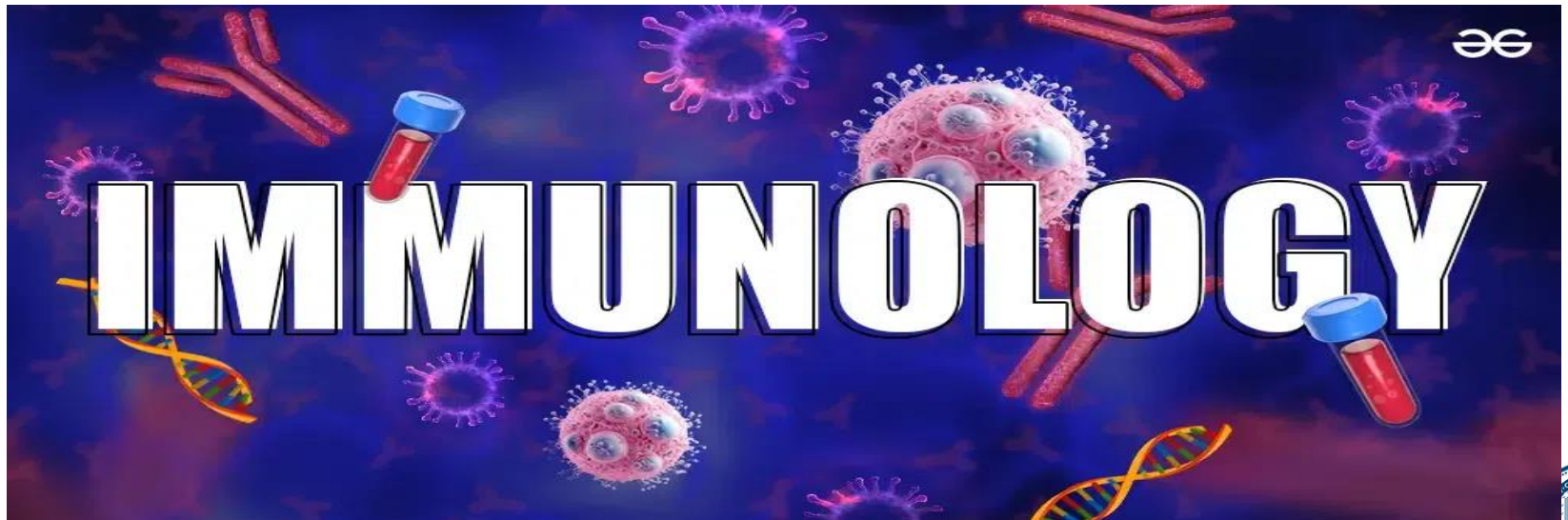


Organs and Cells of Immune System

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Organs and Cells of Immune System

Organs concerned with immune reactions are called lymphoid organs. They contain lymphoid cells.

Lymphoid organs are of 2 types:

1. Primary lymphoid organs
2. Secondary lymphoid organs



Primary lymphoid organs

Are the major site of lymphopoiesis. The lymphoid cells proliferate, differentiate and mature into immune competent cells in the absence of antigenic stimulation. The primary lymphoid organs are large at birth and they atrophy with age progression; major primary lymphoid organs are

1. Thymus (site of T-cell maturation in human)
2. Bone marrow (site of B cell maturation in human)
3. Bursa of fabricious (site of B-cell maturation in bird)



Thymus:

is the site of T cell differentiation and maturation, consist of the cortex and the medulla, cells found in thymus are; stroma cells, epithelial cells, macrophages, dendritic cells and thymocytes (the cells migrate from the bone marrow to the thymus and then become thymocytes).

