

Immunology

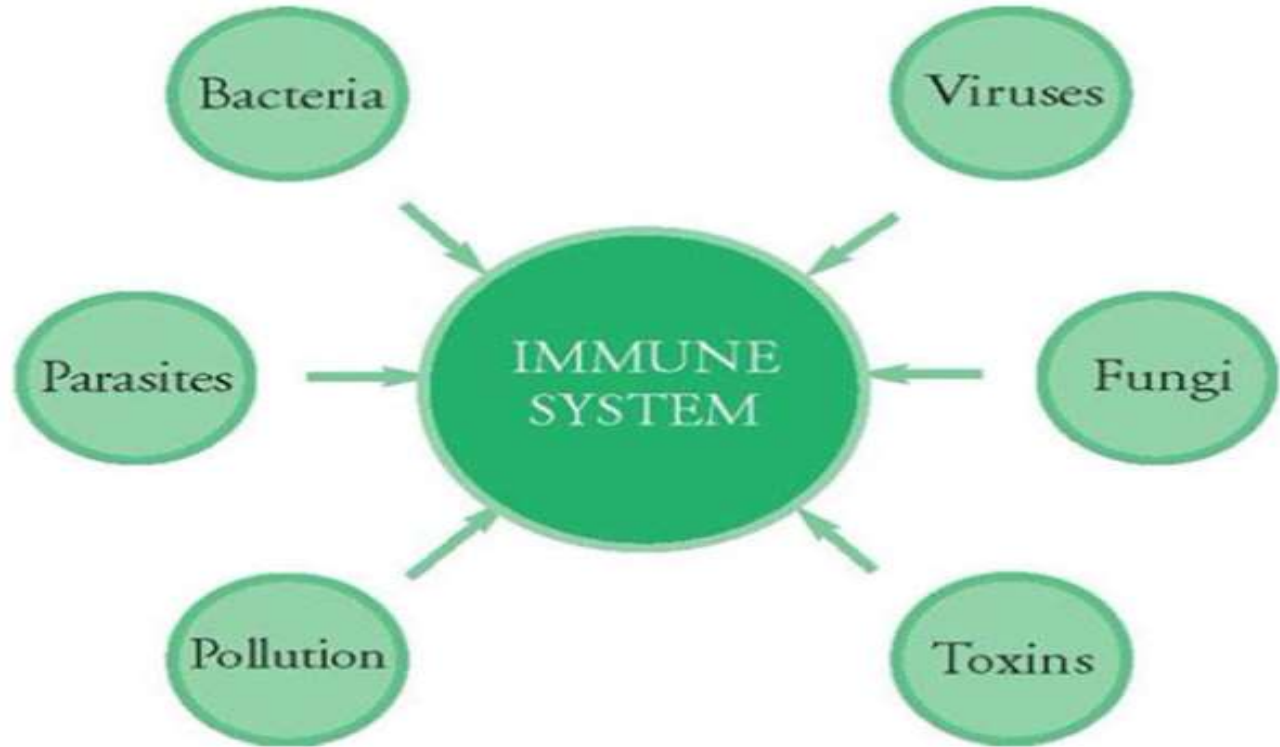
Reference

- ✓ Essential Immunology - Roitt.
- ✓ Immunology - Kuby

What protects us from pathogens?

- ✓ Immune System





Terminology

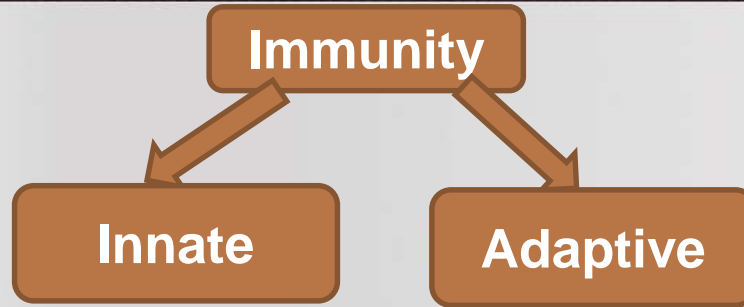
- ✓ **Immune:** Natural or acquired resistance to a disease
- ✓ **Immunity:** Immunity refers to a state of acquired or innate resistance or protection from a pathogenic microorganism or its products or from the effect of toxic substances such as snake or insect venom
- ✓ **Immunology** is that branch of biomedical science concerned with the response of the organism to immunogenic (antigenic) challenge, the recognition of self from nonself, and all the biological (in vivo), serological (in vitro), physical, and chemical aspects of immune phenomena

- **Immune system:** The immune system includes the molecules, cells, tissues, and organs that are associated with adaptive immunity such as the host defense mechanisms, mainly against infectious agents.
- **Immune response:** A collective and coordinated response to the introduction of foreign substances in an individual mediated by the cells and molecules of the immune system.
- Steps of immune response
 - Recognition
 - Response

Types of Immune response

- **Effector response** - Once a foreign organism has been recognized, the immune system recruits a variety of cells and molecules to mount an appropriate response, called an effector response, to eliminate or neutralize the organism.
- **Memory Response** - Later exposure to the same foreign organism induces a memory response, characterized by a more rapid and heightened immune reaction that serves to eliminate the pathogen and prevent disease.

