CELLS AND ORGANS OF THE IMMUNE SYSTEM

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Overview of the immune system

- Immunity or capability to protect from pathogen and non-self is a combined or coordinated function of different components, called components of the immune system.
- It consists of various cells and organs of the immune system.
- Cells secrete various mediator molecule required to communicate with other cells. They are also involved in direct cell-mediated immune response.
- Organs of the immune system produced and maintain the population of immune cells.

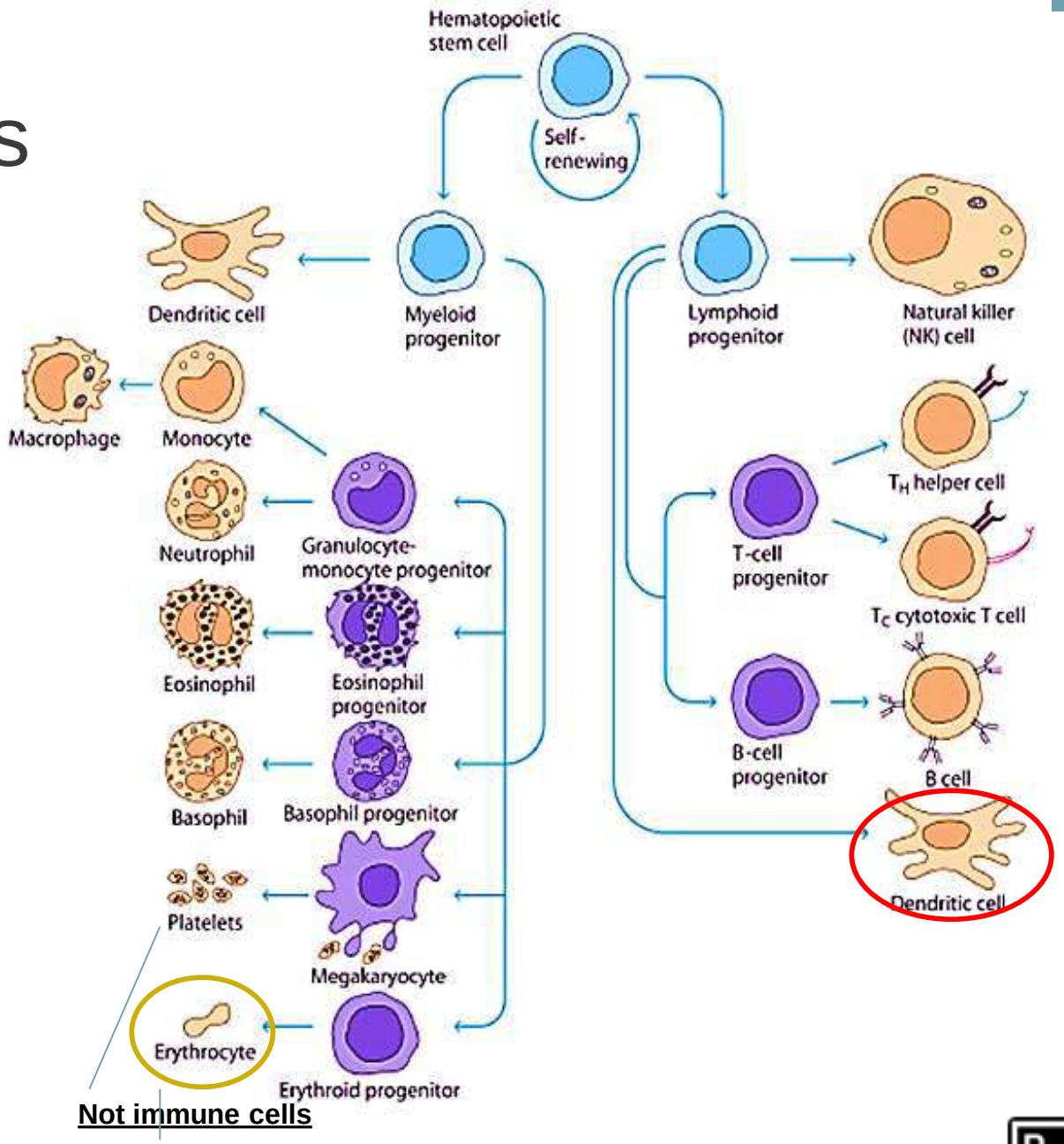
Cells of the immune system

- Cells of the immune system are distributed throughout the body.
- They are of two types – Myeloid cells and lymphoid cells.
