

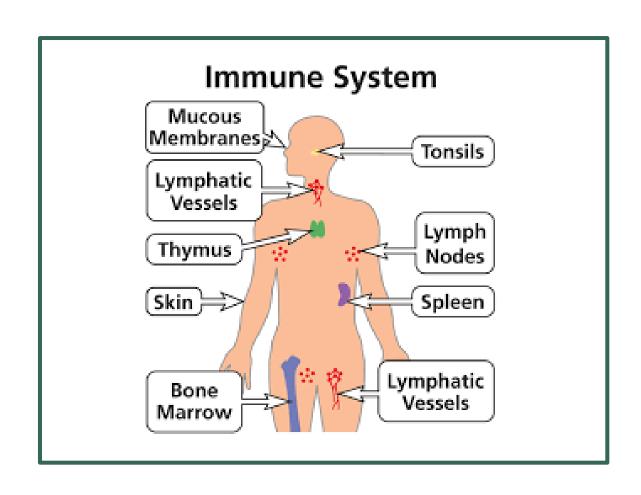
VACCINOLOGY

Dr Noreen Shah
Principal Lecturer
Dept Of C. Med

Learning Objectives

- At the end of this presentation the students shall be able to:
- Describe the importance of vaccination in the control of infectious diseases
- List the main types of vaccine with examples
- Describe difference between live attenuated and inactivated vaccines
- Describe the role of vaccines in preventing disease
- Differentiate between vaccination and immunization
- Describe Expanded Program of Immunization (EPI) of Pakistan
- Describe the factors responsible for failure of vaccination programs in Pakistan.

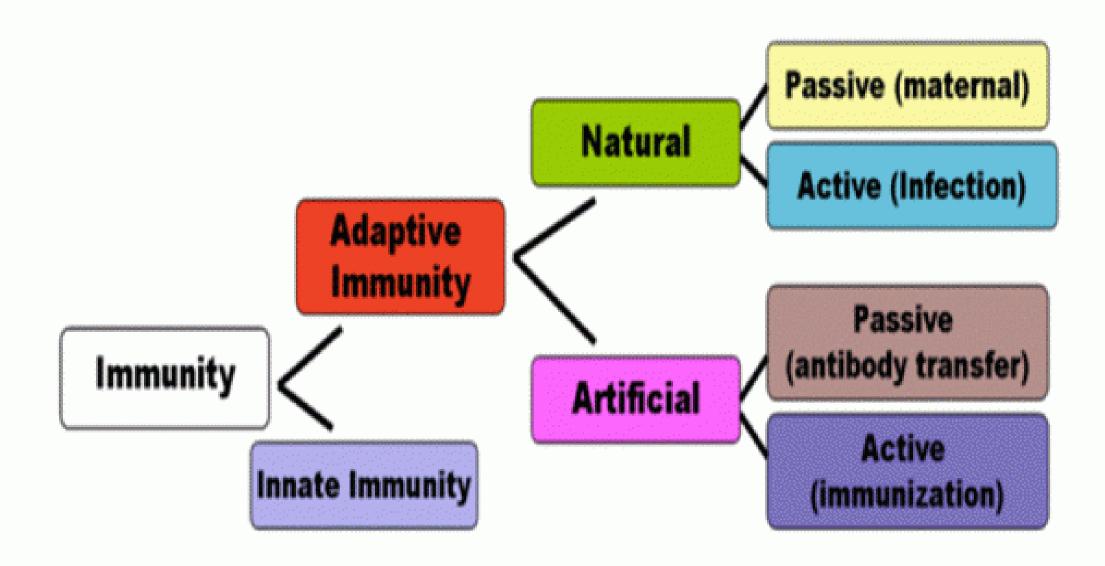
Define Immunity



The ability of an organism to resist a particular infection or toxin by the action of specific antibodies or sensitized white blood cells.

- The **immune system** is made up of different organs, cells, and proteins that work together.
- There are two main parts of the immune system:
- The **innate immune system**, with which we are born.
- The **adaptive immune system**, which develop when our body is exposed to microbes or chemicals released by microbes.

Immunity and its types



1. The Innate Immune System

- It is inherited and is active since birth.
- It refers to nonspecific defence mechanisms that come into play immediately or within hours of an antigen's appearance in the body.
- These mechanisms include physical barriers such as skin, chemicals in the blood, and immune system cells that attack foreign cells in the body.

