Overview of vaccinations

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Learning outcomes

By the end of this lecture the students should be able to:

- Identify the desired properties of an ideal vaccine.
- Describe different methods for Production of vaccines.
- Advantages and limitations of different types of vaccines.

Immunization

Immunization:

The process of eliciting a **long-lived state of protective immunity** against a disease-causing pathogen.

Immunization can be achieved by:

1. Exposure to the **live pathogen** followed by recovery.
2. **Vaccination:** intentional exposure to forms of a pathogen that do not cause disease (a vaccine).
3. The **transfer of antibodies** from mother to fetus or the **injection of antiserum** against a pathogen both provide immune protection.

Immunization

Note: Both **first and second methods** engage antigen-specific lymphocytes and result in the generation of memory cells, providing long-lived protection, while in **the third method** the state of immunity is only temporary (without the development of memory B or T cells specific to the organism).

Objective of Vaccination

1. Stimulate immunologic memory → **protect recipient against future disease** → subsequent infection will be subclinical.
2. **Prevent transmission** of infection to contacts → increase herd immunity & reduce circulation of microorganism in community.

Characteristics of an Ideal Vaccine

1. **High efficacy** in target populations.
2. Few or no **adverse reactions**.
3. **Safe** in immune-compromised individuals & pregnant women.
4. **Easy** & **inexpensive** to deliver to developing countries.
5. **Stable** during transport & storage.
6. Induces **life-long immunity**.
7. Stimulates both **humoral & CMI responses**.

