UNIT 3

COMPONENTS OF IMMUNE SYSTEM–II

Structure

3.1 INTRODUCTION

This unit aims to provide basic concept to the adaptive immune system of the body. The adaptive or acquired immune system comes into action once the pathogen has breached the innate immune system. The innate immune system passes on stimulatory signals to activate the adaptive immunity. We would study about various cells and molecules involved in the adaptive immunity response. B cells on activation produce plasma cells that secrete antibodies and generate memory cells that are dormant cells which are activated on subsequent pathogen exposure. The T cells go on to produce cytotoxic T lymphocytes that are involved in direct killing of the pathogen.

An overview of the humoral and cell mediated immune systems is also provided. The humoral immune response involves various components in the body fluids like antibodies, complements and antimicrobial peptides; while the cell mediated immune system has cell components to neutralize the pathogen. We would also understand the difference between primary and secondary immune responses. Then we would proceed to understand the interrelationship between the innate and adaptive immune systems via NK cells.

Objectives

After studying this unit, you should be able to:

- gain an insight about the adaptive immune system,
- differentiate between naturally and artificially acquired immunity,
- list the various features of adaptive immunity,
- explain B and T lymphocytes,
- discuss the role of cytokines and chemokines,
- give examples of cytokines with their functions,
- differentiate between humoral and cell-mediated immunity,
- list the steps of antibody activation,
- list the features of primary and secondary response, and
- explain the role of NK cells as a bridge between innate and adaptive immune systems.

3.2 ADAPTIVE IMMUNITY

Foreign pathogens and antigens are selectively recognised and eliminated by the adaptive immune system when the innate immune system fails to defend the body against the pathogen invasion. However, it is capable of responding only when a stimulus is provided by the innate immune system.

The Adaptive or Acquired immune response takes much longer time than the innate immune response to become activated and respond. It can take days or even weeks but adaptive immunity is more pathogen specific and also has memory. Adaptive immune response is generated post exposure to a pathogenic antigen or after a vaccination. The responses are tailor made to challenge specific antigen unlike the innate immune system.

The differences between innate and adaptive immunity are given in Table 3.1.

Table 3.1: Differences between innate and adaptive immunity.

	Lines of defense	Timeline	Cells	Antigen dependency	Example
Innate (Non-specific)	First	Immediate response (0-96 hours)	NK cells, macrophages, neutrophils, dendritic cells, mast cells, basophils, eosinophils.	Independent	Skin, hair, cough, mucous membranes phagocytes, granulocytes.
Adaptive (Specific)	Second	Long term (>96 hours)	T and B lymphocytes	Dependent	Pus, swelling, redness, pain.

3.2.1 Four Characteristics of Adaptive Immune Response

Adaptive immune responses are carried out by white blood cells called lymphocytes. Four major features of adaptive immune response are as follows:

i) **Antigen specificity:** This allows the immune system to detect even minor differences among antigens. Antibodies can recognize even single amino acid differences among protein molecules.

ii) **Diversity:** The property of adaptive immune system to generate enormous diversity in the recognition molecules allows it to identify billions of molecules on foreign antigens and pathogens.

iii) **Immunologic memory:** This attribute of generating memory against specific antigen/ pathogen post primary encounter with the antigen allows providing up to life long immunity to various pathogens due to formation of memory B and T cells after initial exposure.

iv) **Distinction between self and non-self:** It is critical that the immune system reacts and responds not only to non-self-molecules as response to self-molecules can lead to several fatal conditions like autoimmune disorders.

There are two types of adaptive immunity namely

a) **Humoral Immune Response** (Antibody Response) mainly involves B cells and antibodies.

b) **Cell mediated Response** mainly involves T cells.

Before studying Humoral Immune Response and cell mediated response in this unit let us discuss about B and T lymphocytes, cytokines and chemokines in the following section.

3.3 B LYMPHOCYTES

They are lymphocytes that are named so due to their occurrence from the site of maturation in birds called the *Bursa of Fabricius.* In mammals like mice and humans, **B lymphocyte maturation occurs in the bone marrow. They are distinct from other lymphocytes and cells in the respect that they display membrane bound antibody molecules.** These antibody molecules have the same antigen specificity and antigen binding sites.

Several other molecules are found on the B-cell surface (Table 3.2)

Bursa of Fabricius: is a chestnut size sac like lymphoid organ in birds,located dorsal to the rectum, anterior to the sacrum, communicating with the posterior portion of the cloaca. In birds B cells mature here.

Table 3.2: Molecules expressed on B cell surface.

Sr. No	Molecule expressed	Role
1.	B220	Frequently used as marker for precursor B cells and mature B cells.
2.	CR1 and CR2	They are receptors for the complement products to bind.
3.	CD32	Receptor for IgG
4.	MHC Class II molecule	They allow B-cells to act as Antigen Presenting Cells
5.	CD 40	Interacts with the CD40 on helper T cell surface.

The interaction of naive B cells antibodies with antigen, as well as with macrophages and T-cells, causes rapid proliferation of B cells leading to the production of B-cell clones. These cells differentiate into memory B cells and plasma cells (Fig 3.1). **The plasma cells rapidly secrete antibodies while the memory cells act on subsequent exposure with the antigen.**

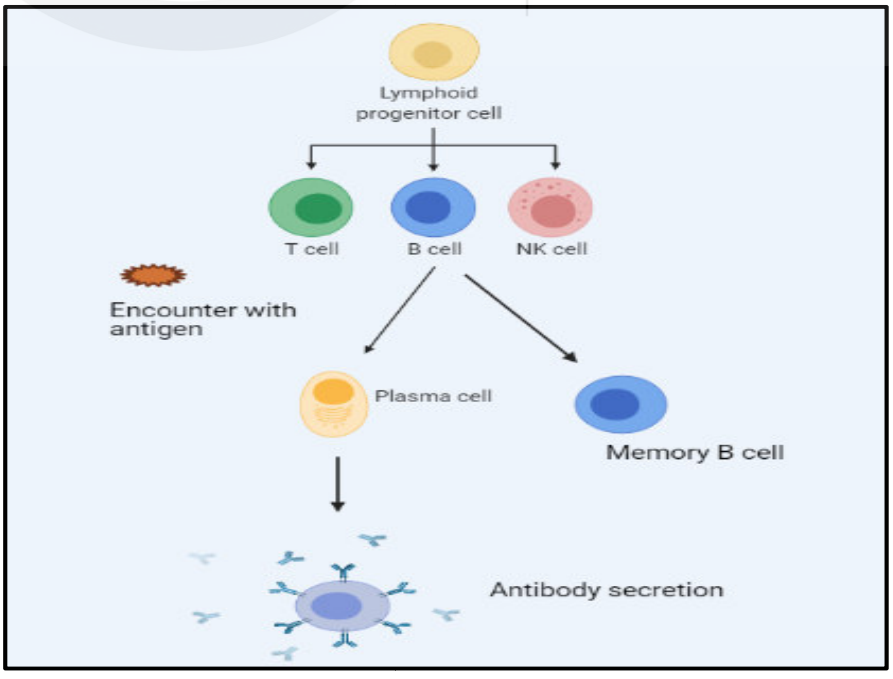


Fig 3.1: Differentiation of B lymphocyte in plasma cells and memory B cell.