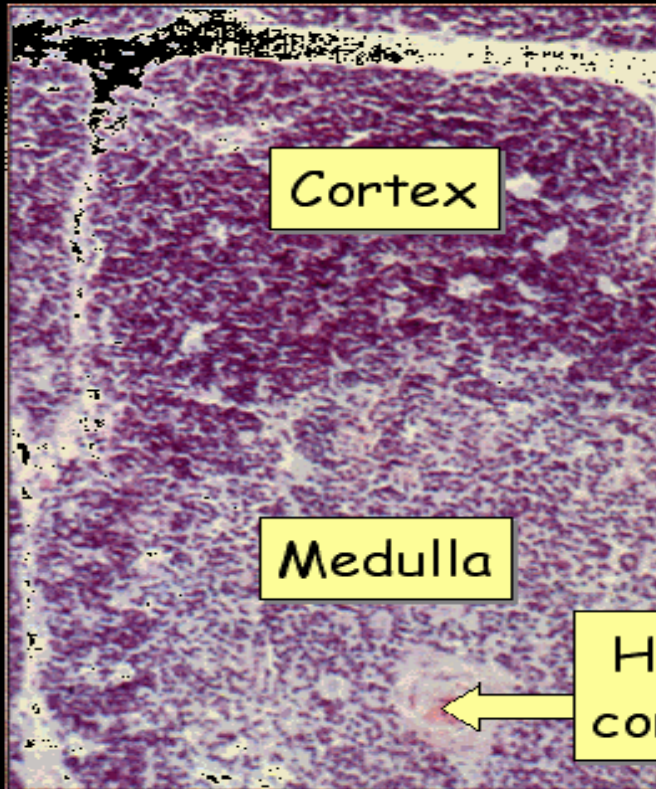
1.The structure of Thymus



THE UNIVERSITY OF AUCKLAND
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HEALTH SCIENCES

30 August 2007

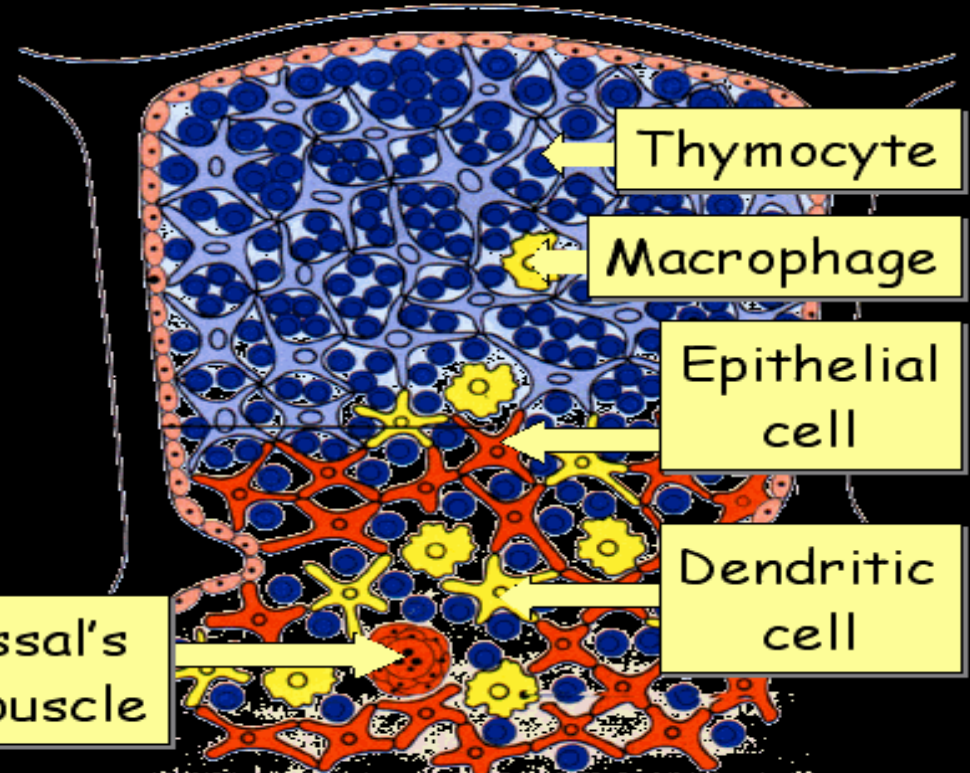
Thymus Structure



Cortex

Medulla

Hassal's
corpuscle



Thymocyte

Macrophage

Epithelial
cell

Dendritic
cell

T-cells will be clustered in the cortex; these clusters will differentiate in medulla and have their own surface molecules thus called cluster of differentiated lymphocytes (CD) e.g. , CD2, CD3, CD4, CD8, CD19. In cortex any thymocyte acquire receptors for self Ag will be killed by apoptosis (programmed cell death) this process called **negative selection**.