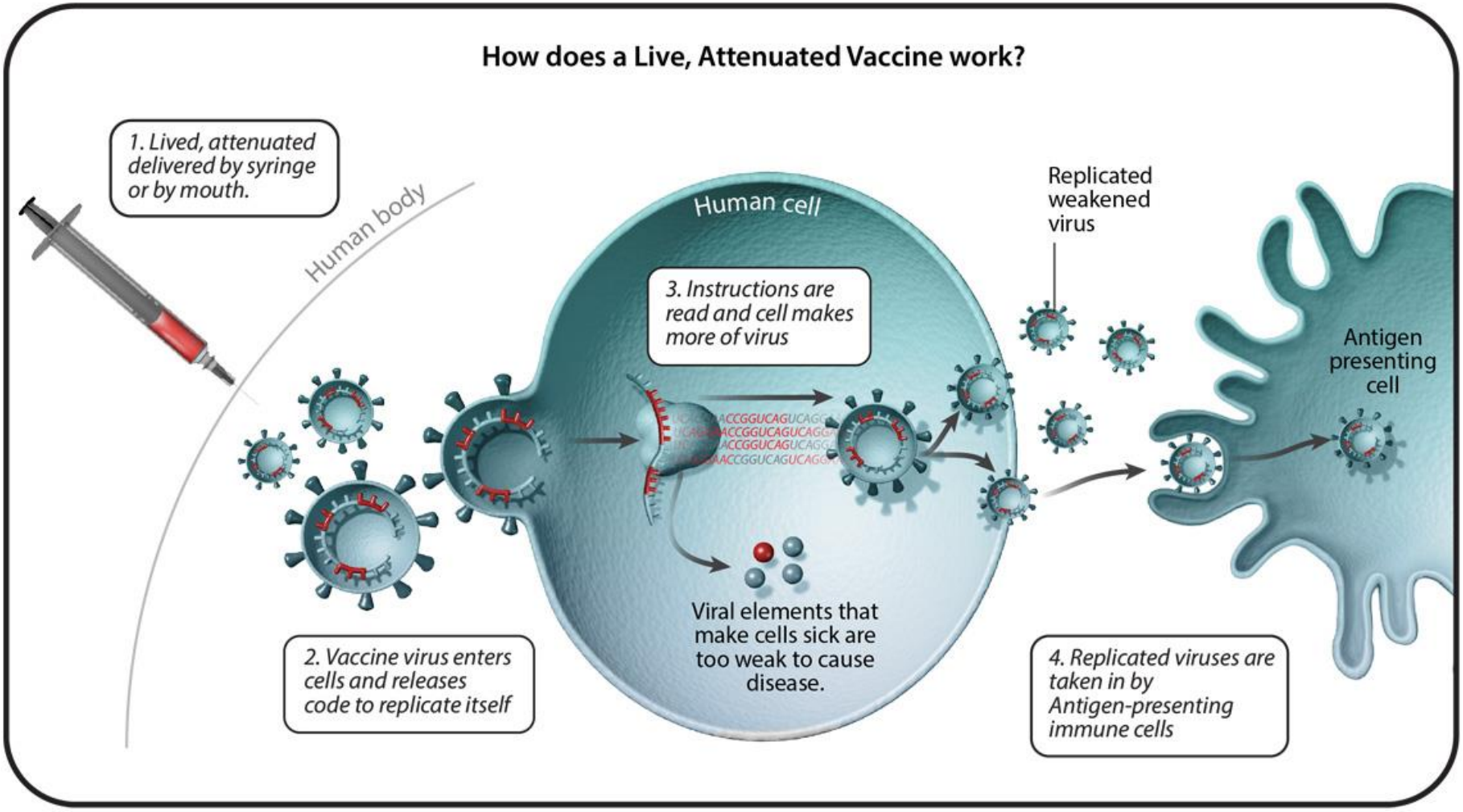
Methods for Production of Vaccines

1. Live attenuated Vaccines:

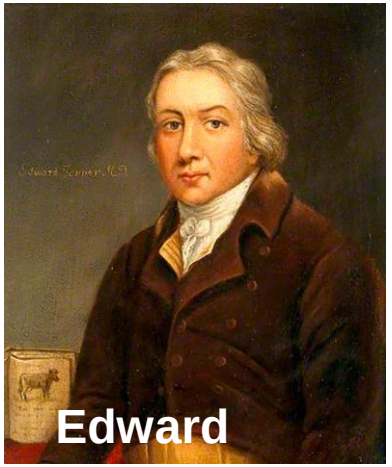
How does a live attenuated vaccine work?

- The vaccine virus **replicates** in recipient → amplifies amount of antigen (Ag) available for presentation to host immune system → host **immune response (IR)** resembling what occurs after natural infection.

1. Live attenuated Vaccines:



1. Live attenuated Vaccines:



Sources of live attenuated vaccines:

1. **Naturally occurring attenuated virus strain.**
2. **Related virus from heterologous host**:

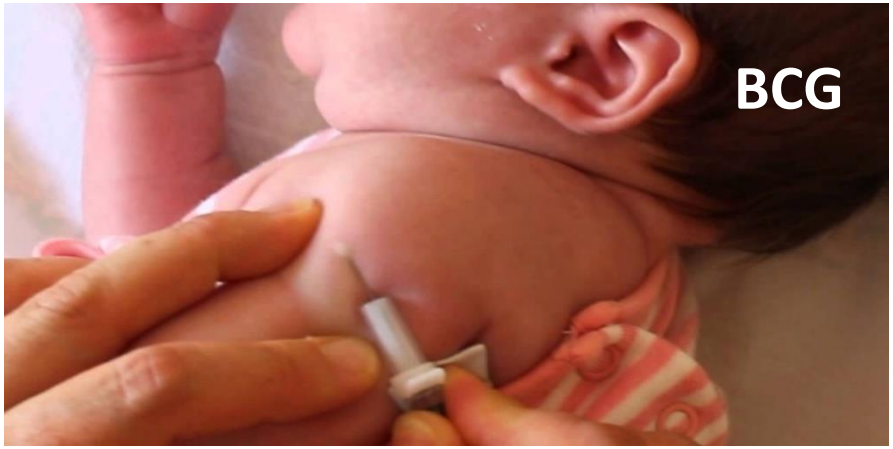
- Example: cowpox virus (cattle pathogen) is antigenically related to smallpox virus (human pathogen)

- cowpox virus was the 1st vaccine introduced to control **human smallpox** → produce mild lesion in humans, but conferred protection against severe disease.

1. Live attenuated Vaccines:

Sources of attenuated virus vaccines:

3. **Serial passage in heterologous host/cultured cells:** → accumulation of numerous point mutations in viral genes → loss of virulence for natural host. Example: Sabine oral polio vaccine (**OPV**) and **BCG**.