3.4 T LYMPHOCYTES

T lymphocytes are cells that mature in the thymus. They have T Cell Receptors (TCRs) that are membrane bound receptors that do not directly recognise the antigen. Most T-cells can recognise antigens only when they are coupled with Major Histocompatibility molecule found on antigen presenting cells like macrophages and dendritic cells and on tumor cells.

Several molecules are displayed on the membrane of T cells.

1. *T-cell Receptor (TCR)*
2. *CD45 and CD28.*

Two distinct subpopulations of T cells can be distinguished based on the expression of CD4 and CD8 molecules:

1. **$CD4^+$ cells:** They can recognise antigen bound to class II MHC molecules and usually function as helper T cells (T_H). Activity of T_H cells is depicted in Fig 3.2.
2. **$CD8^+$ cells:** They recognise antigen bound to class I MHC molecules and function as cytotoxic T cells (T_C). Fig 3.3 depicts the activity of T_C cells.

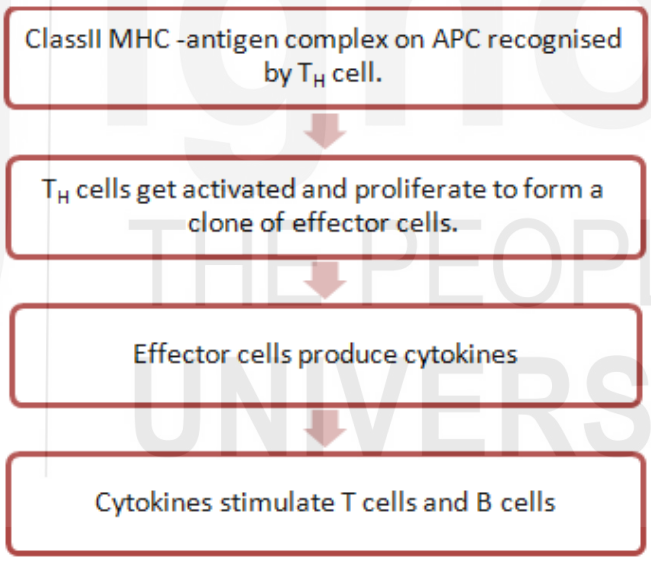


Fig 3.2: Flowchart depicting the activity of helper T-cells (T_H).

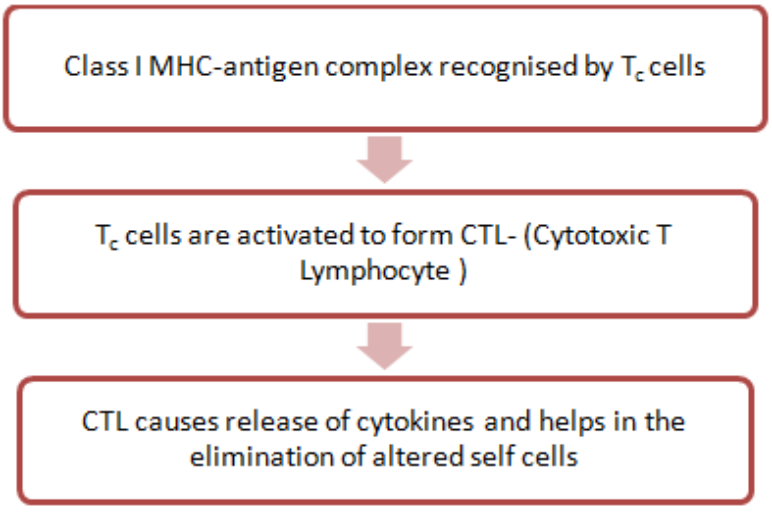


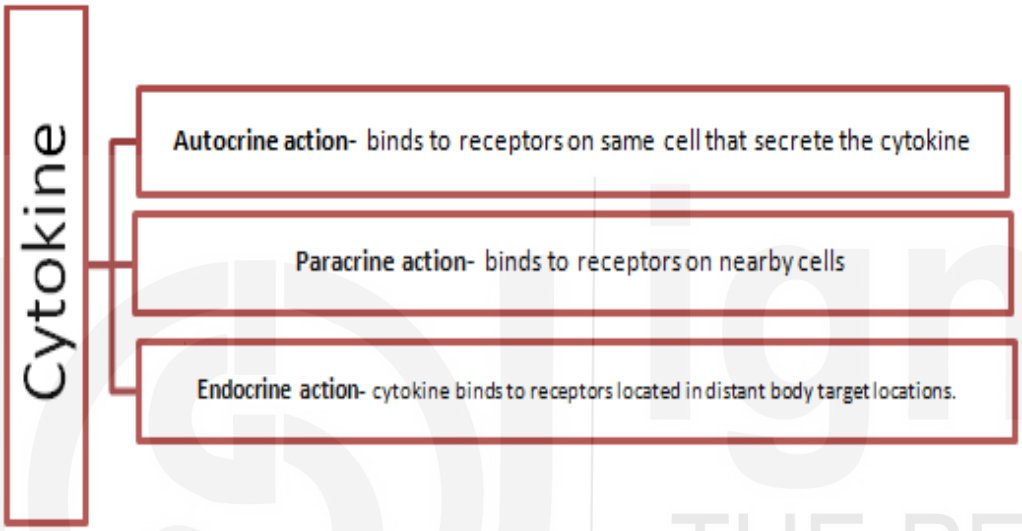
Fig 3.3: Flowchart depicting the activity of cytotoxic T-cells (T_C).

3.5 CYTOKINES

Cytokines are group of proteins secreted by white blood cells and many other cells of the body in response to external stimuli. They are low molecular weight proteins or glycoproteins with regulatory roles.