- Myeloid cells are related to bone marrow cell lineage that resembles bone marrow tissue. 400 billion myeloid cells are produced daily in the process known as haemopoiesis. Production of myeloid cells are also known as myelopoiesis.
- Lymphoid is related to lymph which is a clear yellowish, slightly alkaline, and coagulate fluid. Cells produced by bone marrow like myeloid cells but they are matured in lymphoid tissues. Normally there are 10^{12} (normal reference range is 1 – 5 x 10^{9} liter of blood) lymphoid cells in the body. Generation of lymphocytes in the bone marrow is known as lymphopoiesis or lymphoid hematopoiesis.

Hematopoiesis

Generation of blood cells from self renewing hematopoietic stem cell (HSCs)

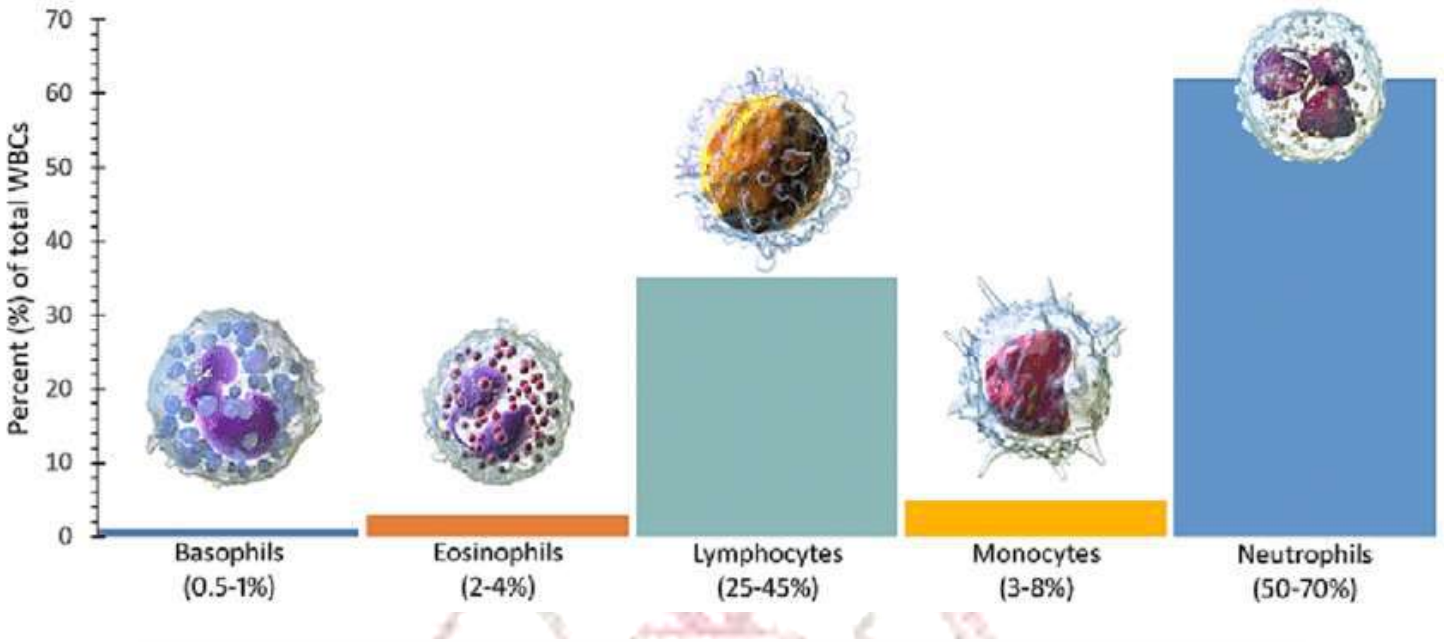
- **Common myeloid progenitor (CMP)** → **RBCs & Other**
- **Common lymphoid progenitor (CLP)** → **Lympho-cytes**



