Unit-II Cells and Organs of the immune system

1. Haematopoiesis.

Defination- Haematopoiesis is the production of all the cellular components of blood and blood plasma. It occurs within the haemopoietic system, which includes organs and tissues such as the bone marrow, liver and spleen.

simply, haematopoiesis is the process through which the body manufactures blood cells. It begins early in the development of an embryo, well before birth and continues for the life of individual.

Anatomy of Haematopoiesis -

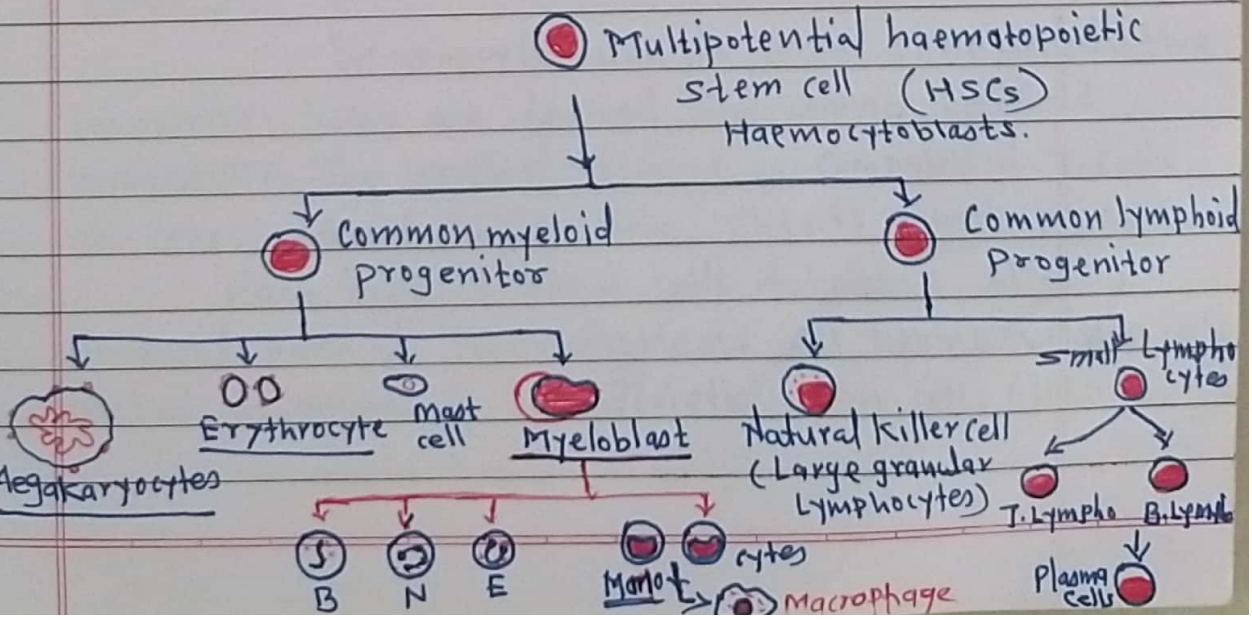
In First Trimester - yolk sac
Second Trimester - Liver & spleen
Third Trimester - Central & peripheral skeleton
Adulthood - Axial skeleton, vertebral bodies, Ribs, pelvis etc.

In adult - RBCs & platelets develops in bonemarrow.

In infants & children - spleen & liver

Particularly spleen, lymph nodes & thymus produce lymphocytes (WBCs) & Tissues in liver ~~spleen~~ Spleen, lymph nodes produce monocytes (another types of WBCs.)

Organization of Haematopoiesis :-



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Haematopoietic stem cells (HSCs)

Haematopoietic stem cells reside in medulla of the bone marrow and have the unique ability to give rise to all of the different mature blood cell types & tissues. HSCs are self-renewing cells. When they differentiate, at least some of their daughter cells remain as HSCs. so the pool of stem cells is not depleted. This phenomenon is called asymmetric division.

