Chapter 11. Immunoprophylaxis and Immunization Schedule

Table of Contents

CHAPTER PREVIEW

- Active Immunoprophylaxis
- Passive Immunoprophylaxis
- National Immunization Schedule

Immunoprophylaxis against microbial pathogens can be classified into active immunoprophylaxis (or vaccination) and passive immunoprophylaxis (or immunoglobulin administration).

VACCINATION (ACTIVE IMMUNOPROPHYLAXIS)

Vaccine is an immunobiological preparation that provides specific protection against a given disease. Following vaccine administration, the immunogen (active ingredient of the vaccine) stimulates the immune system of the body to produce active immunity in the form of protective antibody and/or immunocompetent T cell response.

Vaccines may be of various types based on their method of preparation by using live modified organisms, inactivated or killed organisms, extracted or cellular fractions, toxoids, subunit or combinations of all these. Vaccines of future prospects include DNA vaccine and viral vector vaccine.

Live Attenuated Vaccine

Live vaccines, such as BCG *(Table 11.1)* are prepared from live (usually attenuated) organisms.

- The live attenuated organisms lose their ability to induce full blown disease, but retain their immunogenicity

- Attenuation is achieved by passing the live organisms serially through a foreign host, such as chick embryo/tissue culture or live animals
- Live vaccines in general, are more potent immunizing agents compared to killed vaccines
- They are capable of inducing mucosal immunity by stimulating secretory IgA antibody production at the local mucosal sites.

Precautions while Using Live Attenuated Vaccines

- **Contraindications:** Live vaccines should not be administered in individuals with immunodeficiency diseases or any conditions that suppresses the immunity, such as leukemia, lymphoma, malignancies, on corticosteroid or any other immunosuppressive drug therapy
- **Pregnancy** is another contraindication, unless the risk of infection exceeds the risk of harm to the fetus by giving the live vaccine
- When *two live vaccines* are required to be given; they should be administered with an interval of at least 4 weeks
- **Dosage:** Most live vaccines are given in single dose format as effective immunity is achieved with a single dose.

Table 11.1. Example of commonly used vaccines.

Bacterial	***Viral***
Live attenuated vaccines	
BCG vaccine	Measles vaccine
Typhoral vaccine	Mumps vaccine
	Rubella vaccine
	Live attenuated influenza vaccine
	Chickenpox vaccine
	Oral polio vaccine (OPV)
	Rotavirus vaccine
	Yellow fever 17D vaccine
	Hepatitis A vaccine
	Japanese B encephalitis vaccine (14-14-2 strain)
Killed/inactivated vaccine	
Typhoid vaccine	Injectable polio vaccine (IPV)
Cholera vaccine	Killed influenza vaccine
Pertussis vaccine	Rabies vaccine
Plague vaccine	Covaxin for COVID-19
Toxoid vaccine	**Subunit vaccine**
DT (Diphtheria toxoid) TT (Tetanus toxoid)	Hepatitis B vaccine HPV (Human papillomavirus) vaccine
Cellular fraction	**DNA/RNA vaccine**
Meningococcal vaccine	COVID-19 vaccines such as Moderna or Pfizer vaccines

Bacterial	***Viral***
Pneumococcal vaccine	**Viral vector vaccine**
Haemophilus influenzae type b (Hib) vaccine	Covishield vaccine (COVID-19)
Combined vaccine	
DPT vaccine (Diphtheria, pertussis and tetanus)	Mumps, measles, rubella (MMR) vaccine
Pentavalent vaccine (DPT + Hib + Hepatitis B)	
Note: Details about individual vaccine is discussed in the respective chapters.	

Exception is oral polio vaccine (OPV) which is given as multiple doses at spaced intervals to achieve effective immunity

- **Risk of gaining the virulence:** The attenuation of the live vaccine has to be done in an effective way otherwise there is always a risk of gaining the virulence back
- **Storage:** Live vaccines must be stored cautiously to retain effectiveness, especially the OPV and measles vaccine.

Inactivated or Killed Vaccine

It consists of organisms, which are grown in culture under controlled conditions and then killed using methods, such as heat or formaldehyde.

- They are generally safer but less efficacious than live vaccines
- Compared to the live vaccines, killed vaccines require large doses, adjuvants, and multiple doses to confer immunity. In most cases, a booster dose is also needed
- Adjuvants increase the immunogenicity of the vaccine antigen (e.g. alum is used as adjuvant in DPT vaccine)
- Killed vaccines are usually administered in subcutaneous or intramuscular routes. The only absolute contraindication is a severe local or general reaction to the previous dose.

Various characteristics of killed and live vaccines are given in **Table 11.2**.

