

UNIT 2

Innate and adaptive immunity:- Elements of immune system: Hematopoiesis, T-cells, B-cells, myeloid cells, antigen presenting cells, cell mediated subset of T-Cells, helper and suppressor cells, cell mediated and humoral immunity, antibody dependent cell mediated cytotoxicity, natural killer cells.

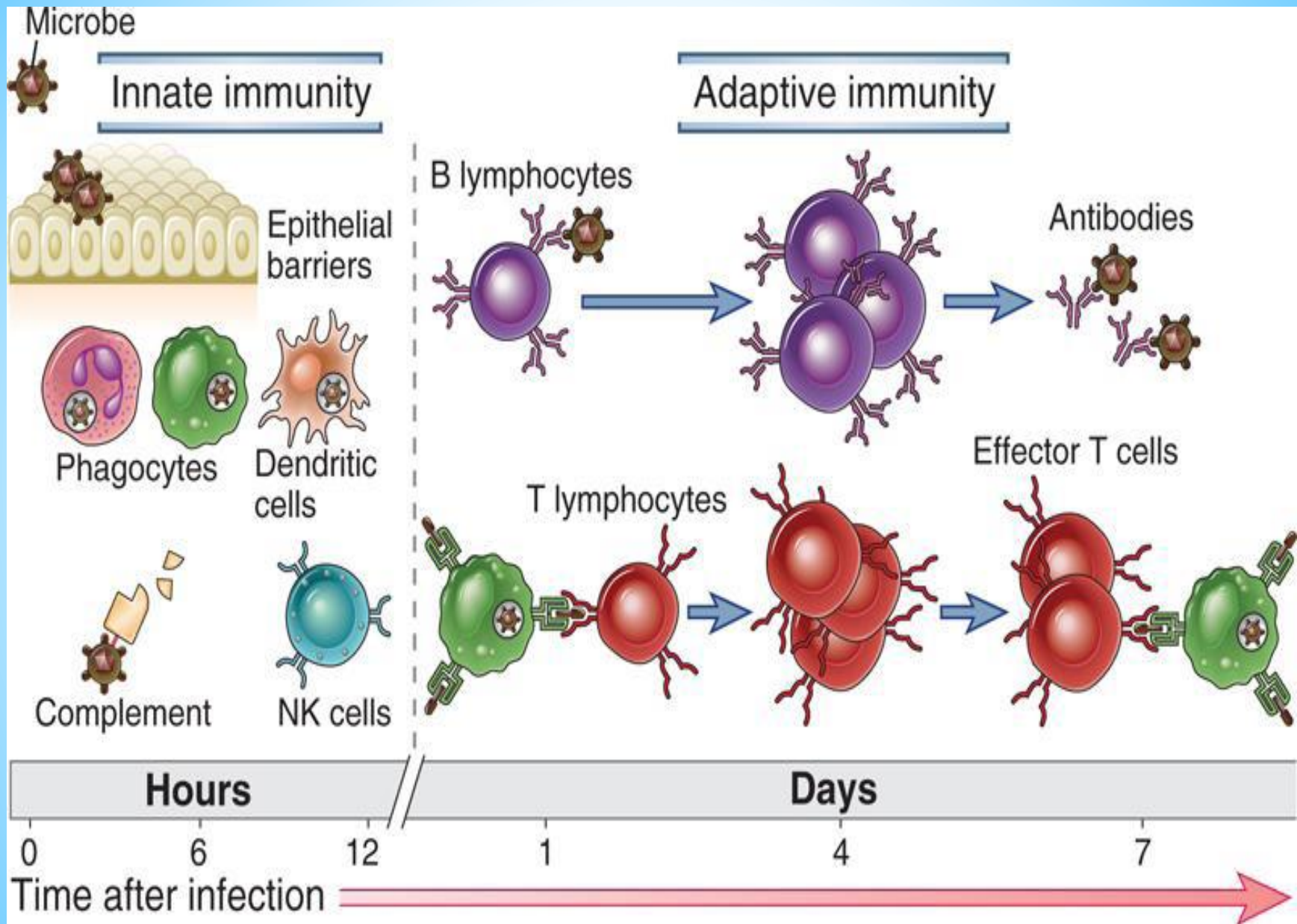
Innate and adaptive immunity

INNATE IMMUNITY

- The resistance that an individual possesses by virtue of his genetic and acquires during life constitutional make up
- Early defense response against microbes
- Immune response Non specific
- Innate response do not alter on repeated exposure
- Memory effect absent
- Not affected by immunization or prior