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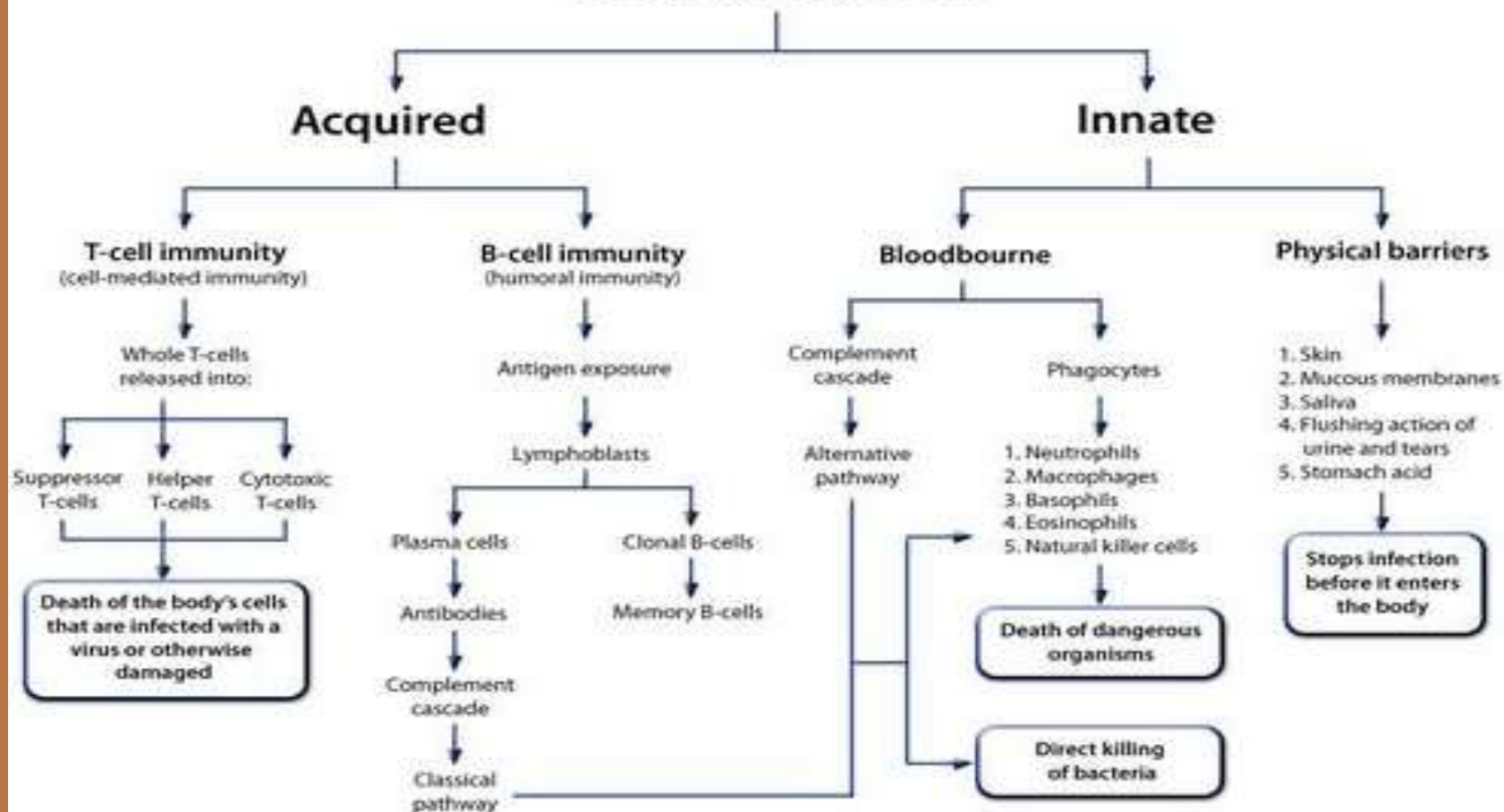