The other daughters of HSCs (myeloid and lymphoid progenitor cells) can follow any of the differentiation pathways that lead to the production of one or more specific types of blood cells, but cannot renew themselves.

The pool of progenitors is heterogeneous and can be divided into two groups, long-term self renewing HSC and only transiently self-renewing HSC, also called short terms. This is one of the main vital processes in the body.

Red blood cells, Megakaryocytes, Mast cell, Basophils, Eosinophils, Neutrophils, monocytes, Macrophages develops from Common myeloid progenitor which are involved in diverse roles of innate immunity & blood clotting.

Lymphocytes are the corner stone of adaptive immunity. They are derived from common lymphoid progenitors. The lymphoid lineage is composed of T. cells, B-cells, natural killer cells This is lymphopoiesis.

Each type of blood cells follows a slightly different path of haemadopoiesis. All begins as stem cells called multipotent haemopoietic stem cells (HSC.)

Red blood cells and platelets-

1. RBCs: Common myeloid progenitor (CMP) cells change five times before finally becoming red blood cells also known as erythrocytes.

2. platelets: CMP cells transform into three different cell types before becoming platelets.

White blood cells

There are several types of white blood cells each following an individual path during haematopoiesis All white blood cells initially transforms from CMP cells into myeoblasts. After that the process is as follows

* Before becoming a neutrophil, eosinophil or basophil a myeoblast goes through four further stages of development.
* To become a macrophage a myeoblast has to transform three more times.

A second pathway of haematopoiesis produce T & B cells. To produce lymphocytes, multipotent haematopoietic stem cells transform into common lymphoid progenitors, which then become lymphoblasts. Lymphoblasts differentiate into infection-fighting T cells & B cells. Some B cells differentiate into plasma cells after exposure to infection.

Some blood disorders can affect healthy blood cells in the blood, even when haematopoiesis occurs.

Haematopoiesis is a constant process that produce a massive number of cells. Estimates vary, and the precise number of cells depends on individual needs. But in a typical day, the body might produce 200 billion red blood cells, 10 million white blood cells, and 400 billion platelets

-: Cells of immune system :-

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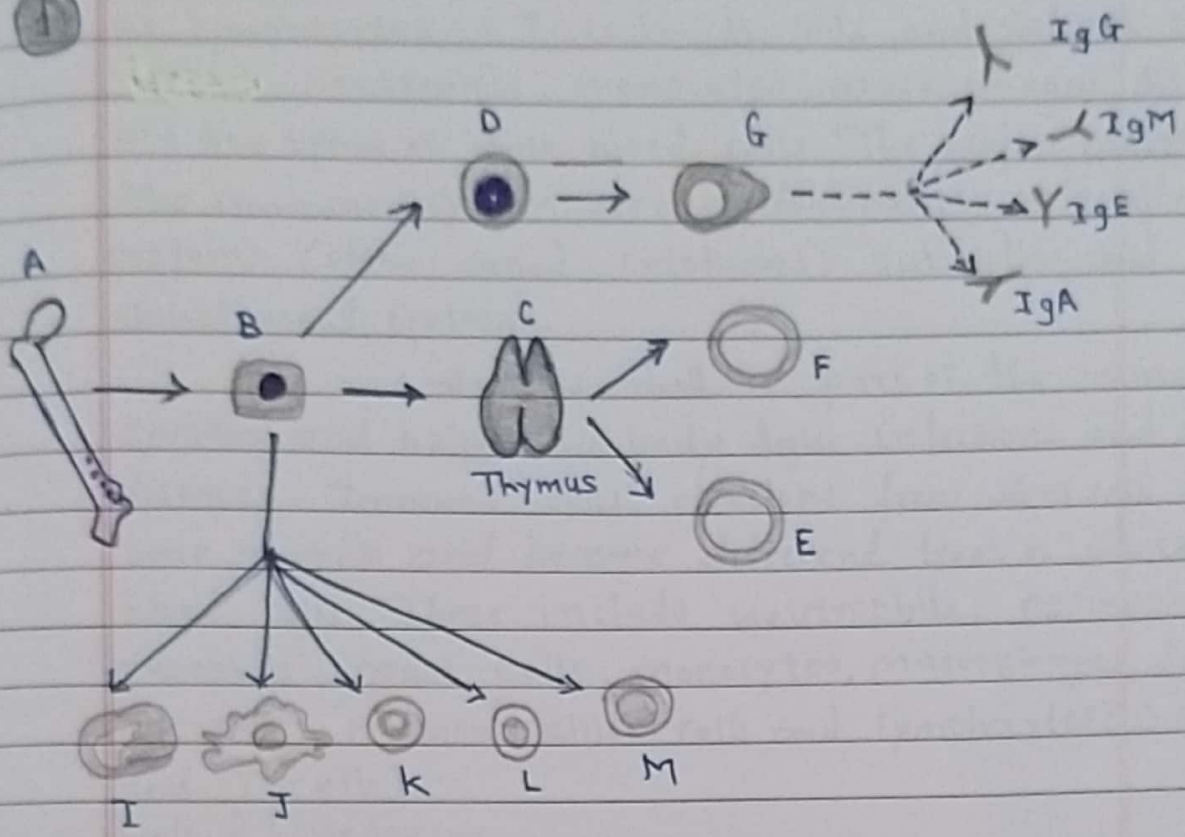