Toxoid Vaccine

The exotoxins produced by certain bacteria can be detoxicated to form toxoid by treating with acidic pH, formalin or by prolonged storage.

- Toxoid is a form of toxin that loses its virulence property but retains immunogenicity
- When a toxoid preparation is given as vaccine, it induces formation of neutralizing antibodies that are capable of neutralizing the toxin moiety produced during an infection; rather than acting upon the organism
- Examples include diphtheria toxoid (from *Corynebac-terium diphtheriae)* and tetanus toxoid (from *Clostridium tetani)*.

Extracted or Cellular Fractions Vaccine

Vaccines, in certain instances, are prepared from extracted cellular fractions; examples include meningococcal vaccine, pneumococcal vaccine and *Haemophilus influenzae* type b vaccine—all are prepared from the capsular polysaccharide antigens of the respective organism.

Table 11.2. Characteristics of killed and live vaccines.

Characteristics	*Killed vaccine*	*Live vaccine*
Number of doses	Multiple	Single*
Need for adjuvant	Yes	No
Duration of immunity	Shorter	Longer
Effectiveness of protection	Lower	Greater
Mimics natural infection	Less closely	More closely
Immunoglobulins produced	IgG	IgA and IgG
Mucosal immunity	Absent	Induced
Cell-mediated immunity	Poor	Induced
Reverts back to virulent form	No	Possible
Stability at room temperature	High	Low
Immunodeficiency and pregnancy	Safe	Unsafe
*Exception is oral polio vaccine (OPV), which is given as multiple doses at spaced intervals to achieve effective immunity.		

Subunit Vaccines

For certain viruses, only a particular subunit of the virus is necessary to initiate the immunity, e.g. hepatitis B surface antigen (HBsAg) is the immunogenic component of hepatitis B virus. So, this viral component alone can be used as vaccine rather than the whole virus.

- Examples of subunit vaccines include hepatitis B vaccine and human papillomavirus (HPV) vaccine
- DNA recombinant technology is used for the preparation of such sub-viral components.

Combinations

If more than one immunizing agents are included in a vaccine preparation, it is called combined vaccine. The aim of the combined vaccine is to—

- Simplify administration and
- Augment the immunogenicity of the immunogen. For example, in DPT vaccine, the pertussis component acts as an adjuvant, which increases the immunogenicity of both diphtheria toxoid and tetanus toxoid.

Newer Vaccine Approaches

DNA or RNA Vaccine

DNA or RNA vaccines have recently been marketed. They have many advantages such as cost effectiveness and mounting a stronger and wider range of immune response.

The small pieces of DNA or RNA containing genes from the pathogenic microorganism are injected into the host. The gene of interest gets integrated with the host cell genome and starts transcribing the proteins against which the host mounts an immune response. The classical examples are COVID-19 vaccines such as Moderna or Pfizer vaccines.

Viral Vector Vaccines

The classical example is Covishield vaccine for COVID-19. These vaccines use a safe virus (e.g., Adenovirus) to encode the desired gene (e.g. S gene). Such vaccine when injected cannot cause disease but serves as a platform to produce proteins (e.g. spike proteins) that will stimulate the host immune system.

Cold Chain

"Cold chain" refers to a system of transport, storage, and handling of vaccines, starting at the manufacturer level and ending with the site of administration of the vaccine to the client. The optimum temperature for refrigerated vaccines is between +2°C and +8°C. For frozen vaccines the optimum temperature is –15°C or lower. In addition, protection from light is a necessary condition for some vaccines. Improper cold chain maintenance is one of the most common causes of vaccine failure; especially oral polio vaccine which is the most sensitive vaccine to heat; must be stored at –20°C.

- Vaccines which must be stored in the freezer compartment are polio and measles vaccines
- Vaccines which must be stored in the COLD part but never allowed to freeze are—DPT, TT, Td, BCG, hepatitis B, *H. influenzae* type b and diluents.

Vaccine Vial Monitor

Vaccine vial monitor is a tool to monitor the stability/potency of a vaccine and to check the efficiency of cold chain.

It is heat sensitive label lining the vaccine vial. It contains an outer blue circle and an inner white square. With time and exposure to higher temperature, the inner square changes its color gradually from white towards blue, whereas the outer circle is not heat sensitive; it remains blue throughout **(Table 11.3 and Fig. 11.1)**.