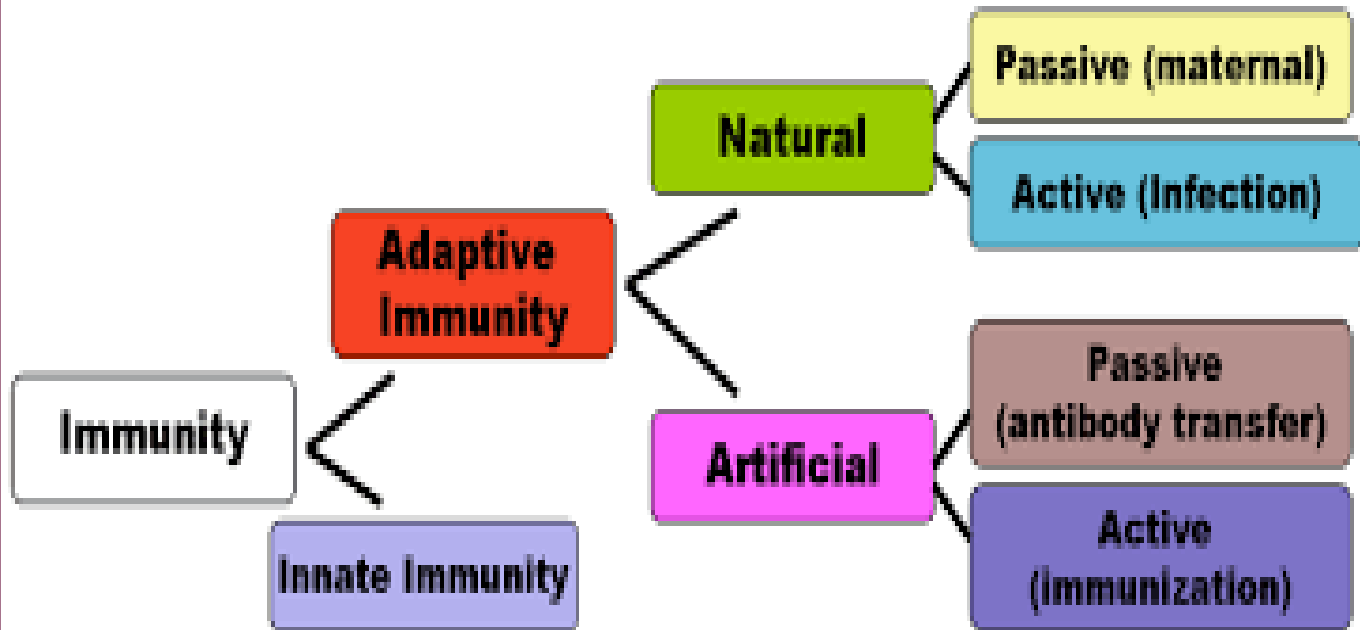
- First line of defense
- Relies on mechanisms that exist before infection
- Response generated within hours
- Limited specificity
- No memory subsequent response of identical intensity to primary response

- Second line of defense (if innate fails)
- Relies on mechanisms that adapt after infection
- Response generated within days
- Diverse specificity
- Memory - Improves with successive encounter with pathogen

Immunity	Cellular Components	Humoral Components
Innate	Phagocytic cells: -monocytes, macrophages, neutrophils NK cells Mast cells	Complement Acute phase proteins: -C reactive proteins Cytokines Interferon
Adaptive	T lymphocytes: -Helper T cell (CD4+ T) -Cytotoxic T cell (CD8+ T) -Suppressor T cell B lymphocytes	Immunoglobulins