Hematopoiesis

- In humans, hematopoiesis begins in the embyonic yolk sac during the first weeks of development and continue whole life – location changes to yolk sac (1st week) → *liver (3rd week to 7th weeks of gestation)* → *bone marrow (whole life)*.
- Early in the process, a multipotent stem cell differentiates along one of the two pathways, giving rise to either a common myeloid progenitor cell (CMP) or a common lymphoid progenitor cell (CLP).
- Progenitor cells then terminally differentiated into various cell types by losing their capacity for self-renewal.
- Common myeloid progenitor cell generates progenitors of red blood cells (erythrocytes), and white blood cells or leukocytes, such as neutrophils, basophils, monocytes, mast cells, dendritic cells), and platelet-generating cells called megakaryocytes.
- Common lymphoid progenitor cells generate lymphocytes, such as B cell, T cells, NK (Natural Killer) cells.
- These cells are generated and matured on a mesh-like scaffold of stromal cells, which includes fat cells, endothelial cells, fibroblasts cells, and macrophages.
- Stromal cells provide hematopoietic-inducing microenvironment consisting of a cellular matrix and factors that promote growth and differentiation of HSCs.

Differential count of different cells



Absolute count = Diff % x Total WBC count

Normal WBC Differential	
Neutrophils	30-75 %
Eosinophils	0-6
Basophils	0-2
Monocytes	0-10
Lymphocytes	20-45

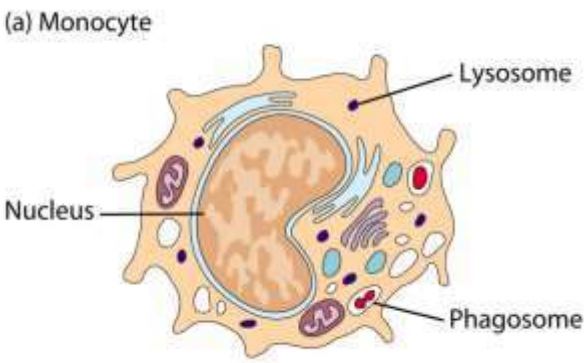
Normal Absolute Counts	
Neutrophils	1,500-8,000
Eosinophils	0- 600
Basophils	0- 200
Monocytes	0- 800
Lymphocytes	1,000-4,500

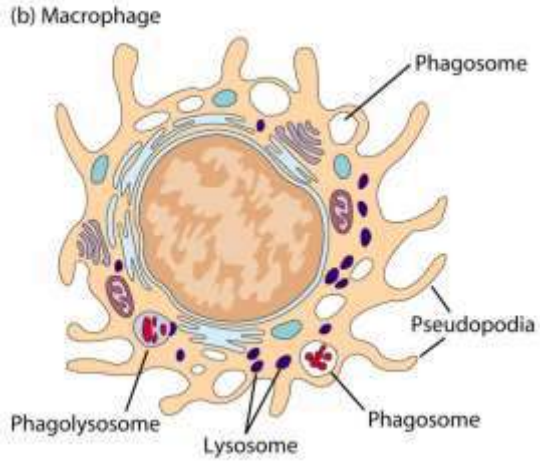
Types of cells

Mononuclear cells: Known as monocytes; found in blood; when migrated to tissue it transforms into macrophages (MΦ).