ACQUIRED IMMUNITY

- Resistance to infection which individual
- Later defense response microbes
- Immune response is highly specific
- Adaptive response improves with each exposure successive encounter with same pathogen
- Memory effect present
- Is improved by immunization contact



Innate or Natural or Nonspecific Immunity (L. innatus = inborn):

- Innate immunity is inherited by the organism from the parents and protects it from birth throughout life.
- It is genetic and constitutional make up.
- It acts as first line of defense against infections, micro organisms, their products before they cause disease.
- It lacks specific responses to specific invaders.
- It providing different barriers to the entry of the foreign agents into our body.

Innate immunity consists of four types of barriers

- Physical barriers,
- Physiological barriers,
- Cellular barriers and
- Cytokine barriers

1. Physical Barriers:

They are mechanical barriers to many microbial pathogens. These are of two types. Skin and mucous membrane.

(a) Skin:

The skin is physical barrier of body. Its outer tough layer, the stratum corneum prevents the entry of bacteria and viruses.

(b) Mucous Membranes:

- Mucus secreted by mucous membrane traps the microorganisms and immobilizes them.
- Microorganisms and dust particles can enter the respiratory tract with air during breathing which are trapped in the mucus.
- The cilia sweep the mucus loaded with microorganisms and dust particles into the pharynx (throat). From the pharynx it is thrown out or swallowed for elimination with the faeces.

2. Physiological Barriers:

The skin and mucous membranes secrete certain chemicals which dispose off the pathogens from the body. Body temperature, pH of the body fluids and various body secretions prevent growth of many disease causing microorganisms.

Some of the important examples of physiological barriers are as follows:

- (a) **Acid of the stomach** kills most ingested microorganisms,
- (b) **Bile** does not allow growth of microorganisms,
- (c) **Cerumen (ear wax) traps** dust particles, kills bacteria and repels insects,

(d) **Lysozyme** is present in tissue fluids and in almost all secretions except in cerebrospinal fluid, sweat and urine. Lysozyme is in good quantity in tears from eyes. Lysozyme attacks bacteria and dissolves their cell walls. Lysoenzyme is also found in saliva

(e) **Nasal Hair:** They filter out microbes and dust in nose,

(f) **Urine:** It washes microbes from urethra,

(g) **Vaginal Secretions:** It is slightly acidic which discourages bacterial growth and flush microbes out of vagina,

(h) **Sebum (sweat):** It forms a protective acid film over the skin surface that inhibits growth of many microbes.

3. Cellular Barriers:

These are certain **white blood corpuscles (leucocytes), macrophages, natural killer cells, complement system, inflammation, fever, antimicrobial substances, etc.**

(i) Certain Leucocytes:

Neutrophils and **monocytes** are major phagocytic leucocytes.

(a) Polymorpho-nuclear Leucocytes (PMNL- neutrophils):

- Polymorphonuclear cells are recruited to the site of infection where they phagocytose invading organisms and kill them intracellularly.
- In addition, PMNs contribute to collateral tissue damage that occurs during inflammation.

(b) Monocytes:

- They are the largest of all types of leucocytes and somewhat amoeboid in shape.
- They have clear cytoplasm (without cytoplasmic granules). The nucleus is bean-shaped.
- Monocytes constitute about 2-10% of the blood leucocytes. They are motile and phagocytic in nature and engulf bacteria and cellular debris.
- Their life span is about 10 to 20 hours. Generally they change into macrophages after entering tissue spaces.