Immune system

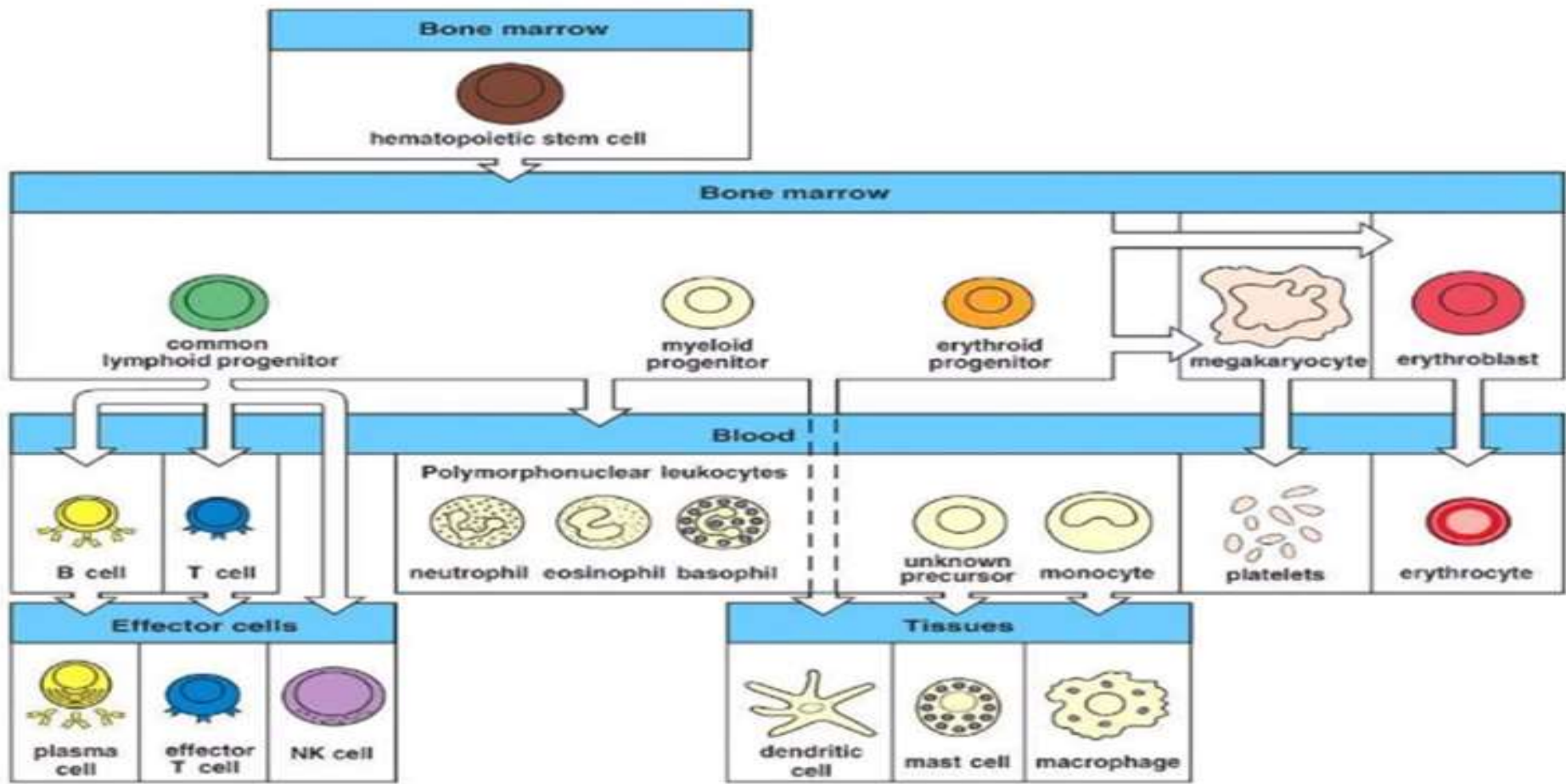




- ✓ **The immune system may fail (immunopathology). This can lead to immunodeficiency, hypersensitivity, or autoimmune diseases.**
- ✓ **Normal immune reactions can be inconvenient in modern medicine, for example blood transfusion reactions and graft rejection.**

Cells Of Immune System

- ◆ All the cells of the immune system develop from precursors in the bone marrow, after which they circulate in the blood and live in lymphoid organs (lymph nodes, spleen, tonsils) and in virtually all the tissues of the body.
- ◆ They can rapidly migrate to any site of infection, where they are needed.



Bone marrow

hematopoietic stem cell

Bone marrow

common lymphoid progenitor

myeloid progenitor

erythroid progenitor

megakaryocyte

erythroblast

Blood

B cell

T cell

Polymorphonuclear leukocytes



neutrophil eosinophil basophil

unknown precursor

monocyte

platelets

erythrocyte

Effector cells



plasma cell

effector T cell

NK cell

Tissues



dendritic cell

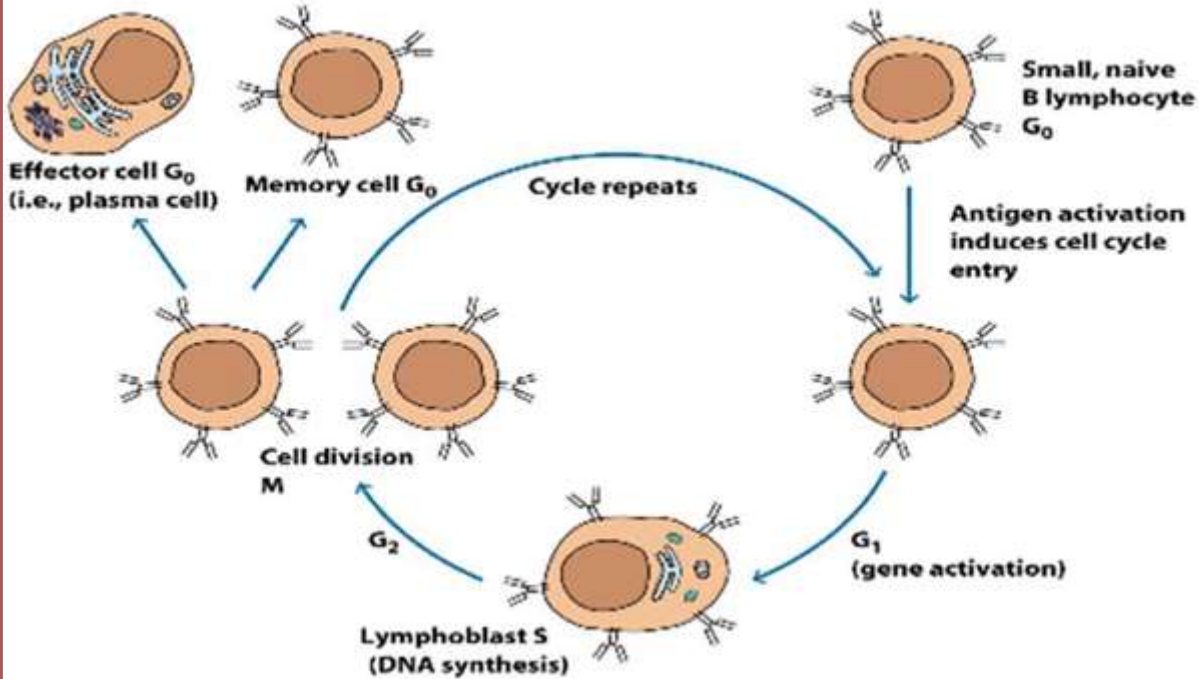
mast cell

macrophage

Lymphocytes

- ◆ Lymphocytes are wholly responsible for the specific immune recognition of pathogens, so they initiate adaptive immune responses.
- ◆ Generated from lymphoid progenitor in bone marrow.
- ◆ Constitute 20-40% of WBC
- ◆ Based on surface markers and function classified into:
 - ✓ B-lymphocyte
 - ✓ T-lymphocyte
 - ✓ Natural killer (NK) cells

B and T-Lymphocytes



- ◆ Small, non-phagocytic, motile & agranular
- ◆ Develop in bone marrow and migrate to different tissues
- ◆ Site of maturation differ

B Lymphocytes (B cells)

