BHARATHIDASAN UNIVERSITY

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Programme: M.Sc., Biomedical Science

Course Title : Medical Virology

Course Code : BM59C19MV

Unit-V

Vaccines and Antiviral Chemotherapy

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VACCINES
AND
ANTIVIRAL CHEMOTHERAPY

Key co-relation between vaccines and antiviral chemotherapy

VACCINES

- Stimulates the immune system
- Disease prevention
- Long term immunity
- Control and eradicate many diseases

ANTIVIRAL CHEMOTHERAPY

- Drugs to treat viral infection
- After exposure
- Combat active infections
- Reduce the severity of an illness

VACCINES

Vaccines train your immune system to create antibodies, just as it does when it’s exposed to a disease. However, because vaccines contain only killed or weakened forms of germs like viruses or bacteria, they do not cause the disease or put you at risk of its complications.

How does vaccine work?

1. Vaccines reduce risks of getting a disease by working with your body's natural defenses to build protection. It;

- Recognizes the invading germ, such as the virus or bacteria.
- Produces antibodies. Antibodies are proteins produced naturally by the immune system to fight disease.
- Remembers the disease and how to fight it. If you are then exposed to the germ in the future, your immune system can quickly destroy it before you become unwell.

2. Our immune systems are designed to remember. Once exposed to one or more doses of a vaccine, we typically remain protected against a disease for years, decades or even a lifetime. This is what makes vaccines so effective. Rather than treating a disease after it occurs, vaccines prevent us in the first instance from getting sick.

Ingredients found in some vaccines

STABILIZERS:

To keep the vaccine effective after manufacturing.

Eg:Sugars, gelatin

ADJUVANTS:

To help boost the body's response to the vaccine.

Eg:Aluminum salts

RESUDUAL INACTIVATING INGREDIENTS:

To kill viruses or inactivate toxins during the manufacturing process.

Eg:Formaldehyde

RESIUDUAL ANTIBIOTICS:

To prevent contamination by bacteria during the vaccine manufacturing process.

Eg:Neomycin, Kanamycin, Streptomycin

PRESERVATIVES:

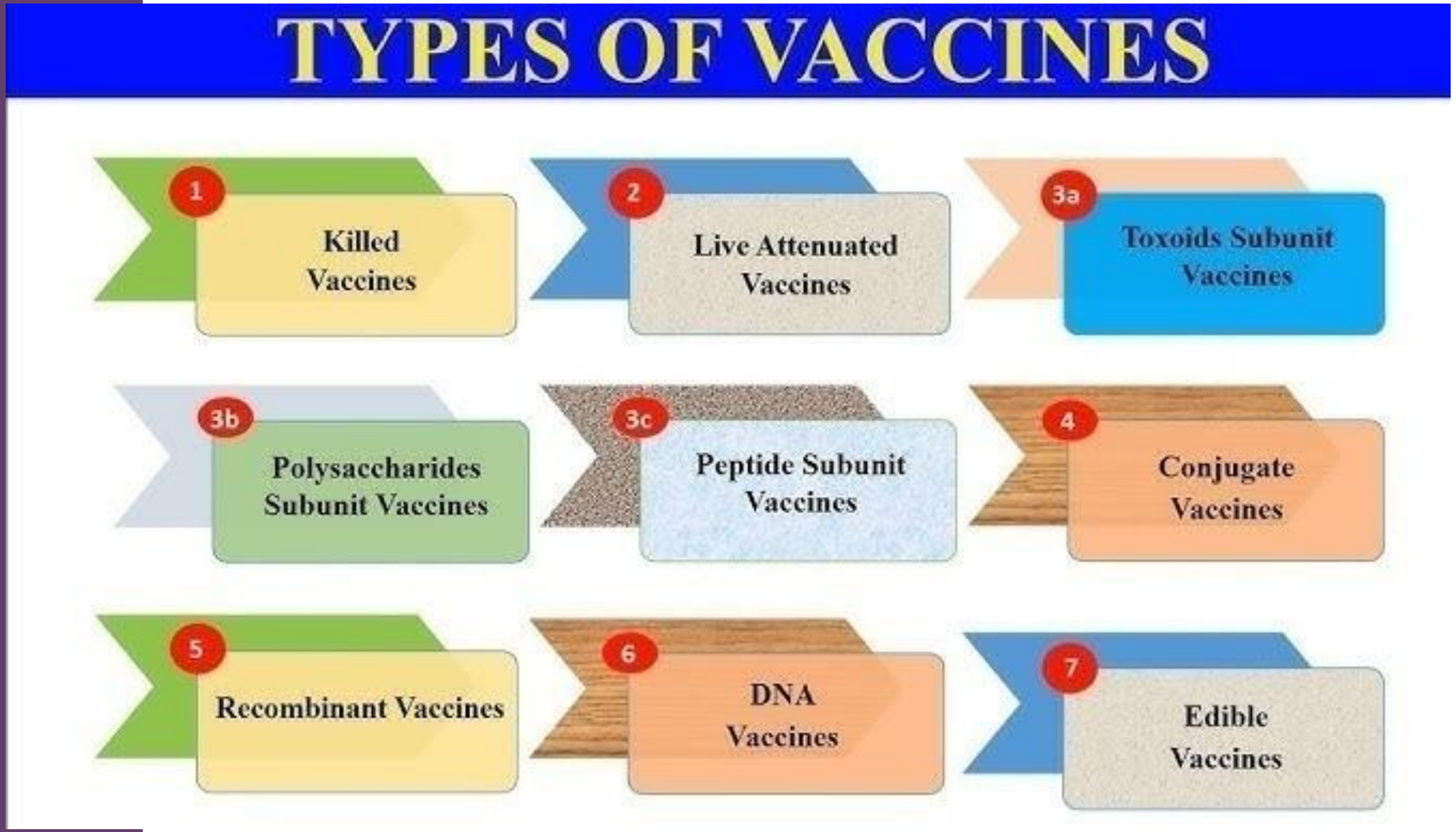
To prevent contamination.