INNATE IMMUNITY

Pathogenic invasion --> Bacteria

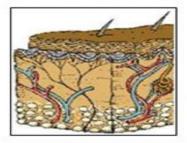


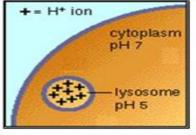


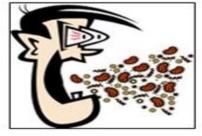




1st Line Defense









Skin

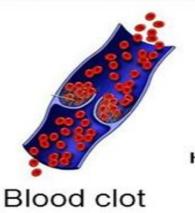
Ciliated cells

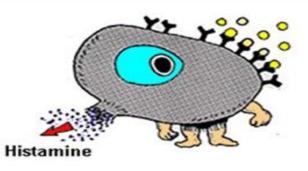
Lysozyme

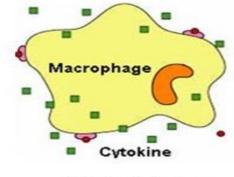
Coughing

Vomitting

2nd Line Defense













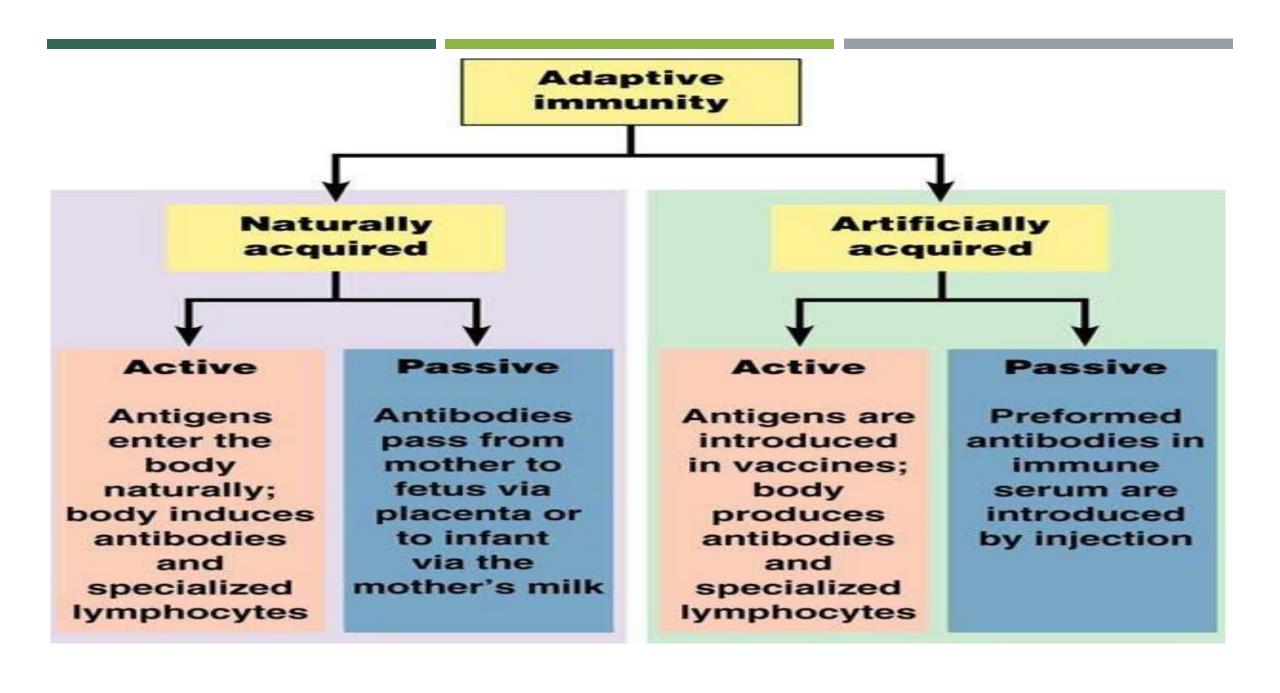
Mast cell

Cytokines

Leukocytes

2. Acquired/adaptive Immunity:

- It is the immunity which is developed later in life.
- E.g. if an individual is infected with chicken pox virus, he/she become resistant to same virus.
- Acquired immunity is provided by Antibodies and certain T-lymphocytes.
- These are specific to specific microorganism therefore acquired immunity is also known as Specific immunity.



Mechanism

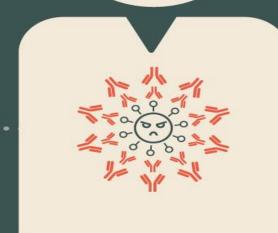
The vaccine
introduces an
inactivated/weakened
form of the
virus/bacteria
into the body

The body's immune system produces antibodies to defend against the virus/bacteria

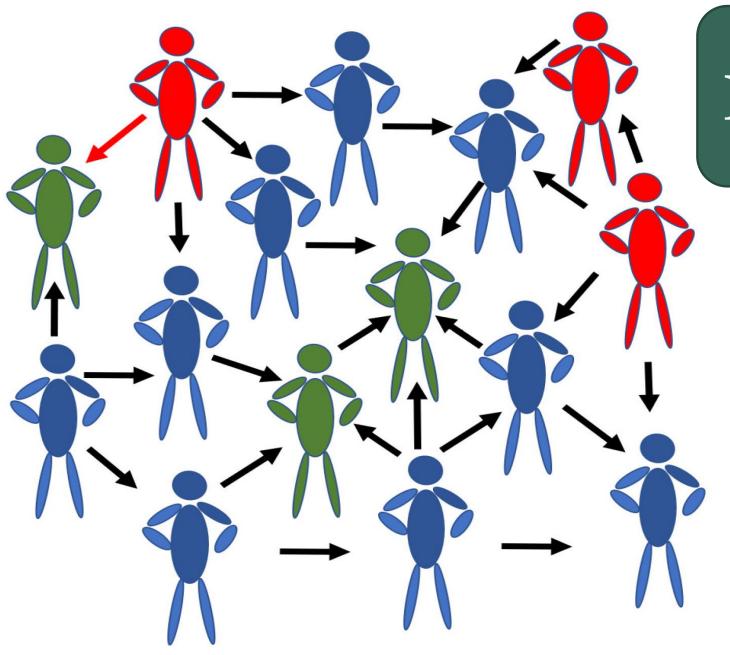


Vaccines
enhance your
body's natural
defenses,
without causing
illness





When the real active virus/bacteria enters the body, it is recognized by the defense system which may eliminate it



Herd immunity



COVID-19 POSITIVE



VACCINED OR IMMUNIZED



UNPROTECTED



NO VIRUS SPREADING



VIRUS SPREADING

- Herd immunity is a form of immunity that occurs when the vaccination of a significant portion of a population (or herd) provides a measure of protection for individuals who are not or cannot be immunized.
- This can effectively stop the spread of disease in the community.
- It is particularly crucial for protecting people who cannot be vaccinated.
- These include children who are too young to be vaccinated, people with immune system problems, and those who are too ill to receive vaccines (such as some cancer patients).

- The proportion of the population which must be immunised in order to achieve herd immunity varies for each disease but the underlying idea is simple: (once enough people are protected, they help to protect vulnerable members of their communities by reducing the spread of the disease).
- E.g. Herd immunity for measles is about 95% of people to be vaccinated
- However, when immunisation rates fall, herd immunity can break down leading to an increase in the number of new cases. For example, measles outbreaks Pakistan.