1. Live attenuated Vaccines:

Sources of attenuated virus vaccines:

4. Selection of cold-adapted mutants:

- Example: **cold-adapted influenza vaccines**: intranasal administration → mutant virus replicates at low temp of nasal cavity (~33°C), but not at temp of the more susceptible lower respiratory tract.

1. Live attenuated Vaccines:

Advantages of live attenuated vaccines:

- IR like what occurs after natural infection → good cell mediated immunity (CMI).
- Can be administered orally, which induces mucosal immunity & IgA synthesis → more protection at the site of viral entry.
- Duration of immunity: usually many years.
- Number of doses needed: Low (usually single dose)
- Number of viruses needed in vaccine dose: Low.

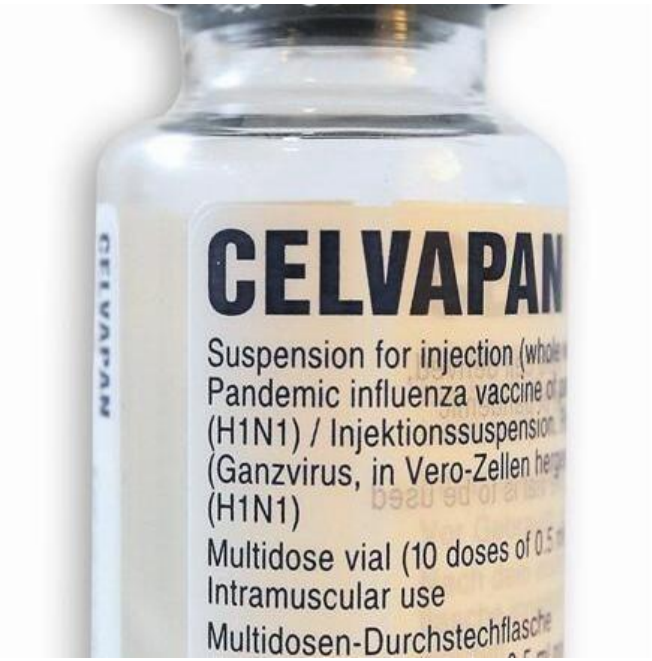
1. Live attenuated Vaccines:

Disadvantages of live attenuated vaccines:

- The possibility of reversion to virulent virus → Cause disease.
- Not safe for immune-compromised persons and pregnant women.

2. Inactivated (Killed) Vaccines:

- Involves exposing virulent microorganism to chemical/physical agent (e.g, formalin) → destroy infectivity while retaining Immunogenicity. Example: Salk inactivated polio vaccine **(IPV)** and **Inactivated Influenza vaccine.**



2. Inactivated (Killed) Vaccines:

Advantages of inactivated vaccines:

- No possibility of reversion to virulent virus.
- Safe for immune-compromised persons and pregnant women.

2. Inactivated (Killed) Vaccines:

Disadvantages of inactivated vaccines

- The need to use large amounts of Ag to elicit adequate Ab response (1ry vaccination course includes 2-3 injections; further "booster" doses are required to maintain protective immunity).
  - Number of doses needed: multiple doses
  - Number of viruses needed in vaccine dose: High.

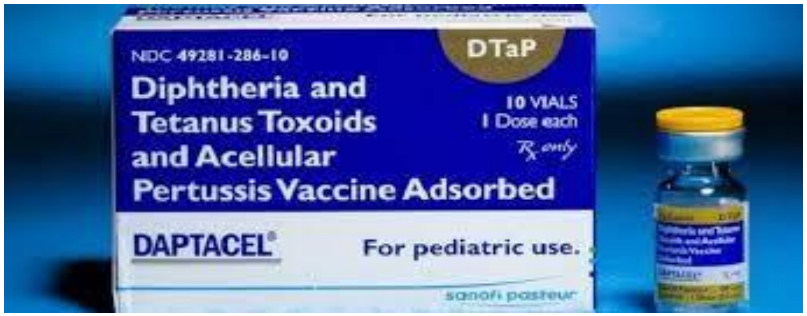
2. Inactivated (Killed) Vaccines:

Disadvantages of inactivated vaccines:

- The chemical or physical agent used to eliminate infectivity may be damaging enough to modify immunogenicity: This result in
  - IR shorter in duration (years but more limited than live attenuated vaccines).
  - Weaker IR (weak CMI and weak mucosal IR) → less effective.