Cytokines **trigger signal transduction pathways** and **eventually lead to alteration of gene expression** in target cells by **binding to specific receptors located on the target cell.** It is the presence of these receptors that determines whether or not a cell is susceptible of action of a particular cytokine molecule.

The cytokines may have:



Cytokines are involved in the stimulation or inhibiting the activation and proliferation of many cells, regulation of antibody secretion and also the secretion of other cytokines. In this way they are able to regulate the magnitude and duration of the immune response.

The binding of cytokines to the target cells leads to increased expression of cytokine receptors and also causes secretion of more cytokine molecules which go on to affect other target cells. Therefore, even a small amount of cytokines secreted by antigen activated lymphocytes can affect the activity of many immune cells. For example, a plethora of interacting cells like B cells, NK cells, macrophages, T_c cells, granulocytes and HSCs- (Hematopoietic Stem Cells) are activated by the cytokines released by T_H cells.

3.5.1 Different Features of Cytokines

Cytokines exhibit different features as discussed below:

1. **Pleiotropy:** It is the exhibition of different biological effects on different target cells by the same cytokine. For example, IL-4 secreted by activated T_H cells goes on to activate B cell, thymocyte and mast cells.
2. **Redundancy:** It is when the same function is performed by two cytokines. Thus, it becomes difficult to attribute a function to one particular cytokine. For example, IL-2, IL4 and IL-5 secreted by activated T_H cells cause B cell proliferation.

3. **Synergy:** Synergy occurs when the additive function of two cytokines is more than the function of a single cytokine.

4. **Antagonism:** The effect of one cytokine inhibits the function of other cytokine.

5. **Cascade induction:** It is the initiation of a sequence of events where the production of cytokine by a cell activates another cell. Now the activated cell secretes more cytokines which further activate more target cells.

3.5.2 Nomenclature of cytokines

Cytokines are principally named on the basis of the cells that produce them. For example:

- **Lymphokines:** cytokines produced by lymphocytes.
- **Monokines**: cytokines produced by macrophages and monocytes.
- **Interleukins:** cytokines secreted by leukocytes and act on other leukocytes.
- Some cytokines are also called by their common names. For example, tumor necrosis factors.

3.5.3 Functions of some cytokines

Functions performed by some cytokines are as discussed below:

- **TNF-α (tumor necrosis factor-α):** It is synthesized by macrophages and has several functions like: inflammation, formation of acute phase proteins in liver, neutrophil activation and loss of body fat and muscle.
- **Interferon-α:** It is secreted by macrophages. It creates an antiviral state in nucleated cells, activates NK cells and increases the expression of MHC I expression.
- **Interleukin -2:** This is secreted by T-cells and causes B cell proliferation, T cell proliferation and activation of NK cells.
- **Interferon-γ:** This is secreted by $CD8^+$ T cells and NK cells. Serves to activate macrophages, stimulates better antigen presentation and increases the overall expression of MHC molecules.

3.5.4 Chemokines

Chemokines are cytokines that act as chemo-attractants. They play an important role in migration of cells between blood and tissues through venules during the process of chemotaxis. (Chemotaxis is the stimulation of cell movement in response to chemical stimuli such as cytokine gradients). Chemokines are also known to influence development of lymphoid organs and T-cell differentiation. They mediate tumour cell metastasis and also function as neuro-modulators in the nervous system.

Chemokine receptors are required for the action of chemokines on the target cells. These receptors belong to G-protein coupled receptors (GPCRs) family and help in initiating intracellular signalling pathways (Fig 3.4).

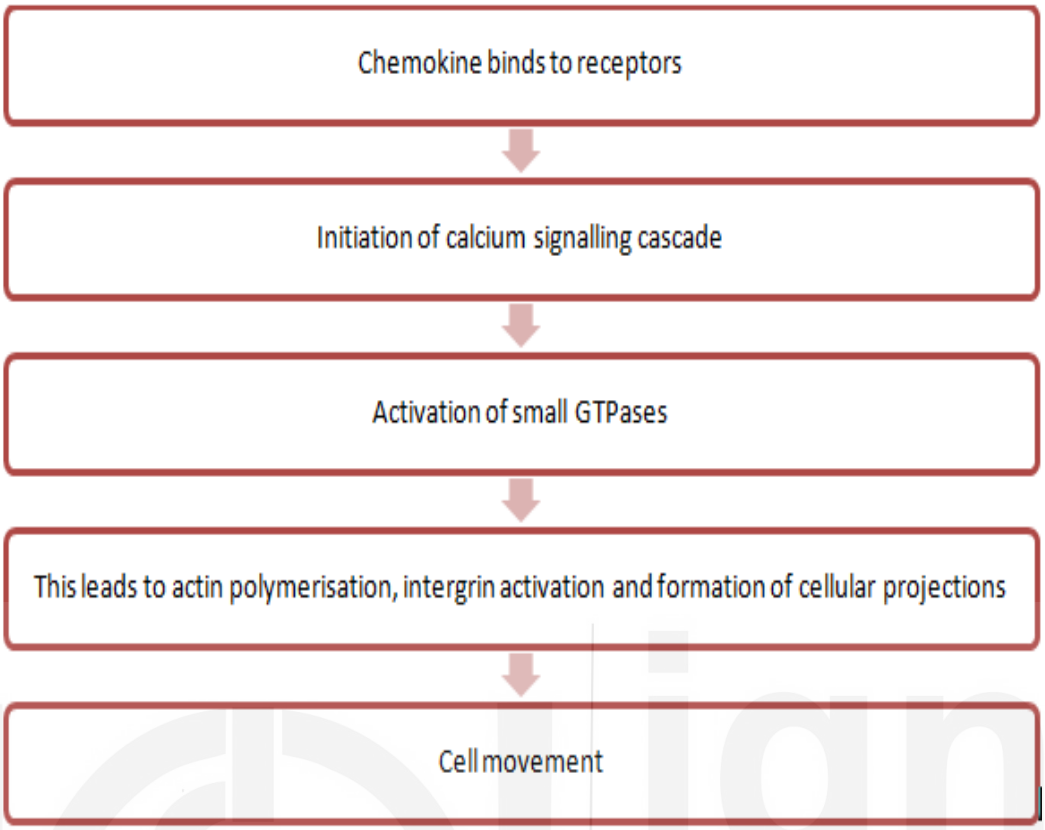


Fig 3.4: Mechanism of action of Chemokines

SAQ 1

State 'True' or 'False':

i) B lymphocyte maturation in mammals like mice and humans occurs in the bone marrow.

ii) Redundancy is not a feature of cytokines.

iii) TCRs do not directly recognise antigens.