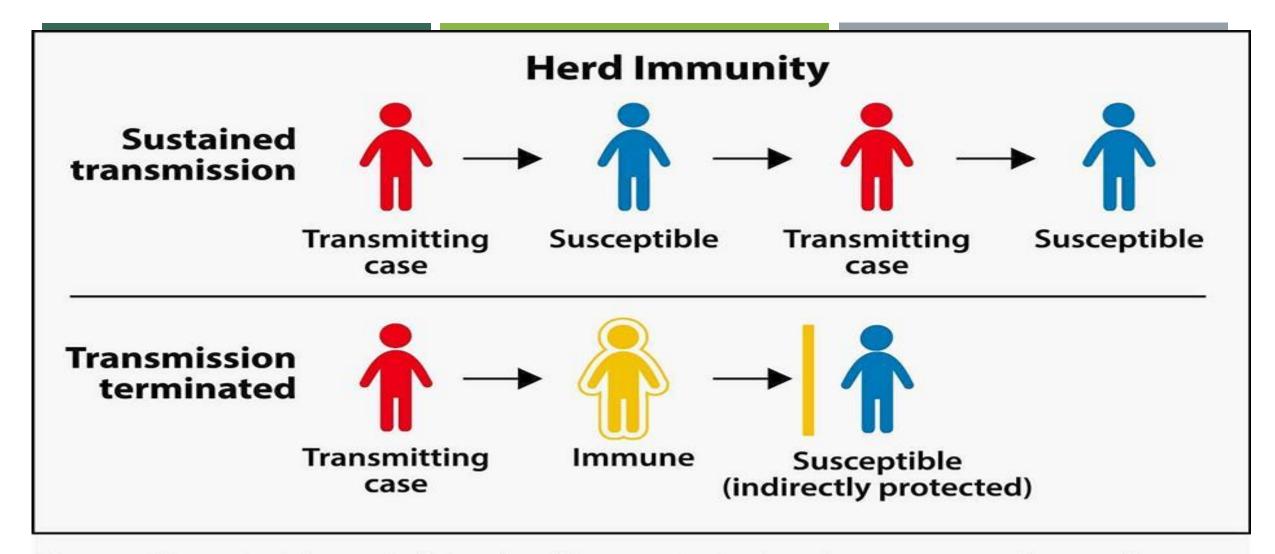
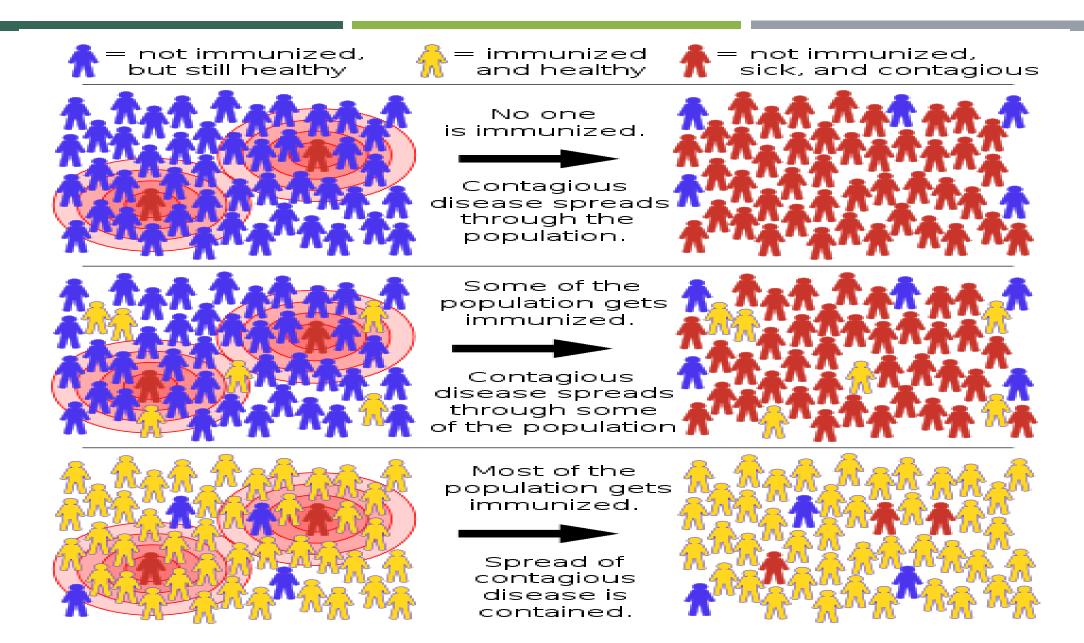


Figure - The principle underlying herd immunity is that the presence of enough immune persons in a community interrupts the transmisssion of an infectious agent, thereby providing indirect protection for unimmunized (or "susceptible") persons.



Q: Does herd immunity work for all diseases?

• No. Herd immunity only works for diseases that are spread directly between people (i.e. are 'contagious'), like measles. One example where it would not work is **tetanus**

Q: How many children need to be vaccinated for herd immunity to work?

This varies depending on the germ and how contagious it is.

Q; Why is it important that children are vaccinated if they can be protected through herd immunity?

• For many diseases children, particularly young children, are at the highest risk of the disease and also have the most severe illness. The best way to protect someone against a disease is to vaccinate them directly, rather than rely on 'indirect' protection through herd immunity.

NAME:

Directions \square

Pick out 2 circles and mark them red.

☐ Pick out 12 circles and mark them green.

 \square Mark the rest blue.

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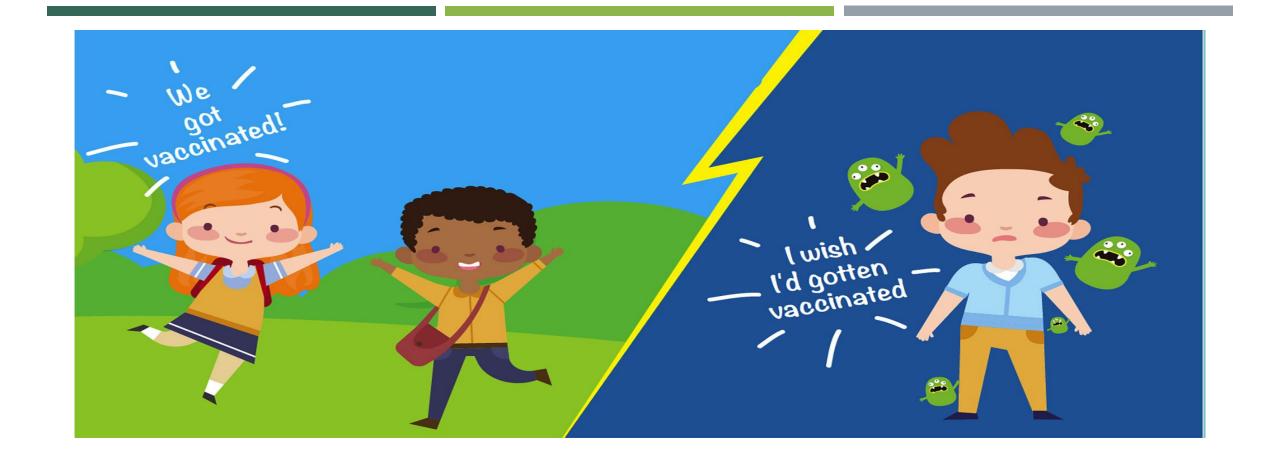
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- 1. What percentage of this population is vaccinated? Use a proportion to find out. 36/50 = n/100
- 2. What percentage of the group is unvaccinated? How can you find the answer?