3. Subunit Vaccines:

- Involves using only specific, purified macromolecules derived from the pathogen. Examples:
  - Inactivated exotoxins (toxoids): The Diphtheria and Tetanus components of the Diphtheria Pertussis Tetanus (**DPT**) vaccine.



  - Capsular polysaccharides: *Haemophilus influenzae* type B (**Hib**) vaccine.

3. Subunit Vaccines:

Advantages of subunit vaccines:

- No possibility of reversion to virulent virus.
- Safe for immune-compromised persons and pregnant women.

Disadvantages of subunit vaccines:

- The inability to activate Th cells → No CMI, Instead, they induce humoral immunity, and little, if any, development of memory cells.

3.a. Recombinant antigen vaccines

- Considered a type of subunit vaccines.
- Involves using **recombinant-DNA technology** to produce large amounts of antigenic proteins.
- The gene encoding viral protein that confer protection is cloned into expression plasmid & expressed in any cell system.
- Example: **Hepatitis B vaccine**

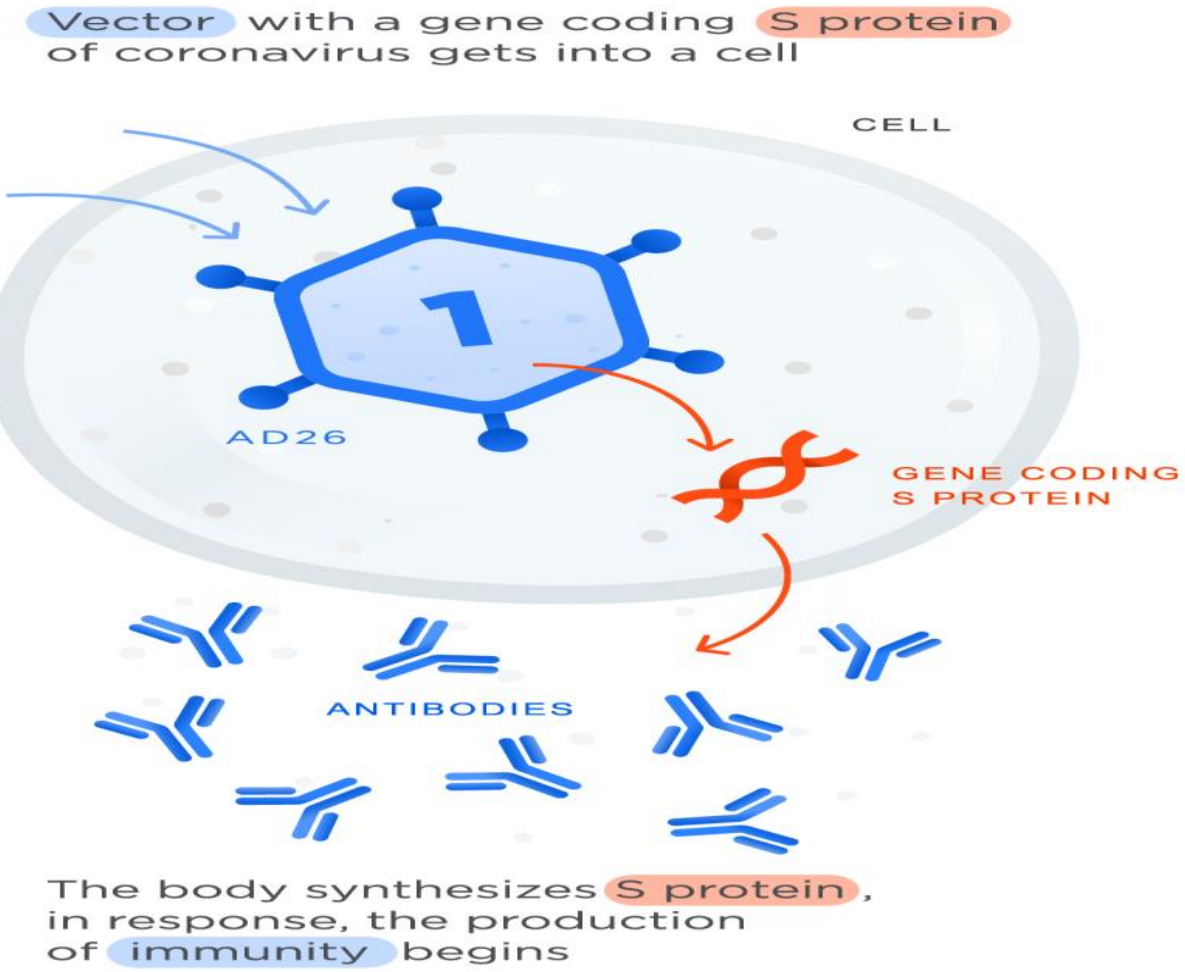
3.b. Virus-Like Particles (VLP)

