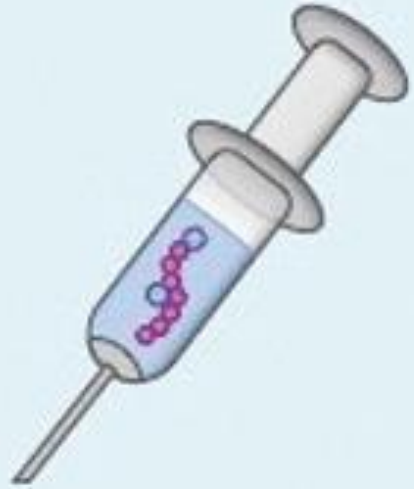
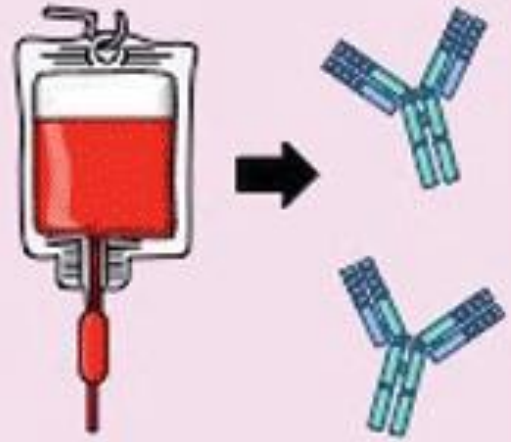
Medical Immunology



Anas Abu-Humaidan
M.D. Ph.D.

Lecture 15

Active Immunity VS Passive Immunity

Natural	Artificial	Natural	Artificial
			
Infection	Vaccination	Maternal antibodies	Monoclonal antibodies

Passive vs. active immunity

Acquired immunity is attained through either **passive** or **active** immunization.

- **Passive immunization** refers to the transfer of **"ready-made" antibodies**, from one individual to another. It can occur:

1) **naturally** by **transplacental transfer** of **maternal** antibodies to the **developing fetus**, or through **colostrum** and **breast milk** rich in IgA.
2) it can be induced **artificially** by **injecting** a recipient with **exogenous antibodies** targeted to a specific pathogen or toxin.

- Examples:

Natural: Maternal 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 prophylactically in the case of **immunodeficiency diseases**, or specific antibodies used in the treatment of several types of acute infections such as **rabies**.

Passive vs. active immunity

Acquired immunity is attained through either **passive** or **active** immunization.

- **Active immunity** refers to the process of exposing the body to an antigen to **generate an adaptive immune response**: the response takes days/weeks to develop but may be long lasting—even lifelong (**unlike passive immunity**). It can occur:

1) Naturally through infection with a certain pathogen.
2) Artificially through administration of vaccines containing weekend or inactive pathogen.

Examples:
Natural: Wild infection 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.

If you went 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. **How would you describe to Jenner the immunology of vaccines**? Starting from the injury to the epithelial barrier and **activation of innate immunity** to the **formation of protective antibodies.**

Vaccination/ overview

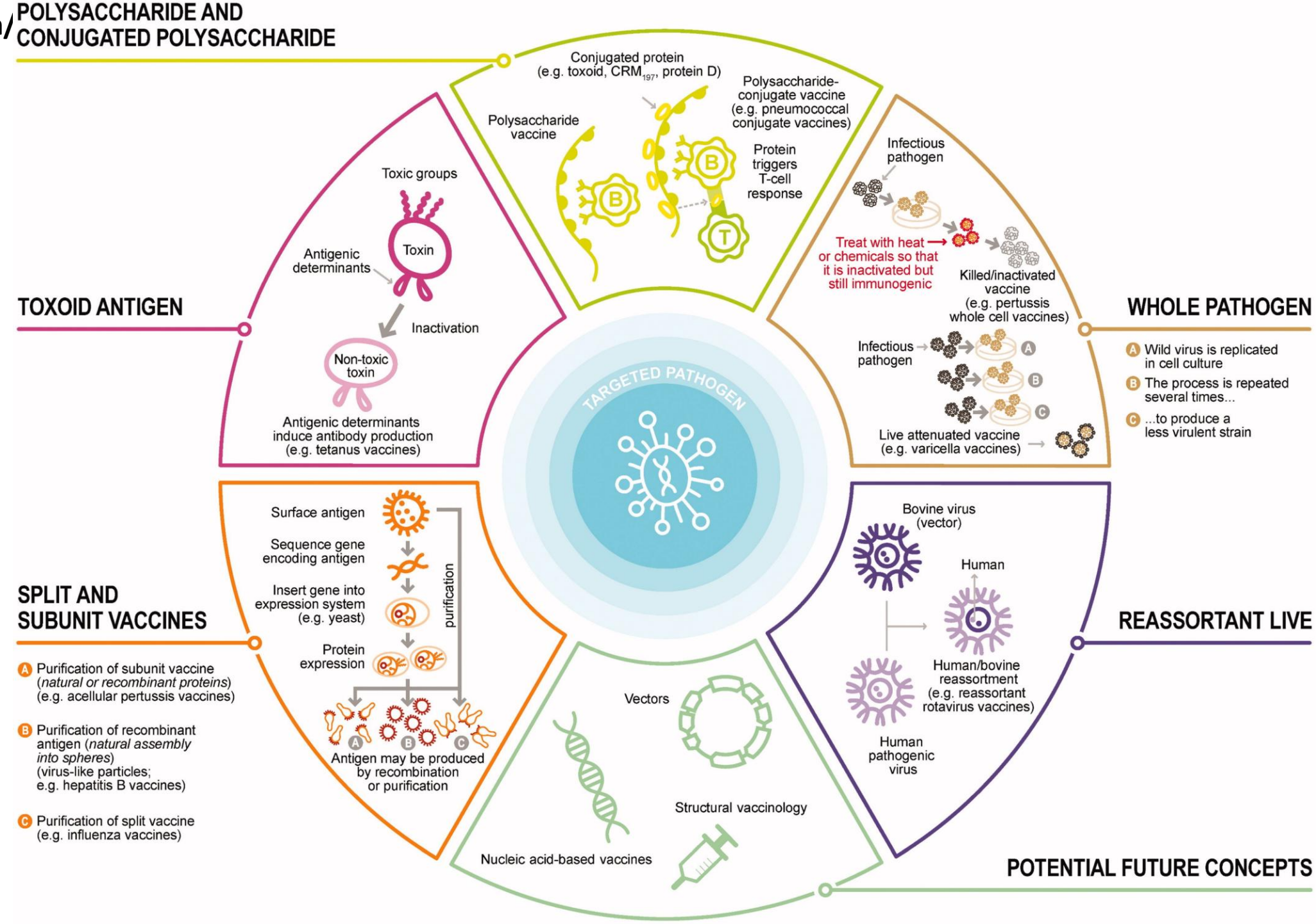
- The aim of vaccination is to **induce a protective immune response** to the targeted pathogen **without the risk** of acquiring the disease and its potential complications.

