EXTENSIVE QUESTIONS

18. Describe the human skin as an impenetrable barrier against invasion by microbes.

Ans: Skin: An Impenetrable barrier against microbial invasion:

The skin is made up of two layers I.e. epidermis and dermis.

Epidermis is superficial multiple cell thickened layer white **dermis** inner comparatively thick layer containing glands hair follicles receptors nerves and blood vessels.

Keratin:

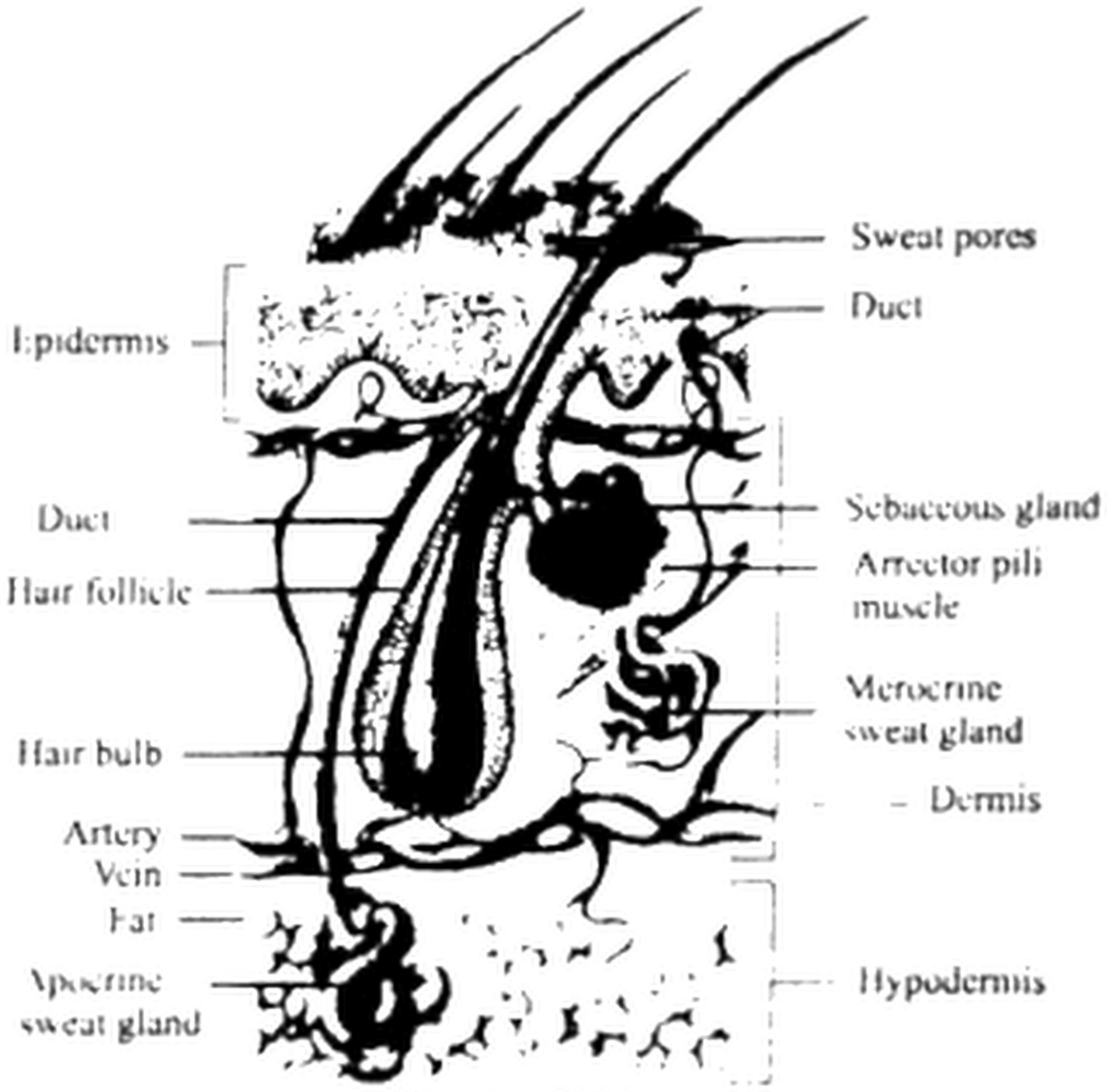
Most cells of epidermis are keratinocytes, which produce a protein mixture called

keratin:

The outer surface of the skin also consists of dry dead cells. Consequently, most microbes that land on the skin cannot obtain the water and nutrients they need.

Sebaceous Glands and Sweat Glands:

In addition, the dermis part of skin also contains the sebaceous glands and sweat glands. **Sebaceous glands** produce **sebum**, an oily substance **whereas sweat glands** secrete **sweat**, a salty fluid that generally provides cooling effect to the body. Secretion from sweat glands and sebaceous glands usually cover the skin. These secretions contain natural antibiotics such as lactic acid that inhibit the growth of bacteria and fungi. These multiple defence make the unbroken skin an extremely effective barrier against microbial invasion.



Glands of Skin

Skin as an impenetrable barrier against microbial Invasion

19. What is the role of macrophages and neutrophils in killing bacteria?

Ans: Killing cells of blood:

Phagocytes:

There are white blood cells in the body called **phagocytes:**

Phagocytosis:

A phagocyte is a cell that destroy other abnormal body cells (cancerous cells) or invaded microorganisms by engulfing or ingesting them. This process is called **phagocytosis.** Two types of blood cells are phagocytes macrophages and neutrophils.

Macrophages:

Macrophages are divided from monocytes that leave the blood are called macrophages.

Monocytes:

Monocytes are formed in bone marrow. From bone marrow, through blood macrophages are transported to the areas of the body where they are needed. Macrophages are generally found in the organs such as the lungs, liver, spleen, kidney and lymph nodes, rather than remaining in the blood.