- Considered a type of subunit vaccines.
- Involves using **recombinant-DNA technology** to produce large amounts of capsid proteins of certain non-enveloped viruses.
- The gene encoding capsid proteins is cloned into expression plasmid & expressed in any cell system → capsid proteins assemble into VLPs **"empty virus particles"** that they are totally devoid of nucleic acid & therefore non-infectious.
- Example: human papilloma virus (**HPV**) vaccine.

4. Recombinant vector vaccines

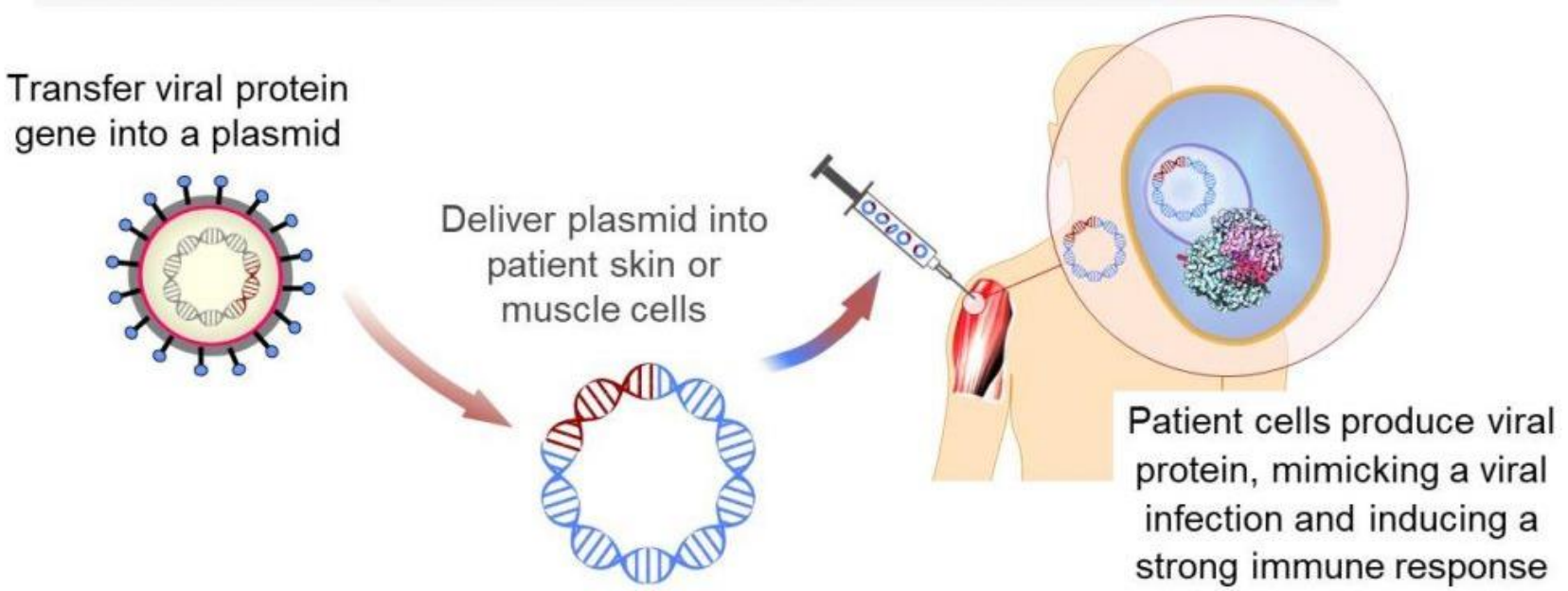
- Involve using **recombinant DNA technology** to insert gene encoding a protective Ag into genome of non-pathogenic bacterial or viral vectors.
- The vector multiplies & presents the viral Ag to immune system → both humoral & CMI responses are elicited.
- Example:
  - **AstraZeneca:** Adenovirus vectored COVID-19 vaccine.