Eg:Thimerosal

TYPES OF VACCINES

There are various types of vaccines in which some of them includes:

- Live attenuated vaccines
- Inactivated vaccines
- Subunit vaccines
- Toxoid vaccines
- mRNA vaccines
- Viral vector vaccines
- Biosynthetic vaccines

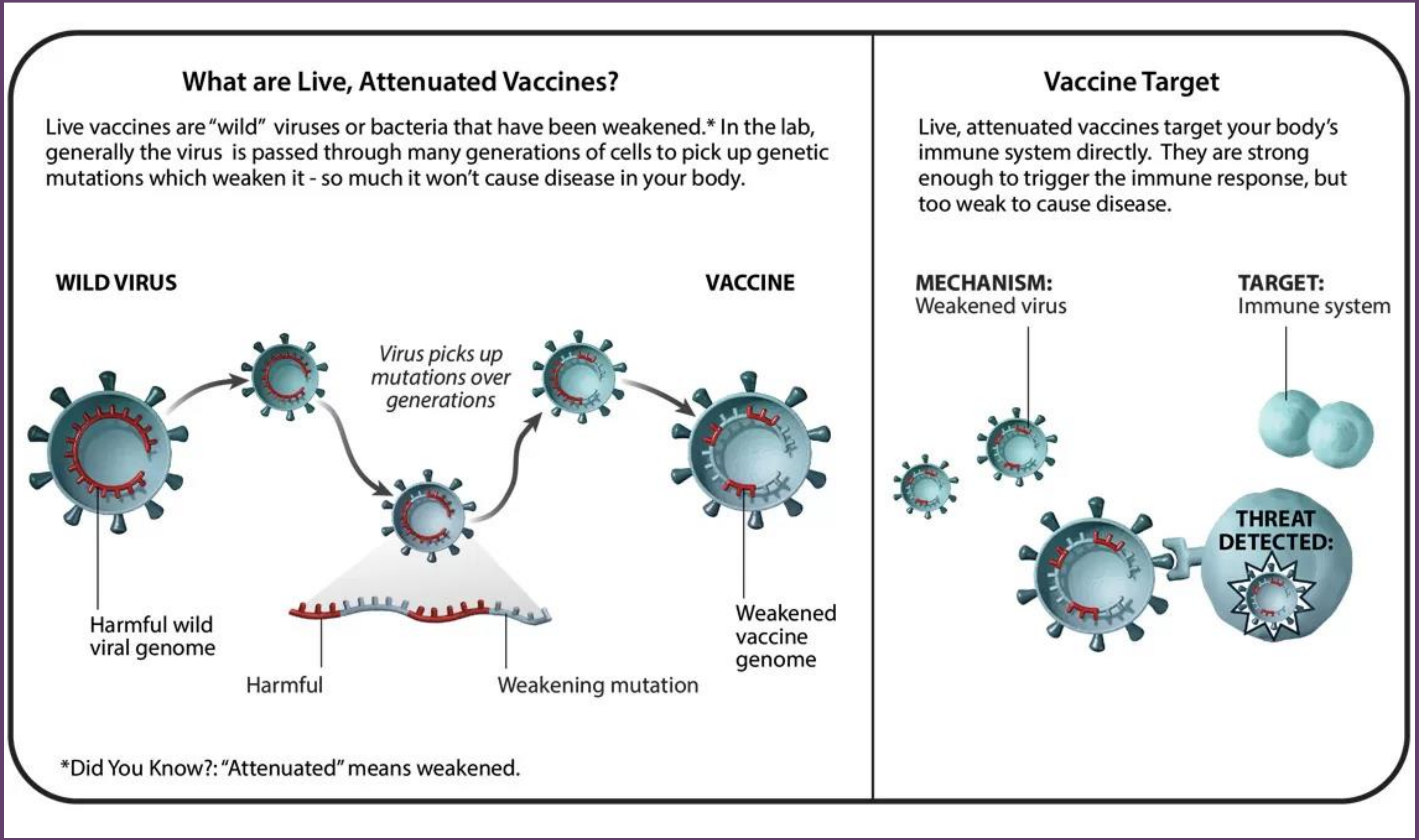


LIVE ATTENUATED VACCINES

1. Live vaccines are attenuated or modified in a way that the pathogen is not able to cause disease itself but can produce a robust immune response.
2. Typically, live vaccines lead to a stronger and more prolonged immune response in comparison to inactivated vaccines.
3. As these live viruses being attenuated, they are unable to replicate to the same extent as live unattenuated viruses. This means that they are no longer able to sufficiently infect the host, but can do so enough for the host to develop broad and robust immunity.

EXAMPLES:

Influenza (flu) vaccines (LAIV), Measles, Mumps & Rubella (MMR), Polio, Smallpox, Chickenpox, Yellow Fever


What are Live, Attenuated Vaccines?
Live vaccines are "wild" viruses or bacteria that have been weakened.* In the lab, generally the virus is passed through many generations of cells to pick up genetic mutations which weaken it - so much it won't cause disease in your body.
WILD VIRUS
VACCINE
Virus picks up mutations over generations
Harmful wild viral genome
Harmful
Weakening mutation
Weakened vaccine genome
*Did You Know?: "Attenuated" means weakened.
Vaccine Target
Live, attenuated vaccines target your body's immune system directly. They are strong enough to trigger the immune response, but too weak to cause disease.
MECHANISM:
Weakened virus
TARGET:
Immune system
THREAT DETECTED:

INFLUENZA VACCINES: (IV)