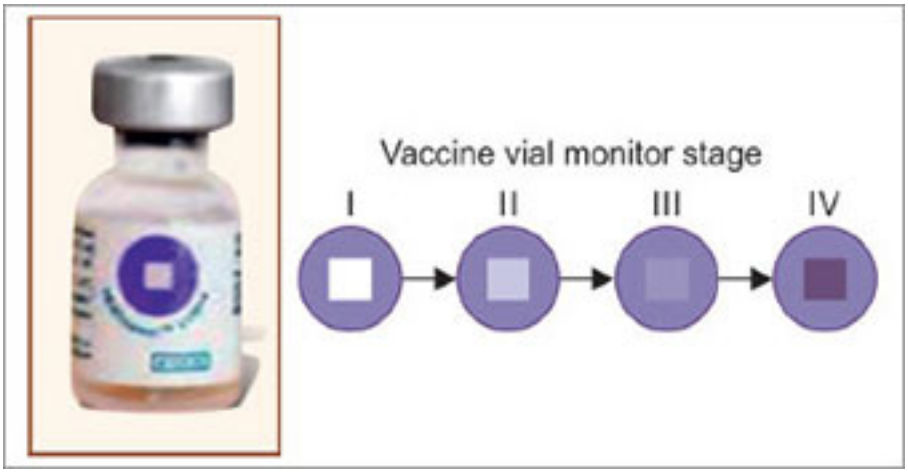
NATIONAL IMMUNIZATION SCHEDULE (NIS)

Immunization is one of the most logical and cost effective strategies of any country for the prevention of childhood sicknesses and disabilities and is thus a basic need for all children. The following is the national immunization schedule recommended by the Ministry of Health, Government of India and it includes those vaccines that are given free of cost to all children of our country *(Table 11.4)*.

Table 11.3. Staging of vaccine vial monitor.

	Inner square	***Outer circle***	***Vaccine***
Stage 1	White	Blue	Can be used
Stage 2	Light blue	Blue	Can be used
Stage 3	Blue	Blue	Discard
Stage 4	Dark blue	Blue	Discard

Fig. 11.1. Various stages of vaccine vial monitor (Vaccine is usable up to stages I and II and should be discarded for stages III and IV)



Source: Pondicherry Institute of Medical Sciences, Puducherry *(with permission).*

PASSIVE IMMUNOPROPHYLAXIS (IMMUNOGLOBULINS)

Passive immunoprophylaxis is given in the form of commercially available ready made *immunoglobulins* prepared against the pathogenic microorganism. Unlike vaccines, immunoglobulins act faster, without involvement of host immune apparatus.

Passive immunization is useful in the following circumstances:

- For immunocompromised individuals who cannot synthesize antibodies
- For post-exposure prophylaxis to achieve an immediate effect.

For the treatment of toxin mediated diseases to ameliorate the effect of toxin. Antibiotics cannot neutralize the toxin; hence, they cannot be used for the treatment of toxin mediated diseases.

Passive immunoprophylaxis available against various microbial diseases is given in **Table 11.5**.

Table 11.4. National Immunization Schedule (NIS) for infants, children and pregnant women.

Vaccine	***When to give***	***Maximum age***	***Dose***	***Dilution***	***Route***	***Site***
For pregnant women						
TT/Td-1	Early in pregnancy	<36 weeks of pregnancy (if missed, can be given later)	0.5 mL	No	IM	Upper arm
TT/Td-2	4 weeks after TT/Td-1*		0.5 mL	No	IM	Upper arm
TT/Td-Booster	If received 2 TT/Td doses in a pregnancy within the last 3 years*		0.5 mL	No	IM	Upper arm

Vaccine	***When to give***	***Maximum age***	***Dose***	***Dilution***	***Route***	***Site***
For infants						
BCG	At birth or as early as possible	Till 1 year	0.05 mL (0.1 mL for >1 month)	Saline	ID	Left upper arm
Hepatitis B - Birth dose	At birth or as early as possible	Within 24 hour	0.5 mL	No	IM	Anterolateral side of mid-thigh
OPV-0	At birth or as early as possible	Within first 15 days	2 drops	No	Oral	Oral
OPV 1, 2 and 3	At 6 weeks, 10 weeks and 14 weeks	5 years of age	2 drops	No	Oral	Oral
Pentavalent[#] 1, 2 and 3	At 6 weeks, 10 weeks and 14 weeks	1 year of age	0.5 mL	No	IM	Anterolateral side of mid-thigh
PCV[^] (3 doses)	At 6 weeks and 14 weeks, booster at 9-12 months	–	0.5 mL	–	IM	Anterolateral side of mid-thigh
Rotavirus[##]	At 6 weeks, 10 weeks and 14 weeks	1 year of age	5 drops	No	Oral	Oral
IPV	Two fractional doses at 6 and 14 weeks of age	1 year of age	0.1 mL	No	ID	Right upper arm
Measles /MR 1st Dose	9 completed months–12 months	5 years of age (only measles vaccine)	0.5 mL	Sterile water	SC	Right upper arm
JE - 1**	9 completed months–12 months	15 years of age	0.5 mL	Phosphate buffer	SC	Left upper arm
Vitamin A (1st dose)	At 9 completed months, given along MR vaccine	5 years of age	1 mL (1 lakh IU)	No	Oral	Oral
For Children						
DPT booster-1	16–24 months	7 years of age	0.5 mL	No	IM	Anterolateral side of mid-thigh
MR 2nd dose[$]	16–24 months	5 years of age	0.5 mL	Sterile water	SC	Right upper arm
OPV Booster	16–24 months	5 years of age	2 drops	No	Oral	Oral