- Each pathogen (or vaccine) expresses (or contains) antigens that induce **cell-mediated immunity** by activating highly specific subsets of **T lymphocytes** and humoral immunity by stimulating **B lymphocytes** to produce specific antibodies.

- After elimination of the pathogen, the adaptive immune system generally establishes immunological memory.

- Vaccines may contain **live-attenuated pathogens**, **inactivated pathogens**, or only **parts of pathogens** and may also contain **adjuvants** to stimulate the immune responses.

Vaccination/



Vaccination/ Live attenuated vaccines

- **Live attenuated vaccines** 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 long-term 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

Vaccination/ Live attenuated vaccines

- 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

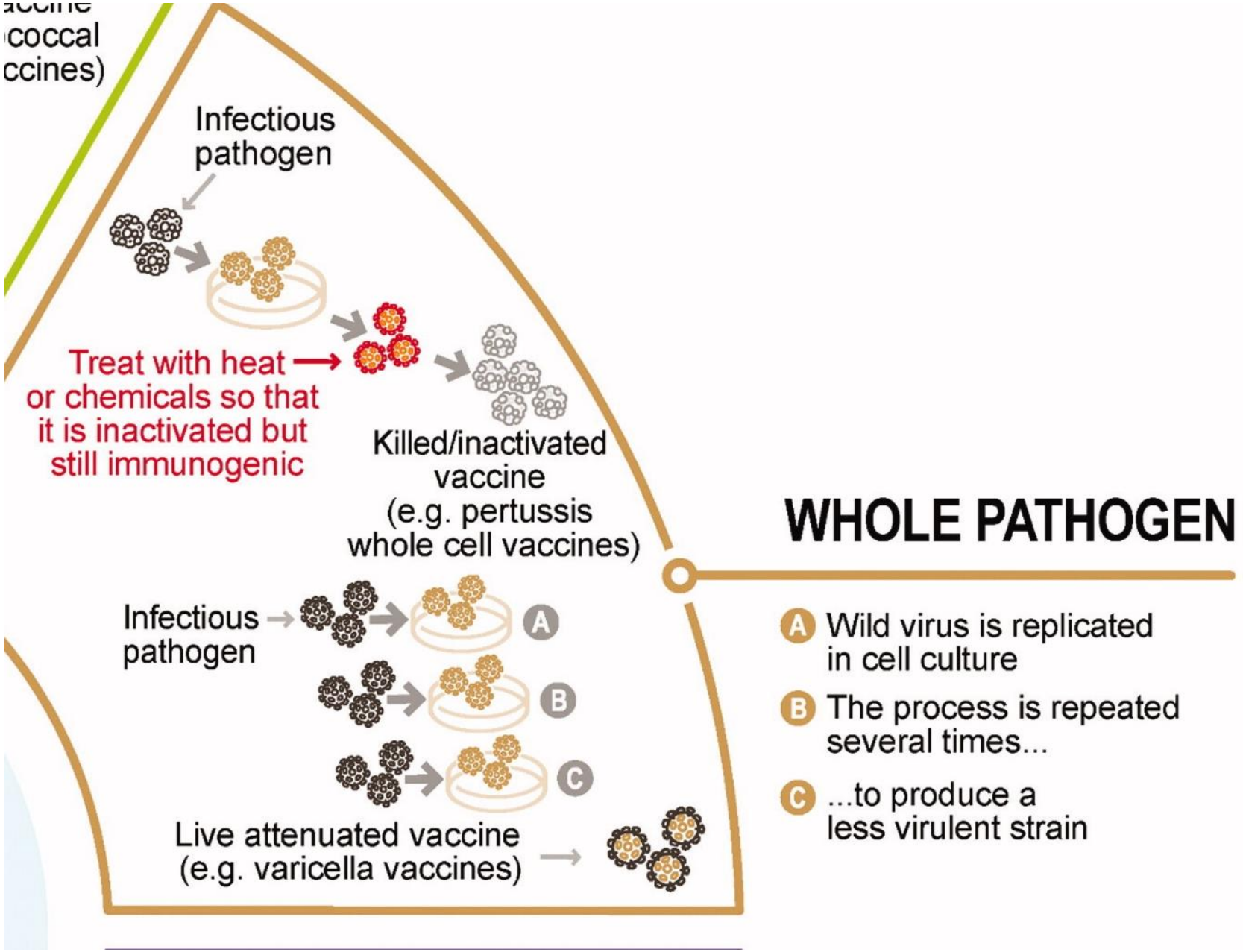
- The **only live attenuated bacterial** vaccine currently in use is the bacillus Calmette-Guérin **(BCG) vaccine**, which was developed almost a century ago

- **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.

Vaccination/ overview



Vaccination/ Non-live vaccines

- **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.