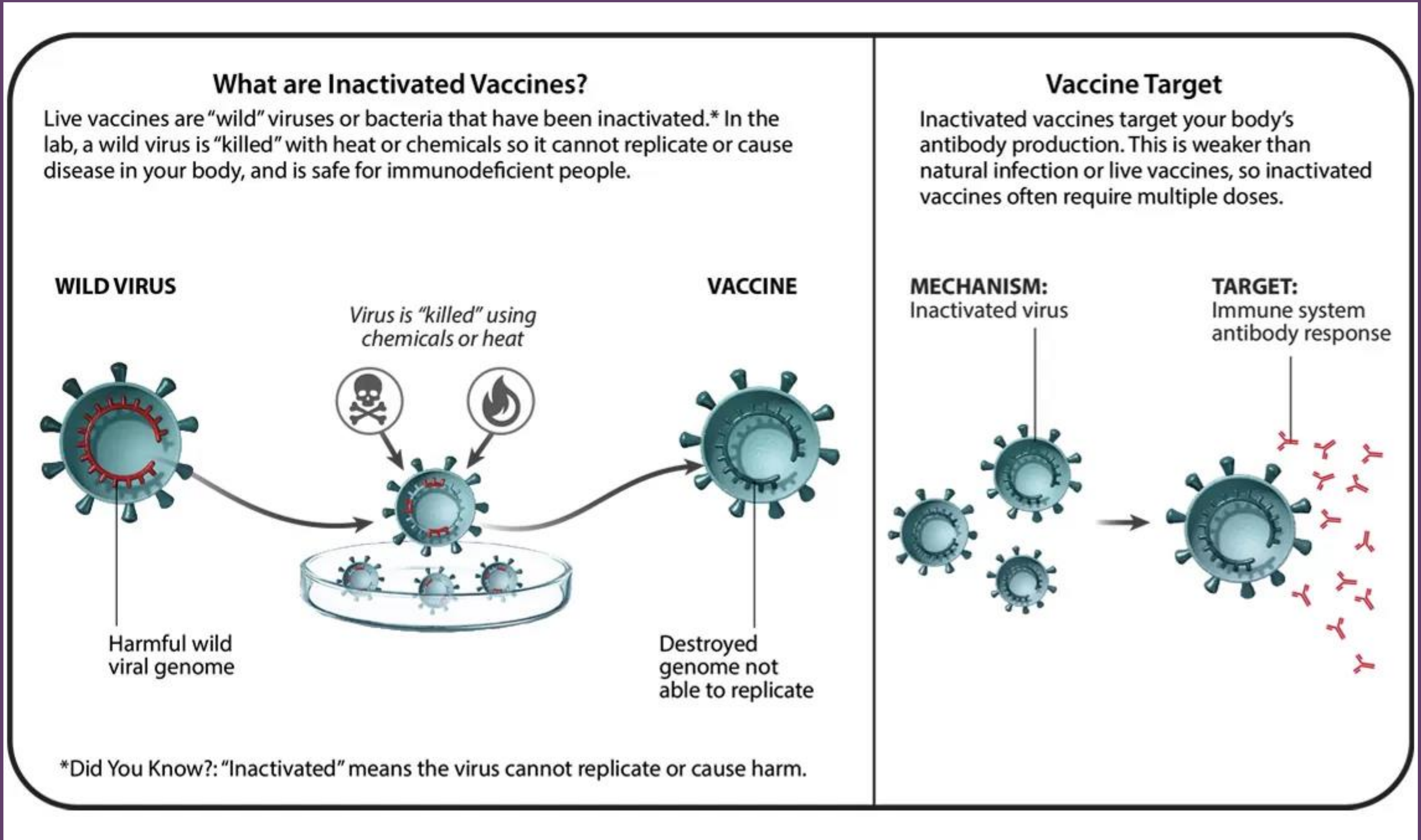
- These is an example for live attenuated vaccines.
- 90% protection in adults under 65 years
- 40% of adults over 65
- IVs are usually administered via the nose – mimicking the natural infection route of the influenza virus.
- The influenza A virus has 8 RNA segments.
- In the live attenuated vaccine, a combination of 6 attenuated segments combined with 2 normal (WT) segments – engineered into plasmids – creating a 6:2 reassortment IV.
- IVs are typically attenuated in 10–11-day old chicken embryonated eggs by serial passaging.

KILLED/INACTIVATED VACCINES:

- Inactivated vaccines are composed of dead, or inactivated, viruses and bacteria, and therefore differ from live but attenuated vaccines.
- The virus is inactivated with the help of two methods:

  Chemical method

  Physical method
- After the inactivation process the viral particle is purified and other components like adjuvants and stabilizers are added in order to formulate the vaccine so that it can be effective.


What are Inactivated Vaccines?
Live vaccines are "wild" viruses or bacteria that have been inactivated.* In the lab, a wild virus is "killed" with heat or chemicals so it cannot replicate or cause disease in your body, and is safe for immunodeficient people.
WILD VIRUS
Virus is "killed" using chemicals or heat
VACCINE
Harmful wild viral genome
Destroyed genome not able to replicate
*Did You Know?: "Inactivated" means the virus cannot replicate or cause harm.
Vaccine Target
Inactivated vaccines target your body's antibody production. This is weaker than natural infection or live vaccines, so inactivated vaccines often require multiple doses.
MECHANISM:
Inactivated virus
TARGET:
Immune system antibody response

- Inactivated virus are mostly used as booster shots after the administration of other vaccines.
- The immune response to live vaccines is similar to encountering the virus itself, whereas inactivated vaccines show little or no cellular immunity. This also means that inactivated vaccines can be used to boost to supplement previous vaccinations.
- Examples of inactivated vaccines: Polio, Hepatitis A, and Rabies

INACTIVATED VACCINES AGAINST COVID-19:

- Sinovac Biotech has created an inactivated whole virus particle vaccine, with an extra immune booster referred to as alum.
- This has been successful against SARS viruses.