SAQ 2

Match the following items given in Column A with Column B.

Column A	Column B
i) CD45 and CD 28	a) Macrophages
ii) Monokines	b) Receptor for IgG
iii) B-cells	c) Expressed on T-cells
iv) Interferons	d) Bear antibody on surface
v) CD32	e) Antiviral state

3.6 HUMORAL IMMUNITY

Humoral immunity depends on molecules found in the "*humor*", that is the body fluids. It is mediated by molecules like antibodies, various complement proteins and antimicrobial peptides. Therefore, it is also as **Antibody Mediated Immunity.**

Humoral immunity involves the production of antibodies and simultaneous occurring of events like the activation of helper T-cells and production of cytokines. It is also involved in various effector functions of antibodies like:

- Neutralization of pathogens and toxins.
- Classical pathway of complement activation
- Opsonisation of pathogen and help in phagocytosis.
- Eventual pathogen clearing.

3.6.1 Antibodies

Antibodies are immunoglobulins found in blood, tissue fluids and various secretions of the body. They are globular proteins that are synthesized and produced by plasma cells that are formed by activated B-cells. Five different classes of antibodies are found in the body. They are: **IgG, IgM, IgA, IgE and IgD.** You will study about them in detail in Unit 7 of this course.

Antibodies are used by the adaptive immune system to neutralize various pathogens like viruses and bacteria. The antibodies can bind to specific targets and cause agglutination and precipitation reactions. As a result various immune complexes are formed that can be cleared from the body. Antibodies also promote phagocytosis by various cells like macrophages and activate the complement system.

3.6.2 Steps of Humoral Immunity

Various steps of humoral immunity are discussed below and shown in Fig 3.5.

1. **Production of B-cells:** The production of B cells occurs in bone marrow. They have B-cell receptors (BCRs) displayed on their surfaces which are specific for particular antigens. These mature B-cells that go on to encounter pathogens in lymphoid organs, to where they have migrated.

2. **The activation of B-cells:** The mature B cell encounters antigen in the lymphoid organs. The antigen binds to the BCR which is then internalised by endocytosis. The antigen fragments are then presented with MHC-II molecules.

3. **The proliferation of B-cells:** The helper T-cell get activated on binding to B-cell. The activation of helper T-cells results in release of various cytokines that go on further to activate the B-cells to proliferate rapidly. Soon a clone of B-cells is formed and these cells eventually form memory cells or plasma cells. The plasma cells secrete large amounts of antibodies while the memory cells are in a temporary resting state which gets activated on subsequent encounter with the pathogen.

4. **Antigen –antibody reaction:** The antigen and antibody then react forming an immune complex which is cleared from the body.

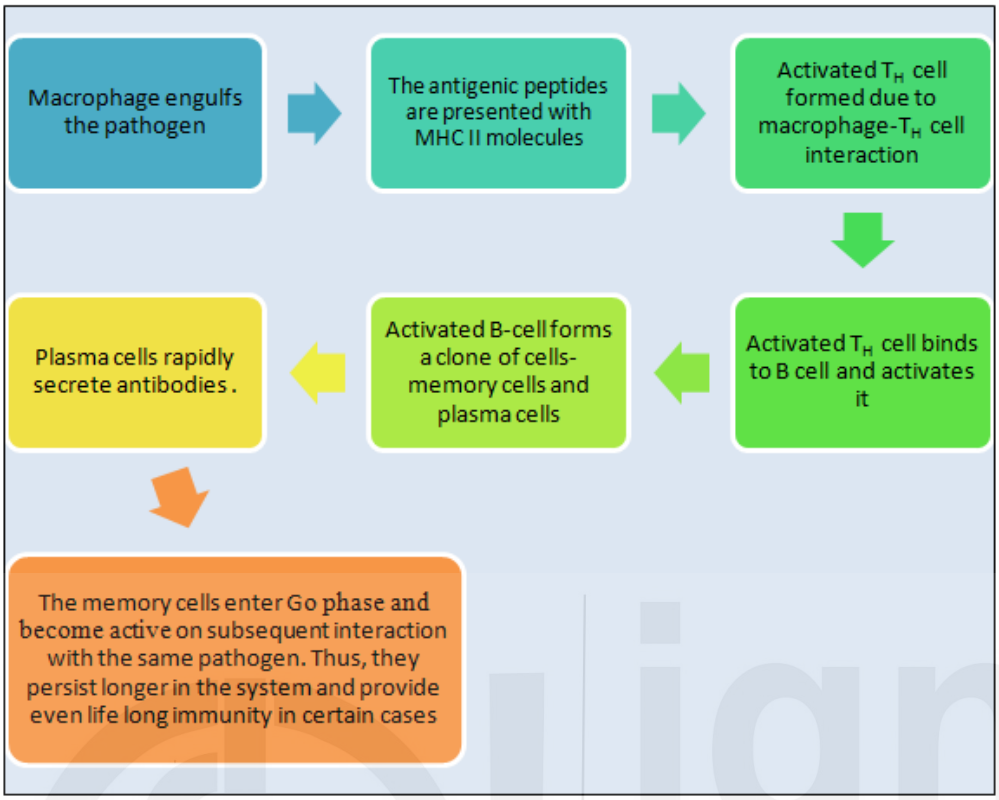


Fig 3.5: The steps of Humoral Immune Response.

3.7 CELL MEDIATED IMMUNE RESPONSE (CMI)

The cell mediated immune response is the method of the body to fight against pathogens like bacteria and viruses. It is also responsible for the killing of cancerous cells and in the graft-rejection process.

The foreign antigen is recognised by macrophages and dendritic cells of the innate immune system. They internalise the pathogen, degrade it and present their antigenic peptides on their surface with class II MHC molecules. This MHC-antigenic complex is responsible for the activation of adaptive immune system.

$CD4^+$ and $CD8^+$ T cells are formed from T-cell precursors in the thymus. The MHC Class II complex on APCs interact with the $CD4^+$ T cells while the $CD8^+$ T cells interact with the antigen- Class I MHC complex found on infected or cancerous cells. The $CD8^+$ T cells transform into Cytotoxic T lymphocytes (CTL) and are responsible for the destruction of the infected or the cancerous cell. (Fig 3.6)

The $CD4^+$ cells prior to the interaction with MHCII- antigen complex present on APCs are called as **naive cells.** The naive cell on activation can form memory T cell or other T_H-cell variants-

- Interferons are produced by Type I helper T-cells that cause pathogen digestion with the APCs. They also stimulate CTL and B-cell activity.
- Interleukins that promote B cell activity are produced by Type II helper T-cells.