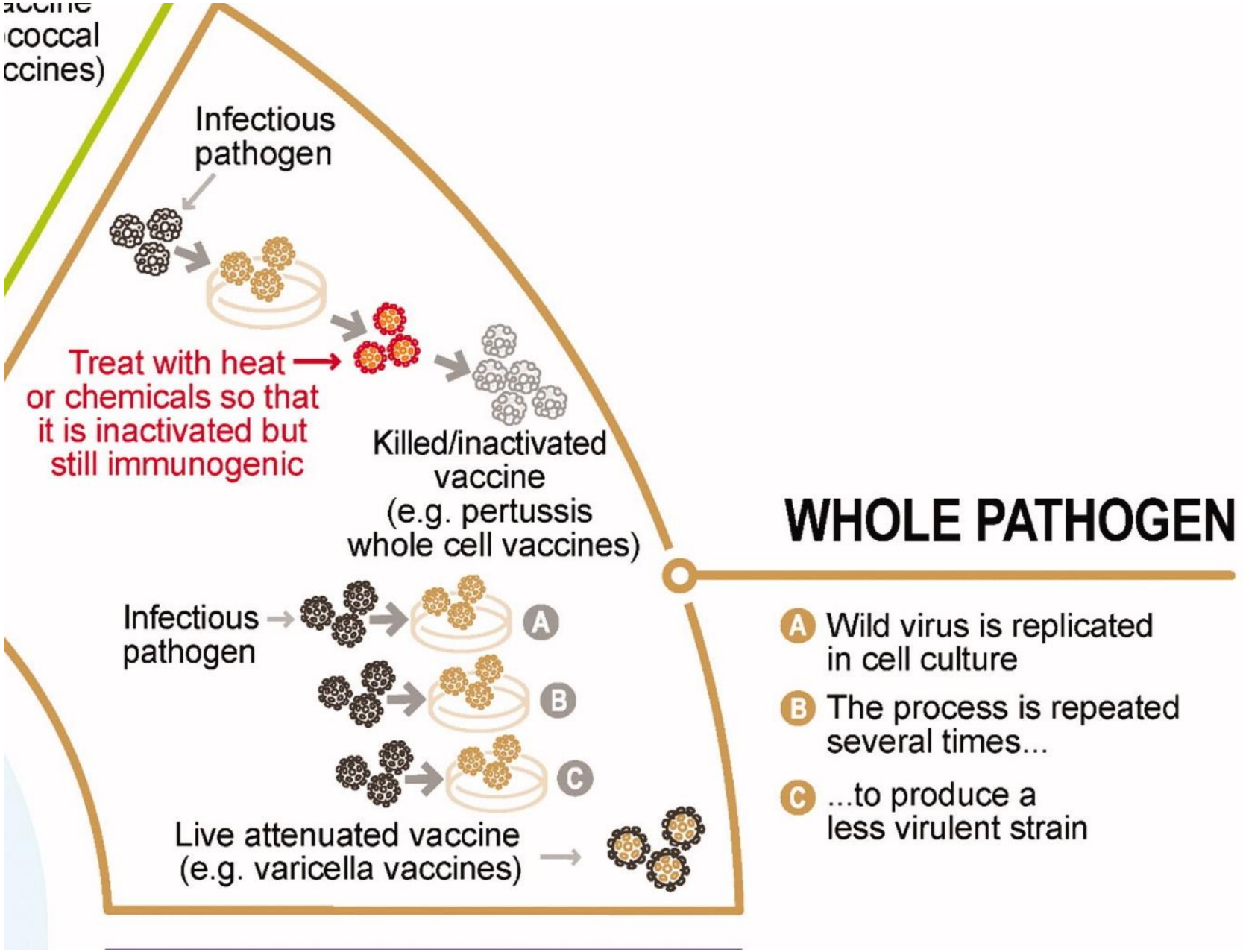
- Non-live vaccines can contain inactivated **whole pathogens** or **only parts of them** such as **proteins** or **polysaccharides** (**subunit vaccines**).

Vaccination/ Non-live vaccines / 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.**

Vaccination/ overview



Vaccination/ Non-live vaccines/ Subunit vaccines

- 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**.

Vaccination/ Non-live vaccines/ Subunit vaccines

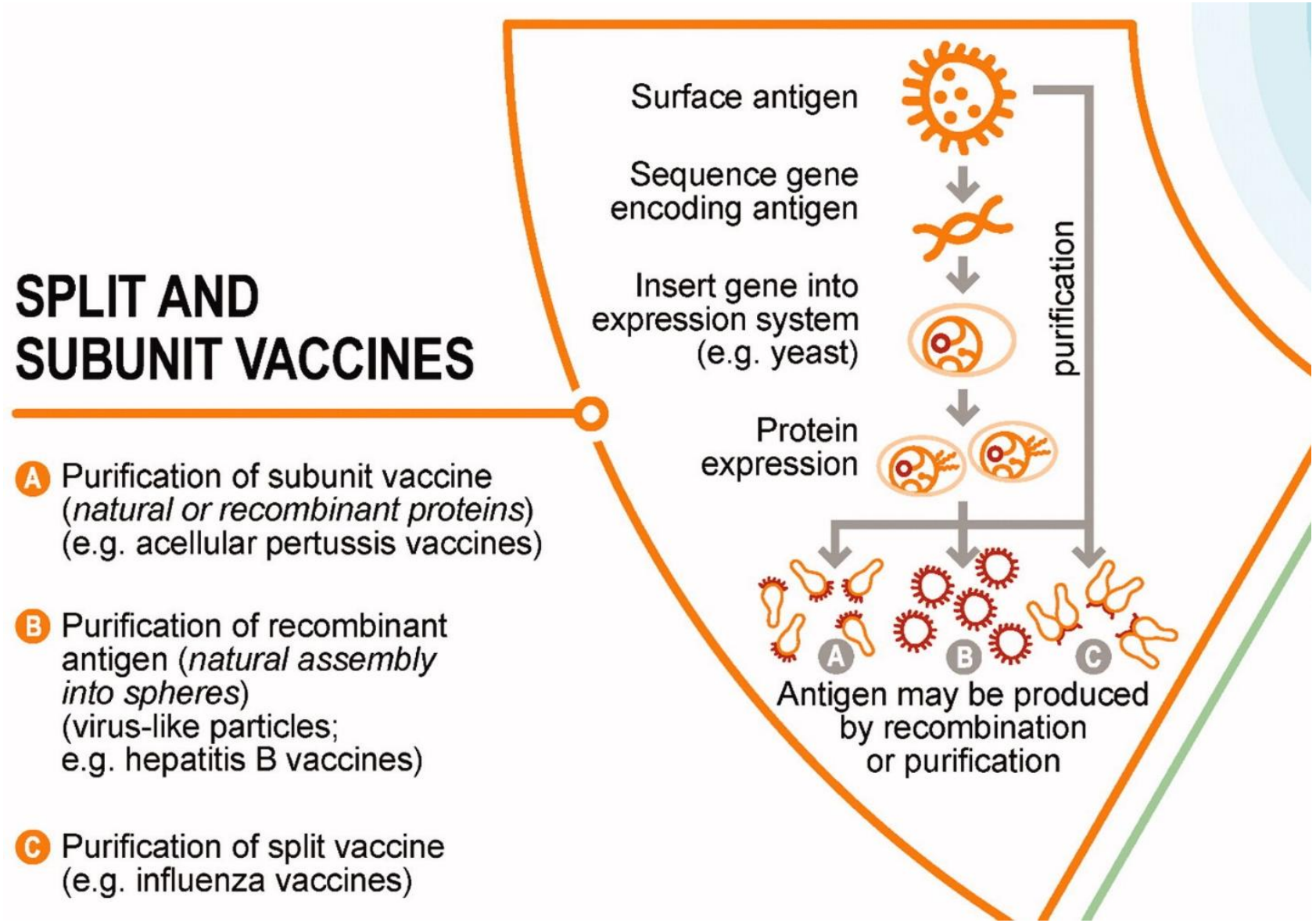
- Antigenic proteins can be **purified** from preparations of the whole pathogen, as for the acellular pertussis vaccines, or can be **produced by recombinant genetic engineering**.

- **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.