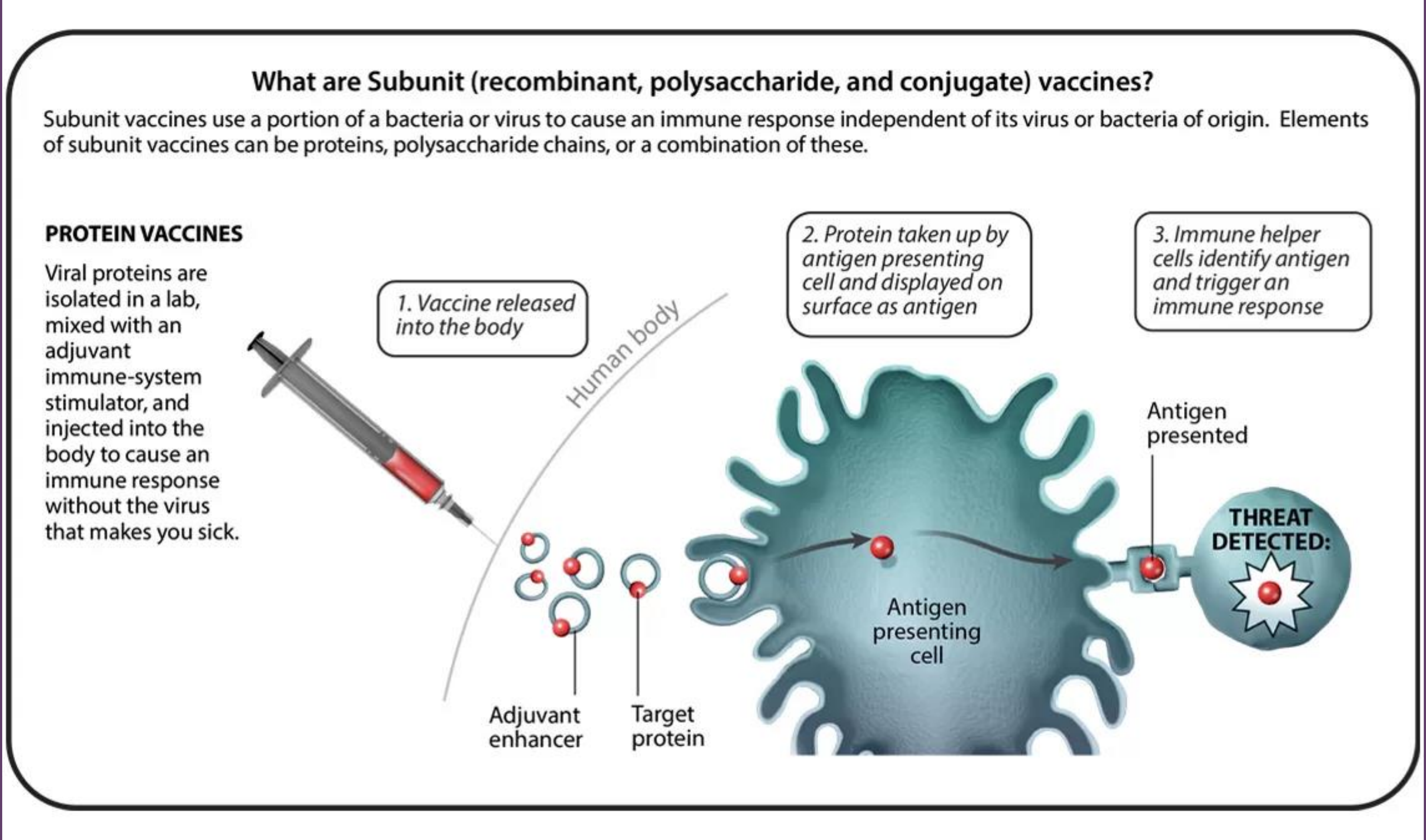
SUBUNIT VACCINES:

- Subunit vaccines are made from a piece of a pathogen, not the whole organism, so they do not contain any live pathogens.
- Some important subunit vaccines are

Polysaccharide vaccines

Conjugate vaccines

Protein-based



POLYSACCHARIDE VACCINES:

= Use long chains of sugar molecules (polysaccharides) found on the surface of certain bacteria to stimulate an immune response.
= This response typically involves the production of B-cell antibodies which tend to stimulate a T-cell-independent immune response, meaning they do not involve helper T-cells.
= This results in a less robust and shorter-lasting immune memory compared to vaccines that involve T-cell activation.
= Importantly, these vaccines do work in children under 2.

CONJUGATE VACCINES:

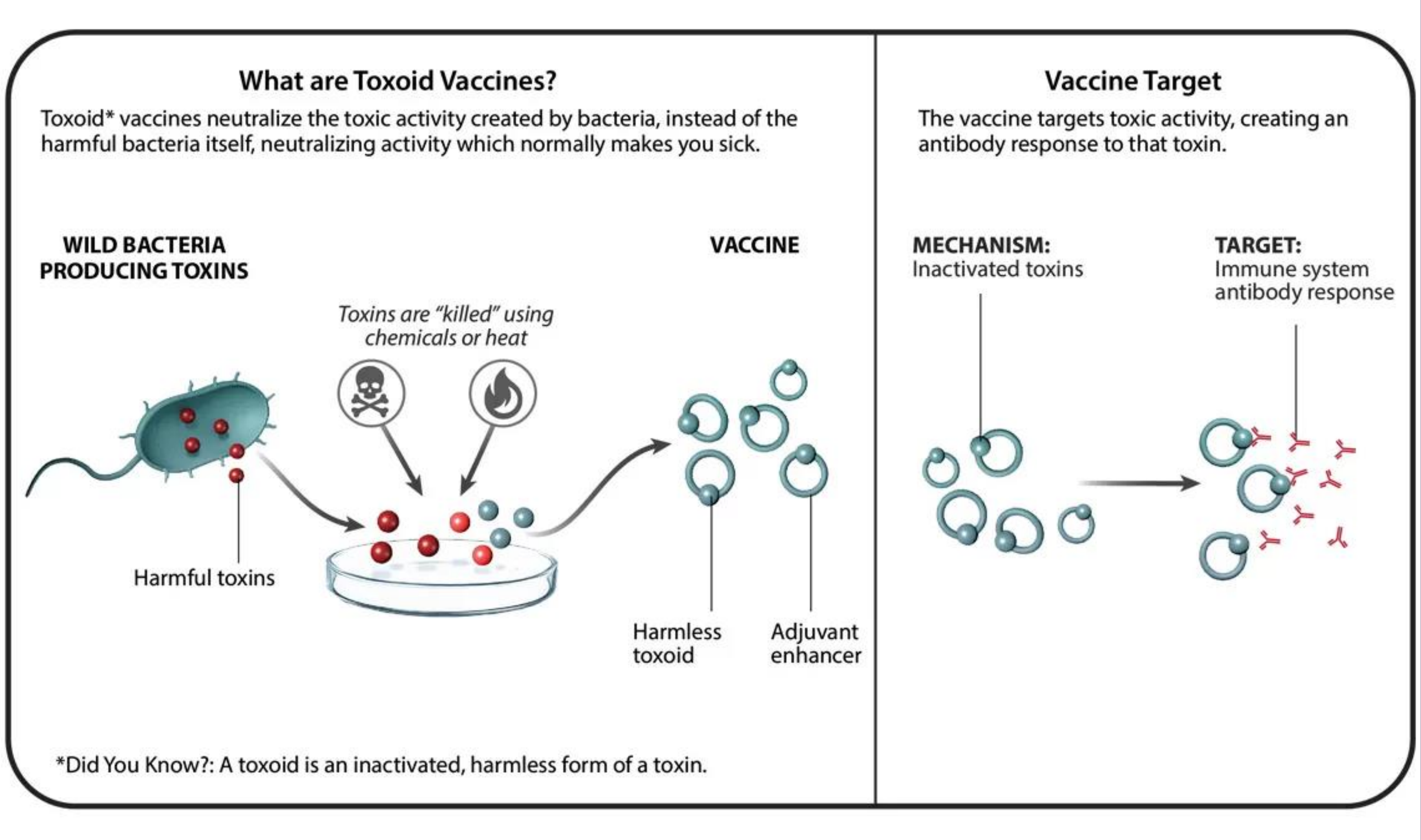
= Conjugate vaccines are a type of vaccine designed to improve the immune response to bacterial infections, especially in young children. = These vaccines link (or "conjugate") a polysaccharide (sugar molecule) from the surface of bacteria to a carrier protein.
= This combination stimulates a more robust and long-lasting immune response, overcoming the limitations of pure polysaccharide vaccines.
= Activates both T-cells and B-cells.

PROTEIN-BASED VACCINES:

= Protein-based vaccines allows to make a protective response against a protein on the surface of a virus/bacteria, or against a secreted toxin.
= In this case, the immune response is against the protein components of the bacteria or virus, not the sugar coat.
= Certain proteins on the surface of bacteria or viruses help the pathogen cause disease, so inducing an immune response against them can help the body fight against the infection or the toxic effects of the toxin.

TOXOID VACCINES

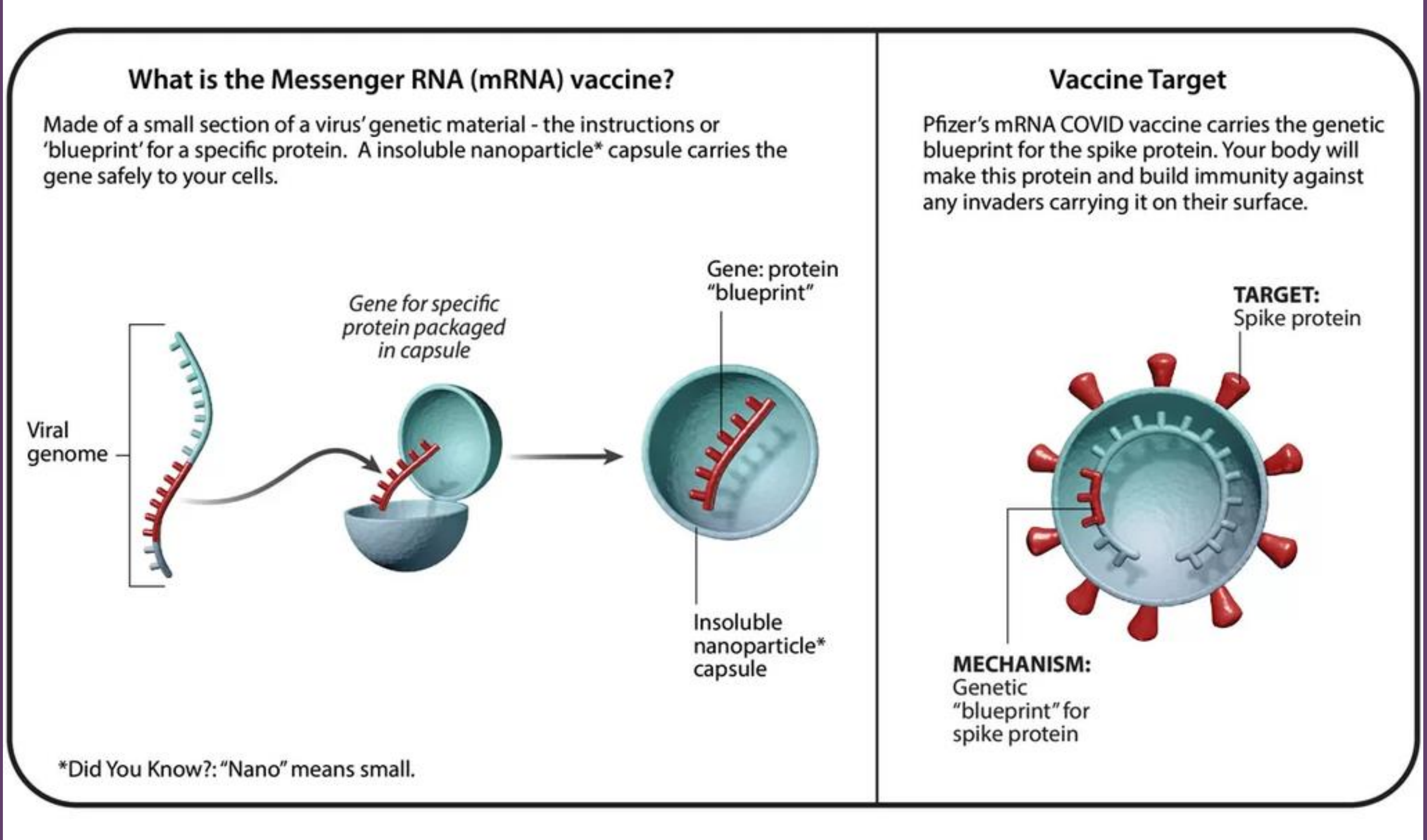
Toxoid vaccines use inactivated toxins to target the toxic activity created by the bacteria, rather than targeting the bacteria itself.