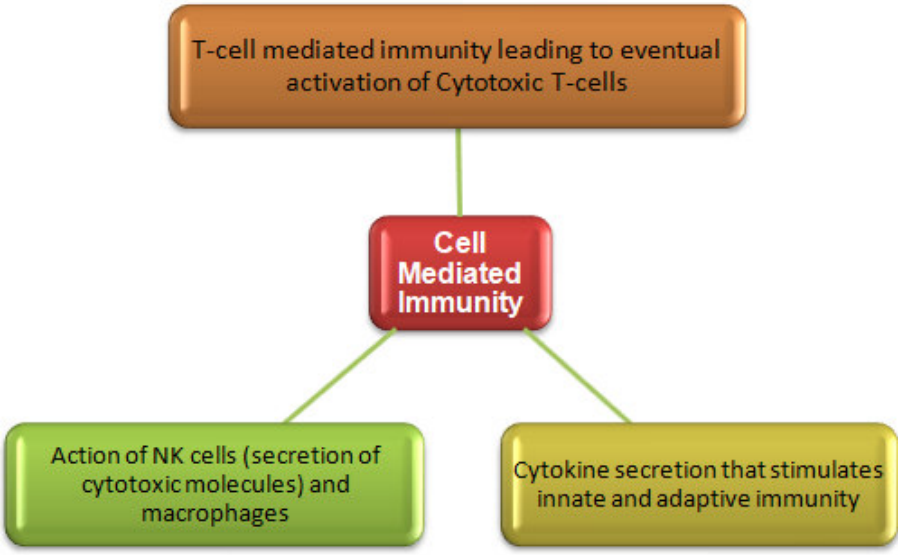


Fig 3.6: Mode of action of Cell-Mediated Immunity.

You have studied about humoral and cell mediated immunity. In Table 3.2 differences between the two types of immunity are listed.

Table 3.2: Differences in Humoral and Cell mediated Immunity.

Sr. No.	Humoral Immunity	Cell-mediated Immunity
1.	The response is mediated by antibodies.	The response is mediated by cells.
2.	Only helper T cells are involved.	Both $CD4^+$ and $CD8^+$ T cells are involved.
3.	Mediated by B cells, T cells and macrophages.	Mediated by helper T-cells, cytotoxic T cells, NK cells and macrophages.
4.	Involves B-cell receptors.	Involves T-cell receptors.
5.	Participates in homografts rejections and in GVHD- Graft versus host disease.	The preformed antibodies may lead to early graft rejection.
6.	No role in immune surveillance.	Has role in defense against cancer cells and also in immune surveillance.

SAQ 3

Fill in the blanks with appropriate words:

i) $CD4^+$ and $CD8^+$ T cells are formed from …….. in the thymus.

ii) The $CD8^+$ T cell transforms into ..... that are responsible for the destruction of the infected or the cancerous cell.

iii) …… participates in homografts rejections and in GVHD-Graft versus host disease.

3.8 PRIMARY AND SECONDARY IMMUNE RESPONSES

3.8.1 Primary Immune Response

Primary humoral response is generated when primary contact with the exogenous antigen is established. It leads to the production of plasma cells that secrete large amounts of antibodies and memory B cells.

The magnitude and kinetics of primary humoral response depend on several factors like:

- Nature and type of antigen.
- The involvement of adjuvants.
- Route of antigen administration.
- The species of the organism.

The primary response has a long lag period during which several activities occur like; clonal selection of B cells, their clonal expansion and subsequent differentiation into plasma cells or memory cells. An exponential increase in the serum antibody level is seen after the log phase. A plateau is reached after some time and then the antibody levels gradually decline.

The process of antibody production has four distinct stages as discussed below and shown in Fig 3.7.

1. ***Lag phase:*** It is the phase when primary contact with the antigen is established. IgM appears and engages the antigenic element. The length of the lag phase is variable. For example- the pneumococcal polysaccharide persists for several hours while the Diphtherial toxin lasts for 2-3 weeks.
2. ***Log phase:*** Rapid increase in the antibody levels.
3. ***Plateau:*** An equilibrium state where the antibody production and decay is balanced.
4. ***Decline phase:*** The antigenic stimulus is removed and the serum antibody level begins to fall.

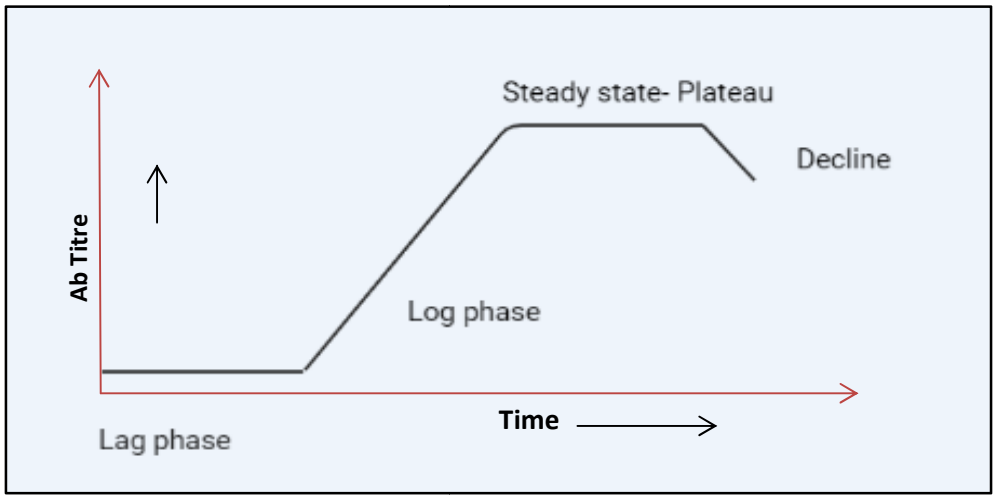


Fig. 3.7: Stages of antibody production.

Initially a rise in the serum IgM levels is seen and later it is replaced by IgG antibody. The IgM has higher avidity, which means that it is capable of engaging more diverse antigens. The IgG on the other hand is more specific to a particular antigen and thus appears in later stages of the immune response. The primary response can last from a few days to a several weeks depending on the antigen and the severity of the infection.

The memory cells that are generated during this process move out of the cell cycle and progress into the G_o phase, where the cell is less metabolically active. These memory cells last for variable durations in the body and some may last for even the entire lifetime. It is the population of memory T cells and memory B cells that together elicit the secondary immune response on subsequent encounter with the same antigen.