Importance of vaccination in the control of infectious diseases:

- Vaccination is one of the most effective and cost efficient medical technology, resulting in the control, elimination or near elimination of numerous infectious diseases e.g. (small pox eliminated/polio is near for elimination)
- Vaccines also protects from serious illness and death
- It also prevent the outbreak of infectious diseases
- Saves between 2 3 million children's lives per year.
- Today vaccines are available to protect against at least 20 diseases
- However, one in five children still miss out on routine life-saving immunization.

- Vaccines are required throughout our lives to help protect against serious diseases.
- Vaccines have greatly reduced infectious diseases that once regularly harmed or killed many infants, children, and adults.
- Vaccination is important because it not only protects the person who gets the vaccine, but also helps to keep diseases from spreading to others, like family members, neighbours, classmates, and other members of your communities.
- Vaccine-preventable diseases have a costly impact, resulting in doctor's visits, hospitalizations, and premature deaths. Sick children can also cause parents to lose time from work.

List of Types of vaccines with examples

Live Attenuated (LAV)

Inactivated (Killed Antigen)

Subunit (Purified Antigen)

Toxoid (Inactivated Toxins)

RNA-Based

Tuberculosis
Oral polio
vaccine (OPV)
Measles
Rotavirus

Yellow fever

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

Haemophilius
influenzae
type B (Hib)

Pneumococcal
(PCV-7, PCV-10,
PCV-13)

Hepatitis B
(HepB)

Tetanus toxoid (TT) Diptheria toxoid Nonreplicating

In vivo selfreplicating

In vivo
dendritic cell
non-replicating

Approved vaccines according to WHO

Next-generation vaccines

Lubrizol Life Science Health

Vaccine And Its Types:

- A substance used to stimulate the production of antibodies and provide immunity against one or several diseases. Prepared from the causative agent of a disease, its products, or a synthetic substitute.
- Treated to act as an antigen without inducing the disease.
- There are 5 main types of vaccines.



1. Live Attenuated Vaccines:

- Weakened form of the germ that causes a disease.
- Create a strong and long-lasting immune response.
- 1 or 2 doses of most live vaccines give a lifetime protection.

Limitations:

- As these are live vaccines cannot be given to immunocompromised people.
- Rare risk of reversion to a virulent strain of germ.
- They need to be kept cool.

EXAMPLES:

- i. Oral Polio Vaccine (OPV)
- ii. Measles
- iii. Typhoid oral
- iv. Measles, Mumps, Rubella (MMR)
- v. Yellow fever
- vi. Hepatitis A
- vii. Rota virus
- viii. Intranasal influenza
- ix. Typhus







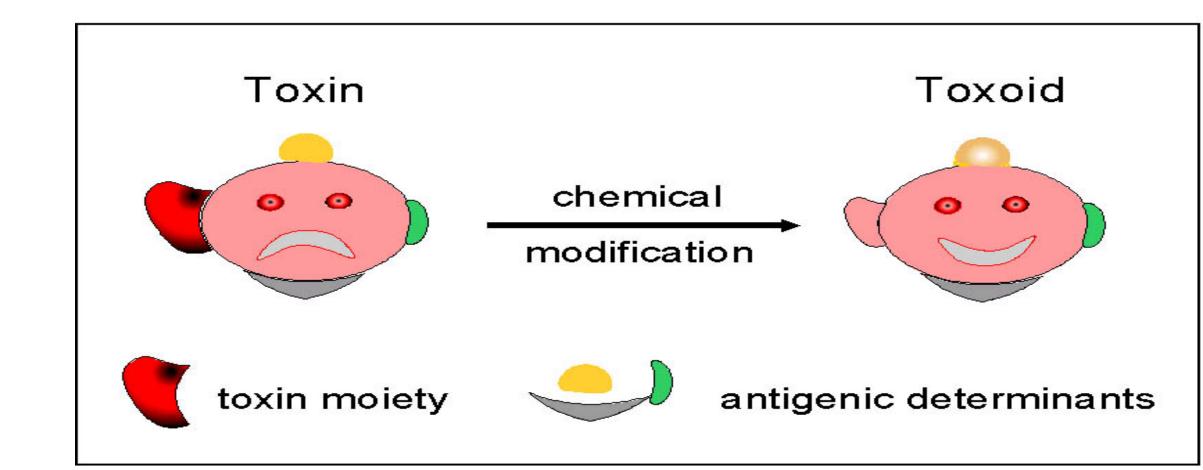
2. Inactivated Vaccines

- Are the killed version of the germ that causes a disease.
- Usually do not provide immunity (protection) as strong as live vaccines.
- So several doses may be needed over time (booster shots) in order to get ongoing immunity against diseases.
- Examples: Inactivated vaccines are used to protect against: Hepatitis A, Flu (shot only), Polio (shot only), Rabies

3. Toxoid Vaccines

- Toxoid vaccines use a toxin (harmful product) made by the germ that causes a disease.
- They create immunity to the parts of the germ that cause a disease instead of the germ itself.
- That means the immune response is targeted to the toxin instead of the whole germ.
- Limitations: booster shots are needed
- E.g. Diphtheria, Tetanus

Modification of Toxin to Toxoid



4. Subunit vaccines

- As compared to a whole-pathogen vaccine approach, a subunit vaccine will only include certain components that originate from disease-causing bacteria, parasites, or viruses.
- These components (antigens) are highly purified proteins or synthetic peptides that are considered to be significantly safer than whole-pathogen vaccines.
- There are three types of subunit vaccines
- Protein based
- Polysaccharide
- Conjugate vaccines

A. Protein-based subunit /recombinant vaccines:

- > Protein based subunit vaccines present an antigen to the immune system without viral particles, using a specific, isolated protein of the pathogen.
- > A weakness of this technique is that isolated proteins, if denatured, may bind to different antibodies than the protein of the pathogen.
- **Examples:** A cellular pertussis (aP), Hepatitis B

B. Polysaccharide vaccines:

- These vaccines contain chains of sugar molecules (polysaccharides) found in the cell walls of some bacteria.
- Not be effective in infants and young children
- Induce only short-term immunity
- Examples: Pneumococcal, Meningococcal and Salmonella Typhi

C. Conjugate subunit vaccines

- In comparison to plain polysaccharide vaccines, they benefit from a technology that binds the polysaccharide to a carrier protein that can induce a long-term protective response even in infants. bind a polysaccharide chain to a carrier protein to try and boost the immune response.
- Example: Homophiles influenza type b (Hib) and Pneumococcal conjugate vaccines

5. Nucleic acid vaccines



- Use genetic material either RNA or DNA
- When this material gets into human cells, it uses cells' protein to make the antigen that will trigger an immune response.
- Advantages: Easy to make, and cheap.
- As antigen is in large quantities, so the immune reaction is strong.
- RNA vaccines need to be kept at ultra-cold temperatures, -70 C or lower. Moderna vaccine is stored at minus 20° C
- Challenges low- and middle-income countries that do not have specialised cold storage equipment.