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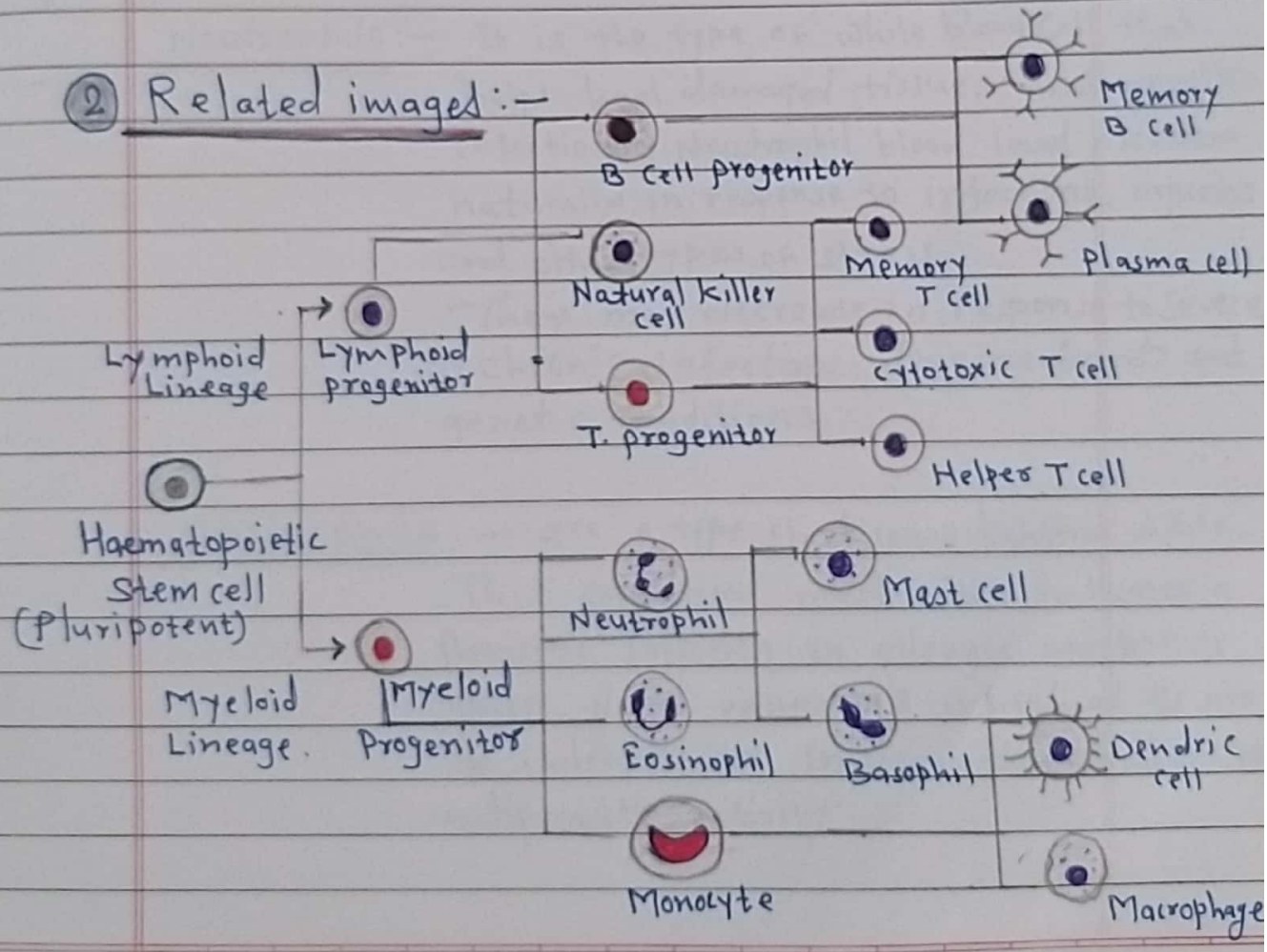