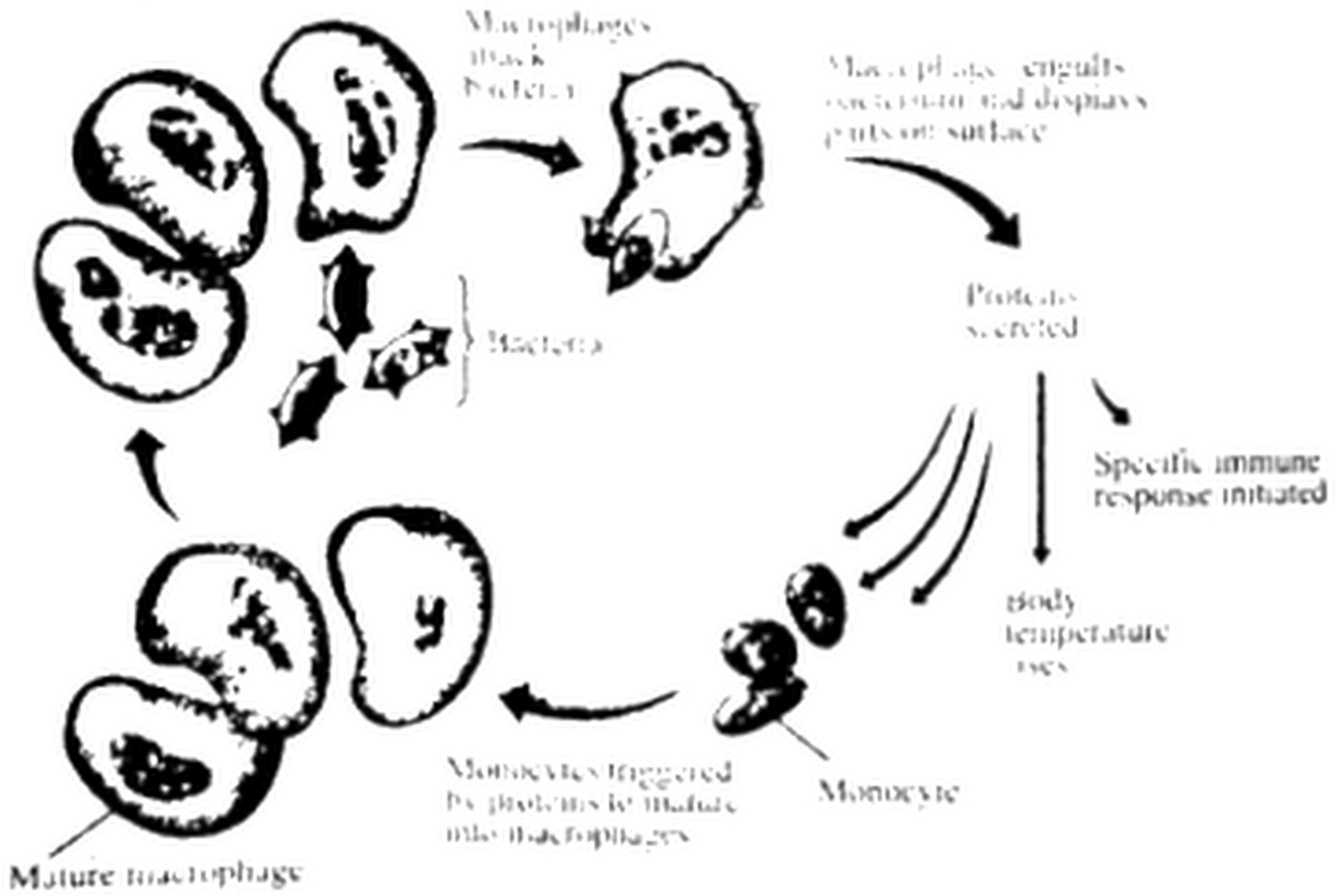
Functions of Macrophages:

i. In these organs, they patrol within the free spaces among the cell and provides protection by trapping and destroying microorganisms entering the tissue.

ii. As macrophages interact with microbes they not engulf and destroy them, they also display some parts of microbes on their surface so that other body cells may also be informed.

iii. The macrophages also secrete many different proteins when they perform phagocytosis of the microbes. Some of these proteins trigger the maturation of monocytes into macrophages, thereby increasing their numbers.

iv. Another protein Interleukin-I, singles the brain to raise the body temperature producing fever. Some other protein also stimulates the specific immune response.



Response of macrophages to foreign particles

Neutrophils:

These belong to the granulocyte type of WBCs. They are highly short-lived and highly mobile as they squeeze between cells of capillary walls and can enter parts of issue where other cell/molecules would not be able to enter otherwise.

Functions of Neutrophils:

I. They move like *Amoeba* forming pseudopodia
II. They proceed rapidly to infected area to perform their duty and they often die after single phagocytic event.
III. Net ophil also release lysosomal enzymes and certain chemicals kill microorganisms and cause inflammation

20. Explain the protective protein of complementary system with diagram.

Ans: Protective proteins of Complement System:

The complement system consists over thirty types of small proteins found in

the blood. In general, synthesized by the liver and normally circulating in active state.

They are activated on the entry of foreign particle. Once a **complement protein** is activated. It activates another protein which further activates other protein of the system and so on. The result of the complement activation is stimulation of phagocytes to clear foreign and damaged material, development of intimation to attract additional phagocytes at the site of infection and activation of the cell killing membrane attack complexes. The complement system is an important supporter of the immune system that enhances (complement) the ability of antibodies and phagocytic cells to clear microbes and damaged cells from the body promotes inflammation and attacks the pathogen's plasma membrane.

Action of the complement system against a bacterium

Example:

An example of protective protein of complement system is **protein, a** membrane attack complex that produce holes in the bacterial cell walls and plasma membranes of bacteria. The holes allow fluids and salt to enter the bacterial cell, thus, bacterial cell swells and eventually burst.

Interferons:

Interferons (IFNs) belong to the large class of protein known as **cytokines,** molecules used for communication between cells during infection.

They are made and released by host cells in response to the presence of several pathogens specially viruses.

Functions of interferons:

Interferons are named for their ability to "**interfere**" with viral replication as interferons activate molecules which prevent the virus from producing and replicating its RNA or DNA. In this way interferons limit cell-to-cell, spread of viruses in the body. IFNs also activate immune cells, such as natural killer cells and macrophages that in turn destroy virally infected cells.

21. Explain in detail inflammatory response with diagram.

Ans: Inflammatory Response:

The inflammatory response is a major component of the non- specific defence. Any damage to tissue, whether caused by an infections microorganism or by physical injury, even just a scratch or an insect bite triggers this response inflammation can be localized or systemic (widespread). Local inflammation is an inflammatory response confined to a specific area of the body.