(ii) Macrophages:

- Monocytes circulate in the bloodstream for about 8 hours, during which time they enlarge and then migrate into the tissues and differentiate into specific tissue macrophages.
- Macrophages are long lived and are highly motile phagocytic.
- Macrophages serve different functions in different tissues and are named to reflect their tissue location. Some examples are given below:
 - i. **Pulmonary alveolar macrophages** in the lung
 - ii. **Histiocytes** in connective tissues
 - iii. **Kupffer cells** in the liver
 - iv. **Glomerular Mesangial cells** in the kidney
 - v. **Microglial cells** in the brain
 - vi. **Osteoclasts** in bone

Natural Killer Cells

- Natural killer cells are called “natural” killers because they are ready to kill as soon as they are formed.
- Natural killer cells recognize and attach to infected cells or cancer cells, then release enzymes and other substances that damage the outer membranes of these cells.
- Natural killer cells are important in the initial defense against viral infections.
- Also, natural killer cells produce cytokines that regulate some of the functions of T cells, B cells, and macrophages.

Complement System

The complement system consists of more than 30 proteins that act in a sequence: One protein activates another and so on. This sequence is called the complement cascade. Complement proteins have many functions in acquired immunity as well as innate:

- Killing bacteria directly
- Helping destroy bacteria by attaching to them and thus making the bacteria easier for neutrophils and macrophages to identify and ingest
- Attracting macrophages and neutrophils to a trouble spot
- Neutralizing viruses
- Helping immune cells remember specific invaders
- Promoting antibody formation
- Enhancing the effectiveness of antibodies
- Helping the body eliminate dead cells and immune complexes (which consist of an antibody attached to an antigen)

(v) Inflammation:

- Inflammation is a defensive response of the body to tissue damage.
- The conditions that may produce inflammation are pathogens, abrasions (scraping off) chemical irritations, distortion or disturbances of cells, and extreme temperatures.
- The signs and symptoms of inflammation are redness, pain, heat and swelling.

- Inflammation is an attempt to dispose of microbes, toxins, or foreign material at the site of injury to prevent their spread to other tissues, and to prepare the site for tissue repair. Thus, it helps restore tissue homeostasis.
- Broken mast cells release histamine. Histamine causes dilation of capillaries and small blood vessels.
- As a result more blood flows to that area making it red and warm and fluid (plasma) takes out into the tissue spaces causing its swelling. This reaction of the body is called inflammatory response.

(vi) Fever:

- Fever may be brought about by toxins produced by pathogens and a protein called endogenous pyrogen (fever producing substance), released by macrophages.
- When enough pyrogens reach the brain, the body's thermostat is reset to a higher temperature, allowing the temperature of the entire body to rise.
- Mild fever strengthens the defence mechanism by activating the phagocytes and by inhibiting the growth of microbes.
- A very high temperature may prove dangerous. It must be quickly brought down by giving antipyretics.

4. Cytokine Barriers:

- Cytokines (Chemical messengers of immune cells) are low molecular weight proteins that stimulate or inhibit the differentiation, proliferation or function of immune cells.
- They are involved in the cell to cell communication. Kinds of cytokines include interleukins produced by leucocytes, lymphocytes produced by lymphocytes, tumour necrosis factor and interferon's (IFNs).
- Interferon's protect against viral infection of cells.

Adaptive immunity

Adaptive immunity



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graph TD; A[Adaptive immunity] --> B[Naturally acquired]; A --> C[Artificially acquired]; B --> D[Active]; B --> E[Passive]; C --> F[Active]; C --> G[Passive]; D --- D1[Antigens enter the body naturally; body induces antibodies and specialized lymphocytes]; E --- E1[Antibodies pass from mother to fetus via placenta or to infant via the mother's milk]; F --- F1[Antigens are introduced in vaccines; body produces antibodies and specialized lymphocytes]; G --- G1[Preformed antibodies in immune serum are introduced by injection];
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The diagram is a hierarchical flowchart. At the top is a yellow box labeled 'Adaptive immunity'. A line from this box branches into two arrows pointing to 'Naturally acquired' (left, purple background) and 'Artificially acquired' (right, green background). From 'Naturally acquired', two arrows point to 'Active' (orange background) and 'Passive' (blue background). From 'Artificially acquired', two arrows point to 'Active' (orange background) and 'Passive' (blue background). Each of these four boxes contains a detailed description of the process.