Macrophages: Macrophages are phagocytes and act as scavenger; they produce cytokines and hydrolytic enzymes; can be activated by IFN-γ cytokines; they present antigen in association with MHC II (Major histocompatibility antigen II). They are sub-classified based on the tissue where they reside, such as Alveolar cells residing in lung, Kupffer cell residing in liver, microglial cells residing in brain, and osteoclast cells residing in the bone.

Monocytes range between 7 and 9um in diameter while MΦ are about 21um diameter in size.





Types of cells

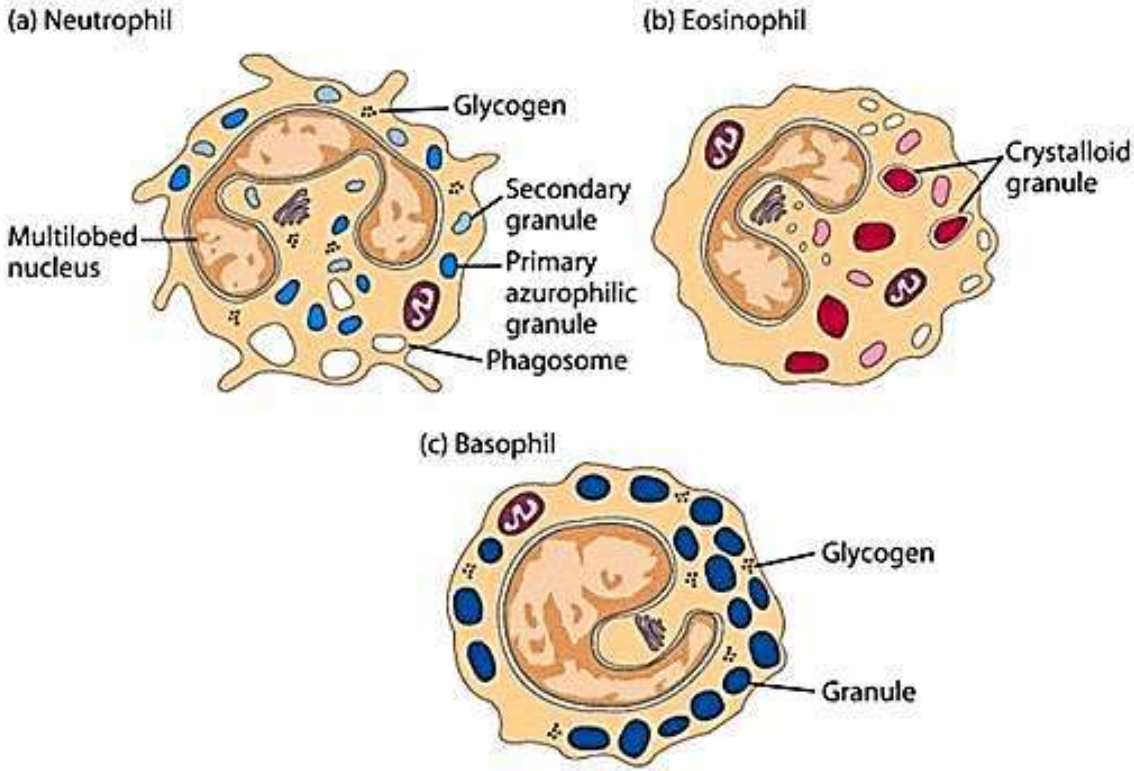
Dendritic cells: They are known as professional antigen presenting cells capable of presenting antigen through both MHC I and MHC II; thy are of two types: Langer cells (LCs) and circulating DCs.

- Langerhans cells (LCs) are found in skin, while circulating DCs are found circulating.
- Circulating DCs are of two kinds myeloid (MDCs) and plasmacytoid.
- Myeloid DCs are further sub-classified as MDC1 and MDC2.
- Interstitial DCs are found in the organs such as heart, lungs, intestines , etc.
- Interdigitating DCs populate usually T cell areas of lymph nodes and thymic medulla.