6. Combination vaccines

Combination vaccines consist of two
 or more vaccines in the same preparation.



- This approach has been used for over 50 years in many vaccines e.g. Pentavelant, Hexavalent and MMR.
- Combination products simplify vaccine administration and allow for the introduction of new vaccines without requiring additional health clinic visit and injections.

Advantages of combination vaccines:

- Reduce the cost of stocking and administering
- Reduce cost of extra health care visits
- Improve timeliness of vaccination (some parents and health-care providers object to administering more than two or three injectable vaccines during a single visit because of a child's fear of needles and pain, and because of concerns regarding safety)
- Facilitate addition of new vaccines into immunization programs.

COMMON COMPONENTS OF VACCINES

Active components

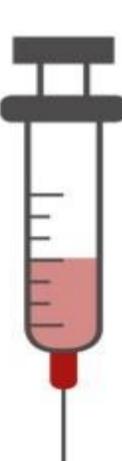
- Antigen
 - Virus, Bacteria, Toxin

Adjuvants

- Enhance immune response to vaccine
 - Aluminum

Antibiotics

- Prevent bacterial contamination
 - Neomycin, Gentamycin
 Polymycin B



Preservatives

Prevent contamination
 e.g., repeated puncture of
 a multi-dose vaccine vial
 - Magnesium, Thimerosal

Stabilizers

- Protect the vaccine from adverse conditions such as the freeze-drying process
 - Sugar : Lactose, Sucrose
 - Amino acid : Glycine
 - Protein : Gelatin, Albumin

Trace components

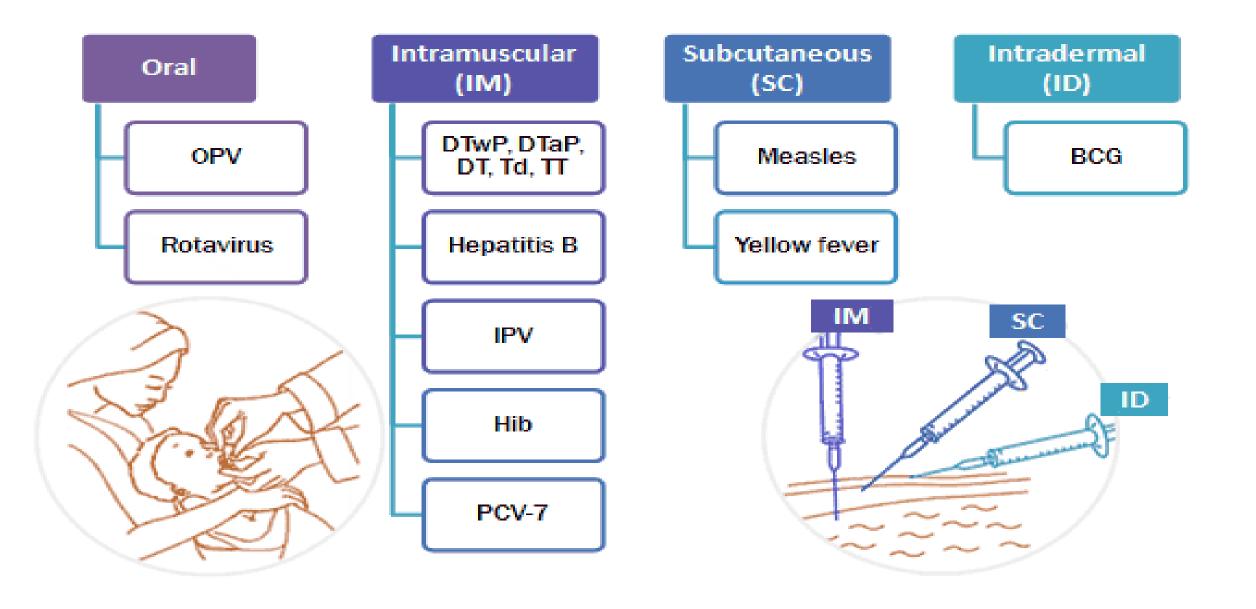
 Left over from vaccine production process
 Formaldehyde

Quiz

- A pregnant woman passes antibodies to her unborn baby through the placenta to protect against certain diseases. About how long does this natural immunity last after birth?
- A. 1 year
- B. 2 years
- C. 5 years
- Bacterial meningitis strikes babies more often than any other age group. Which vaccine will help prevent one previously common type of meningitis?
- A. Tetanus
- B. Hib
- C. HIV
- D. Varicella

- Which diseases do the combined DTPa vaccines cover?
- A. Diphtheria, Tuberculosis And Polio
- B. Diphtheria, Tetanus And Polio
- C. Diphtheria, Tetanus And Pertussis
- D. Diphtheria, Tetanus And Pneumococcal Disease
- E. Diphtheria, Tuberculosis And Pneumococcal Disease
- Vaccine against viruses are usually:
- A. Given at birth
- B. Expansive
- C. Either live attenuated or killed
- D. Mainly polysaccrides

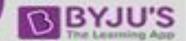
Routes of administration of different vaccines



Describe difference between live attenuated and inactivated vaccines

	Features	Live Attenuated Vaccines	Killed Vaccines
1	Agent used	Live attenuated organism	Killed organism
2	Immune response	High	Low
3	Duration	Antibodies persists for long time	Short time
4	Booster Immunization	Booster not needed	Boosters needed frequently
5	Adjuvant	Not required	Required
6	Cold chain	Required	Not required
7	Cost	Cheap	Costly
8	Safety	Chance of reversal	Safe
9	Production	Easy to produce	Difficult to produce

DIFFERENCE BETWEEN VACCINATION AND IMMUNIZATION





VACCINATION

VACCINATION IS THE ADMINISTRATION OF ANTIGENIC MATERIAL (A VACCINE) TO STIMULATE AN INDIVIDUAL'S IMMUNE SYSTEM TO DEVELOP ADAPTIVE IMMUNITY TO A PATHOGEN.