Vaccination/ Non-live vaccines/ Subunit vaccines



Vaccination/ Non-live vaccines/ Toxoid vaccines

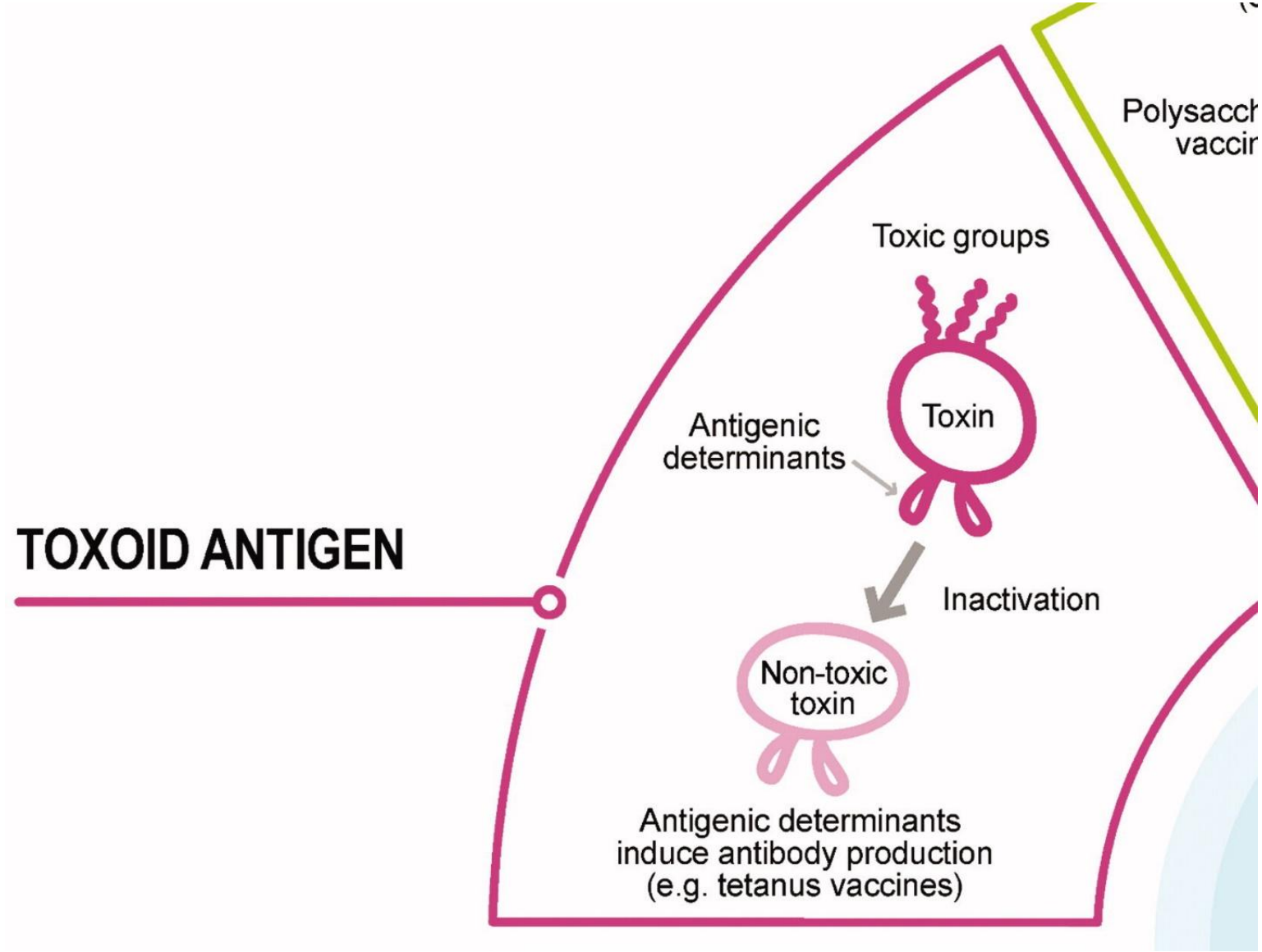
- Some bacteria such as **Clostridium tetani**, Clostridium difficile or **Corynebacterium diphtheriae** cause disease by releasing **pathogenic toxins**. Vaccines against these diseases are produced by **detoxifying the toxin** using heat, chemicals (e.g. formaldehyde) or both.

- 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.

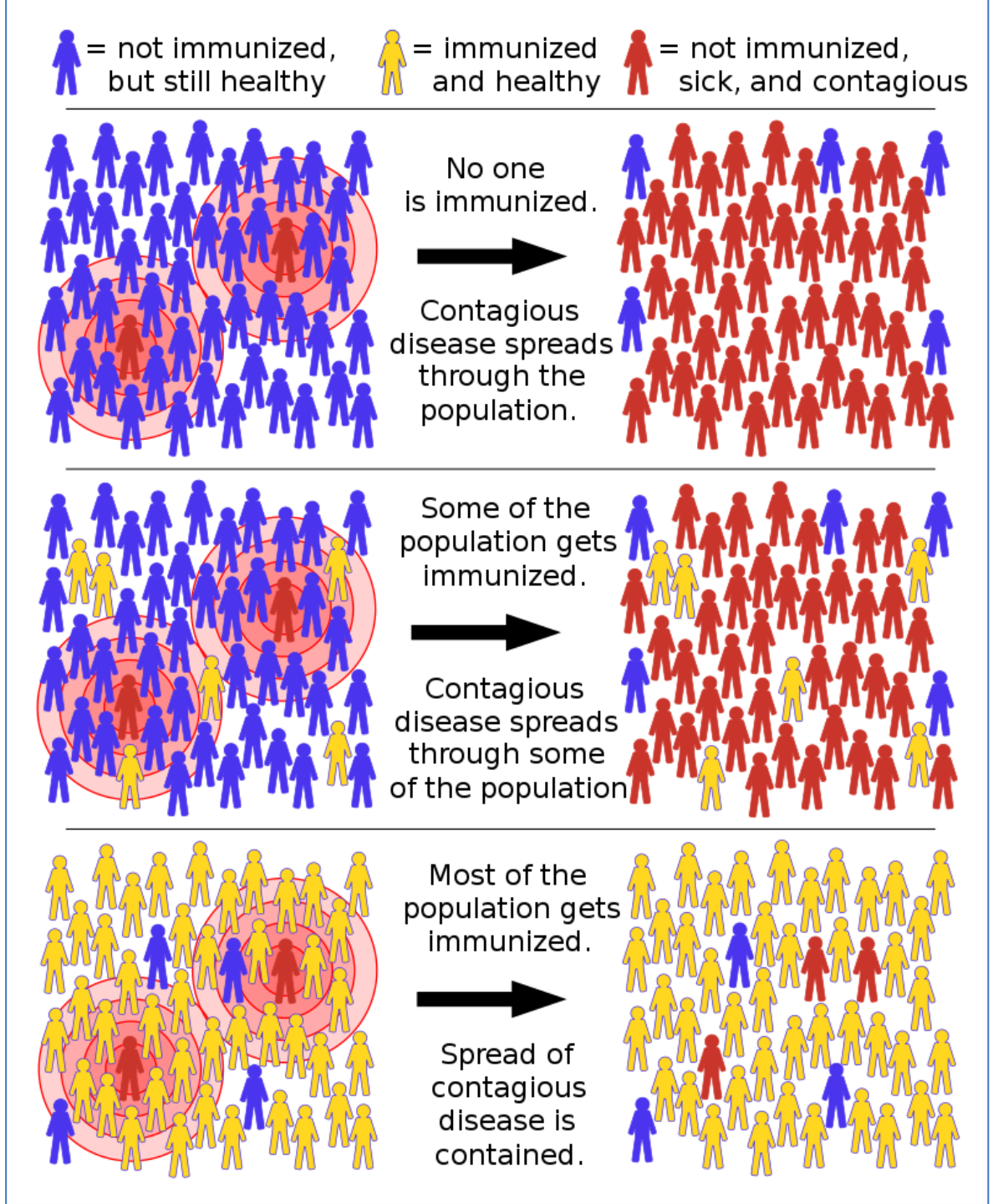
Vaccination/ Non-live vaccines/ Toxoid vaccines