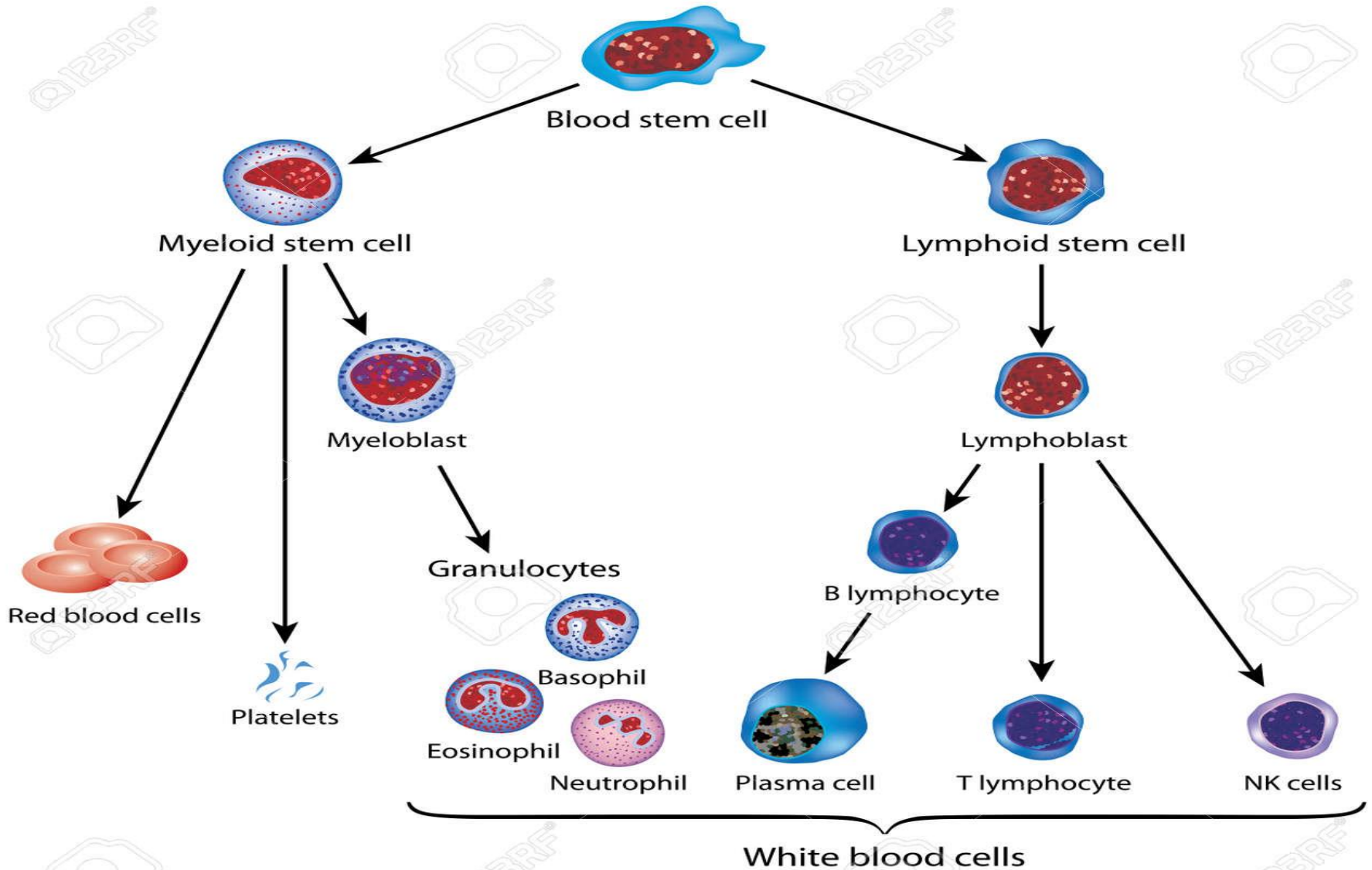


In medulla **positive selection** occur when cells acquire molecules (receptors) by which recognized Ags in association with class I MHC and class II MHC molecules. These two processes negative and positive selection are called **T-cells educations**.