IMMUNIZATION

IMMUNIZATION IS THE PROCESS WHEREBY A PERSON IS MADE IMMUNE OR RESISTANT TO AN INFECTIOUS DISEASE, TYPICALLY BY THE ADMINISTRATION OF A VACCINE.





The Expanded Program On Immunization (EPI)

Objectives of EPI

- To affirm the commitment of the Government of Pakistan to provide safe, effective and costeffective vaccination against vaccine preventable diseases
- To set national standards and guidelines for immunization aligned with the global goals and evidence base
- To encourage the generation of local evidence for vaccination against vaccine preventable diseases
- To increase equitable coverage of immunization services against vaccine preventable diseases
- To decrease vaccine preventable diseases associated morbidity and mortality
- To improve immunization services through expansion of service delivery and cold chain

- The Expanded Programme on Immunization (EPI) was launched in Pakistan in 1974
- The Aim was to protect children by immunizing them against childhood tuberculosis, poliomyelitis, diphtheria, pertussis, tetanus and measles.
- Later, with the support of development partners, a number of new vaccines e.g. hepatitis B, haemophilus influenzae type b (Hib) and pneumococcal vaccine (PCV10) were introduced in 2002, 2009 and 2012, and inactivated polio vaccine in 2015, respectively.
- Rotavirus vaccine was introduced in 2017 prevent against fatal diarrhoea due to rotavirus.

- The Pakistan EPI programme has adopted its goals and strategies in accordance with priorities set at the global and regional level.
- EPI was launched in Pakistan in 1978 to protect children by immunizing them against childhood tuberculosis, poliomyelitis, diphtheria, pertussis, tetanus and measles.
- It also aims to protect mothers and new-born against tetanus.
- Later hepatitis B, haemophilis influenza type b (Hib) and pneumococcal vaccine
 (PCV10) were introduced in 2002, 2009 and 2012, respectively.
- Inactivated polio vaccine (IPV) was added in 2015.

- Rotavirus vaccine was introduced in 2017in EPI schedule.
- A child needs only 5 visits during the first year and one visit during the second year of life to complete the vaccination with 6 visits against 9 dreadful diseases.
- The National Immunization Technical Advisory Group (NITAG), was established in 2008, by the Ministry of Health in accordance with WHO guidelines.

- A programme policy document was developed in 2015 with the support of partners.
- The document lays out policy direction and guidelines for involvement of lady health workers and private sector in immunization service delivery.
- The key goal of new immunization policy **Pakistan's Vision 2025** is to reduce infant mortality rate from 74 to less than 40/1000 births & reduce maternal mortality rate from 276 to less than 140/1000 births and continue reducing the infant mortality rate through immunization targets and activities in order to achieve **SDG 3**



1994
National Polio Immunization Days

2009

Pentavalent vaccine introduced

2015
Inactivated Polio Vaccine (IPV)

1976

Pilot project with 6 basic antigens (BCG, Measles, Diphtheria, Pertussis, Tetanus and Polio)



1981

Activities intensified



2002

Hepatitis B vaccine introduced



2012

Pneumococcal vaccine (PCV10)



2017

Rotavirus Vaccine



Diseases covered by EPI

- 1. Poliomyelitis
- 2. Childhood Tuberculosis
- 3. Neonatal Tetanus
- 4. Diphtheria
- 5. Pertussis (Whooping Cough)
- 6. Hepatitis-B
- 7. Haemophilus influenzae type b
- 8. Measles
- 9. Rota virus diarrhoea

Penta valent Vaccine

Vaccine	No. of doses	Administration site	Age	Dose/ time	Storage temp
BCG	1	Vaccine is given intradermal on right deltoid	Soon after birth	o.o5ml At birth	+ 2 to +8 ° C
OPV	4	Orally	1 st soon after birth 2 nd 4 wks. 3 rd 10 wks. 4 th 14 wks.	4 doses 1 st year of life	- 15 to - 25 °C at federal level + 2 to + 8 ° C at district level
Pentavelan t + Pneumococ cal	3	Deep IM at anterolateral aspect right thigh	1 st 6 wks. 2 nd 10 wks. 3 rd 14 wks.	o.5 ml	+ 2 to + 8 °C

Vaccine	No. of doses	Administration site	Dose	Dose/ time	Storage temp
Measles	2	Subcutaneous	9 month 15 month	o.5 ml	+2 to +8 °C
Hepatitis B	3	Deep IM – anterolateral aspect of left thigh	1 st 6 wks. 2 nd 10 wks. 3 rd 14 wks.	o.5 ml	+2 to +8 °C
Rota virus	2	Orally – least 4 wks. apart		1 ml	+2 to +8 °C
IPV	1	Deep IM at anterolateral aspect of left thigh	14 wks.	o.5 ml	+2 to +8 °C

Dose of Td (according to card or history)	When to give	Expected duration of protection	
Td1	At first contact or as early as possible in pregnancy	None	
Td2	At least 4 weeks after Td1	1 - 3 years	
Td3	At least 6 months after Td2 or during subsequent pregnancy	At least 5 years	
Td4	At least one year after Td3 or during subsequent pregnancy	At least 10 years	
Td5	At least one year after Td4 or during subsequent pregnancy	For all childbearing years and possibly longer	