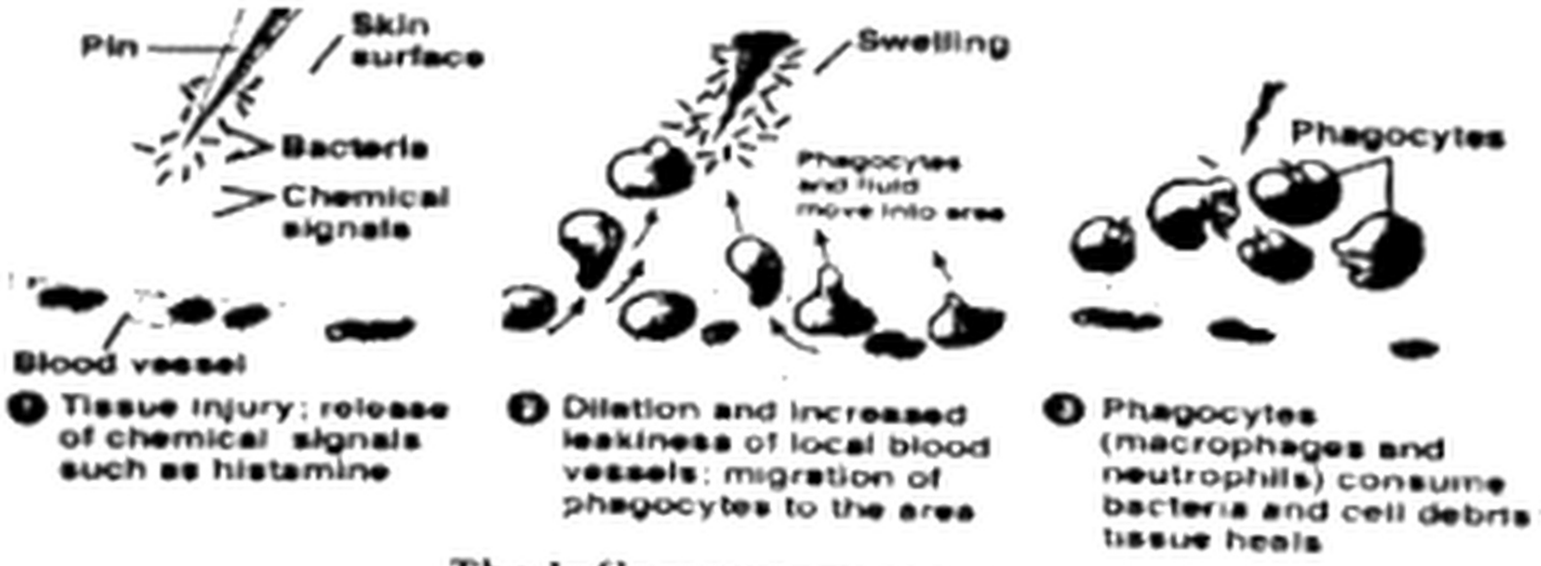
Signs of Inflammation:

The classical signs of inflammation are heat, pain redness, swelling, and loss of function.

Inflammatory Response:

Inflammation literally means "setting on fire". The finger shows the chain of events that make up the inflammatory response. In case where a pin has broken the skin and infected it with bacteria. The first thing that happened when a

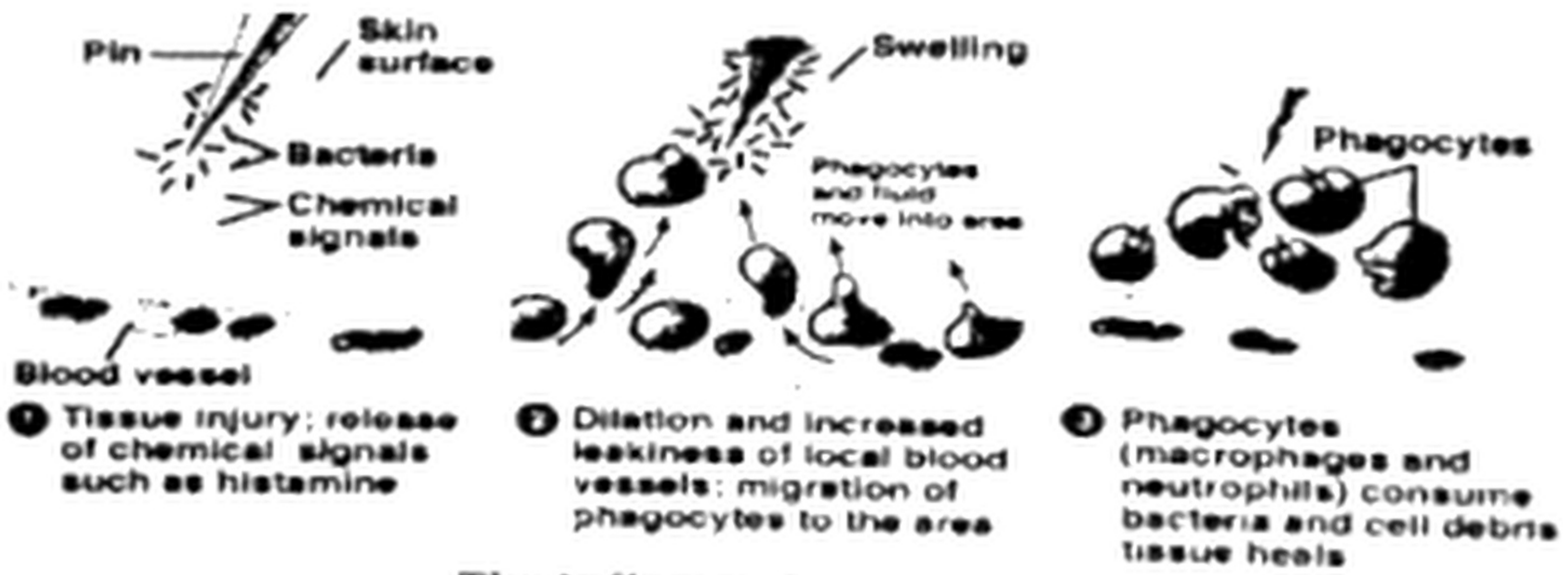
tissue is injured is that the damaged cells release chemical alarm signal such as **histamine.** The chemical sparks the mobilization of various defence. Histamine for instance induces neighboring blood vessels to dilate and blood vessels start leaking. Blood supply to the damaged area increases, and blood plasma passes out of the leaky vessels into the interstitial fluid of the affected tissues.



The Inflammatory response

Function of inflammation:

The function of inflammation is a eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult (to attack physically) and the inflammatory process, and to initial tissues repair. The inflammatory response also helps to prevent the spread of infection to the surrounding tissues.



The Inflammatory response

22. Explain temperature response against infection.

Ans: Temperature Response:

Pyrogens:

Fever or pyrexia is the raised body temperature than normal. The invaded microorganisms often release certain chemical, which are generally termed as **pyrogens**.

High Temperature:

These pyrogens cause the temperature set point of the **hypothalamic thermostat** of the body to rise, as a result, all the mechanisms for raising the body temperature are brought into play, such as heat conservation and increased heat production. Since, higher body temperature than normal facilitates the microbial growth in the body, this is the reason why invaded microorganisms want to increase the host's body temperature.

Endogenous Pyrogens:

On the other hand, certain white blood cells in response to the infection, also release hormones collectively called **endogenous pyrogens** (self-produced fire makers) that further increase the temperature set point of hypothalamus because higher body temperature than normal increase for activity of phagocytic white blood cells that attack upon bacteria.

Effects of high Temperature:

I. The endogenous pyrogens also cause other cells to reduce the concentration of iron in the blood because many bacteria require more iron to reproduce at temperature of 38° C or 39° C than at 37° C, so fever and reduced iron in the blood combine to slow down their rate of reproduction.

ii. Fever also increases the production of interferons that travel to other cells and increase their resistance to viral attack.

iii. The higher body temperature may directly inactivate the virus particles, particularly enveloped viruses, which are more heat-sensitive than non-enveloped viruses.

Iv. Replication of some viruses in reduced at higher temperatures, therefore, fever may inhibit replication.