Examples: Tetanus vaccine,
Diphtheria vaccine

mRNA VACCINES

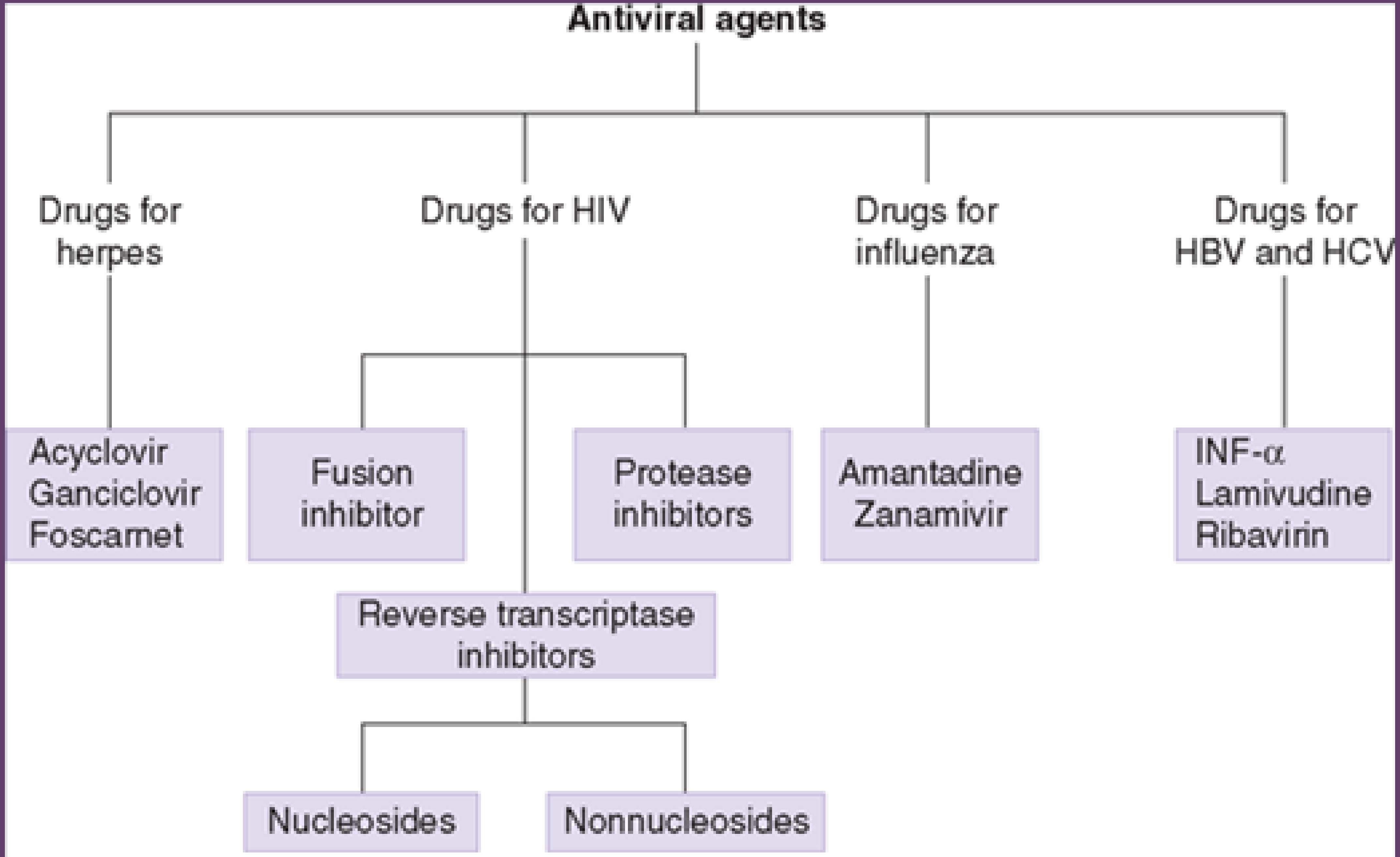
- mRNA vaccines are a type of vaccine that use messenger RNA (mRNA) to instruct cells to produce a protein that triggers an immune response.
- When an mRNA vaccine is delivered, the RNA material teaches our body how to make a specific type of protein that is unique to the virus, but does not make the person sick.
- **That way, if a person is ever exposed to that virus in the future, the body would like have the tools (antibodies) to fight against it.**



ANTIVIRAL CHEMOTHERAPY

- Antiviral chemotherapy refers to the use of drugs to treat viral infections by inhibiting the replication of viruses within the host.
- Since viruses rely on the host's cellular machinery to reproduce, developing effective antivirals is challenging, as these drugs must target viral components without damaging the host cells.