New immunization schedule

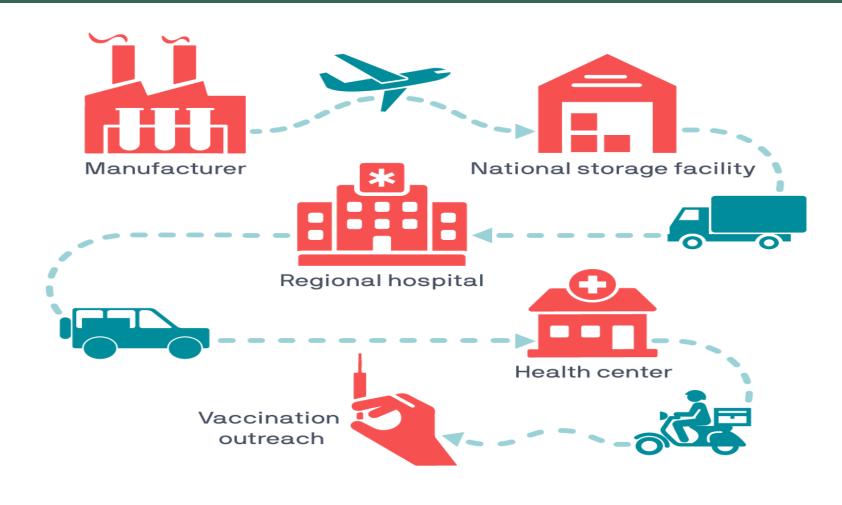
Disease	Cause of Infection	Vaccine	Doses	Age of administration	
Childhood TB	Bacteria	BCG	1	Soon atter birth	
Poliom yelitis	Virus	OPV	4	OPV0:soon after birth OPV1:6 wks OPV2:10 wks OPV3:14 wks	
Diphtheria	Bacteria				
Tetanus	Bacteria	Pentavalent		Penta1:6 wks Penta2:10 wks Penta3:14 wks	
Pertussis	Bacteria	vaccine	3		
Hepatitis B	Virus	(DTP+HepB+ Hib)			
Hib pneum onia and meningitis	Bacteria	~,			
Pineumionia and mieningitisidue to S. pheumoniae	Bacteria	Pinumiococcal conjugate vaccine (PICV10)	3	Pneumo1:6 wks Pneumo2:10 wks Pneumo3:14 wks	
Measles	Virus	Measles	2	Measles1:09 months Measles2:15 months	
Diarrhea	Virus	Diarrhoea	2	Rota 1: 6 /2 : 10 weeks	



COLD CHAIN

- Vaccines are sensitive biological products that may become less effective or destroyed, when exposed to temperatures outside the recommended range.
- Cold chain refers to the process used to maintain optimal conditions during the transport, storage, and handling of vaccines.
- Starting at the manufacturer and ending with the administration of the vaccine to the client.
- The optimum temperature for refrigerated vaccines is between +2°C and +8°C.

Cold chain



Temperature monitoring devices

- 1. Cold Rooms and Freezer Rooms
- 2. Refrigerators and Freezers: Data loggers and dial thermometers
- 3. Transportation in Cold Boxes and Vaccine Carriers
- 4. Electronic freeze indicators
- 5. Cold Chain Monitor
- 6. Vaccine Vial Monitor
- 7. Electronic Shipping Indicator.

Cold room

Cold boxes





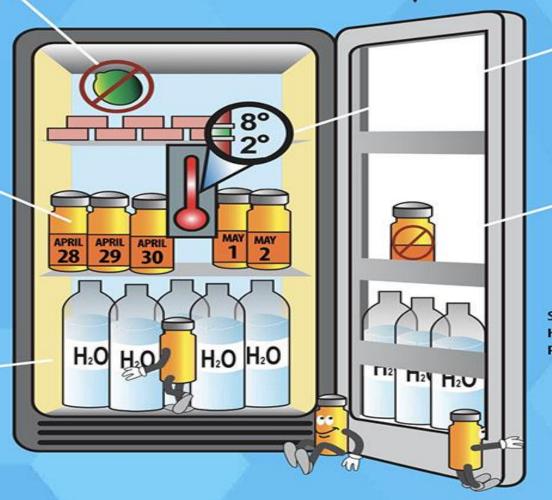
Store only vaccine in refrigerator

Stock vaccine according to expiry date.
"First to expire, first out."

Never leave vaccine outside the refrigerator

Store full bottles of water on empty shelves and in the door

Check and log temperature twice a day



Open the door only when necessary

√ Keep

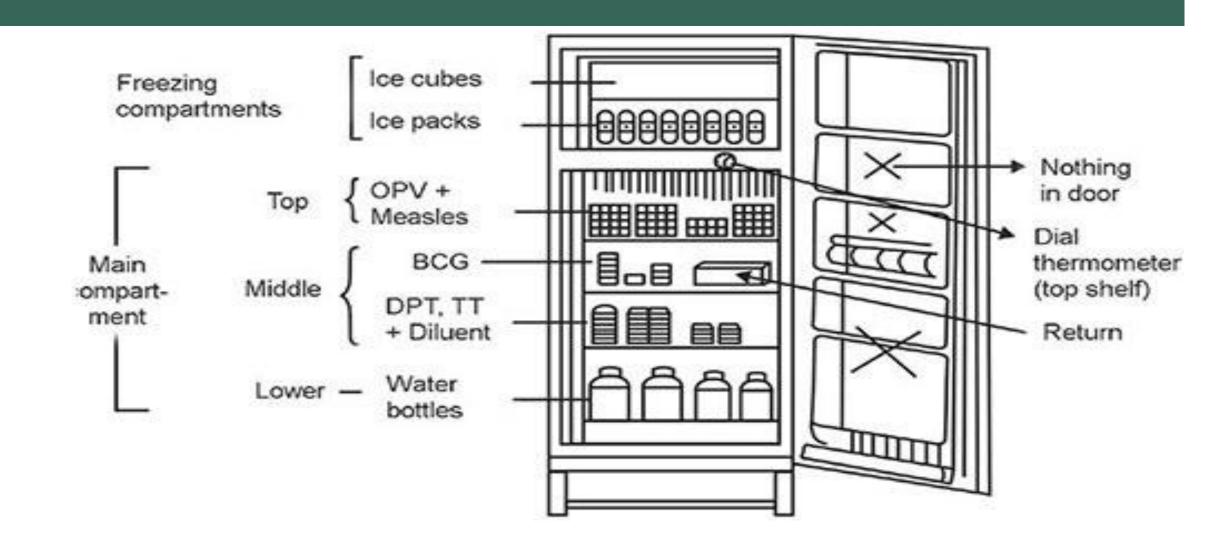
vaccines at

+2°C to +8°C

Don't store vaccine on the door shelves

Source: National Vaccine Storage and Handling Guidelines for Immunization Providers 2007

EPI vaccines are placed in different compartments of refrigerator



Sensitivity of vaccines to heat and freezing

- Vaccines Are Grouped Into Six Categories
- The most heat sensitive vaccines are in group A and the least sensitive in group F.
- Group A: OPV
- **Group B:** Influenza
- Group C: IPV, Measles/ Measles-rubella/ Measles-mumps-rubella (Freeze-dried)
- **Group D:** Cholera, Hexavalent, Pentavalent, Hib (Liquid) Measles (Freeze-dried) Rotavirus (Liquid And Freeze-dried) Rubella (Freeze-dried) **Group E:** BCG, Tetanus, TD, Td
- **Group F:** Hepatitis B Hib (Freeze-dried), Meningococcal A, Pneumococcal

Sensitivity to freezing

Sensitivity to light

- Cholera
- Hexavalent
- Pentavalent
- Hepatitis B
- Hib (liquid)
- Inactivated poliovirus (IPV)
- Influenza
- Pneumococcal
- Rotavirus Tetanus, DT, Td

- Vaccines that are as sensitive to light as they are to heat include
- BCG
- Measles
- Measles-rubella
- Measles-mumps-rubella
- Rubella

EFFECTIVE COLD CHAIN

Three main elements combine to ensure proper vaccine transport, storage, and handling.