Bone marrow: is the site of generation of all circulating blood cells in the adult, including immature lymphocytes, and is considered as the site of B cell maturation



blood cell development



2. Secondary lymphoid organs

Lymphocytes are made functional in the secondary lymphoid organs. The secondary lymphoid organs are small and poorly developed at birth and they grow progressively with age. The secondary lymphoid organs include:

1. Lymph nodes
2. Spleen
3. Mucosal associated lymphoid tissues (MALT), such as gut-associated lymphoid tissue (GALT).



Lymph nodes: are the organs in which immune responses to lymphoid- borne antigens are initiated, they have many functions.

- Filter and eliminate foreign antigens.
- Site of immune response.
- Site of lymphocytes residence and source of recirculation cells.

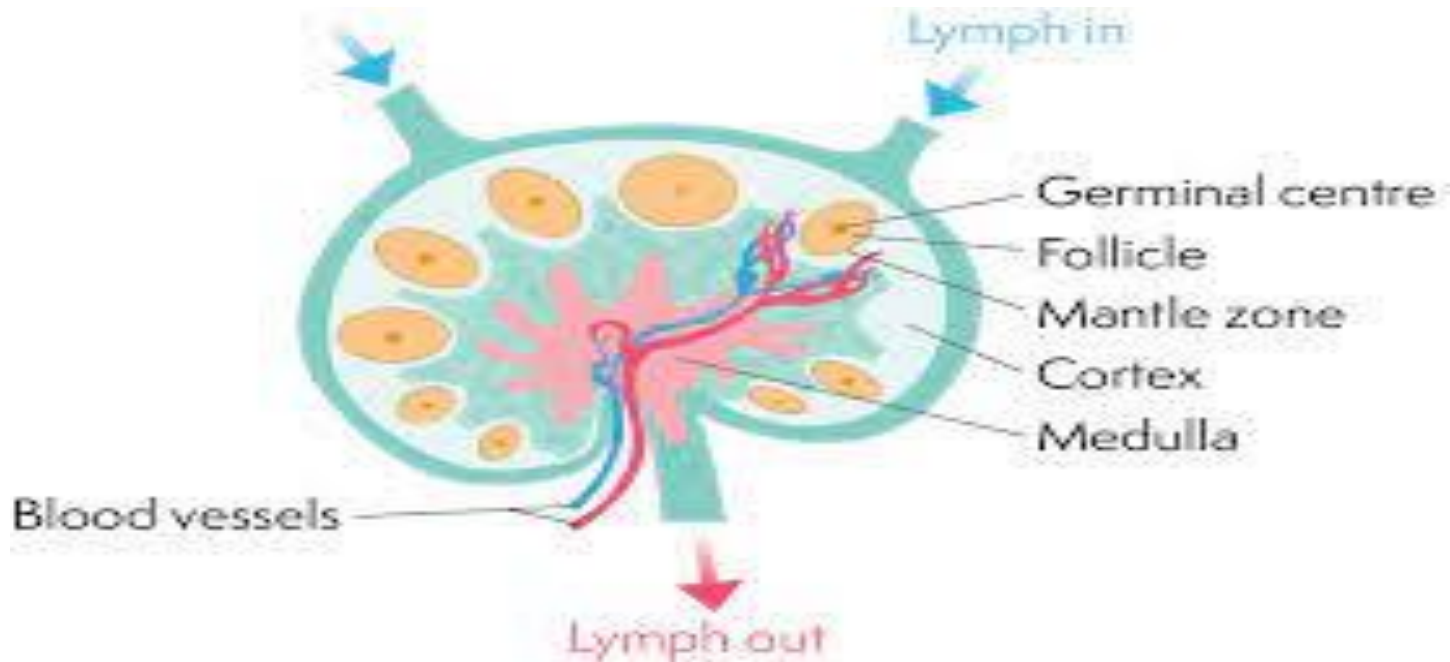
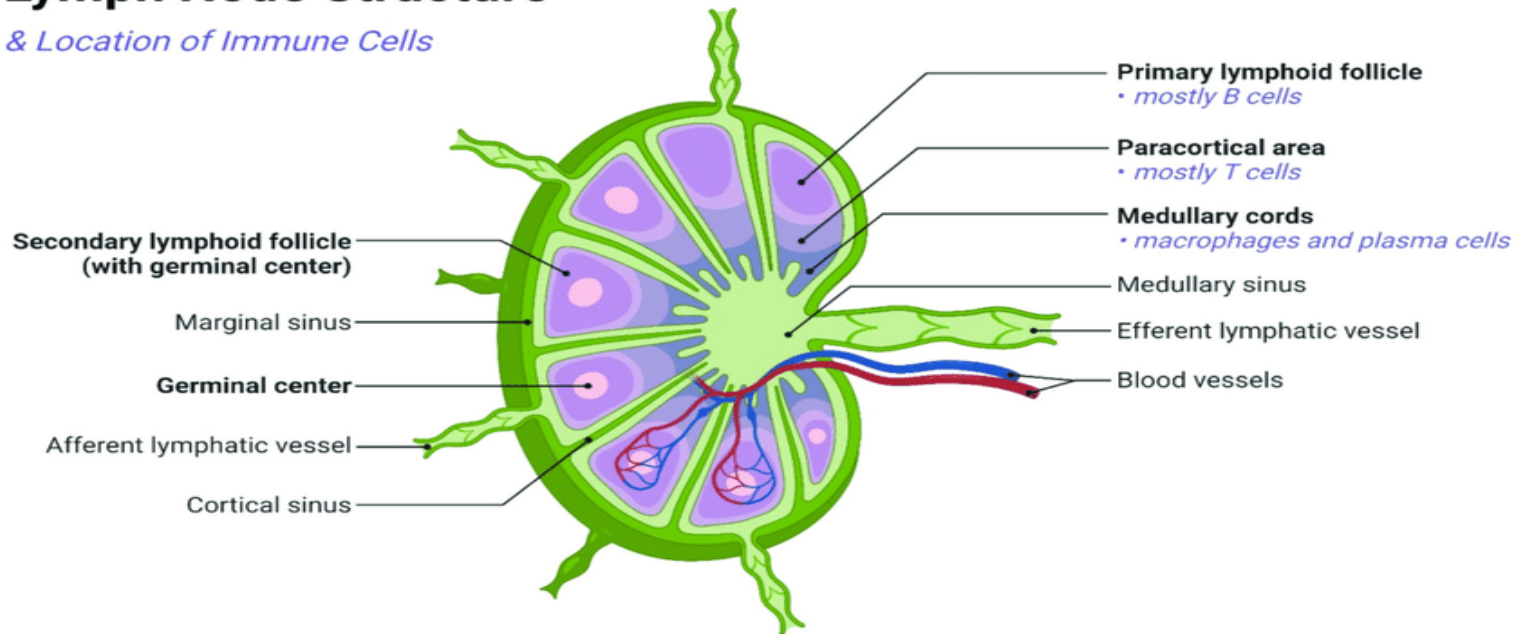
The spleen: is the major site of immune responses to blood-borne antigens

- Site of immune cell residence.
- Site of immune response.
- Produce some active substances, such as complement.
- Filtration.



Lymph Node Structure

& Location of Immune Cells



Mucosal associated lymphoid tissues (MALT)

The MALT of the gastrointestinal and respiratory tracts is colonized by lymphocytes and antigen presenting cell that initiate immune responses to ingested and inhaled antigens.

Cells of the immune system

Stem cells of the immune system originated from the yolk sack in the first six weeks of gestation, after that liver take this function, then bone marrow will be responsible for originate and proliferate stem cell under some hormones and enzymes.