However, fever is nonspecific defence against microbial infections, but often, high degree fever becomes destructive for body's own metabolic system and ultimately body is collapsed. Therefore, physicians use to prescribe antipyretic drugs to the patients of high degree fever.

23. What are the ways fever kills microbes?

Ans: **Fever** or **pyrexia** is the raised body temperature than normal.

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24. Describe the role of monocytes in immune system.

Ans: Role of Monocytes in third line of defence:

As already described in second line of defence that monocytes are kind of WBCs, **which are** produced by lymphoid tissues. The monocytes circulate in blood for 10 to 20 hours and ultimately, they leave the blood and come into intercellular space of tissues. In the tissues, they swell and attain a larger size to become tissue **microphages.**

Interleukin-1:

When macrophages perform phagocytosis of invaded

microorganisms after digesting them, they not only display microbial antigens on their surfaces but also begin to secrete about 100 different compounds including various enzymes, interferons and a protein called **Interleukin-1.**

Role of Interleukin-1:

The Interleukin-1 secrete by macrophages activates the T cells that in turn begin to secrete Interleukin-2, which then activates the B cells, Interleukin-1 also promotes a general response to injury, causing fever and activating other mechanisms that defend the body against invasion.

25. What is the role of T cells in cell mediated response.

Ans: Role of T cells in third line of defence (cell mediated immune response):

The cells originate from stem cells in the bone marrow. After early embryonic development, the newly forming T cells migrate to **thymus gland** for processing. The thymus makes T cells immunocompetent that is capable of immunological response. The immune response provided by T cells is called **cell mediated immune response.**

Activations of T cells:

In case of infection, macrophages perform phagocytosis of invaded microorganism and detect particular **antigens (nonself molecules)** of the organism.

Major Histocompatibility Complex (MHC):

Macrophages isolate and display these antigens on their surface with the help of their own proteins (self-protein) called **major histocompatibility complex (MHC).**

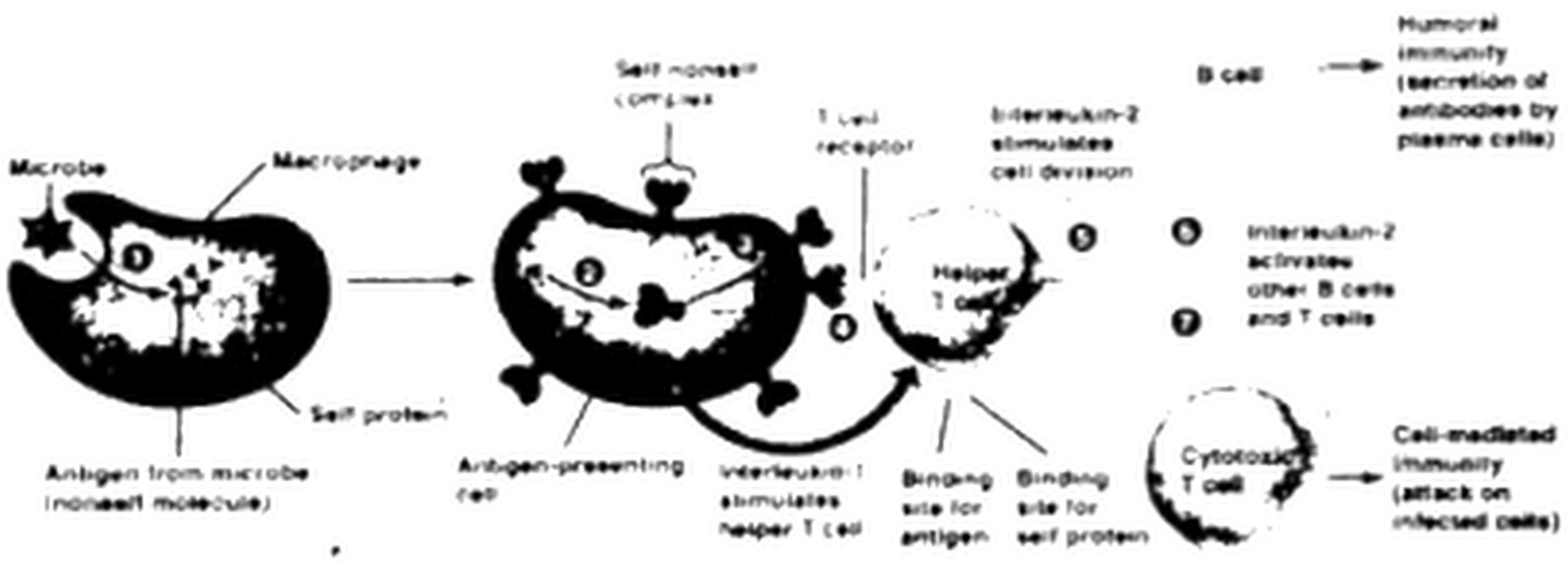
In this way macrophages come **antigen-presenting cells (APCs).** Macrophages also secrete **Interleukin-1** that stimulates and attracts helper T cells towards the displayed antigen.

T Cell Receptor (TCR):