4. Recombinant vector vaccines



5. DNA Vaccination

- Involve using **naked DNA** as an immunogen.
- Recombinant plasmids are constructed to contain genes encoding protective Ags → upon injection by gene gun, DNA in plasmid is transcribed & mRNA is translated → expressed proteins elicit IR similar to that during infection. Both humoral & CMI are elicited.



5. DNA Vaccination

Advantages:

- Multiple Ags of different microorganisms can be included in single plasmid.
- No need to prepare large amounts of protein Ag.
- Ags are expressed in native conformation resembling that on virion → CMI & Ab responses are elicited.

Disadvantages:

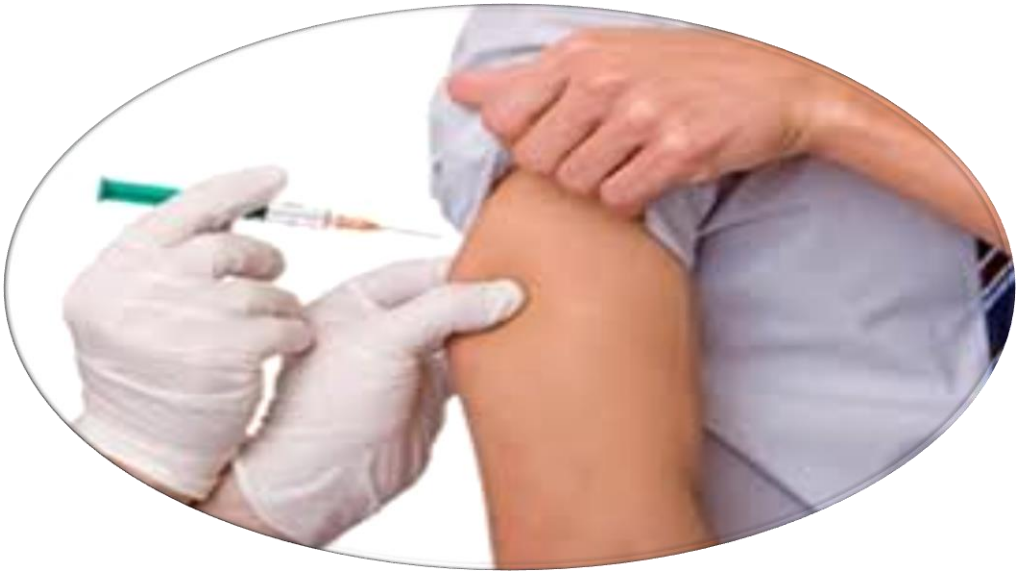
- For reasons not fully understood, the efficacy of DNA vaccines demonstrated in mice is not always reproduced in humans.

Advantages and Limitations of Attenuated, Inactivated, and DNA Vaccines

Property	Attenuated Virus Vaccine	Inactivated Virus Vaccine	DNA Vaccine
Route of administration	• Injection • Inhalation • Oral	• Injection	• Gene gun
Amount of virus in vaccine dose	Low	High	Nil
Number of doses	Usually single	Multiple	Usually single
Duration of immunity	Many years	Years (more limited)	Not known
CMI response	Good	weak	Good
Use in immune-compromised or pregnancy	No	yes	yes
Reversion to virulence	Can occur	No	No

II- Immunization of HCP

- **HCP may be exposed to infectious disease agents that may be transmitted through the airborne route, direct contact and the blood-borne route.**



- **For example:**
  - **Airborne: Many airborne infectious agents are vaccine preventable (e.g., rubella, chickenpox), and determining HCP immunization status for such infections is an essential element in the employee health program.**

  - **Blood-borne:**
    - **Hepatitis B is one of the three major BBPs of concern to HCP that can be prevented by immunization.**

Table of Vaccines that are recommended for HCP

Vaccine	Indication	Vaccine/Route/ Schedule	Booster dose
Hepatitis B	All HCP	3 doses i.m. 0, 1, 6 months;	Not recommend
Td (Tetanus)	Persons without a history or an unknown history	3 doses i.m. 0, 1-2 months, 6 months	•Every 10 years •If exposed to a dirty wound and last booster dose is > 5y
Rubella	Un-immunized women of child-bearing age	Single dose i.m. or s.c.	