- ◆ **Site of maturation:** Bursa of fabricius in birds & Bone marrow in mammals
- ◆ Secrete proteins called antibodies, which bind to and eliminate extracellular microbes
- ◆ Each B cell is genetically programmed to express a antibody for a particular antigen.
- ◆ Display membrane-bound immunoglobulin (antibody). Other surface markers:
 - CD45-marker
 - MHC Class II molecules-antigen presentation Complement receptors CR1 & CR2
 - B7-interact with T cell and CD 40-to interact with T cell

- Once antigen is encountered

Differentiation requires interaction with T cells & macrophages

1) PLASMA CELLS - produce large amounts of the antibody, but in a secreted form, die within 1-2 weeks

2) Memory B cells - same membrane-bound antibody as parent B cell, longer life span

T Lymphocytes (T cells)

- ◆ Site of maturation: Thymus.
- ◆ Based on different roles that T cells are classified
- ◆ **T cell receptor** :-Only recognize antigen that is bound to cell membrane proteins called major histocompatibility complex (MHC) of antigen presenting cells
- ◆ **Surface markers**
- ◆ CD 28-interact with B cell (B7)
- ◆ CD 45-signal transduction.
- ◆ Upon activation differentiate:
- ◆ Effector T cells
- ◆ Memory T cells

TYPES

- ◆ **T helper cells (TH)**
- ◆ CD4 glycoprotein surface marker
- ◆ Recognize antigens bound to MHC class II molecules
- ◆ "help" activation of B cells. Te cells, macrophages in immune response by release of several cytokines
- ◆ **Type 1 helper T cells or TH1 cells** interact with mononuclear phagocytes and helps them destroy intracellular pathogens
- ◆ **Type 2 helper T cells or TH2 cells-** interacts with B cells and helps them to divide, differentiate, and make antibody

➤ **T cytotoxic cells (TC)**

- CD8 glycoprotein surface marker
- Recognize antigen bound to MHC class I molecules
- Recognition of MHC-antigen complex initiates differentiation into effector cell called cytotoxic T lymphocyte (CTL)
- Responsible for the destruction of host cells that have become infected by viruses or other intracellular pathogens by direct cell-cell interactions – cytotoxicity

➤ **T suppressor cells (T₂)**

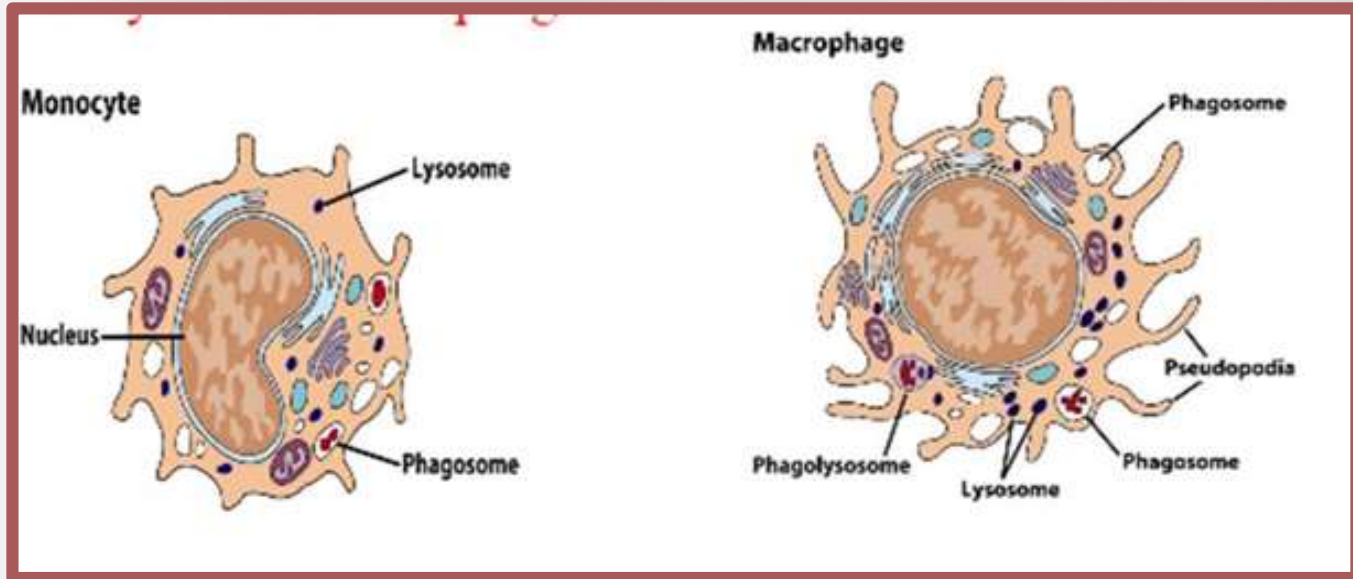
- CD4 and CD25 glycoproteins surface markers • Help suppress the immune system

Natural Killer Cells

- ◆ Subset of lymphocytes derived from bone marrow (5-10%)
- ◆ Large and bear cytoplasmic granules (large granular Recognize tumor or virus-infected cells and lyse them lymphocytes)
- ◆ Innate immunity - do not require prior contact with antigen. and are not MHC restricted
- ◆ Surface markers differ from T & B cells
- ◆ Marker CD16- which can recognize a region of antibody Ig G that has attached to cell infected by virus
- ◆ Bring about Antibody dependent cell mediated cytotoxicity (ADCC) of Ig G coated target cell