Naturally acquired

Active

Antigens enter the body naturally; body induces antibodies and specialized lymphocytes

Passive

Antibodies pass from mother to fetus via placenta or to infant via the mother's milk

Artificially acquired

Active

Antigens are introduced in vaccines; body produces antibodies and specialized lymphocytes

Passive

Preformed antibodies in immune serum are introduced by injection

- Adaptive immunity refers to antigen-specific immune response.
- The adaptive immune response is more complex than the innate. The immunity that an individual acquires after the birth is called acquired or adaptive or specific immunity.
- Adaptive immunity also includes a "memory cells" formed by B cells and T cells that makes future responses against a specific antigen more efficient.
- It is specific and mediated by antibodies or lymphocytes or both which make the antigen harmless.

Characteristics of Acquired Immunity:

(i) Specificity:

It is the ability to differentiate between various foreign molecules (foreign antigens).

(ii) Diversity:

It can recognize a vast variety of foreign molecules (foreign antigens).

(iii) Discrimination between Self and Non-self:

It can recognize and respond to foreign molecules (non-self) and can avoid response to those molecules that are present within the body (self) of the animal.

(iv) Memory:

- When the immune system encounters a specific foreign agent, (e.g., a microbe) for the first time, it generates immune response and eliminates the invader. This is called first encounter.
- The immune system retains the memory of the first encounter. As a result, a second encounter occurs more quickly and abundantly than the first encounter.
- The cells of the immune system are derived from the pluripotent stem cells in the bone marrow.

- Pluripotent means a cell that can differentiate into many different types of tissue cells.
- The pluripotent stem cells can form either myeloid stem cells or lymphoid stem cells.
- Myeloid stem cells give rise to monocytes, macrophages and granulocytes (neutrophils eosinophil's, and basophils). RBCs and blood platelets (lymphoid stem cells) form B lymphocytes (B cells), T lymphocytes (T-cells) and natural killer (NK) cells.

Components of Acquired Immunity:

Acquired immunity has two components:

- **Humoral immunity or Antibody mediated immune system (AMIS)**
- **Cellular immunity or cell mediated immune system (CMIS).**

Antibody Mediated Immune System or Humoral Immunity

Antibody Mediated Immune System (AMIS) or Humoral Immunity:

- It consists of antibodies (specialised proteins produced in the body in response to antigen) that circulate in the body fluids like blood plasma and lymph.
- The word ‘humor’ pertains to fluid. B lymphocytes (B cells) produce antibodies that regulate humoral immunity.
- The T-lymphocytes themselves do not secrete anti-bodies but help B lymphocytes produce them.

- Certain cells of the bone marrow produce B lymphocytes and mature there.
- Since B lymphocytes produce antibodies, therefore, this immunity is called **antibody mediated or humoral immunity**.
- Humoral immunity or antibody-mediated immune system (AMIS) provides defense against most extracellular bacterial pathogens and viruses that infect through the respiratory and intestinal tract.

Formation of Plasma B cells and Memory B cells:

- When antibodies on B cell's surface bind antigens (any substances that cause antibodies formation) the B cell is activated and divides, producing a clone (descendants of a single cell) of daughter B cells.
- These clones give rise to plasma B cells and memory B cells. This phenomenon is called clonal selection.

(a) Plasma B Cells (Effector B cells):

- Some of the activated B cells enlarge, divide and differentiate into a clone of plasma cells.
- Although plasma cells live for only a few days, they secrete enormous amounts of antibody during this period.

(b) Memory B Cells:

- Some activated B cells do not differentiate into plasma cells but rather remain as memory cells (Primed cells).
- They have a longer life span.
- The memory cells remain dormant until activated once again by a new quantity of the same antigen.

Role of AMIS:

The AMIS protects the body from

(i) viruses

(ii) some bacteria and

(iii) toxins that enter the body fluids like blood

and lymph.

**Cell-Mediated Immune
System or T-Cell
Immunity**

Cell-Mediated Immune System (CMIS) or T-Cell Immunity:

- A healthy person has about a trillion lymphocytes. Lymphocytes are of two types: T lymphocytes or T cells and B lymphocytes or B cells.
- Both types of lymphocytes and other cells of the immune system are produced in the bone marrow.
- The process of production of cells of immune system in the bone marrow is called haematopoiesis.