3.8.2 The Secondary Immune Response

The secondary immune response is generated on subsequent exposure to the antigen and its interaction with memory B cells generated during the primary response. In secondary response, the lag phase is shorter but the magnitude is greater and persists longer. There is secretion of antibodies other than IgM that are more specific to the antigen.

Reasons for rapid and higher magnitude response in Secondary Response

1. The population of naive B-cells is much lower that the more antigen specific memory B cells.
2. The memory B cells are more readily activated than naive B-cells.

The production of higher affinity and different antibodies other than IgM is due to the processes of:

1. Affinity maturation
2. Class switching.

Therefore, the antibodies produced are equipped with better effector functions that are customised for a particular pathogen. There is a 100-1000 fold increase in antibody concentration as compared to primary response and the predominant antibody in this case is IgG along with IgA and IgE. In Table 3.3 Primary and Secondary Responses are compared and comparison of Ig levels in serum in both the responses is depicted in Fig. 3.8.

Table 3.3: Differences between Primary and Secondary Immune Responses.

Sr. No.	Primary Response	Secondary Response
1.	Occurs following first exposure to a foreign antigen.	It occurs on encountering the same antigen subsequently.

2.	A longer lag phase is observed that may last from a few days to a few weeks.	The lag phase is very short.
3.	Weaker response.	Effective, rapid and more specific response.
4.	Appears mainly in spleen and lymph nodes.	First seen in bone marrow, then in lymph nodes and spleen.
5.	IgM antibody predominates.	IgG antibody predominates, also small amounts of IgM, IgA, IgE. (Fig 3.8)
6.	The response occurs by naïve B cells and naïve T cells.	Response occurs by memory B and T cells.
7.	Rapid decline in antibody levels is seen and become undetectable after some time.	Antibodies persist for longer time.

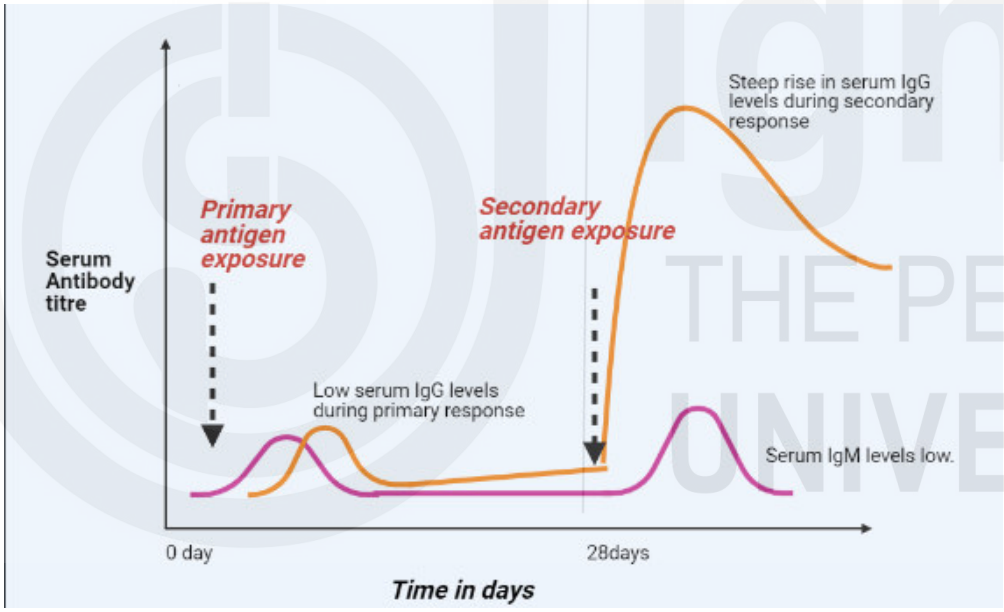


Fig 3.8: Comparison of serum Ig levels in primary and secondary immune response.

3.9 HOW DO THE INNATE AND ADAPTIVE IMMUNE SYSTEMS WORK TOGETHER?

As seen earlier, foreign pathogens and antigens are selectively recognised and eliminated by the adaptive immune system when the innate immune system fails to defend the body against the pathogen invasion. It is capable of responding only when a stimulus is provided by the innate immune system.

An antigen is a non-self or foreign molecule that is recognised by cells of the innate immune system. The information is then passed on to the adaptive immune system. These cells are called antigen-presenting cells (APC) and they recognise, engulf and pass on the activation signal to the adaptive system.

The pathogen/antigen is phagocytosed by APCs and then digested into many smaller fragments. These antigenic fragments are then transferred to the surface of the APC. This fragment will act as a signal for other immune cells activation. Dendritic cells and macrophages act as professional antigen presenting cells.

Once the antigen is phagocytosed, a phagosome is formed which then fuses with a lysosome to form a phagolysosome where the antigen is broken down, and then attached to class II MHC molecules. The class II MHC molecules-antigen peptide complex is then moved to the cell surface and present the antigen peptides. Various immune cells respond when antigen is presented by MHC-II molecules. One of the main cells to respond is Helper T-cells. They release cytokines and cause further activation of cells.

Additionally, the adaptive immunity is fully activated by danger signals displayed on cells. This occurs when the Pattern Recognition Receptors (PRRs) present on APCs like macrophages and dendritic cells recognise general classes of molecules frequently displayed by pathogens but never our own body. These pathogen specific patterns are called Pathogen Associated Molecular Patterns (PAMPs). This triggers events in the cell due to which threat signals are displayed by cells. Also, various cytokines, chemokines and chemotactic lipids are released that bring the adaptive immune system into action. Furthermore, dendritic cells bridges the innate and adaptive immune systems by presenting antigen and communicating the signal of activation to $CD4^+$ Helper T lymphocytes.

3.9.1 Natural Killer Cells-The Bridge between Innate and Adaptive Immune Systems

The functional borders between innate and adaptive immune system is blurred due to the sophisticated biological roles played by NK cells.

The immune system has been divided into: Innate immunity and Adaptive immunity. The innate immunity consists of myeloid and lymphoid cells having limited number of germ line-encoded receptors which cause rapid effector functions. The adaptive immune system consists of lymphocytes- the B and T cells that express a wide variety of antigen receptors. The receptors of these cells are produced by site-specific somatic recombination. Naive B and T cells exert their effector functions after undergoing cell division and maturation on encountering the antigen in lymphoid organs.

NK cells are a population of white blood cells that have been classified as lymphoid cells as:

- They originate from the common lymphoid progenitor cells.
- Many lymphoid markers are expressed by them.
- Morphological similarity.