Mononuclear phagocytes

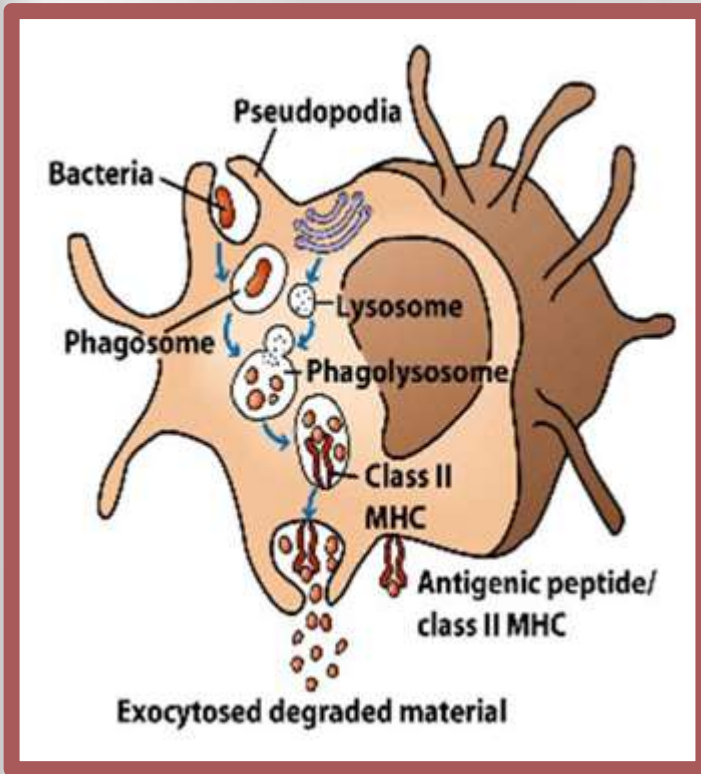
- ◇ Generated from myeloid progenitor in bone marrow Large mononuclear phagocytic cells found in many tissues active in innate immunity. Monocytes and macrophages



- Monocytes circulate in blood and then migrate into tissue and differentiate into specific macrophage

- **Macrophages**

- Intestinal macrophages in gut
- Alveolar macrophages in lung
- Histiocytes in connective tissue
- Kupffer cells in the liver
- Mesangial cells in the kidney
- Microglial cells in the brain
- Osteoclasts in bone
- Professional antigen-presenting cells and effector cells in both humoral and cell-mediated immunity



Complex antigens are phagocytized, the resulting phagosome fuses with a lysosome

The digested antigen is then eliminated through exocytosis: some of it is presented on membrane on MHC

Phagocytosis is enhanced when antibody is attached to the antigen: antibody acts as opsonin (molecule that binds to both antigen and phagocyte)

◆ Activated macrophage - stimulated in some manner or by some substance to increase its functional efficiency with respect to phagocytosis, intracellular bactericidal activity, or lymphokine, i.e.. IL-1. 6. TNF alpha production

◆ Increase in size and number of cytoplasmic granules and a spread of membrane ruffling

Oxygen-dependent killing

Reactive oxygen intermediates

$O_2^{\cdot -}$ (superoxide anion)

OH^{\cdot} (hydroxyl radicals)

H_2O_2 (hydrogen peroxide)

ClO^- (hypochlorite anion)

Reactive nitrogen intermediates

NO (nitric oxide)

NO_2 (nitrogen dioxide)

HNO_2 (nitrous acid)

Others

NH_2CL (monochloramine)