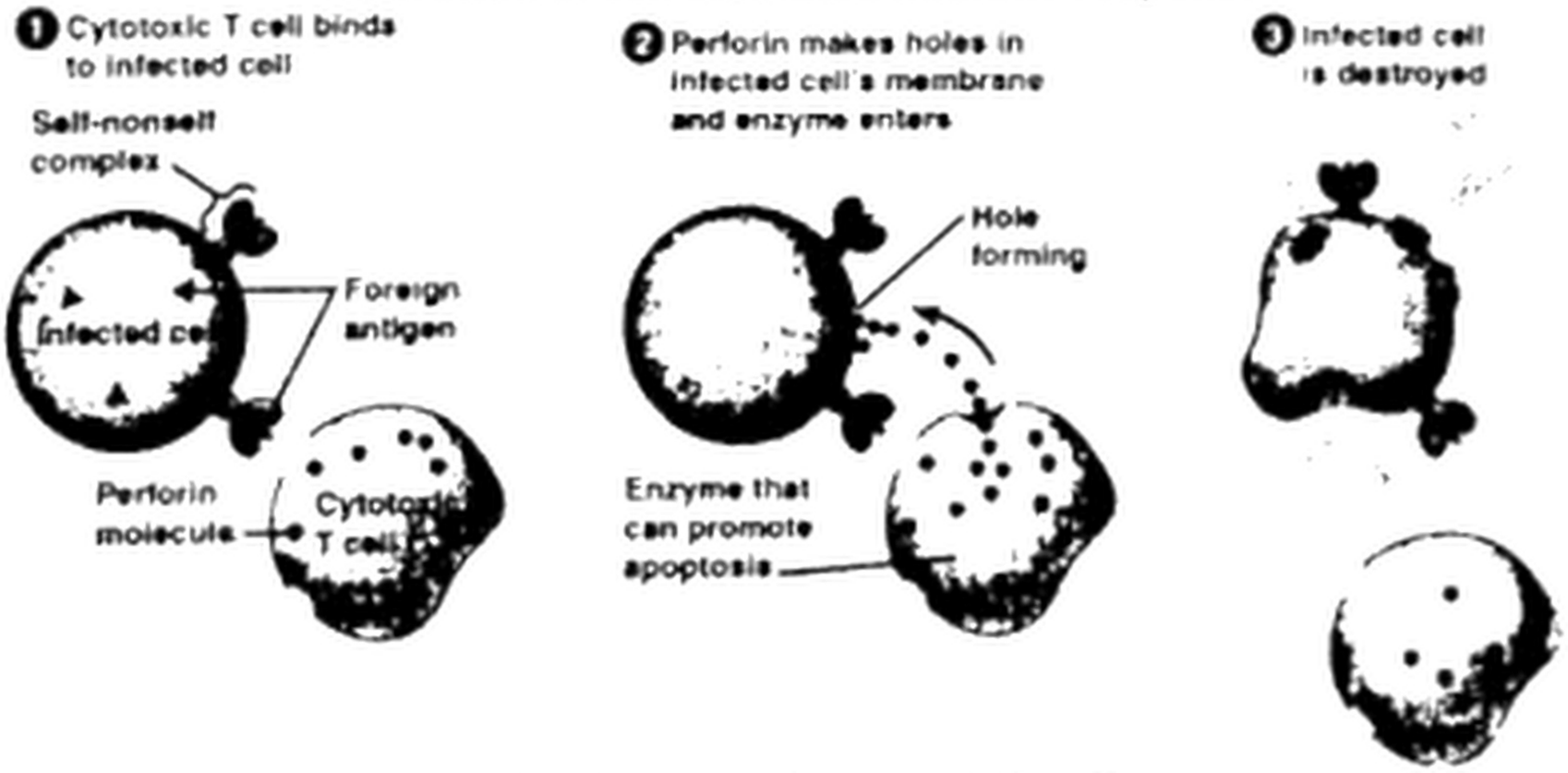
Helper T cells have specific receptor on their surface called T cell receptor (TCR) by which they bind with a particular antigen displayed o APC. Interleukin-1 also stimulates the helper T cells to secrete another protein, the Interleukin-2 that not only compact the helper T cells to divide but also causes the proliferation of certain cytotoxic T cells and B cells.

Cell-Mediated Immunity:

The activation of T-Cells by a specific antigen is called **cell-mediated immunity.** The body contains millions of different T-cells each able to respond to one specific antigen.



Activation of cell mediated immune response



Mode of action of cytotoxic T cells

Types of T cells:

Two main categories of T cells have been identified.

CD8 Cells:

The first group, known as **CD8** cells because they have surface marker designated **CD8**, include cytotoxic T cells and suppressor T cells.

CD4 Cells:

The second group i.e. **helper T cells** also known as **CD4** cells because they have a surface marker designated **CD4.**

When helper T cells are activated. They divide and produce four types of cells, which have specific role in cell-mediated immune response.

(i) Cytotoxic T cells: These cells secrete **cytotoxic** which triggers destruction of the pathogen's DNA or perforins which is a protein that creates holes in the pathogens plasma membrane. The holes cause the pathogen to lyse (rupture).

(ii) Helper T cells: These cells secretor **interleukin 2** which stimulates cell division of T cells and B cells. In other words, these cells recruit even more cells to help fight the pathogen

(iii) Suppressor T cells: When infection successfully removed, these cells begin to secrete certain proteins that inhibit further proliferation of T cell. Therefore, they shut down the immune response.

(iv) Memory T cells: These cells remain dormant after the initial exposure to an antigen. If the same antigen presents itself again, even if it is years later, the memory cells are stimulated to convert themselves into helper T cells and help fight the pathogen.

26. Describe the role of B cells in Humoral antibody mediated immune response.

Ans: Role of B cells in third line of defence:

Humoral/Antibody Mediated Immune Response:

B cells are differentiated in bone marrow B cells express specific receptors on their cell membrane. The B cell receptors (BCRs) allow the B cell to bind a specific antigen against which it will initiate an antibody response. Like T cells there are millions of B cells types, found in the body, each is specific for one particular antigen.

Activation B cells:

B cell activation begins when the B cell binds to an antigen via its BCR. Actually, B cells are stimulated to bind with specific antigen by interleukin-2 proteins, which are secreted by helper T cells.

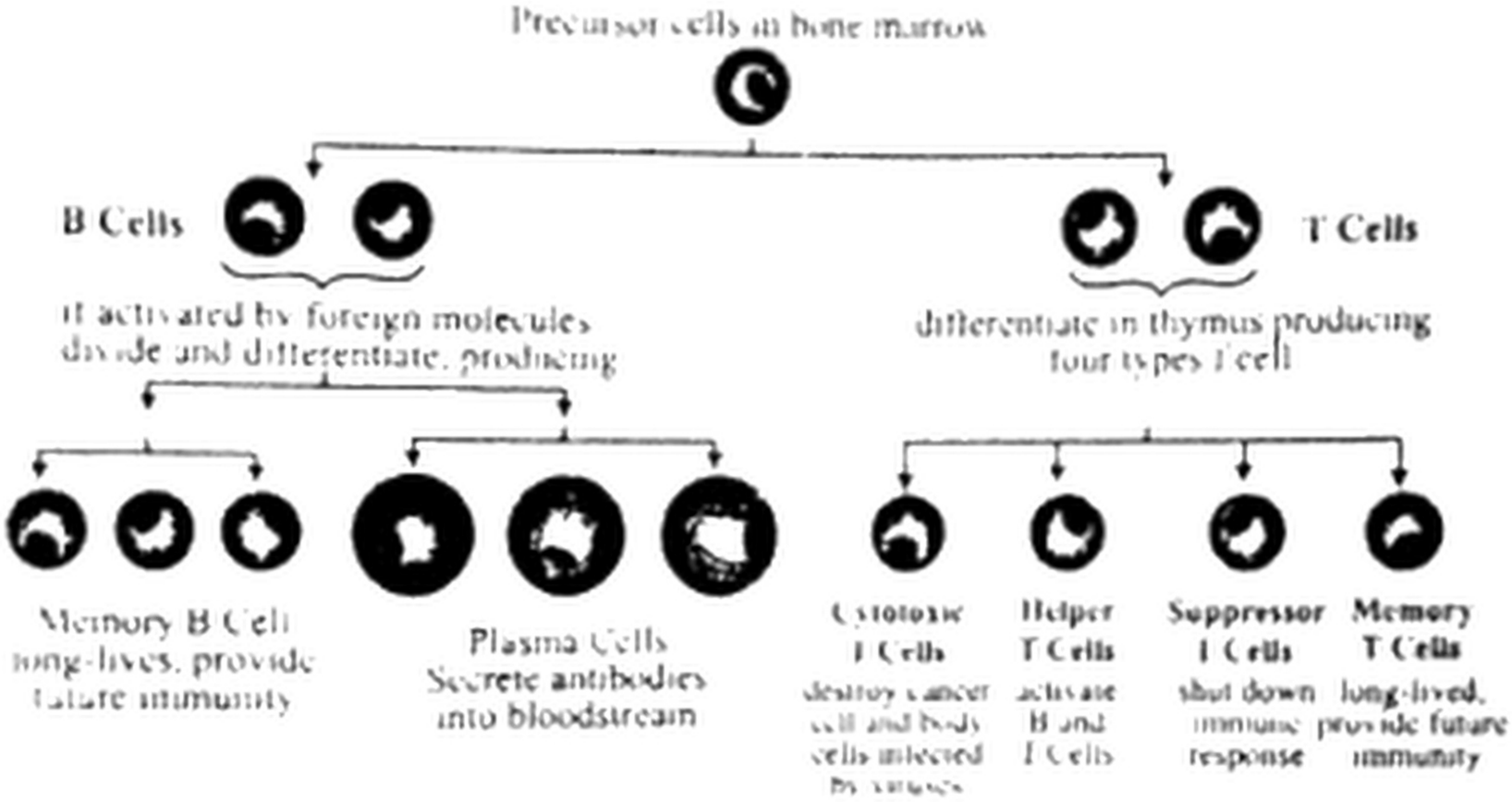
After binding with specific type of antigen, the B cells divide to produce two types of cells **plasma** clone **cells** and **memory B cells.**