The cells of the immune system can be categorized as lymphocytes (T-cells, B-cells and Natural killer cells), Neutrophils, monocytes, macrophages. All these are the types of white blood cells. The major proteins of the immune system are predominantly signaling proteins (often called cytokines) antibodies and complement proteins.

A cells that is part of the immune system and helps the body fight infections and other diseases. Immune cells develops from stem cells in the bone marrow and become different types of white blood cells. These include neutrophils, eosinophils basophils, mast cells, monocytes, macrophages, dendritic cells, natural killer cells and lymphocytes (B cells and T cells).

Cells of Myeloid Lineage:-

1. Neutrophils:- It is the type of white blood cell that helps heal damaged tissues and resolve infections. Neutrophil blood level increase naturally in response to infections, injuries and other types of stress.
They may decrease in response to severe or chronic infections, drug treatments and genetic conditions.

2. Eosinophils:- are a type of disease fighting WBCs. This condition most often indicates a parasitic infection, an allergic reaction or cancer. No of eosinophils is high at the site of infection or inflammation. Antibacterial antiparasitic activity.

3. Basophils :- It play a part in "immune surveillance" Basophils have the ability to help detect and destroy some early cancer cells. Another important function of basophil is that they release the histamine in their granules during allergic condition or asthma attack.

4. Mast Cells :-

Mast cells are types of WBCs located all over the body. people have highest number of mast cells where the body meets environment, the skin, lungs & intestinal tract. It contribute to homeostasis in immune sys. They serve as a first line defense against antigen entering the body due to their location.

5. Monocytes :-

Monocytes fight certain infections and help other WBCs remove dead & damaged cells and fight cancer cells.

6. Dendric cells :- (Tree likes ape)

These cells are responsible for the initiation of adaptive immunity. hence functions as the 'sentinels' of immune system dendritic cells are antigen-presenting cells. Main function to process antigen & present it on the cell surface of the T. cells.

7. Macrophage :-

are specialised cells involved in the detection, phagocytosis and destruction of bacteria and other harmful organisms In addition, they can also present antigens to T-cells and initiate inflammation by releasing molecules of cytokines that activate other cells.

Cells of Lymphoid Lineage :-

1. Natural Killer cells :- (NK cells)

Natural killer cells are lymphocytes in the same family as T and B cells coming from a common progenitor. These cells secretes cytokines such as IFNγ and TNFα, which act on other immune cells like macrophage and dendritic cells to enhance the immune response. NK cells are effector lymphocytes of the innate immune system that control several types of tumors & microbial infections by limiting their spread & subsequent tissue damage.