- Stem cells include lymphoid series (T, B and NK cells) and myeloid series (RBCs, monocytes and granulocytes).

A. Lymphocytes -Lymphocytes are mononucleate, nongranular leukocytes of lymphoid tissue participating in immunity. -They are found in blood, lymph and lymphoid tissue such as spleen, lymph nodes, tonsils and peyer's patches. -They are spherical or oval in shape and arise from haemopoetic stem cells.



1. T-Lymphocytes –

represent about **70%** of the total lymphocyte population. all T cells express **CD3** on their surfaces, along with T cell receptors (**TCRs**) which recognize specific antigens presented in an MHC I or MHC II molecule.

-There are different types of T cells:

1. T-initiator or inducer: have CD+4
2. T-helper: have CD+4, which have two types T-helper1 (Th1) and T-helper2 (Th2).
3. Tdh (delay hypersensitivity): have CD+4.
4. T-cytotoxic: have CD+8, kill viral infected cells and tumor cells .
5. T-Memory: have CD+4 and CD+8, play a role in secondary immune response



Mode of killing of T-lymphocytes:-

- Direct by cell to cell action (cytotoxic cell).
- Indirect by cytokines secretion (helper cell).

2. B-lymphocytes

Lymphocyte that matures in bursa of fabricious or bone marrow and that responsible for humoral immunity is called B lymphocytes.



Mode of killing:

- By specific immunoglobulins. **B-cell development:-** -pro-B-cell: contain CD45 and CD19. -Pre-B-cell: contain intra cytoplasmic μ chain. -Immature B-cell: have surface IgM only. -Mature B-cell: have surface IgM and IgD. When B-cell activated it will differentiated in to plasma cell and secrete Abs (immunoglobulin).



3. Natural killer cells (NK cells)

They form the third population of lymphocytes. The NK cells have 2 or 3 large granules in the cytoplasm. Hence they are also called large **granular lymphocytes**. They destroy the cancer cells and cells infected with virus, do not need antibody for activity, are activated by interferon and interleukin-2.



Mode of killing:-

Kill by Ab dependent cell- mediated cytotoxicity (**ADCC**). Antibodies bind to organisms via their Fab region. NK cells, attach via FC receptors, and kill these organisms not by phagocytosis but by release of toxic substances called **perforins** that found in their granules.



B. Macrophages

Macrophages are large mononuclear phagocytic cells derived from monocytes. Macrophages are concentrated in lymph nodes, spleen, bone marrow and liver.

C. Eosinophils

They are acidophilic leucocytes and are called eosinophils because eosin (acid dye) stains the granules of the cytoplasm of these cells . Granules are rich in hydrolytic enzymes.



D. Basophils

The cytoplasm of these cells containing granules that stains with basic dyes. The basophilic granules contain heparin, histamine, serotonin, platelet activating factor.

E. Neutrophils

Neutrophils form the major part of the white blood cell. They are motile, short lived cells with multilobed nucleus. Major function of the neutrophil is phagocytosis.



Complement system

Complement system is a part of the immune system that helps or complements the ability of antibodies and phagocytic cells to clear pathogens from an organism. It is part of the innate and adaptive immune system.



The complement system consists of a number of small proteins (30 proteins) found in the blood. In general synthesized by the liver (hepatocytes).

- Many components are precursors (pro-proteins) which are functionally inactive until proteolytic cleavage, which removes an inhibitory fragment and exposes the active site.

When stimulated by one of several triggers, proteases in the system cleave specific proteins to activation cascade of further cleavages.

The end-result of this activation cascade is formation of membrane attack complex (MAC).



Complement Activation

The **complement system**, also known as **complement cascade**, is a part of the immune system that enhances (complements) the ability of antibody and phagocytic cells to clear microbe and damaged cells from an organism, promote inflammation, and attack the pathogen's cell membrane. It is part of the innate immune system,

There are three separate pathways which activate the complement system:

1. **classical pathway**: activated by antibody-antigen complexes (immune complexes) on pathogen surfaces.
2. **mannose-binding lectin pathway**: activated when mannose-binding lectin binds to the carbohydrate molecule mannose on pathogen surfaces.
3. **alternative pathway**: C3 reacts directly with pathogen surfaces



- All three of these pathways act to generate the enzyme C3 convertase.
- This cleaves C3 into two parts (C3a and C3b) and activates the rest of the cascade.