Plasma Clone Cells:

The plasma clone cells are specialized to secrete bulk quantity of antibodies. After B cells become plasma cells, they live only for a few days but secrete a great deal of antibody during the time. A **plasma cell** can produce more than 10 million molecules of antibody per hour.

Memory B Cells:

If the same antigen enters the body later the memory B cells divide to make more plasma cells and membranes, B cells that can protect against future attacks by the same antigen. The stimulation of B cells to divide into plasma clone cells and memory B cells and the secretion of antibodies by plasma clone cells is called **Humoral and cell mediated** immune **response.**

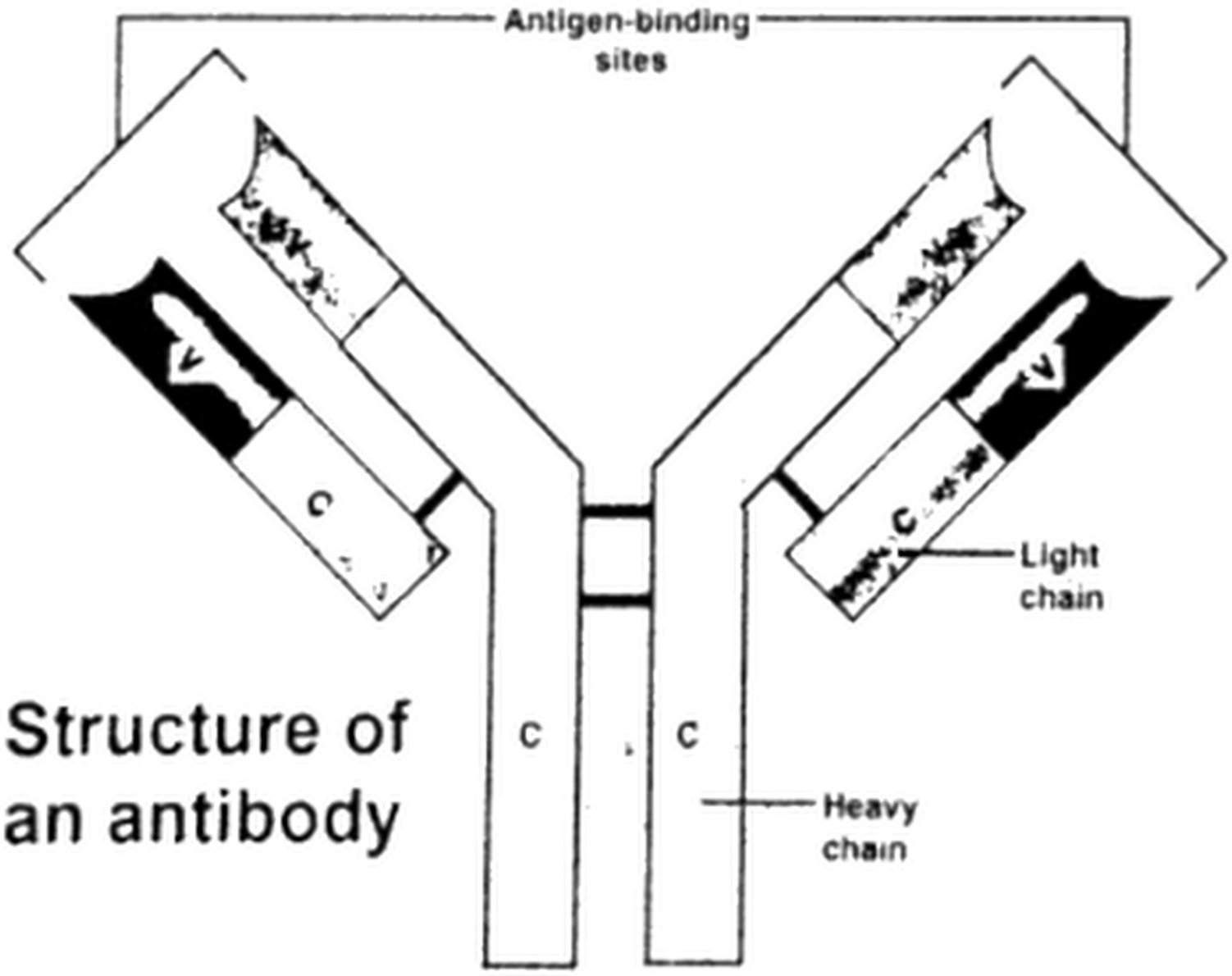


The major cells of Immune system and their roles in the immune system

27. Describe with diagram the structure of antibody.

Ans: Structure of an antibody:

Antibodies (also called immunoglobulin or Ig's) are Y-shaped proteins that circulate through the blood stream and bind to specific antigens, thereby attacking microbes. The antibodies are transported through the blood and the lymph to the pathogen invasion site.



Structure of an antibody

A typical antibody is a Y-shaped molecule which consists of four polypeptide chains, two identical long chains called **heavy** chains and two identical short chains called **light chains.**

Each chain has a **constant segment,** a functional segment and a **variable segment. Constant Segment:**

In the constant segment, (C) of the heavy chains, the amino acid sequence is constant within a particular immunoglobulin class.

Variable Segment:

On the other hand, the variable segment (V) consists of different amino acid sequences in every body. Therefore, they act as anti-binding site. Each antibody has two antigen-binding sites.