2. Bcell progenitors

(a) Memory cells :-

Memory cells are long-lived immune cells capable of recognizing foregin particles they were previously exposed to (thus the memory in their name) As clones, the memory B cells bear the same B cell receptors as those of the parent B cells Therefore, they would be able to detect the same antigen when reexposed.

(b) Plasma Cells :-

Are the type of B lymphocytes. It is also called plasma B cells. plasma cells secrete large quantities of proteins called antibodies. inresponse to being presented specific antigen.

3. T cell progenitors

(a) Memory T Cell :-

Memory T cells are antigen-specific T cells that remain long-term after an infection has been eliminated. The memory T cells are quickly converted into large number of effector T-cells upon reexposure to the specific invading antigen.

Thus providing a rapid response to past infection.

(b) Cytotoxic T cells :-

Are effector cells that destroy virus-infected cells, tumor cells, and tissue grafts that exist in the cytosol or contiguous nuclear compartment. it is also known as $CD8^+$ T cells. These cells carry out their killing function by releasing two types of cytotoxic protein. granzymes - which able to induce apoptosis in any type of target cell & the pore forming protein perforin, which punches holes in the target-cell membrane through which granzymes can enter.

(c) Helper T cells :-

These are arguably the most important cells in adaptive immunity, as they are required for almost all adaptive immune responses. They not only help to activate B cells to produce antibodies and macrophages to destroy ingested microbes, but they also help activate cytotoxic T cells to kill infected target cells.

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: Organs of the immune system:

primary lymphoid organs include the bone marrow & the thymus. They create special immune system cells called lymphocytes.

The secondary lymphoid organs include the lymph nodes, the spleen, the tonsils & certain tissues in various mucous membrane layers in the body

primary Lympoid organs	Secondary lymphoid organs
1. Central lymphoid organs	1. Where antigen is localized so that it can be effectively exposed to mature lymphocytes.
2. Where immature lymphocytes develop.	2. Initiate adaptive immune response
3. In these organs differentiation, proliferation & maturation of stem cells into immuno competent cells takes place	3. Includes - spleen. Lymph nodes, Tonsils Appendix, Peyer's patches
Includes 1. Thymus 2. Bone marrow.	

organs that function as barriers :—

our skin and mucous membranes are the first line of defense against germ entering - from outside the body. They acts as a physical barrier with support from the following.

1> Antibacterial substances can kill germs right from the start. A certain enzymes found in saliva, airways and tear fluid destroys the cell walls of bacteria.

2> Mucus in the bronchi helps trap many of the germs we breathe in so they can be moved out of the airways by hair-like structures called cilia.

3> stomach acid stops most of the germs that enter the body in the food we eat.

4> Harmless bacteria on our skin & many of the mucus membranes in our body also act as part of immune system. In addition, the reflexes that cause us to cough & sneeze help to free our airways of germs.

Primary lymphoid organs:

(1) Bone marrow :—

It is a sponge-like tissue found inside the bones. That is where most immune system cells are produced and then also multiply. These cells move to other organs & tissues through the blood. At birth, many bones contain red bone marrow, which actively creates immune cells. over the course of our life, more and more red bone marrow turns into fatty tissue. In adulthood, only a few of our bones still contain red bone marrow, including the ribs, breastbone and the pelvis.

(2) Thymus :—

It is located behind the breastbone above the heart. This gland like organ reaches full maturity only in children, and is then slowly transformed to fatty tissue. special types of immune system cells called thymus cell lymphocytes (T cells) mature in the thymus. Among other tasks, these cells corordinate the processes of the innate and adaptive immune system. T cells move through the body & constantly monitor the surfaces of all cells for changes.

Secondary lymphoid organs:—

(1) Lymph nodes :—

Lymph nodes are small bean-shaped tissue found along the lymphatic vessels. The lymph nodes acts as filters. Various immune system cells trap germs in the lymph nodes & activate the creation of special antibodies in the blood. swollen painful lymph nodes are a sign that the immune system is active. for example to fight an infection.