TYPES OF ANTIVIRAL DRUGS



Source: Trevor AJ, Katzung BG, Kruidering-Hall M, Masters SB: *Katzung & Trevor's Pharmacology: Examination & Board Review*, 10th Edition: www.accesspharmacy.com

KEY CLASSES OF ANTIVIRAL DRUGS

Nucleoside and Nucleotide Analogs:

= mimic the building blocks of viral DNA or RNA

- Acyclovir (herpesviruses)
- Sofosbuvir (hepatitis C virus)

Protease Inhibitors:

= These block the viral enzyme protease

- Ritonavir (HIV)
- Glecaprevir (hepatitis C)

Polymerase Inhibitors:

= These target viral polymerases

- avipiravir
- Remdesivir (COVID-19)

Reverse Transcriptase Inhibitors (RTIs):

= Primarily used to treat HIV.

= They inhibit reverse transcriptase

- Zidovudine
- Lamivudine

Fusion Inhibitors:

= prevent viruses from fusing with host cell membranes.

= blocks their entry into cells.

- Enfuvirtide (HIV)

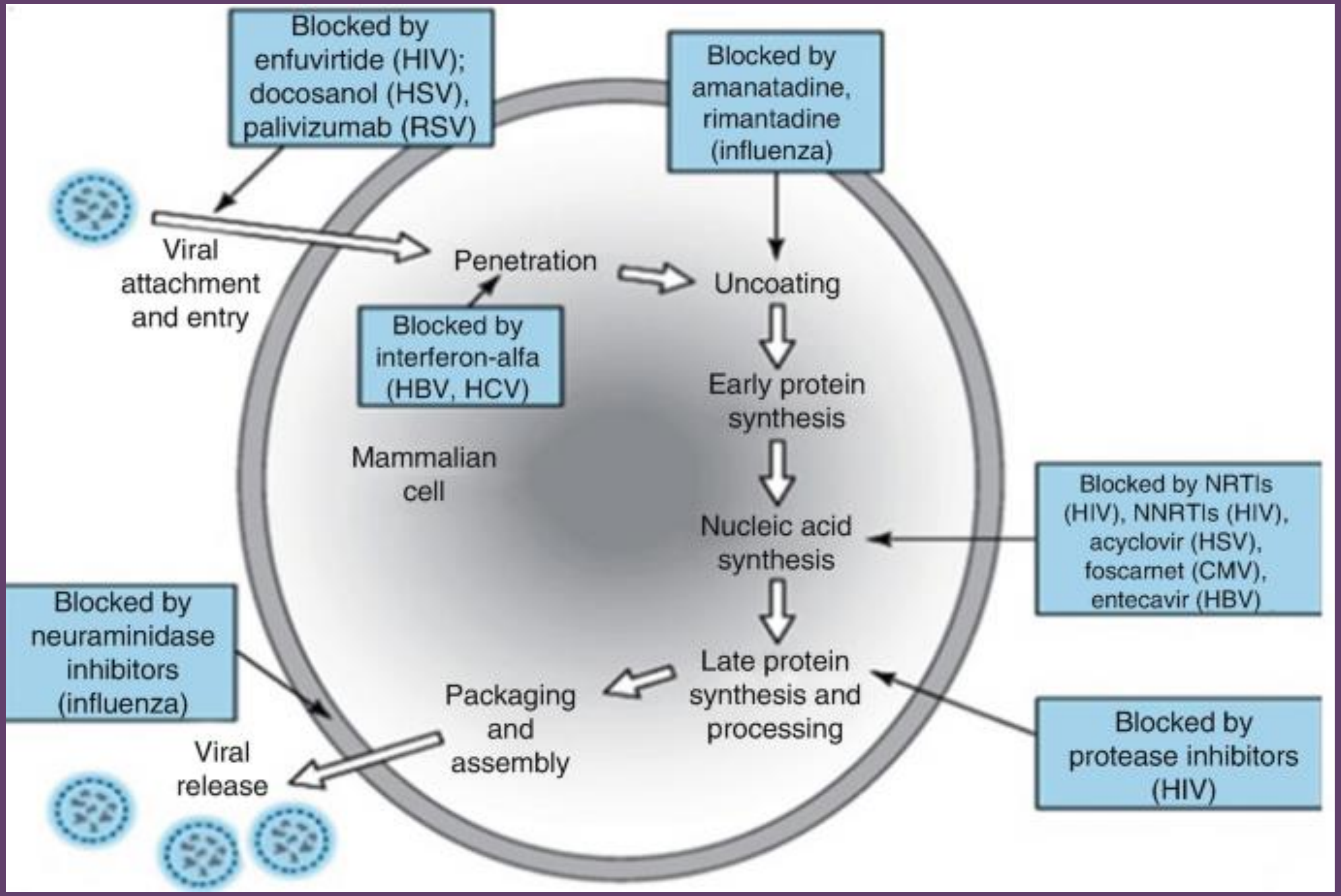
Entry Inhibitors:

= Block the receptors that viruses use to enter cells.

- Example: Maraviroc (HIV).