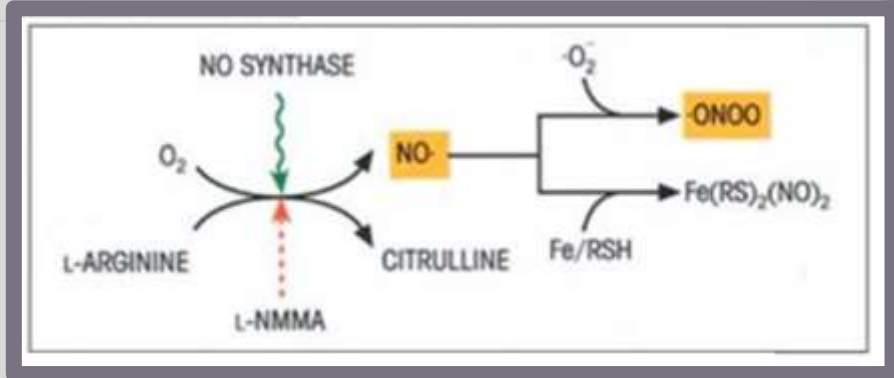
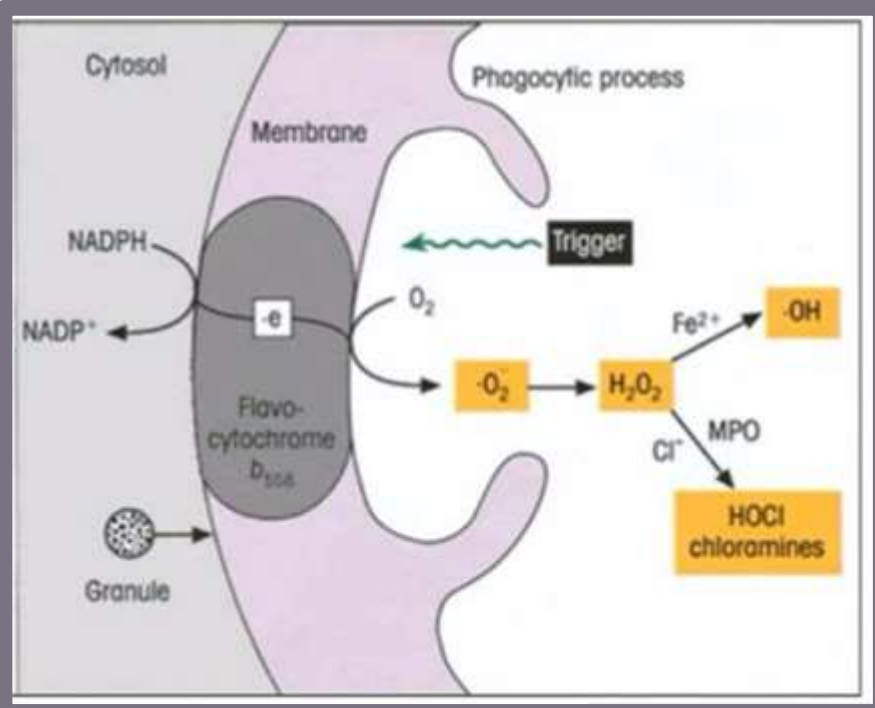
Oxygen-independent killing

Defensins

Tumor necrosis factor α
(macrophage only)

Lysozyme

Hydrolytic enzymes

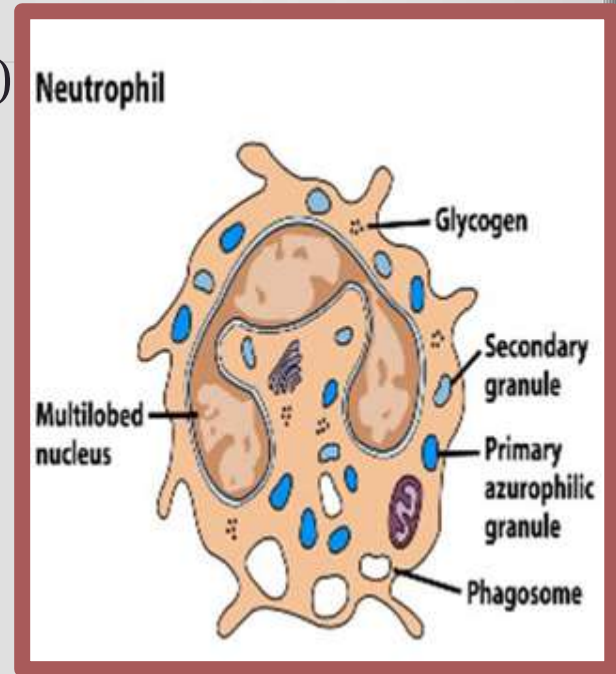


Granulocytes

- Leukocytes are of the myeloid series with irregularly shaped, multi lobed nuclei with large intracellular granules that contain hydrolytic enzymes capable of destroying microorganisms
- Differentiated based on the staining characteristics of their cytoplasmic granules
 - Neutrophils
 - Eosinophils
 - Basophils
- Active in acute inflammatory responses

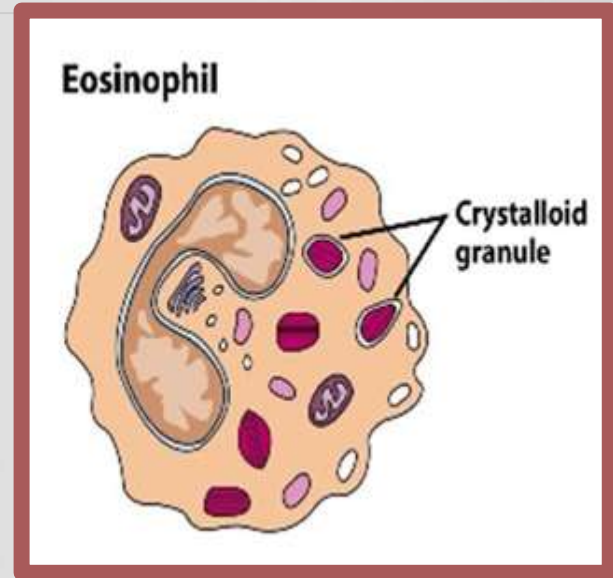
Neutrophils

- ◆ Multi-lobed nucleus, light granules (Polymorphonuclear leukocyte)
Comprise 40 to 75% of the total white blood count
- ◆ Granulated cytoplasm: lytic enzymes & bactericidal substance (lysozyme, peroxidase, collagenase) .
- ◆ Generally first to arrive at site of inflammation. Phagocytize, ADCC
- ◆ Generate antimicrobial agents (oxygen dependent & independent)