Vaccination/ 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.



Vaccination/ Non-live vaccines/ Polysaccharide and conjugate vaccines

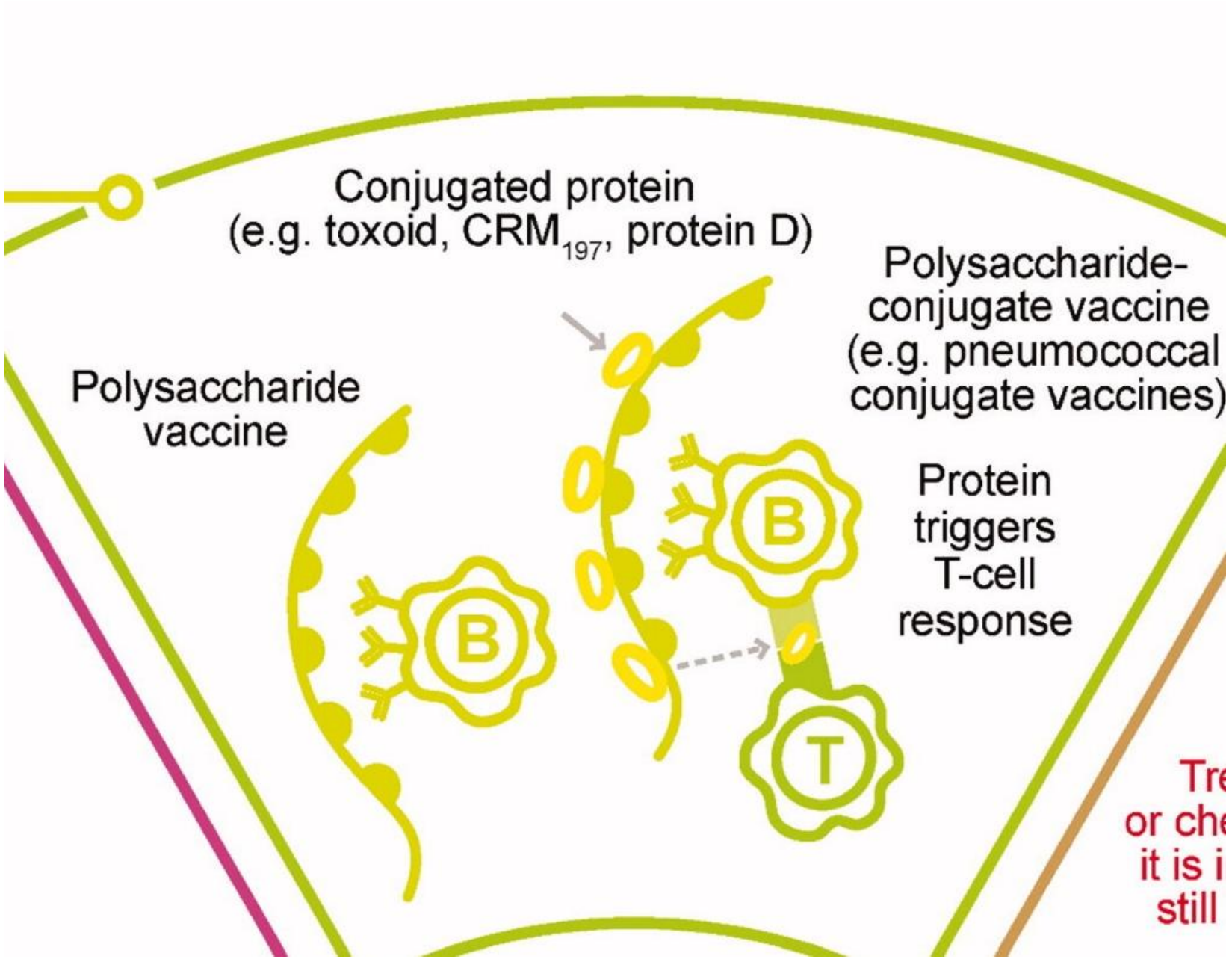
- **Streptococcus pneumoniae**, **Haemophilus influenzae type b** and **N. meningitidis** are three **encapsulated bacteria** that cause severe invasive disease. They possess **polysaccharide capsules** that **facilitate bacteria's survival** when carried in the **nasopharynx** and in the **blood** during 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