Hepatitis B – If previously unvaccinated, give 3-dose series (dose #1 now, #2 in 1 month, #3 approximately 5 months after #2). Give intramuscularly (IM). For HCP who perform tasks that may involve exposure to blood or body fluids, obtain anti-HBs serologic testing 1–2 months after dose #3.

Influenza – Give 1 dose of influenza vaccine annually. Inactivated injectable vaccine is given IM, except when using the intradermal influenza vaccine. Live attenuated influenza vaccine (LAIV) is given intranasally.

MMR – For healthcare personnel (HCP) born in 1957 or later without serologic evidence of immunity or prior vaccination, give 2 doses of MMR, 4 weeks apart. For HCP born prior to 1957, see below. Give subcutaneously (SC).

Varicella (chickenpox) – For HCP who have no serologic proof of immunity, prior vaccination, or diagnosis or verification of a history of varicella or herpes zoster (shingles) by a healthcare provider, give 2 doses of varicella vaccine, 4 weeks apart. Give SC.

Tetanus, diphtheria, pertussis – Give 1 dose of Tdap as soon as feasible to all HCP who have not received Tdap previously and to pregnant HCP with each pregnancy (see below). Give Td boosters every 10 years thereafter. Give IM.

Meningococcal – Give 1 dose to microbiologists who are routinely exposed to isolates of *Neisseria meningitidis* and boost every 5 years if risk continues. Give MCV4 IM; if necessary to use MPSV4, give SC.

Hepatitis A, typhoid, and polio vaccines are not routinely recommended for HCP who may have on-the-job exposure to fecal material.

Tips about hepatitis B vaccination of HCP

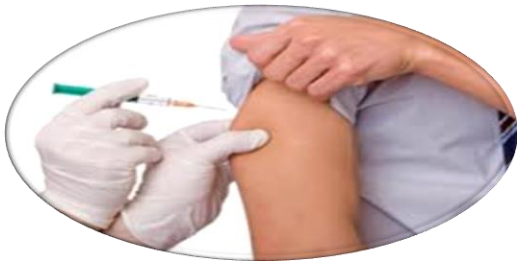
- **All HCP should be offered hepatitis B vaccine prior to beginning assigned tasks.**

- **There is no need to provide booster doses.**

- **If the vaccine supply is limited, offer the vaccine to HCP who are exposed to blood or who have potential for sharps or needle stick.**

Tips about hepatitis B vaccination of HCP

- **Do not perform serologic testing before vaccination.**
- **Perform serologic testing 2 months after the 3rd dose to ensure adequate immune response (HbsAb +ve).**
- **Seroconversion (HbsAb +ve) occurs 1-2 months after the 3rd dose.**
- **Non-responders should repeat the vaccination schedule again (3 doses).**
- **Provide hepatitis B vaccine as post-exposure prophylaxis for unvaccinated HCPs who receive needle stick injuries.**



Tips about hepatitis B vaccination of HCP

- **On Vaccine series interruption:**

"If a HCP has not completed the series, do not restart the series but do complete the series"

- ✓ **If the series of HB vaccine is interrupted after the first dose, administer the second as soon as possible. The second and third dose should be separated by an interval of at least 2 months.**

- ✓ **If only the 3rd dose of vaccine is delayed, administer when convenient.**

Questions

Which of the following vaccine types is contraindicated in immune-compromised patients?

A. Live attenuated Vaccines

B. Inactivated Vaccines

C. Subunit vaccines

D. DNA vaccines

E. Virus-like particles

Questions

Salk polio vaccine is an example of which type of vaccine?

A. Live attenuated Vaccines

B. Inactivated Vaccines

C. Subunit vaccines

D. DNA vaccines

E. Virus-like particles

References

- **Runte, F., Renner IV, P., & Hoppe, M. (2019). Kuby immunology.**

- **Burrell, C. J., Howard, C. R., & Murphy, F. A. (2016). Fenner and White's medical virology. Academic Press.**