MECHANISM OF ANTIVIRAL DRUGS

Antiviral drugs work by interfering with various stages of the viral life cycle, including:



ATTACHMENT AND ENTRY INHIBITION:

- Some antivirals prevent viruses from attaching to or entering host cells, thus blocking the initial step of infection.
- Example: Maraviroc, used in HIV treatment, blocks the CCR5 receptor that HIV uses to enter cells.

UNCOATING INHIBITION:

- **After entering a host cell, viruses must release their genetic material to replicate. Some drugs block this process, preventing the virus from replicating.**

Example: Amantadine and Rimantadine, which were once used against influenza A, inhibit the M2 protein, preventing viral uncoating.

INHIBITION OF VIRAL PROTEIN SYNTHESIS:

- **Some antivirals block the translation of viral proteins needed for the virus to build new particles.**

Example: Antisense therapies or small interfering RNA (siRNA) therapies are under investigation for viral protein synthesis inhibition.

INHIBITON OF VIRAL GENOME REPLICATION:

- Many antiviral drugs target viral replication enzymes, such as DNA or RNA polymerases or reverse transcriptase, preventing the virus from copying its genetic material.

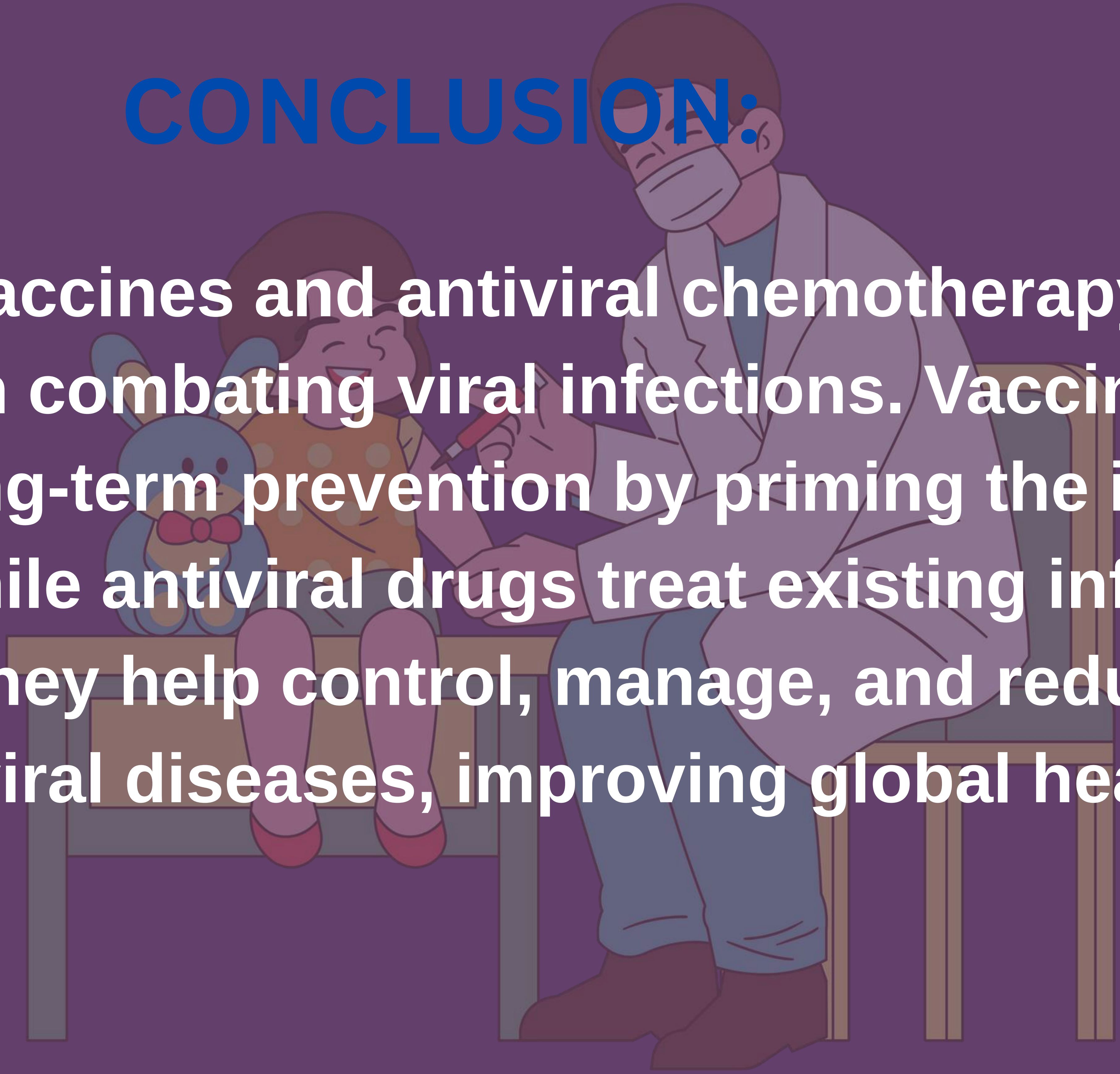
Example: Acyclovir, used to treat herpesvirus infections, is a nucleoside analog that inhibits viral DNA polymerase, halting viral replication.

INHIBITION OF VIRAL ASSEMBLY AND RELEASE:

- Antiviral drugs can prevent viruses from assembling properly inside the host cell or from being released from the cell to infect new cells.

Example: Protease inhibitors (like those used in HIV therapy) block the enzyme that cleaves viral polyproteins into functional units, preventing viral assembly.

CONCLUSION:



Vaccines and antiviral chemotherapy are essential in combating viral infections. Vaccines provide long-term prevention by priming the immune system, while antiviral drugs treat existing infections. Together, they help control, manage, and reduce the spread of viral diseases, improving global health outcomes.

References:

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THANK YOU