- Because T lymphocytes (T cells) mature in the thymus, this immunity is also called T- cell immunity.

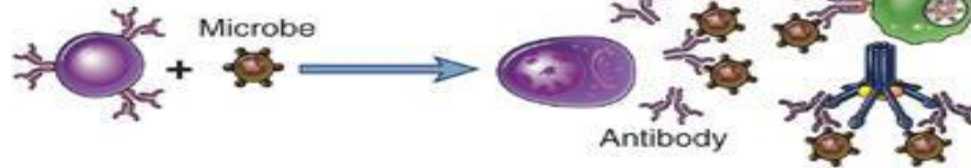
The T-cells play two important functions—effector and regulatory.

- The effector function includes cytolysis (destruction of cells by immune processes) of cells infected with microbes and tumour cells and lymphokine production.
- The regulatory functions are either to increase or to suppress other lymphocytes and accessory cells.

Antigen recognition

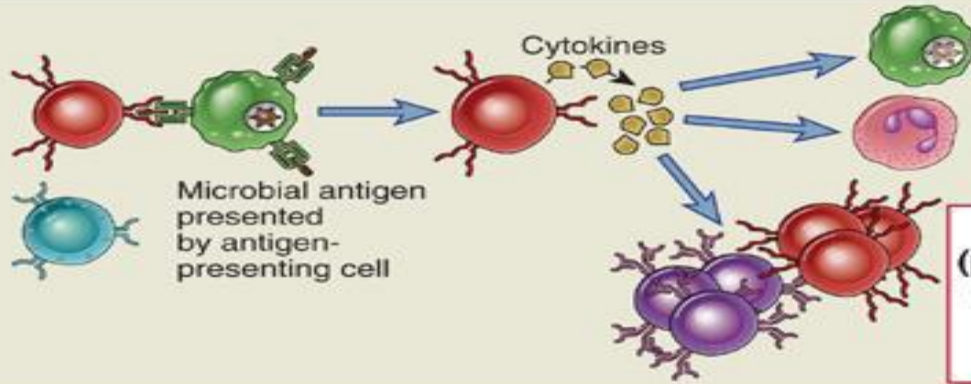
Effector functions

B lymphocyte



Neutralization of microbe, phagocytosis, complement activation

Helper T lymphocyte

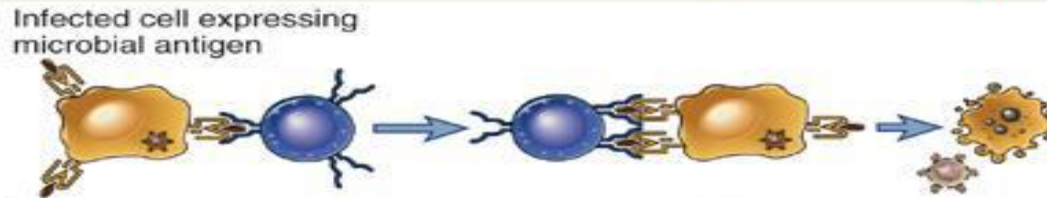


Activation of macrophages

Inflammation

Activation (proliferation and differentiation) of T and B lymphocytes

Cytotoxic T lymphocyte (CTL)



Killing of infected cell

Regulatory T lymphocyte



Suppression of immune response

Natural killer (NK) cell



Killing of infected cell

Types of T-cells and their Functions:

1. Helper T cells (TH):

- TH cells are most numerous of the T cells. They help in the functions of immune system.
- They produce a growth factor that stimulates B-cell proliferation and differentiation and also stimulates antibody production by plasma cells; enhance activity of cytotoxic T cells.

2. Cytotoxic T cells (Tc) or Killer cells:

- These cells are capable of killing microorganisms and even some of the body's own cells directly hence they are called killer cells.
- The antigen receptors on the surfaces of the cytotoxic cells cause specific binding with antigens present on the surface of foreign cell.