NK cells do not express antigen specific receptors on their surface and are thus considered to be a part of the innate immune system. They are cytolytic cells that can kill tumor cells or virus infected cells even in the absence of any prior immunisation, unlike cytotoxic T-cells.

NK cells are also known to produce many cytokines, chemokines and growth factors. In several pathological and physiological conditions, several cytokines like Interferon –γ (IFN-γ), pro-inflammatory cytokines like Tumor necrosis factor-α (TNF-α) and immunosuppressive cytokines like interleukin (IL–10) are also secreted. The NK cells are able to influence T-cell responses through the secretion of interferon –γ. There is a direct interaction between naive T cells and NK cells migrating from the site of inflammation in peripheral tissues to secondary lymphoid compartments. Growth factors like G-CSF (granulocyte colony-stimulating factor), IL-3 and as GM-CSF (granulocyte macrophage colony-stimulating factor) are also produced. The chemokine molecules secreted include CCL2, CCL3, CCL4, CCL5 and CCL8. These chemokines play important role in facilitating the presence of NK cells with dendritic cells at the site of inflammation.

The T cell responses are influenced by the killing of target cells by NK cells by probably-

- Decreasing the load of antigen.
- Cross presentation of target cell debris to $CD8^+$ cytotoxic T cells.

It is established that NK cells have cytolytic effects against tumor cells or virus infected cells, but they also impact dendritic cells, macrophages and neutrophils due to cytokine production and cytotoxicity. Thus NK cells play an important role in influencing subsequent interaction of B and T cells with antigens. Depending upon the nature of antigen, NK cells can negatively or positively influence the B and T cell of the host immunity through the secretion of IFN-γ and IL-10.

SAQ 4

Do as directed:

i) …….. have cytolytic effects against tumor cells or virus infected cells. (Fill the blank)

ii) Initially a rise in the serum IgM levels is seen in primary immunity and later it is replaced by IgG antibody. (True/False)

iii) IgM has more affinity than IgG. (True/False)

3.10 ACQUIRED IMMUNITY

There are two types of acquired immunity viz. naturally acquired and artificially acquired immunity (Table 3.4)

Table 3.4: Differences between Naturally Acquired and Artificially Acquired Immunity.

Sr. No	Naturally Acquired Immunity	Artificially Acquired Immunity
1.	*Active*- This is acquired when the antigen enters the body naturally; the host fights it and recovers naturally.	*Active*- Killed or attenuated pathogen is introduced in the host. This process is called vaccination.

2.	*Passive*- It occurs when the antibodies are passed from mother to the foetus through the placenta or when the antibodies are given to child via breast milk.	*Passive*- Preformed antibodies are given to individual from an immune animal/person.

3.10.1 Naturally Acquired Immunity

Naturally acquired immunity can be divided as active or passive-

1. **Active:** When a pathogen enters the body, the innate immune system passes on a message for the activation of adaptive immune system via antigen presenting cells. The B and T cells are activated via interaction between cells and the secretion of many cytokines, chemokines and other molecules. Eventually, memory B and T cells are formed and immunologic memory of the antigen/pathogen is retained in the body. Also, receptors specific to the pathogen are acquired by the host. On subsequent exposure to the same pathogen, a much exaggerated secondary response is mounted. This also forms the basis for vaccination.

   A wild infection with for example Hepatitis A virus would elicit an immune response. A lifelong protection can be generated post- recovery.

2. **Passive:** New-borns are particularly susceptible to infections as they have no prior exposure to most antigen/pathogens. Thus, the mother provides passive protection to the baby.

   The maternal antibodies (MatAb) are transferred from mother to the foetus through the placenta via FcRn receptor found on placental cells. This happens around the end of first trimester. Thus very high antibody levels are found in the baby at the time of birth. These antibodies have almost the same specificity for antigen as the mother. **The only antibody that can cross the placenta is IgG.**

   Also, breast milk contains large amounts of secreted antibodies (mainly IgA) that protect the new-born till it becomes capable of synthesizing antibodies itself.

   This immunity is however very short lived as no antibodies are synthesized or immunological memory is generated.

3.10.2 Artificially Acquired Immunity

The Artificially acquired immunity can be active or passive.

1. **Active:** This can be acquired by the process of Vaccination. A vaccine contains an antigenic substance that can induce primary immune response without producing any signs or symptoms of the disease. The term “vaccine” was adopted by Louis Pasteur in honour of Edward Jenner who developed the small pox vaccine in 1796.

The vaccination process involves providing immunization by priming the immune system with the antigen deliberately. There are several types of vaccines- their types and example are given in Table 3.5.

Table 3.5: Different types of vaccines and their examples.

Sr. No	Vaccine	Description	Examples
1.	Inactivated vaccines	Composed of potentially pathogenic microorganisms that are no longer capable of causing infection as they have been killed using chemicals/ heat or other treatments.	Cholera Flu Plague
2.	Attenuated vaccines	The potentially pathogenic microorganisms are inactivated/ weakened and are no longer capable of causing infection.	Mumps Rubella virus Yellow fever
3.	Toxoid based vaccines	Used when the disease is caused by pathogenic toxin rather than the pathogen itself.	Tetanus
4.	Subunit/ recombinant vaccine	Immunisation with small pathogenic fragments.	Hepatitis B virus

2. Passive: Passive immunisation is critical when the infection is rapidly spreading and there is insufficient time for the body to develop response and protect itself. Artificially acquired passive immunity is due to the intravenous or intramuscular injection of preformed antibodies from human or animal plasma through antiserum therapy and immunoglobulin therapy. This is short lived as no response is generated and antibodies are superficially administered. **It used in the treatment of several types of acute infections and in the treatment of poisoning.**

However, in this method the major drawback is the risk of developing hypersensitivity reactions, especially when gamma globulins are involved from non-human sources.

SAQ 5

Fill in the blanks:

i) A vaccine contains an …… that can induce primary immune response without producing any signs or symptoms of the disease.

ii) The only antibody that can cross the placenta is ……..…. .

iii) During primary contact with the antigen, memory of this encounter is generated in our system in the form of ……..... .

iv) In …… vaccine the potentially pathogenic microorganisms are inactivated/weakened and are no longer capable of causing infection.