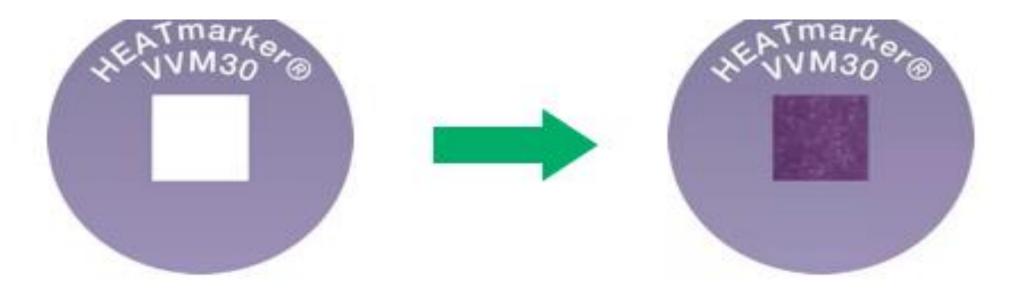
Trained personnel

Transport and storage equipment Efficient management procedures

Electronic freezer/fridge indicator



- These are irreversible temperature indicators that shows if a vaccine has been exposed to freezing temperatures.
- It consists of an electronic temperature measuring circuit and LCD-display.
- If the vaccine is exposed to a temperature below 0.5° C ± 0.5° C for more than 60min the display will change from the "OK" status symbol (\checkmark) into the "ALARM" status symbol (x).
- A small blinking dot in the right-hand corner of the LCD-display indicates that the device is functioning.



Before heat exposure

After excessive heat exposure

Vaccine Vail Monitor

- Vaccine Vail Monitor (VVM) is a thermo chromic label on vials containing vaccines.
- It gives visual indication of whether the vaccines has been kept at a temperature which preserves its potency.
- The vials are designed in response to problem of delivering vaccines to developing countries where.
- i. Cold chain is difficult to preserve and,
- ii. Vaccines became inactive and denatured by exposure to ambient temperatures.

How to read a VVM



Inner square is lighter than outer circle.

If the expiry date has not been passed,

USE the vaccine.



At a later time, inner square is lighter than outer circle. If the expiry date has not been passed, USE the vaccine.



Discard point:

Inner square matches colour of outer circle.

DO NOT use the vaccine.

Inform your supervisor.



Beyond the discard point:

Inner square darker than outer circle.

DO NOT use the vaccine.

Inform your supervisor.



Failure of Vaccination Programs in Pakistan



with all precautionary protocols in place for your & your child's safety, especially during COVID-19 pandemic





- Immunization is one of the most successful public health initiatives in recent times. It is, therefore, worrying to learn the level of under-vaccination in Pakistan.
- Diseases that have been successfully eliminated through the aid of vaccination in other countries have not been eliminated in Pakistan.
- The reasons for this vary and show the uniqueness of the economic, healthcare and environmental landscape of Pakistan, through which public health programmes need to be implemented.

- When compared to globally standardised targets for immunization, Pakistan is trailing behind.
- Not achieving these targets is worrying from both a global perspective and within the national healthcare landscape of Pakistan.
- Research is necessary to bring together findings on the failings of routine immunization and polio campaigns

- The "Expanded Programme of Immunization" (EPI) is the main programme through which routine immunization is provided to the public.
- Within Pakistan, it has encountered many problems since its inception. These includes
- i. Logistical obstacles
- ii. Parental and female awareness and education
- iii. Influence of religious community leaders
- iv. Conflict and war

- v. Reduced focus on EPI funding and technical assistance in relation to specific campaigns like polio
- vi. Poor capacity of human resources has contributed significantly to its poor performance.

These reasons include

- Poor worker motivation
- Political interference
- Underutilization of available human resources
- Worker fatigue due to polio and other regularly conducted campaigns have reduced the time available for EPI

- Theft by workers
- Obstacles in procurement of vaccines and other required items
- Lack of proper cold chain monitoring
- Poor maintenance of equipment
- Inability to pay transportation and/or other costs
- Lack of available time during immunization hours, often due to other obligations to support the family livelihood and traditions.
- Poor or disrespectful treatment from health workers during service contacts

Recommendations

- The EPI needs drastic changes to improve its performance.
- Interprovincial coordination and collaboration needs to be strengthened.
- A situational analysis of the EPI should be carried out in each of the Provinces.
 This assessment could include coverage, mapping of difficult-to-reach populations and fixed service points.
- The available human resources, logistical demands, funding, and demand aspects of the program should also be included.

- EPI implementation plan for each district within each province to consider and address program gaps identified by the situational assessment.
- The responsibility for planning should be delegated to the union council (UC) and district-level staff under the direction of the provincial EPI manager.
- This ensure ownership of the program, use local knowledge, and help to make more realistic estimates of eligible children.

- Integration of immunization services with maternal and child health (MCH),
 integrated management of childhood illnesses (IMCI) programs
- Integration of immunization with primary health care
- Integration of immunization services with the private sector
- The province should develop a comprehensive plan to expand the number of fixed centres to cover all communities with a reorganization of outreach services to address hard-to-reach areas, especially in high-risk districts.
- The logistics system should be improved.

- VVM and cold chain monitoring tools should be introduced
- Vaccine procurement capacity and cold chain equipment maintenance as well as back-up power systems are all in need of improvements.
- Leadership and good management should be fostered through training.
- Regular training of managers (Funding for this course to be offered regularly in each province should be sought either from the Government of Pakistan or from development partners).

- Supervision and monitoring should be restructured. All categories of staff should be encouraged to prepare monthly plans for supervision beforehand, and seek pre-approval at the monthly conference of EPI staff.
- Managers at all levels must closely monitor the completion of supervision by lower-level by on-site spot checks on the staff
- Monitoring, evaluation, and surveillance system of the EPI needs to be strengthened.