- Cell after binding, the cytotoxic T cell secretes hole-forming proteins, called perforins, that punch large round holes in the membrane of the foreign cell.
- Then fluid flows quickly into the cell from the interstitial space. In addition, the cytotoxic T cell releases cytotoxic substances directly into the foreign cell.
- Almost immediately, the foreign cell becomes greatly swollen and it usually dissolves shortly thereafter.

Thus they destroy body cells infected by viruses and attack and kill bacteria, fungi, parasites and cancer cells.

3. Memory T Cells (Primed Cells):

- These cells are also formed by T-lymphocytes as a result of exposure to antigen and remain in the lymphatic tissue (e.g., spleen, lymph nodes).
- They recognize original invading antigens even years after the first encounter.
- These cells keep ready to attack as soon as the same pathogens infect the body again.
- They proliferate and differentiate into cytotoxic T cells, helper T cells, suppressor T cells, and additional memory cells.

4. Suppressor Cells (Regulatory T cells (TR)):

- These cells are capable of suppressing the functions of cytotoxic and helper T cells.
- They also inhibit the immune system from attacking the body's own cells.
- It is believed that suppressor cells regulate the activities of the other cells.
- For this reason, the suppressor cells are classified as regulatory T cells.

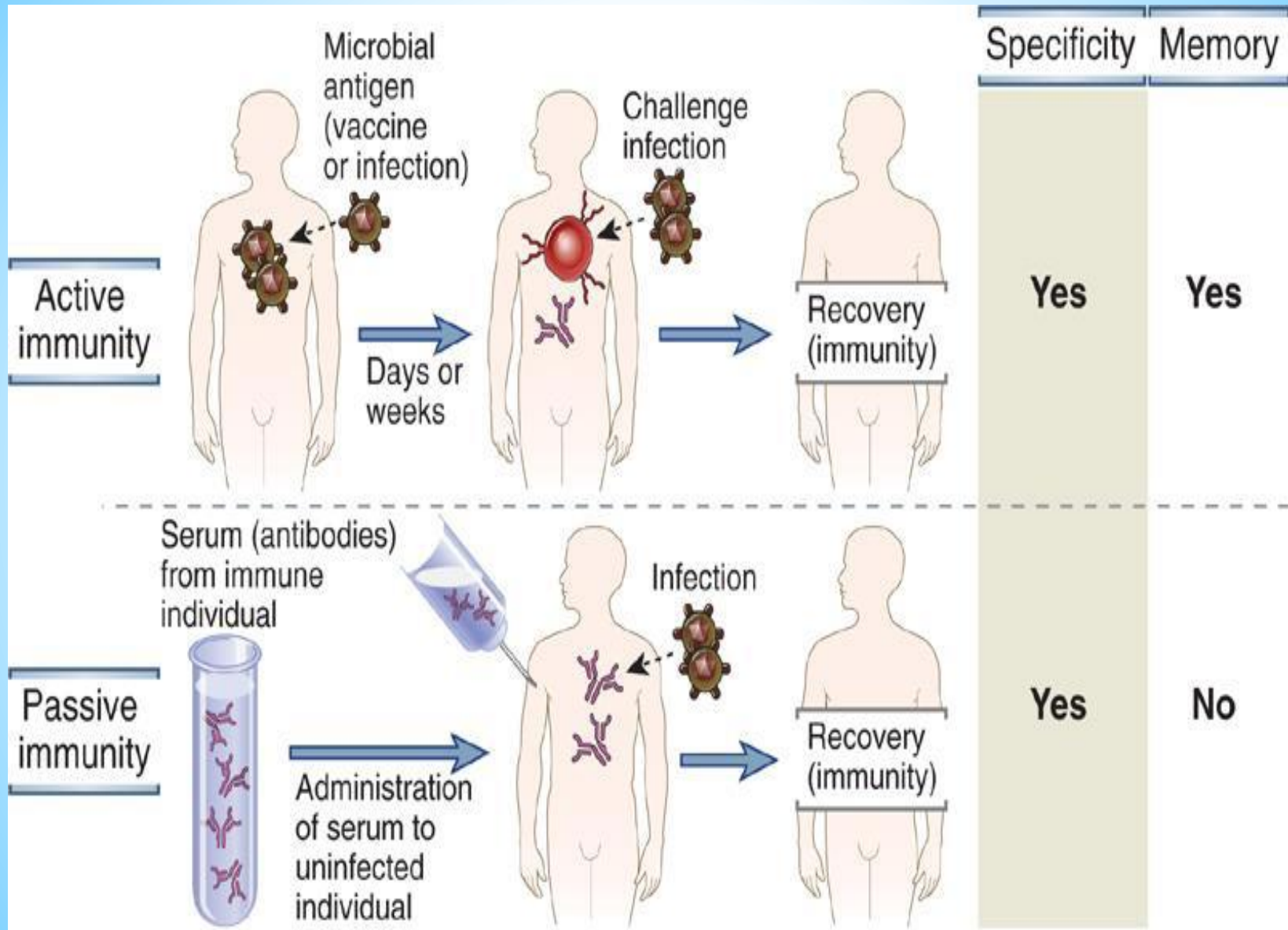
Natural Killer (NK) Cells:

NK cells attack and destroy target cells, participate in antibody dependent cell mediated cytotoxicity. They can also attack parasites which are much larger than bacteria.

Types of Acquired Immunity:

Acquired (= Adaptive) Immunity is of two types:

- **Active immunity**
- **Passive immunity.**



1. Active Immunity:

In this immunity person's own cells produce antibodies in response to infection or vaccination. It is slow and takes time in the formation of antibodies. It is long lasting and is harmless. Active immunity may be **natural** and **artificial**.

(a) Natural active immunity

A person who has recovered from an attack of small pox or measles or mumps develops natural active immunity.

(b) Artificial active immunity

Artificial active immunity is the resistance induced by vaccines.

Examples of vaccines are as follows:

Bacterial vaccines

- (a) Live- BCG vaccine for tuberculosis
- (b) Killed vaccines- TAB vaccine for enteric fever.

Viral vaccines

- (a) Live – sabin vaccine for poliomyelitis, MMR vaccine for measles, mumps, rubella,
- (b) Killed vaccines- salk vaccine for poliomyelitis, neural and non-neural vaccines for rabies. Bacterial products. Toxoids for Diphtheria and Tetanus.

2. Passive Immunity:

When ready-made antibodies are directly injected into a person to protect the body against foreign agents, it is called passive immunity. It provides immediate relief. It is not long lasting. It may create problems. Passive immunity may be **natural and artificial**.

(a) Natural passive immunity

- It is the resistance passively transferred from the mother to the foetus through placenta.
- IgG antibodies can cross placental barrier to reach the foetus. After birth, immunoglobulin's are passed to the new-born through the breast milk.
- Human colostrum (mother's first milk) is rich in IgA antibodies. Mother's milk contains antibodies which protect the infant properly by the age of three months.

(b) Artificial passive immunity

- It is the resistance passively transferred to a recipient by administration of antibodies.
- This is done by administration of hyper-immune sera of man or animals. Serum contains antibodies.
- **For example,** anti-tetanus serum (ATS) is prepared in horses by active immunisation of horses with tetanus toxoid, bleeding them and separating the serum. ATS is used for passive immunisation against tetanus. Similarly anti-diphtheric serum (ADS) and anti-gas gangrene serum (AGS) are also prepared.