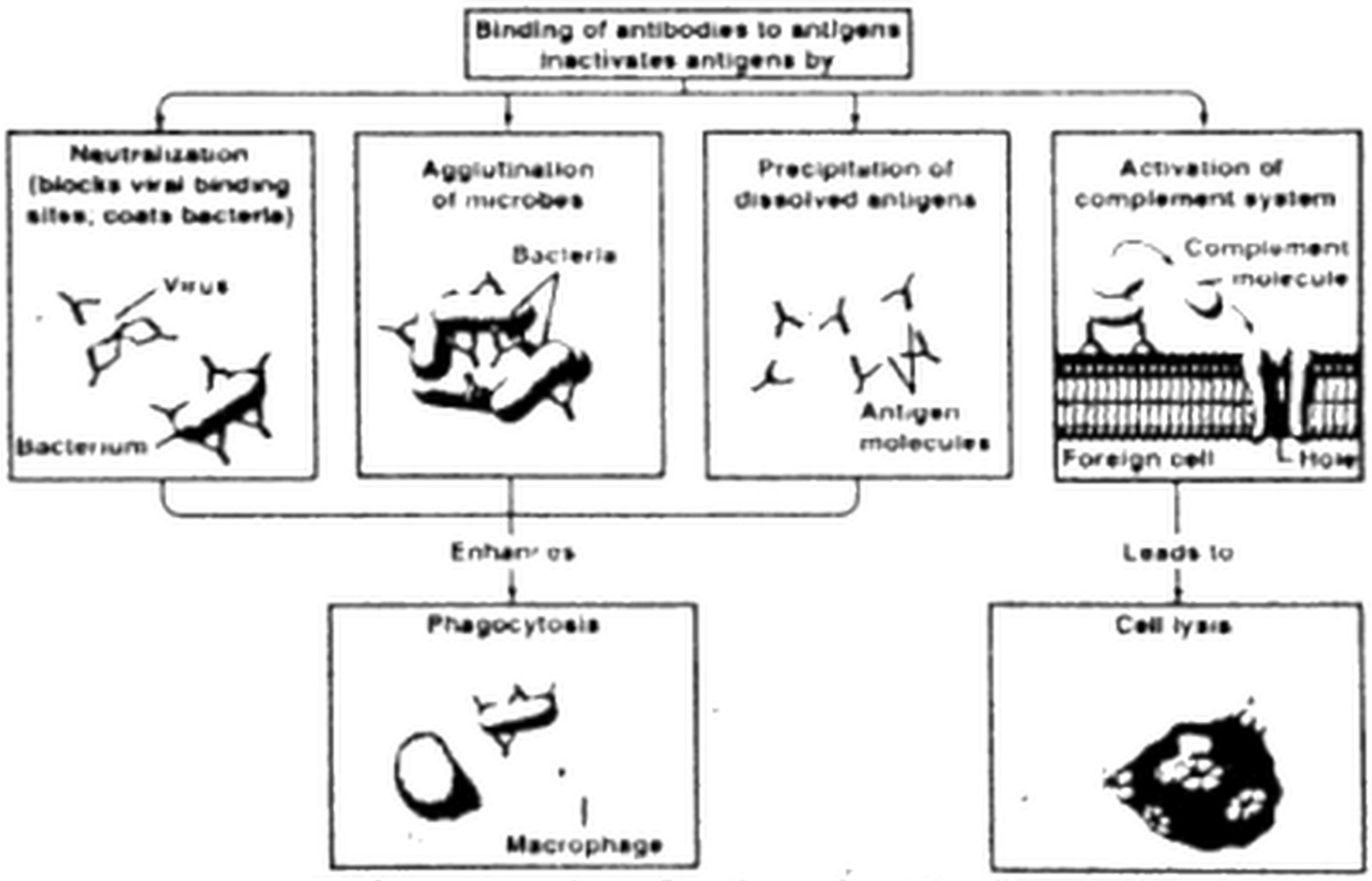
28. Describe the mode of action of an antibody.

Ans: Mode of action of an antibody:

Antibodies work in different ways.

1. Neutralizing an Antigen:

The antibody can bind to an antigen, forming an antigen-antibody complex. This forms a shield around the antigen, preventing its normal function. This is how toxins from bacteria can be neutralized or how a cell can prevent a viral antigen from binding to a body cell thereby preventing infection.



Different modes of action of antibodies

2. Activating Complement:

Complement is a group of plasma proteins made by the liver that normally are inactive in the body. An antigen-antibody complex triggers a series of reactions that activates these proteins. Some of the activated proteins can cluster together to form a pore channel that inserts into a microbe's plasma membrane. This lyses (ruptures) the cell. Other complement proteins can cause chemotaxis and inflammation both of which increase the number of white

blood cells at the site of invasion.

3. Precipitating Antigens:

Sometimes the antibodies can bind to the same free antigen to cross-link them. This causes the antigen to precipitate out of solution making it easier for phagocytic cells to ingest them by phagocytosis (as describe above).

Also, the antigens within the cells walls of the bacteria can cross-link, causes the bacteria to clump together in a process called agglutination, again making it easier for phagocytic cells to ingest them by phagocytosis.

4. Facilitating Phagocytosis:

The antigen-antibody complex signals phagocytic cells to attack. The complex also binds to the surface of macrophages to further facilitate phagocytosis.

29. Describe the types of acquired immunity.

Ans: Types of Acquired Immunity --- Active and Passive Immunity:

There are two ways to acquire adaptive immunity.

(a) Active Immunity **(b)** Passive Immunity

Both types may be acquired naturally or artificially.

Immunization:

Providing immunity artificially is called immunization.

(a) Active Immunity:

Natural Active Immunity:

Natural active immunity is the kind of immunity, which is obtained as a result of an infection. The body manufactures its own antibodies when exposed to an infectious agent. This type of immunity is most effective and generally persists for a long time some times even for life.

Artificial active immunity:

Artificial Active Immunity (vaccination) is achieved by injecting (or administering orally) small amounts of antigen, called the vaccine, into the body of an individual. The process is called **vaccination.** The antigen stimulates the body to manufacture antibodies against another antigen. Often a second, booster is given and this stimulates a much quicker production of antibody which is long lasting and which protects the individual from the disease for a considerable time. Several types of vaccine are currently in use.

In passive immunity, antibodies from one individual are passed into another individual. They give immediate protection, unlike active immunity, which takes a few days or weeks to build up. However, it only provides protection against infection for a few weeks for the antibodies are broken down by the body's natural processes, so their number slowly fall and protection is lost.

(b) Passive Immunity:

Natural passive immunity:

It may be gained naturally. For example, antibodies from a mother can cross the placenta and enter her foetus. In this way they provide protection for the baby until its own immune system is fully functional. Passive immunity may also be provided by **colostrums**, the first secretion of the mammary glands. The baby absorbs the antibodies through its gut.

Artificial passive immunity:

Antibodies, which have been formed in one individual are extracted and then injected into the blood of another individual, which may or may not be of the same species. They can be used for immediate protection if a person has been or is likely to be, exposed to a particular disease. For example, specific antibodies used for combating tetanus and diphtheria used to be cultured in horses and injected into humans. Only antibodies of human origin are now used for humans. Antibodies against the human rhesus blood group antigen are used.