• Classical Pathway Begins with Ag-Ab Binding

soluble Ag-Ab* or bacteria-Ab*



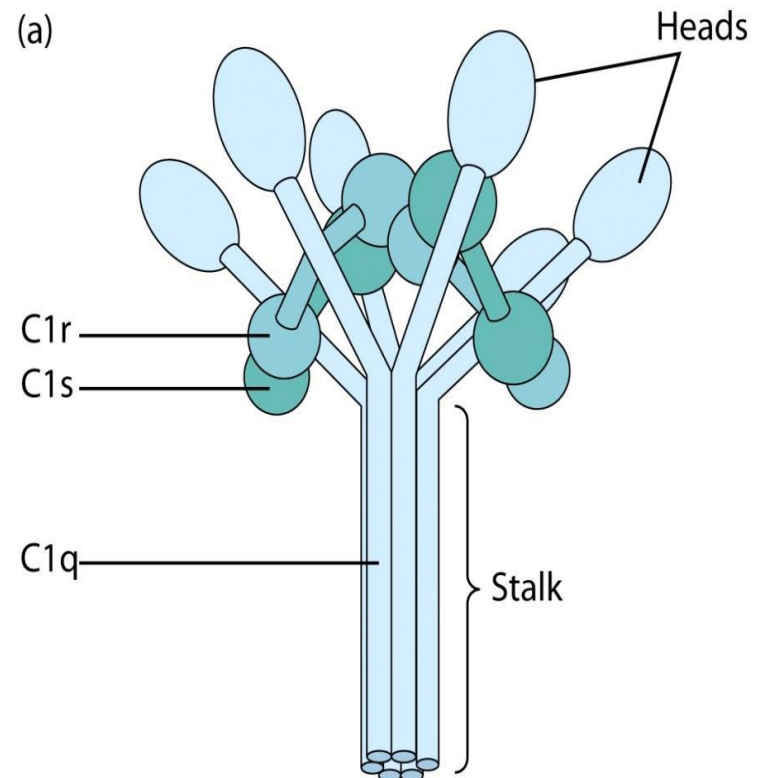
conformational changes
in the Fc portion of Ig



expose a binding site on the
Fc portion for the C1 component
of the complement system

*C1 binds to Ag-bound Ab

C1 molecule



“Classical Pathway”

- **C1q** portion of C1 attaches to the Fc portion of an **antibody**
- Only **IgG** and **IgM** can activate complement
- Once activated **C1s** is eventually cleaved which activates C4 and C2
- C4b & C2a come together to form the **C4b2a** which is the **C3 convertase**
- C3 convertase activates C3 to C3a and C3b

The Alternative Pathway

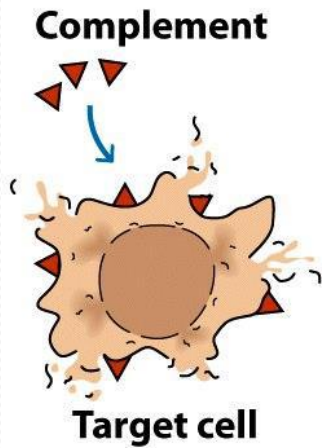
The activation of alternative pathway doesn't need Ab; thus, it is a component of the innate immune system.

- It is initiated by bacterial cell wall.
- C1, C4 and C2 are not involved in the alternative pathway.
- Four serum proteins, C3, factor B, factor D, and properdin, are involved in this pathway.