Vaccine	*When to give*	*Maximum age*	*Dose*	*Dilution*	*Route*	*Site*
JE-2	16–24 months	–	0.5 mL	Phosphate buffer	SC	Left upper arm
Vitamin A*** (2nd to 9th dose)	16–18 months. Then one dose every 6 months up to the age of 5 years	5 years of age	2 mL (2 lakh IU)	No	Oral	Oral
DPT Booster-2	5–6 years	7 years of age	0.5 mL	No	IM	Upper arm
TT/Td	10 years and 16 years		0.5 mL	No	IM	Upper arm

**TT/Td:* Tetanus toxoid (TT) is given alone, or in combination with adult diphtheria toxoid (Td). The second or booster dose is ideally given before 36 weeks of pregnancy, but should be given even if presented late in pregnancy or during labor.

***JE Vaccine* is introduced in selected endemic districts after the campaign: UP, Bihar, Assam, West Bengal and Karnataka.

*** The 2nd to 9th doses of Vitamin A can be administered to children 1–5 years old during biannual rounds, in collaboration with ICDS (Integrated Child Development Services).

#*Pentavalent* vaccine- contains combination of DPT, hepatitis B and *H.influenzae* type b vaccines.

Interval between two doses of pentavalent vaccine or OPV should never be less than 1 month.

##*Rotavirus vaccine:* Given in selected states such as Andhra Pradesh, Assam, Haryana, Himachal Pradesh, Jharkhand, Madhya Pradesh, Odisha, Rajasthan, Tamil Nadu, Tripura and Uttar Pradesh.

^*Pneumococcal conjugate vaccine (PCV):* Given in selected states such as Bihar, Himachal Pradesh, Madhya Pradesh, Uttar Pradesh (12 districts) & Rajasthan (9 districts).

Children who have not been received a single vaccine coming after 1 year: Will be given 3 doses of DPT at an interval of 4 weeks; Measles-1st dose, JE-1st dose (wherever applicable) up to 2 years of age.

Abbreviations: IM, intramuscular; SC, subcutaneous; ID, intradermal; TT/Td, Tetanus and adult diphtheria toxoid; BCG, Bacillus Calmette-Guerin; PCV, Pneumococcal conjugate vaccine.

Table 11.5. Passive immunoprophylaxis.

Immunoglobulin preparations	*Source*	*Indications*
Diphtheria antitoxin	Equine	Treatment of respiratory diphtheria
Tetanus immune globulin (TIG)	Equine, Human	Treatment of tetanus as PEP, for people not adequately immunized with tetanus toxoid
Botulinum antitoxin	Equine, Human	Treatment of botulism
Varicella-zoster immune globulin (VZIG)	Human	PEP for immunosuppressed contacts of acute cases or newborn contacts

Immunoglobulin preparations	***Source***	***Indications***
Rabies immunoglobulin (RIG)	Equine, Human	Treatment of rabies and PEP in people not previously immunized with rabies vaccine
Hepatitis B immunoglobulin (HBIG)	Human	PEP for percutaneous or mucosal or sexual exposure Newborn of mother with HBsAg +ve
Rubella	Human	Women exposed during early pregnancy
Measles	Human	Infants or immunosuppressed contacts of acute cases exposed <6 days previously
Abbreviation: PEP, post-exposure prophylaxis.		

EXPECTED QUESTIONS

1. I. Write short notes on:

1. Live vaccines vs. killed vaccines.
2. National Immunization Schedule.
3. Passive immunoprophylaxis.

2. II. Multiple Choice Questions (MCQs):

1. **All of the following are live attenuated vaccines,** *except:*
    a. MMR
    b. Yellow fever 17D
    c. Salk polio
    d. Sabin polio
2. **All the following vaccines are given at birth,** *except:*
    a. BCG
    b. Hepatitis B
    c. DPT
    d. OPV
3. **Example for subunit vaccine is:**
    a. *H. influenza* b vaccine
    b. Hepatitis B vaccine
    c. Meningococcal vaccine

d. Pertussis vaccine

4. **Vaccine administered intradermally is:**

a. MMR

b. DPT

c. BCG

d. Salk polio vaccine

Answers

1. c	**2.** c	**3.** b	**4.** c