30. Describe the disorder of immune system:

Ans: Disorder of Immune System:

Some conditions that stimulate a defective immune response or destroy immune system are called disorders of immune system.

Allergies:

Allergies are actually a form of immune response. A foreign substance, such as a pollen grain, enters the bloodstream and is recognized as an antigen by a particular type of B cell. This B cell proliferates, producing plasma cells that pour out the antibodies attach to the plasma membranes of histamine-containing cells located in the respiratory and digestive tracts. When pollen grains encounter the attached antibodies, they trigger the release of **histamine**, which causes increased mucus secretion, leaky capillaries, and other symptoms of inflammation.

Symptoms and Causes of Allergies:

Because pollen grains most often enter the nose and throat, the major reactions occur in these locations, resulting in the runny nose, sneezing, and congestion typical of "heavy fever". Antihistamine drugs block some of the effects of histamine, relieving the symptoms of allergies. Food allergies cause equivalent symptoms, including cramps and diarrhea, in the digestive tract.

Autoimmune disease:

Sometimes, a person's immune system does not normally respond to the antigens (self-molecules) borne on the body's own cells and the antibodies are going to produce against bodies own components and begin to destroy them. This problem is called an **autoimmune disease.**

For example:

a) Some types of anemias are caused by antibodies that

destroy a person's red blood cells.

b) Many cases of insulin-dependent (juvenile-onset) diabetes occur because the insulin-secreting cells of the pancreases are the victims of a misdirected immune response. Unfortunately, at present there is no way to cure autoimmune diseases. The autoimmune response can be suppressed with drugs.

31. Describe the role of T cells and B cells in transplant rejection.

Ans: Transplant rejections:

It is occasionally desirable to transplant some tissue or an organ such as the skin, kidney, heart, or liver, from one person to another to replace a non-functional damaged or lost body part. In such cases there is a danger that the recipient cells may recognize the donor's organ or tissue as being foreign. This triggers the recipient's immune mechanisms, which may act to destroy the donor tissue. Such a response is called transplant rejection.

Role of T cells in transplant rejection:

Although the mechanism of rejection probably varies with the nature of the tissue and the degree of incompatibility, all the mechanisms require that the host helper T cells come into contact with the graft tissue's major histocompatibility complex (MHC) antigens. This contact is probably mediated by the dendritic cells of the graft tissue itself. At this point, three different possibilities exist. In the first, **antigen-specific TH cells** stimulate the activation and proliferation of appropriate T cells, which then mount a focused attack on the transplant tissue. In the second, **responsive** antigen-specific TH cells move to the graft site, where they release **lymphokines.** These recruit monocytes/macrophages and T cells to the graft site and maintain them at the scene while they destroy the tissue.

Role of B cells in transplant rejection:

There is a third mechanism in which antibodies plays a role. The responsive

helper T cell interacts with the appropriate B cell clone, producing a shower of antibodies to the implanted tissue's MHC antigens. These can trigger either complement-mediated graft damage or facilitating the phagocytosis of the grafted tissue by macrophages.

32. Explain why a transplant recipient is given immune suppressant drugs and determine what implications this has on his life.

Ans: Organ transplantation has become a routine procedure due to improvement of surgical techniques, better tissue typing and the availability of drugs that more selectively inhibit rejection of transplanted tissues and prevent the patient from becoming immunologically compromised. Transplant rejection occurs as delayed hypersensitivity reaction as a function of lymphocytes and not due to antibodies. Administration of immunosuppressive drugs enhances tolerance. People receiving immunosuppressive drug have side effects like pain, diarrhea, leukopenia, sepsis, lymphoma, thrombocytopenia, skin rashes, anaphylactic reaction, hypertension, hyperkalemia and neurotoxicity (tremors, seizures, hallucination). Hence, each system is affected, so the person starts to feel weakness and gets fatigue easily.

33. Describe malignant melanoma as due to the inability of tumour-infiltrating lymphocyte (TIL) to control the tumour of skin cancer and correlate it with the scientific advancements of inserting a gene of tumournecrosis factor in the lymphocyte.

Ans: Describe malignant melanoma as due to the inability of tumour-infiltrating lymphocyte (TIL) to control the tumour of skin cancer and correlate it with the scientific" C advancements of inserting a gene of tumour necrosis factor in the lymphocyte. Cancer starts when cells in the body begin to grow out of control.

Melanoma:

Melanoma is a cancer that usually starts in the melanocytes a type of skin cell. Melanomas can develop anywhere on the skin, but they are more likely to start on the trunk (chest and back) in men and on the legs in women. The neck and face are other common sites.

Development of Melanoma:

The cancerous growths develop when unrepaired DNA damage to skin cells (most often caused by ultraviolet radiation from sunshine or tanning beds) triggers mutations (genetic defects) that lead the skin cells to multiply rapidly and form malignant tumours. These tumours originate in the pigment-producing melanocytes in the basal layer of the epidermis. **Tumour-Infiltrating Lymphocytes:**

Tumour-infiltrating lymphocytes are believed to represent the immune reaction/response to melanoma cells. Tumour (tumor)-infiltrating lymphocytes (TIL), are white blood cells that have left the bloodstream and migrated into a tumour. They are mononuclear immune cells, a mix of different types of cells (i.e. T cells, B cells, NK cells, macrophages) in variable proportions, T cells being the most abundant cells. They can often be found in the stroma and within the tumour itself.

TILs are not strong enough to control certain types of tumors e.g. malignant melanoma.

Protein Tumour Necrosis Factor (TNF):

For the gene therapy of malignant melanoma first the TIL cell are removed from the patient and reinserted a gene that odes for the protein tumour necrosis factor (TNF). The protein kills tumour cells by preventing from establishing a blood supply. The engineered TIL cells were then returned to the patient blood stream to seek out and invade the malignant melanoma tumours.

34. Describe the discovery of monoclonal antibodies and justify how this accomplishment revolution many aspects of biological research.

Ans: Discovery of Monoclonal Antibodies:

In 1970 Cesar Milstein and Georges Kohler working in Cambridge solve the problem of developing a technique for producing monoclonal antibodies, for which they were awarded Noble Prize 1984.

Monoclonal means belonging to one clone. Each type of antibody is most by one type B cells which cloned itself, in other words multiplies to make many identical copies of itself in response to a particular antigen. Milstein and Kohlar fused B cells with cancer cells, which are immortal to form hybridoma cells. The hybridoma cells continue to multiply and can be cloned so that large quantities of antibodies can be produced. Monoclonal antibodies are harvested from cell cultures rather than animals. The ability to make monoclonal antibodies has been spawned a new industry. A common area of application is medical diagnosis. Monoclonal antibodies are used for determining pregnancy and for diagnosing diseases such as, hepatitis, rabies, cancer, streptococcal throat infections, herpes viruses, leukemias (cancers of white blood cells) and lymphomas etc. A monoclonal antibody has been developed which is very effective at preventing rejection of transplanted kidneys. Monoclonal antibodies can be used to find out the types of antigens present in the donor and increase the accuracy of matching