Vaccination/ Non-live vaccines/ Polysaccharide and conjugate vaccines



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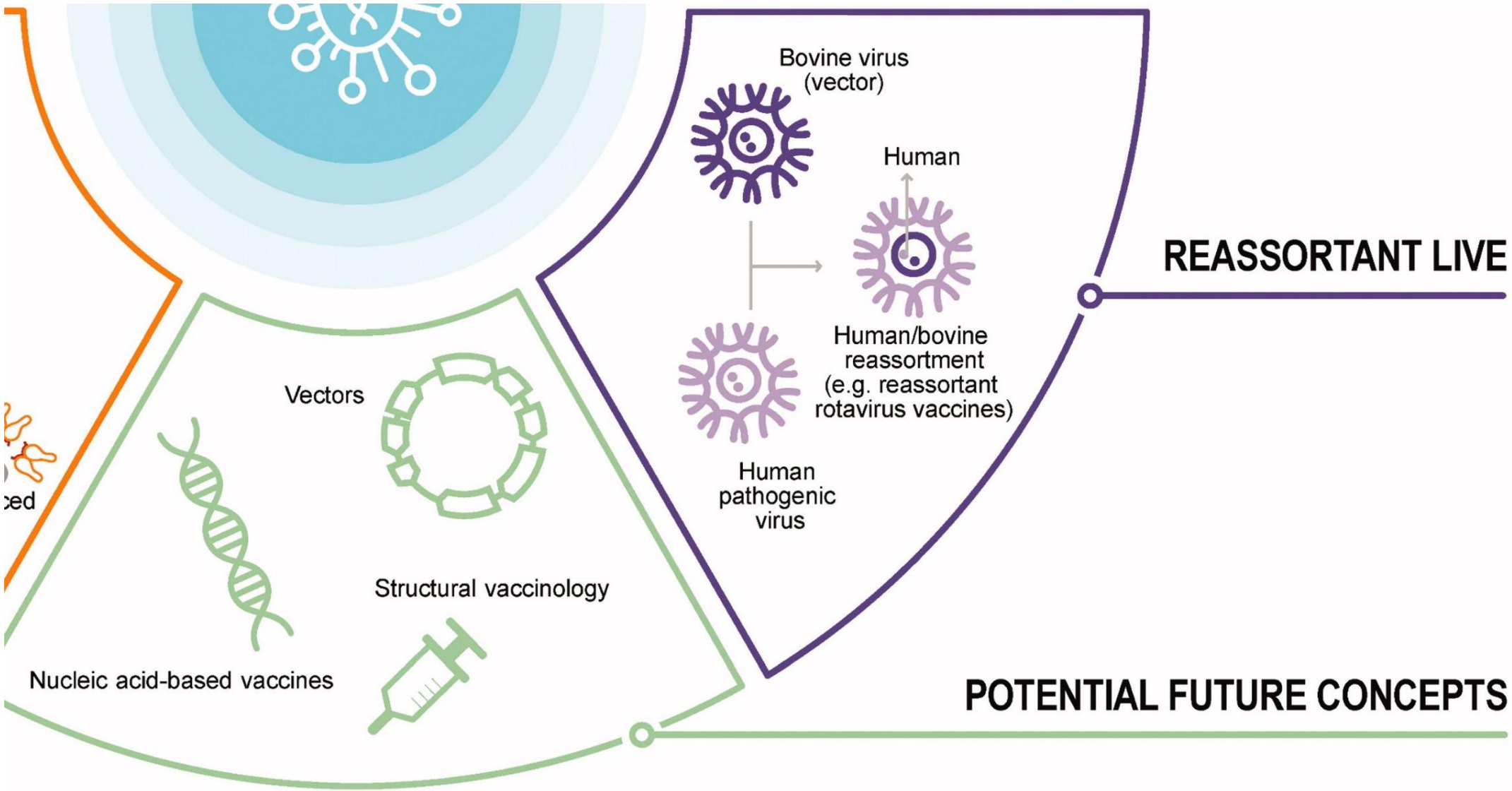
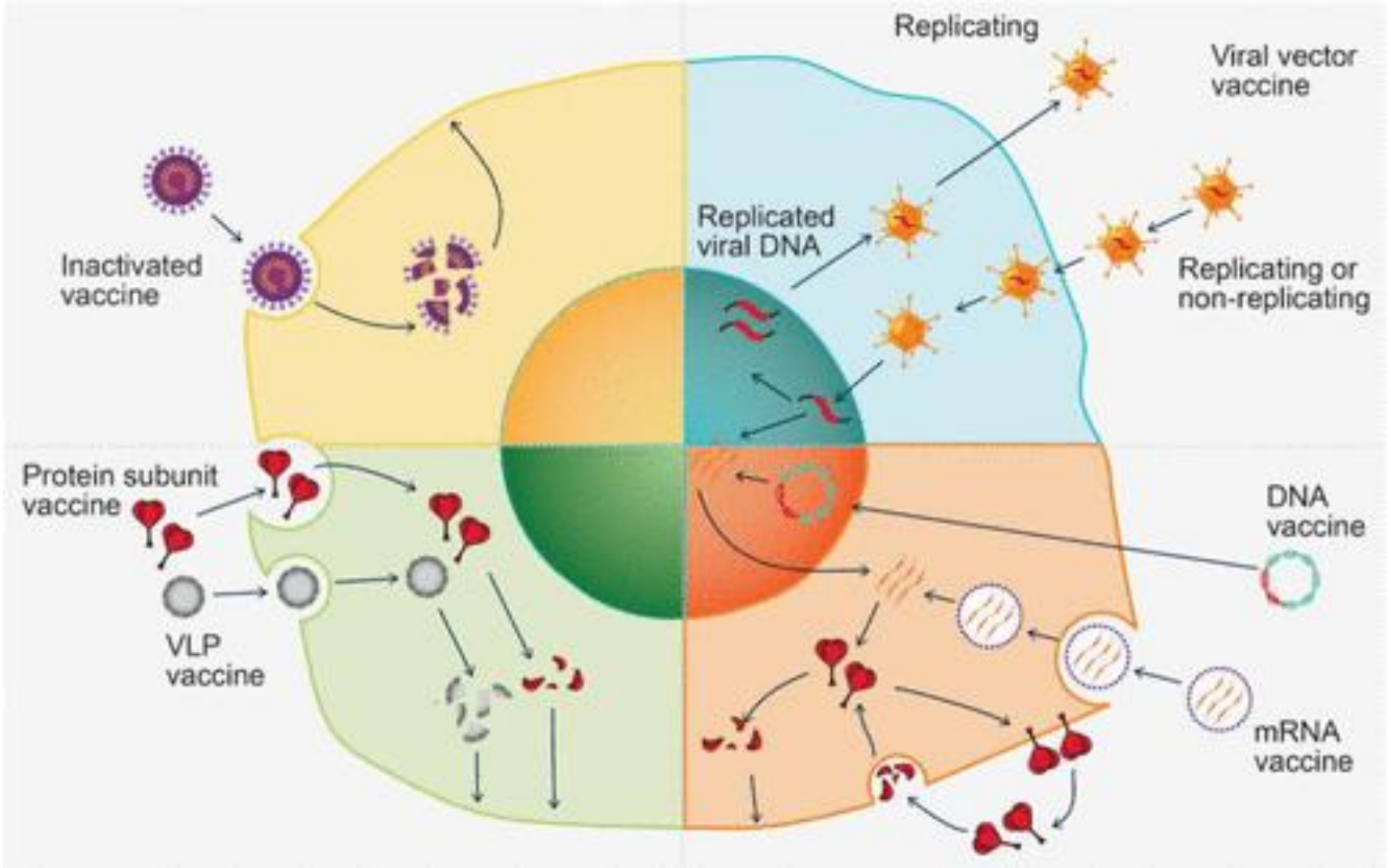
Vaccination/ overview