3.11 SUMMARY

Let us summarise whatever you have learnt in this unit

- Adaptive immune response is generated post exposure to a pathogenic antigen or after a vaccination. The responses are tailor made to specific antigenic challenges and not present naturally like the innate immune system.
- The features of adaptive immunity are diversity, antigen specificity, immunologic memory and self and non-self-differentiation.
- The acquired immunity can be naturally and artificially acquired.
- There are several types of vaccines:-inactivated, attenuated, toxoid and recombinant vaccines.
- B-cells are formed in the bone marrow and on activation form memory and plasma cells.
- A signal transduction pathway is initiated by BCR binding to antigen. This leads to the activation of B-cells.
- T-cells that recognise antigen-MHCII molecule function as helper T-cells.
- T-cells that recognise antigen-MHCI molecule function as cytotoxic T-cells that on activation form cytotoxic T-lymphocytes.
- Cytokines are low molecular weight proteins or glycoproteins with regulatory roles.
- Cytokines trigger signal transduction pathways and eventually lead to alteration of gene expression in target cells by binding to specific receptors located on the target cell.
- Cytokines exhibits several features: redundancy, pleiotropy, synergy and antagonism.
- Humoral immunity is mediated by molecules like antibodies, various complement proteins and antimicrobial peptides. Therefore, it is also known as Antibody Mediated Immunity.
- The cell mediated immune response is the method of the body to fight against pathogens like bacteria and viruses. It is also responsible for the killing of cancerous cells and in the graft-rejection process.
- Primary response is seen on first encounter with the pathogen. It usually has a long lag phase. IgM is the main antibody involved.
- Secondary response is seen on subsequent exposure to the same antigen. It has a much shorter lag phase and is of a greater magnitude.

3.12 TERMINAL QUESTIONS

1. Expand the following terms:

   a) CTL

   b) MHC

   c) T_H cell

   d) APC

2. Match the following:

Attenuated vaccine	Cholera
Toxoid	Mumps
Killed vaccine	Tetanus

3. State as 'True' or 'False'.

   i). Interleukin -10 is a cytokine.

   ii). NK cells need prior antigen exposure to get activated and cause cytolytic activity.

   iii). The memory B-cells are more easily activated than naive B-cells.

4. List the various factors that determine the kinetics of humoral response.

5. Fill in the blanks:

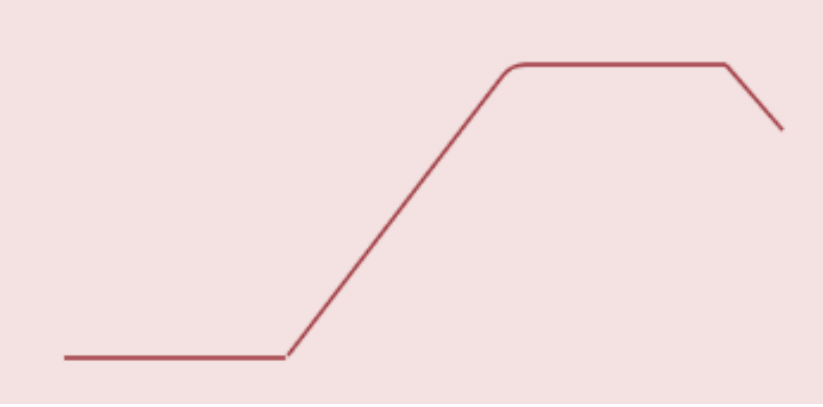
   i). …… is an example of active artificially acquired immunity.

   ii). …… is an example of active naturally acquired immunity.

   iii). Passage of antibodies via mother's milk is an example of ...……..

6. Why is the IgM that appears early in the infection replaced by IgG antibodies in the later exposure?

7. Label the stages of antibody production given in the figure.



8. Fill in the blanks:

   i) Activated B cell clones form ……..... and ……. cells.

   ii) B-cells are called so due to their origin in ……. in birds.

   iii) $CD8^+$ T cell activated transform into …… .

   iv) B-cells mature in …… lymphoid organ.

9. Provide a name for the following situations.

   i) IL-4 secreted by activated T_H cells goes on to activate B cell, thymocyte and mast cells.

   ii) IL-2, IL4 and IL-5 secreted by activated T_H cells all cause B cell proliferation.

3.12 ANSWERS

Self Assessment Questions

1. i) True, ii) False, iii) True.
2. i) c, ii) a, iii) d, iv) e, v) b.
3. i) T-cell precursors
   ii) Cytotoxic T-lymphocyte
   iii) Humoral immunity
4. i) NK cells, ii) True, iii) False, iv) True.
5. i) Antigenic substance.
   ii) IgG.
   iii) Memory B and T cells.
   iv) Attenuated vaccine.

Terminal Questions

1. a) Cytotoxic T lymphocyte.
   b) Major Histocompatibility Complex.
   c) Helper T cell.
   d) Antigen presenting cell.
2. Match the following:

Attenuated vaccine	Mumps
Toxoid	Tetanus
Killed vaccine	Cholera

3. i) True, ii) False, iii) True.

4. Factors that determine the kinetics of humoral response are:

   - Neutralization of pathogens and toxins.
   - Classical pathway of complement activation.
   - Opsonisation of pathogen and help in phagocytosis.
   - Eventual pathogen clearing.

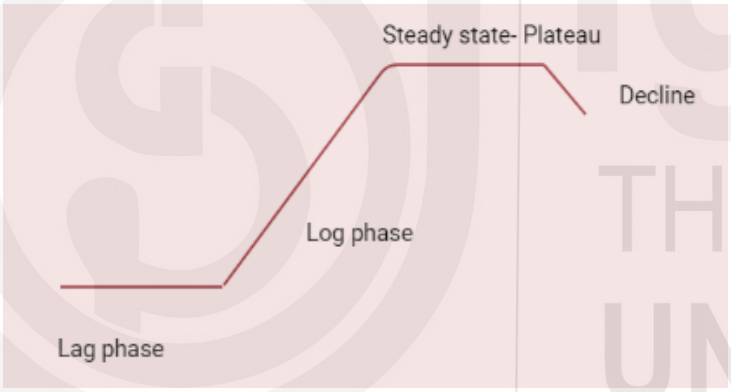
5. i) Vaccination.

   ii) Exposure to antigen and natural recovery of the body.

   iii) Passive naturally acquired immunity.

6. Initially a rise in the serum IgM levels is seen and later it is replaced by IgG antibody. IgM has higher avidity, which means that it is capable of engaging more diverse antigens. The IgG on the other hand is more specific to a particular antigen and thus appears in later stages of the immune response.

7.



8. i) Memory cells and plasma cells.

   ii) Bursa of Fabricius.

   iii) Cytotoxic T lymphocytes.

   iv) Bone marrow.

9. i) Pleiotropy, ii) Redundancy.