(2) Spleen:-

The spleen is located in the upper abdomen, beneath the diaphragm, and is responsible for different kinds of jobs.

(1) It stores various immune system cells, when needed, they move through the blood to the organs. Scavenger cells in the spleen act as a filter for germs that get into the bloodstream.

(2) It breaks down red blood cells (erythrocytes)

(3) It stores and break down platelets which are responsible for the clotting of blood among other things.

There is always a lot of blood flowing through the spleen tissue. At the same time this tissue is very soft. In the event of severe injury, for example in an accident, the spleen may rupture easily. surgery is then usually necessary because otherwise their is a danger of bleeding to death. If the spleen needs to be removed completely, other immune system organs can carry out its roles.

(3) Tonsils :-

The tonsils are also part of the immune system. Because of their location at the throat and palate, they can stop germs entering the body through the mouth or nose. The tonsils also contain a lot of white blood cells, which are responsible for killing germs. There are different types of tonsils: Palatine tonsils, adenoids and the lingual tonsil. All of these tonsilar structures together are sometimes called Waldeyer's ring since they form a ring around the opening of the throat from the mouth & nose. There is also lymphatic tissue on the side of the throat, whic can perform the functions of the palatine tonsils if they are removed.

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(4) Mucous membranes:—

The bowel plays a central role in defending the body against germs. More than half of the body's cells that produce antibodies are found in the bowel wall especially in the last part of the small bowel & in the appendix. These cells detect foreign substances, & then mark & destroy them. They also save information about the substances in order to be able to react more quickly the next time. The large bowel also contains harmless bacteria called gastrointestinal flora. Healthy gut flora make it difficult for germs to spread & enter the body. mucous membranes support the immune system in other parts of the body, too, such as the respiratory and urinary tracts & the lining of the vagina. The immune system cells are directly beneath the mucous membranes, where they prevent bacteria and viruses from attaching.

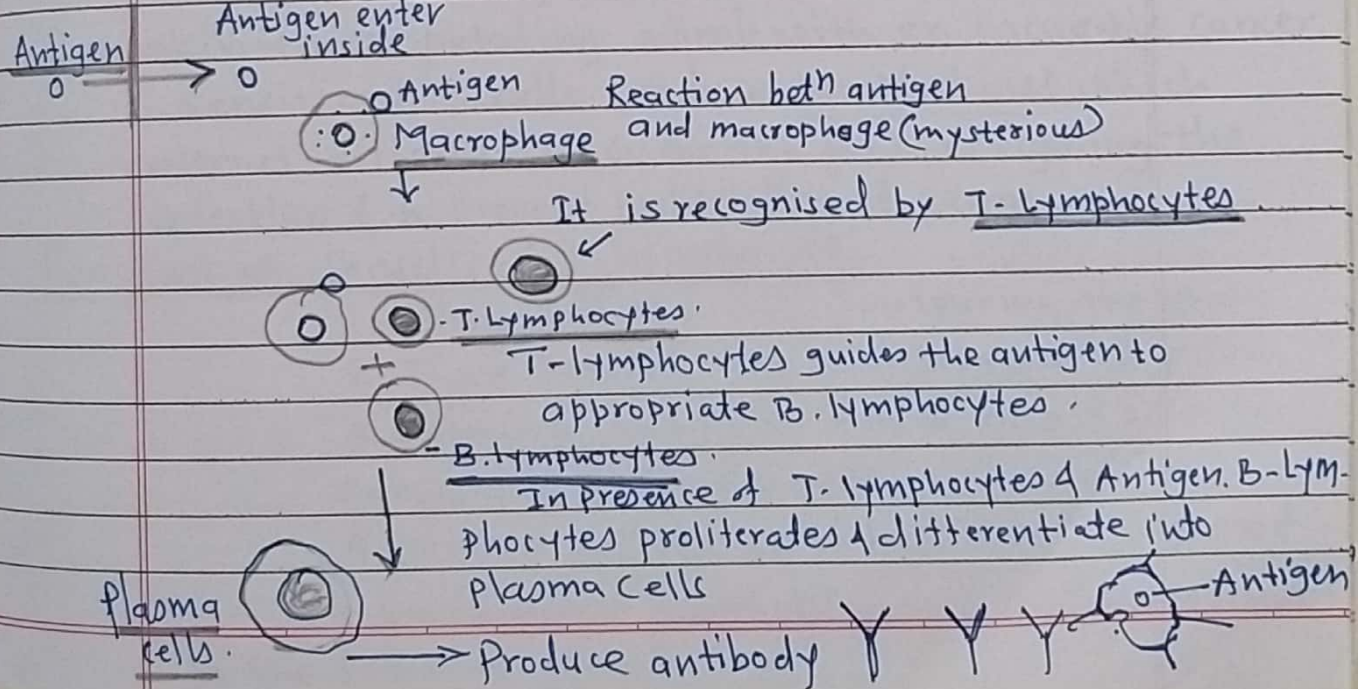
Immune responses (Humoral & cell mediated)