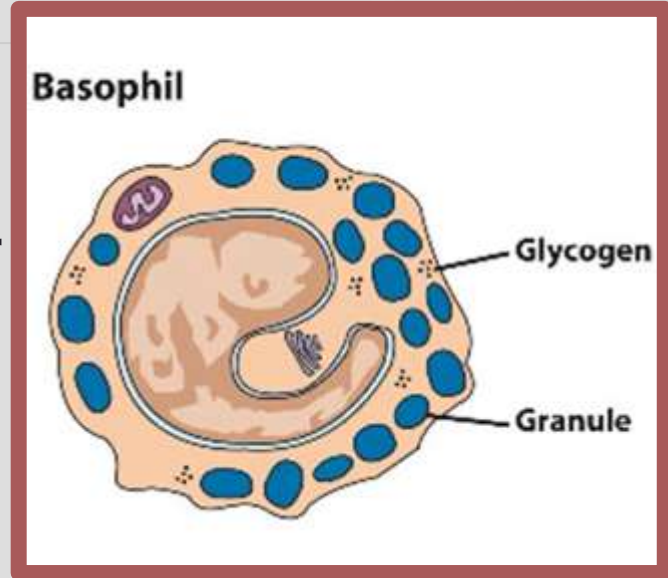
Eosinophil

- ◆ Bilobed nucleus
- ◆ Granulated stained by eosin
- ◆ 2 to 5% of the total white blood cells
- ◆ Phagocytic cell migrate from blood to tissues
- ◆ Distribution - skin, mucosa of the bronchi, and gastrointestinal tract
- ◆ Play a role in parasitic infection



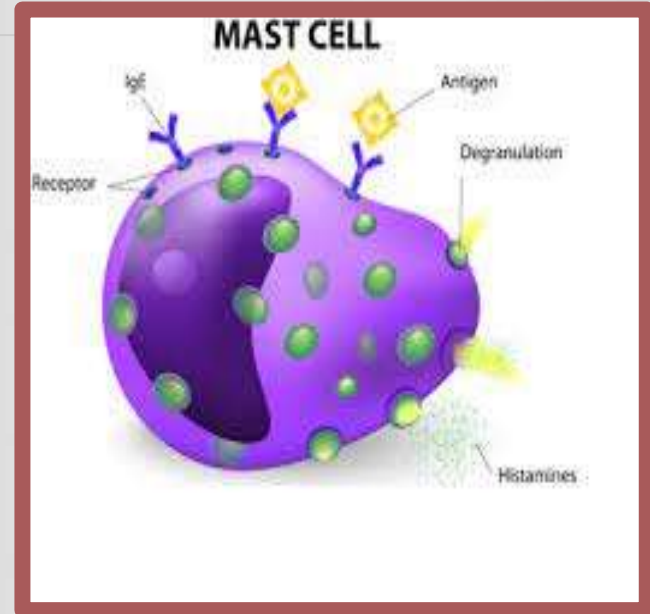
Basophils

- ◆ Lobed nucleus with densely granulated cytoplasm which stains with basic dye
- ◆ Granules- heparin, histamine, platelet-activating factor, and other pharmacological mediators of
- ◆ immediate hypersensitivity
- ◆ Comprise less than 0.5% of peripheral blood leukocytes Non phagocytic granulocytes
- ◆ Play a role in allergic reactions



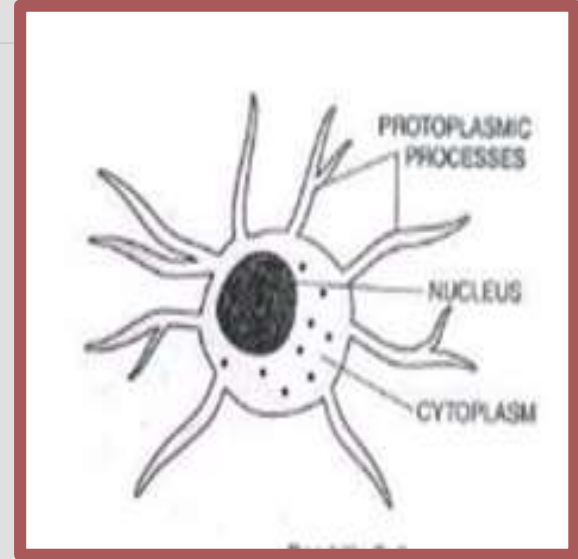
Mast Cells

- ◆ Generated from unknown precursor
- ◆ Generally found in connective tissue, skin, mucosal epithelium
- ◆ Receptors to bind IgE
- ◆ Have large cytoplasmic granules which store histamine and cytokines
- ◆ Play important role in development of allergies & inflammation



Dendritic Cells

- ◆ Long membranous extensions, look like dendrites on nerve cells
- ◆ Professional antigen-presenting cells and powerful activators of T cell responses. Constitutive expression of MHC and B7 molecules
- ◆ Antigen presentation: Immature DC acquire antigen by phagocytosis and it is processed
- ◆ Processed antigen are presented by mature DC to TH cells



- ◆ Subsets are derived from both myeloid and lymphoid lineages

- ◆ Four major groups:
 - ◆ Langerhans DC –Skin
 - ◆ Interdigitating DC-lymph nodes
 - ◆ Monocyte-derived (Myeloid) DC
 - ◆ Plasmacytoid-derived (Lymphoid) DC
 - ◆ **Follicular dendritic cells: Involved with B cell maturation**

THANKS!