Vaccination/ COVID-19 vaccines



(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.**

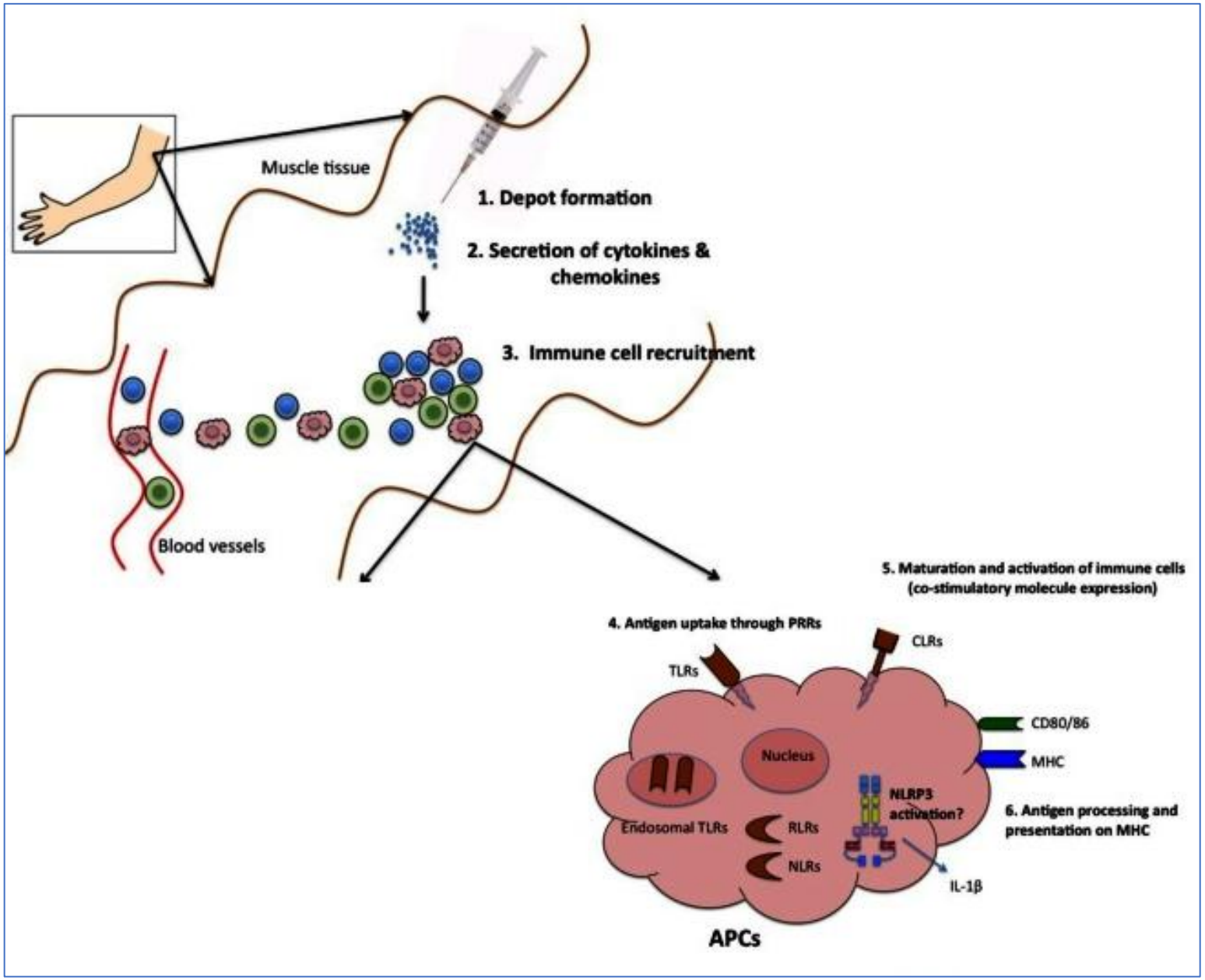
Vaccination/ adjuvants

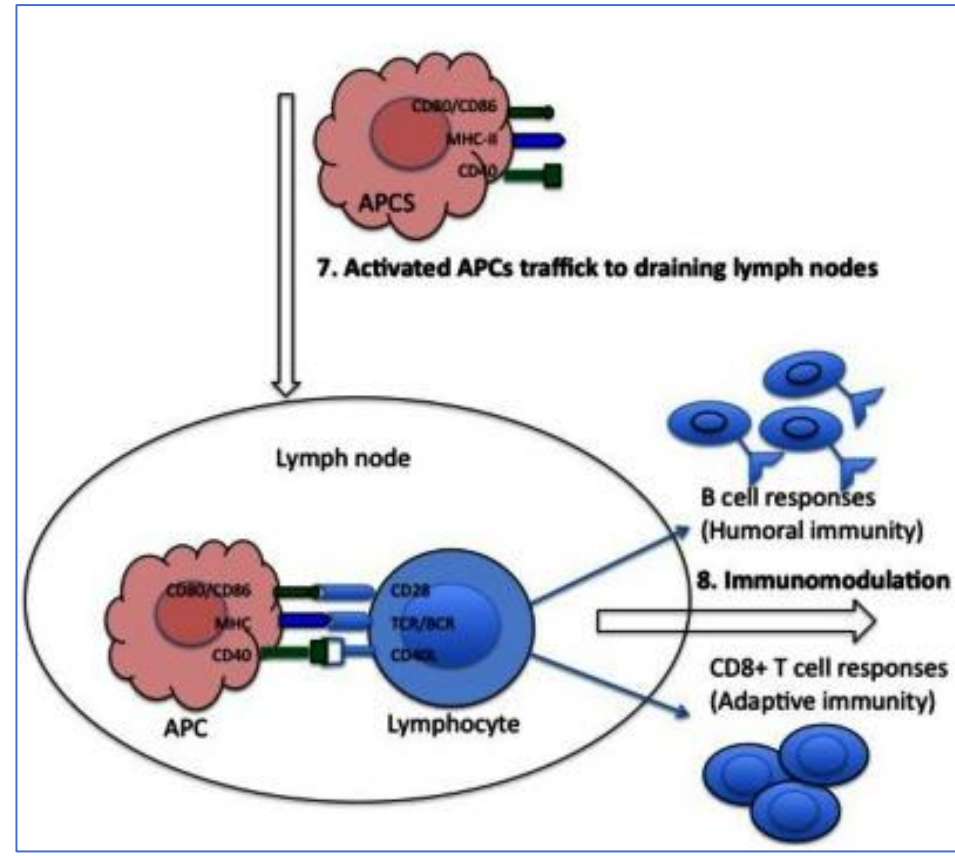
- **Adjuvants** are substances that can **enhance and modulate the immunogenicity of the antigen**. Adjuvants are usually not needed for live attenuated vaccines because these vaccines actively replicate and self-enhance the immune response.