(1) Humoral Immune Response:

The important features of this response is the production of antibodies which circulate in the blood stream and neutralize the toxins or help to eliminate the invading germs. The antibody formation is usually triggered by a protein called antigen. Antigen is a small part of invading agent. If this part is identified, separated and introduced into the blood stream, it alone also triggers the antibody formation. Antigen may be a virus, bacteria, pollen or any chemical substance. If the antigenic component of a number of germs is the same, then same type of antibodies are formed indicating that infection by any of them will afford protection against others also.

Mechanism of Antibody formation.

1- upon entry into the body antigen first comes in contact with the macrophages (phagocytes) in tissues.
2. The reaction of the antigen with the macrophage in some mysterious way leading the macrophages to become fit to be recognised by a T-lymphocyte in the blood stream.
3. The T-lymphocyte then guides the antigen to appropriate B-lymphocytes in lymphoid organs.
4- In the presence of T-lymphocytes and antigen the B-lymphocytes proliferate & ditterentiate into antibody forming cells called plasma cells.
5 plasma cells starts producing antibodies specific for the antigen.
6. Antibody formation is under the control of genes.
7. Antibody bind with antigen & make it inactive/destory it
8. Antibody may get attached to other cells like neutrophils or macrophages conferring on them the ability to detect antigen and ingest it.
9- They may bind the other B. lymphocytes & stimulate their transformation to plasma cells which produce more antigen.



(2) Cellular immune response:

B-lymphocytes are concerned with humoral immunity the cellular immunity involves T-Lymphocytes. There are many germs which take shelter within the cells of the body. for such organisms another response in the body called cellular immunity it includes following events.

1. upon the entry into the body the antigen first comes in contact with macrophages in tissues.
2. Macrophage processes the antigen & bring it in contact with T-lymphocytes.
3. The result of this contact is that the T-cells are converted into killer T-cells, technically called Sensitized T-cells.
4. Sensitized T. cells not only act directly but also by stimulate the proliteration of similar sensitized T-cells all over the body.
5. Sensitized T. cells neither forgive nor forget the enemy because of their good memory, they swing into action promptly whenever the same organism invades the body again.
6. sensitized T-cells hunt for the cells which have been invaded by the germs and kill them. It is an event akin to amputating a limb with an incurable cancer.
7. sensitized T-cells produce lymphokined which attract ditterent WBCs for the help in fighting the infection & to prevent proliferation of germs.

Functions of Sensitized T. Lymphocytes:

1-They kill the cells harbouring the germs.
2. They prevent the proliteration of germs.
3. Stimulate the production of more similarly sensitized T. lymphocytes.
4. Increase resistance of host cells to some types of germs
5. production of lymphokines attract the leucocytes to the fighting ground.