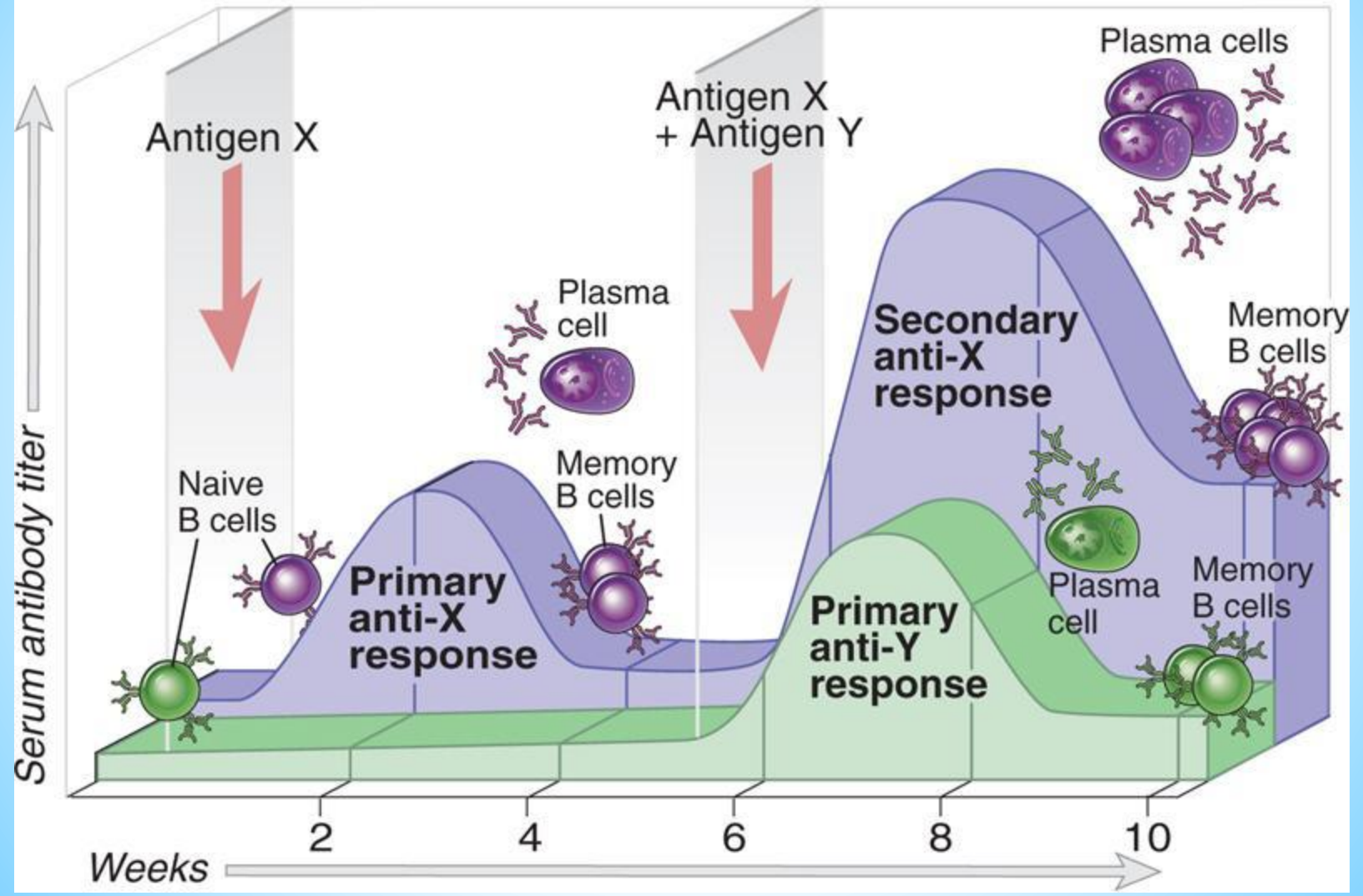
Immune Response

Immune Response:

The immune response involves primary immune response and secondary immune response.

(a) The primary immune response:

After an initial contact with an antigen, no antibodies are present for a period of several days. Then, a slow rise in the antibody titer (arbitrary units) occurs, first IgM and then IgG followed by a gradual decline in antibody titer. This is called the primary immune response.



(b) The secondary immune response:

- Memory cells may remain in the body for decades. Every new encounter with the same antigen results in a rapid proliferation of memory cells. This is also called “**booster response**”.
- The antibody titer after subsequent encounters is far greater than during a primary response and consists mainly of IgG antibodies. This accelerated, more intense response is called the secondary immune response.
- Antibodies produced during a secondary response have an even higher affinity for the antigen.

- A person who had been suffering from diseases like measles, small pox or chicken pox becomes immune to subsequent attacks of these diseases.
- It includes spleen, lymph nodes, tonsils, Peyer's patches of small intestine and appendix.

The increased power and duration of the secondary immune response explain why immunization (method of providing immunity artificially, it is called vaccination) is usually accomplished by injecting antigen in multiple doses