- 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.

Vaccination/ adjuvants





Vaccination/ conclusion

- 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)

Vaccination/ Vaccine program in Jordan

Motherhood & More

برنامج التطعيم للأطفال / الأردن

أقرب 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 المستدمية 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 IPV+OPV +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 ـ 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).

Vaccination/ Vaccine program in Jordan

Motherhood & More

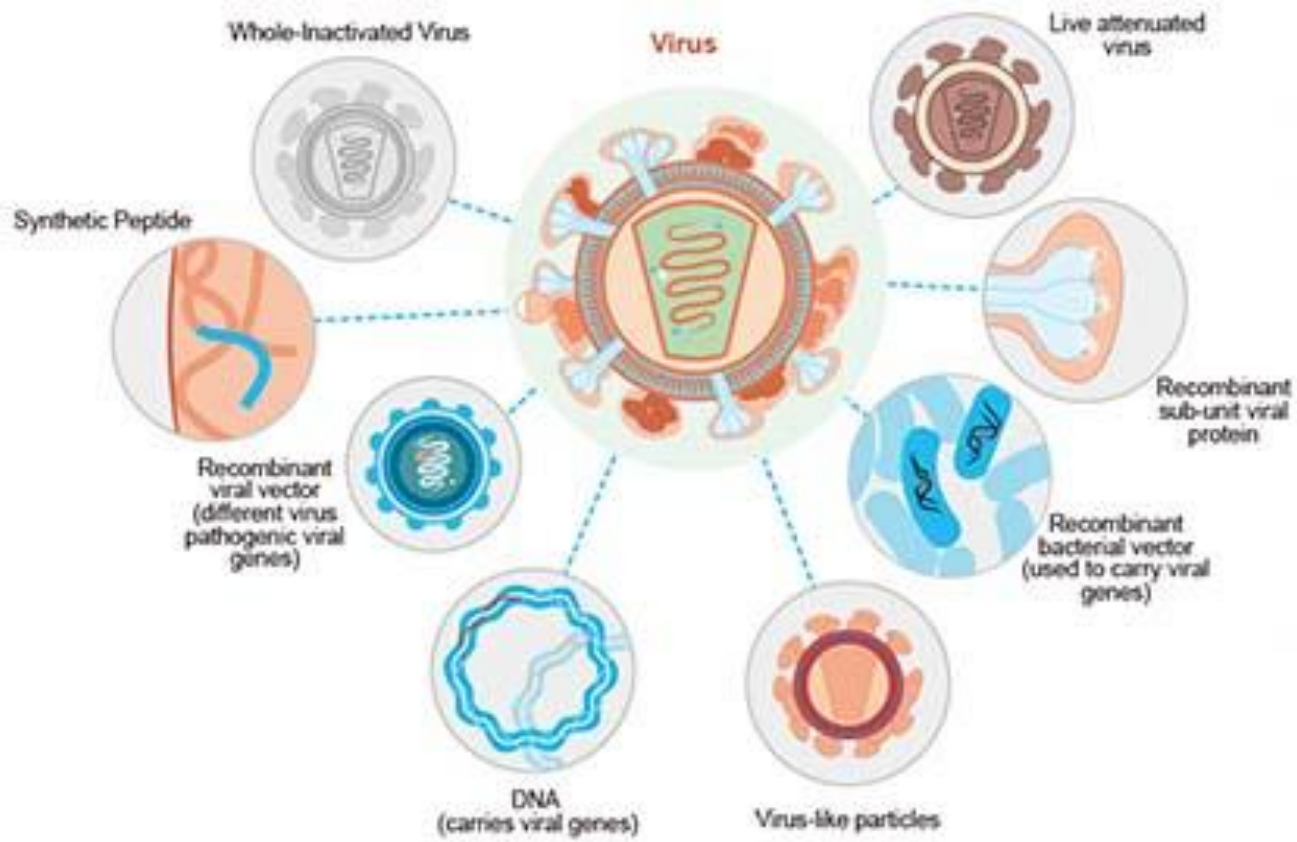
Vaccination Schedule جدول المطاعيم

اسم المطعوم	تاريخ أخذ الجرعات					ملاحظات
	الجرعة الأولى I	الجرعة الثانية II	الجرعة الثالثة III	الجرعة الرابعة IV	الجرعة المدعمة	
التدرن BCG	٨/٧/٢٠١٧					
شلل الأطفال المقتول IPV						
شلل الأطفال الفموي OPV		٦/٩/٢٠١٧	١٨/١٠/٢٠١٧	١١/٩/٢٠١٧	٢٠١٧/١٢/٩	
الثلاثي البكتيري DPT					٢٠١٧/١٢/٩	
الخماسي المحسن DPT IPV +Hib	٥/٨/٢٠١٧	٦/٩/٢٠١٧	١٨/١٠/٢٠١٧			
الخماسي العادي DPT+BV +Hib						
التهاب الكبد الوبائي HBV	٥/٨/٢٠١٧	٦/٩/٢٠١٧	١٨/١٠/٢٠١٧			
المستدمية النزلية Hib						
الحصبة Measles فيتامين أ(١٠٠الف وحدة دولية)	١١/٣/٢٠١٨					
الثلاثي الفيروسي MMR فيتامين أ(٢٠٠الف وحدة دولية)	٥/٦/٢٠١٨	٧/٩/٢٠١٧				
مطعوم الروتافيروس *						
أخرى Others						
هل تم أخذ عينة المسح الطبي للتحري عن الأمراض الوراثية	نعم ☐ لا ☐					

* ملاحظة: عدد الجرعات يعتمد على الشركة المصنعة للمطعوم

Vaccination

Types of Vaccines



Live attenuated (LAV)

- Tuberculosis (BCG)
- Oral polio vaccine (OPV)
- Measles
- Rotavirus
- Yellow fever

Inactivated (killed antigen)

- Whole-cell pertussis (wP)
- Inactivated polio virus (IPV)

Subunit (purified antigen)

- Acellular pertussis (aP).
- *Haemophilius influenzae* type B (Hib).
- Pneumococcal (PCV-7, PCV-10, PCV-13)
- Hepatitis B (HepB)

Toxoid (inactivated toxins)

- Tetanus toxoid (TT).
- Diphteria toxoid

Further reading:

- Cellular and Molecular Immunology. 7th Edition..

Chapter 11. B Cell Activation and Antibody Production

- Review Article

Understanding modern-day vaccines: what you need to know