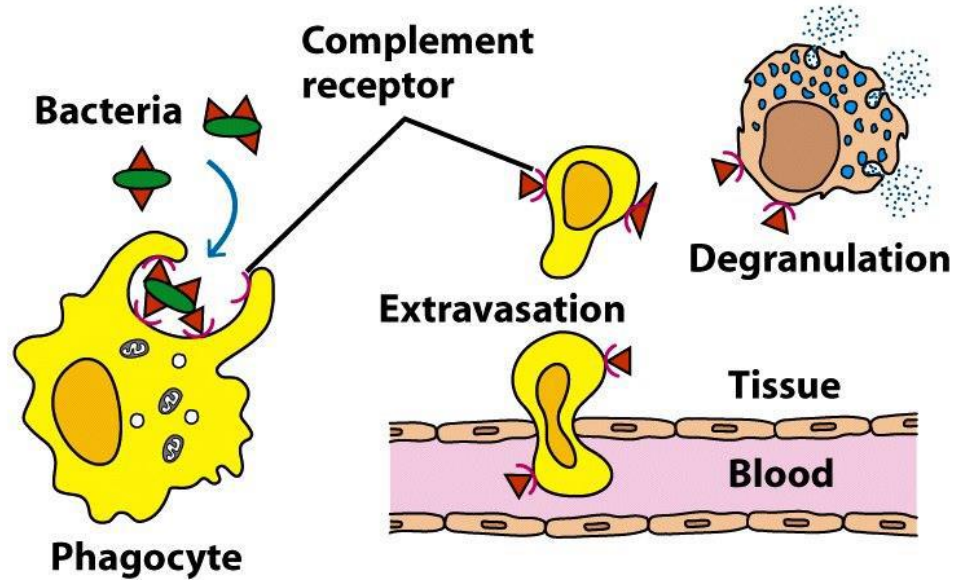
function of complement

- 1. Cell lysis:** The membrane-attack complex can lyse a broad spectrum of cells: G(-) bacteria, parasite, viruses, erythrocyte and nucleated cells (tumor cells).
- 2. Inflammatory response:** C3a, C4a, C5a (called anaphylatoxin) bind to complement receptors on mast cells and basophils and induce degranulation with release of histamin and other mediators.
- 3. Opsonization:** C3b is the major opsonin of the complement system
- 4. Clearance of immune complexes**

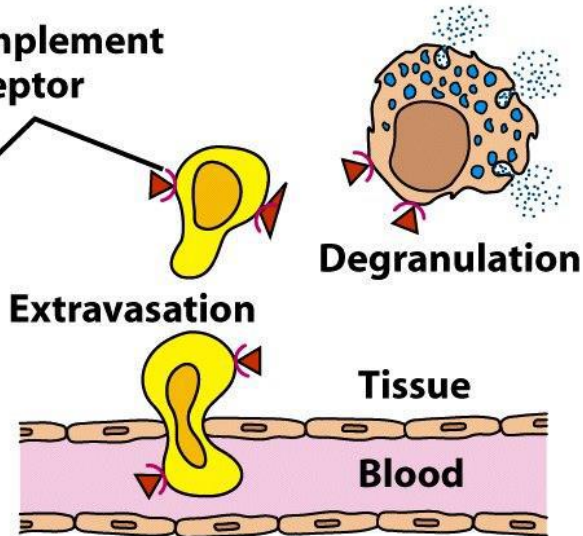
LYSIS



OPSONIZATION



ACTIVATION OF INFLAMMATORY RESPONSE



CLEARANCE OF IMMUNE COMPLEXES

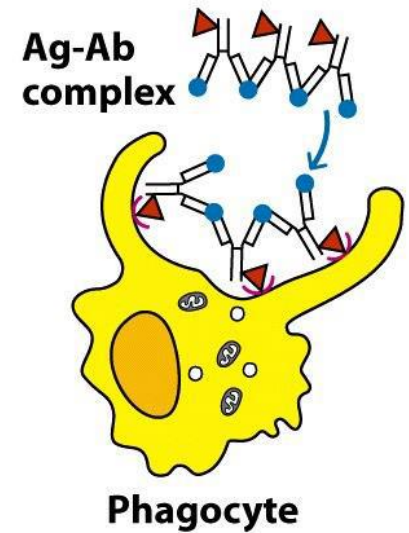


Figure 7-1
Kuby IMMUNOLOGY, Sixth Edition
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