Types of cells

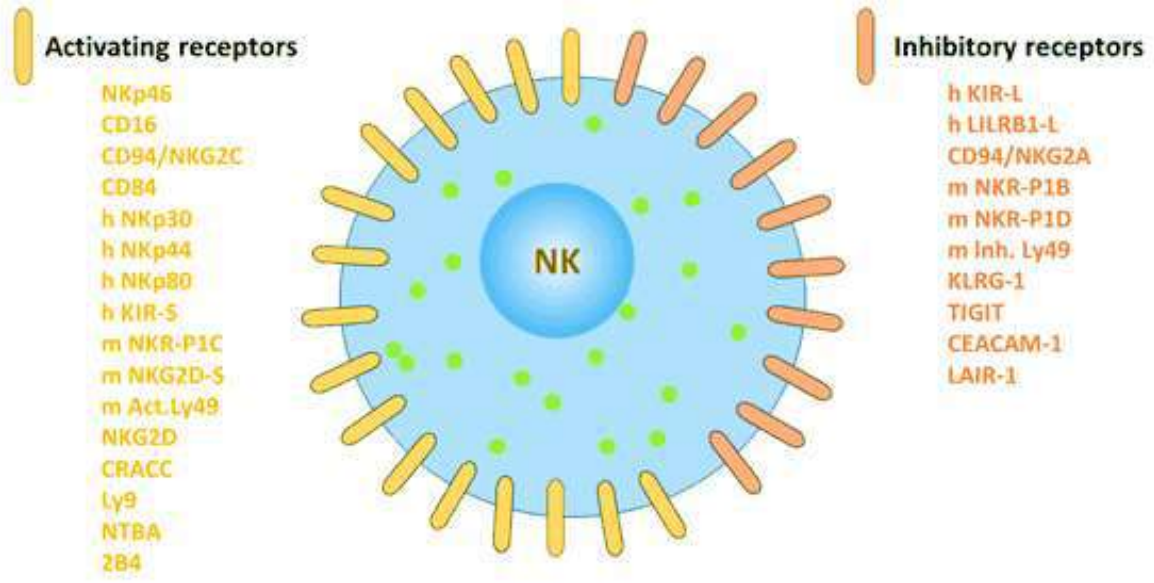
<u>Granulocytic cells</u>: These are characterized by granular nature of cytoplasm. They have multi-lobed nuclei. They are clssified on the basis of cellular morphology and cytoplasmic-staining characteristics as:

- Neutrophils
- Eosinophils
- Basophils



Types of cells

Natural Killer cells: They are also known as NK cells or large granular lymphocytes (LGL), are a type of cytotoxic lymphocyte critical to the innate immune system that belong to the rapidly expanding family of innate lymphoid cells (ILC). They represent 5–20% of all circulating lymphocytes in humans.



Types of cells

Lymphocytes: They are agranular cell with very clear cytoplasm which stains pale blue. They have very large nucleus that stains with dark purple. They are smaller than the granulocytes. They are second most numerous leukocyte, accounting for 25 – 35% of the cells. They are classified as:

i. **T cells of T lymphocytes:** They act against virus infected cells and tumor cells . They are further subclassified as:
   a. **T helper cells or CD4+ T cells:** It helps other immune cells in the generation of effective immune response. It may be of two kinds:
      i. T helper 1 (Th1) cells: It produces inflammatory cytokines known as Th1 cytokines, such as IFN, TNF-β, IL-17, etc.
      ii. T helper 2 (Th2) cells: It producesa anti0inflammatory cytokines known as Th2 cytokines, such as IL-4, IL-5, IL-10, IL-13, etc.
   b. **Cytotoxic T cells or CD8+ T cells:** It is killer cells and kills the infected cells by direct cell-to-cell contact.

ii. **B cells or B lymphocytes:** They produce antibody. They may be transitional, naïve, plasma, and memory cells.

Types of cells

Differential staining morphology of different blood cell types

red blood cells (RBCs):

cytoplasm = orange-pink to rose

monocytes:

cytoplasm = pale gray-blue
nucleus = deep bluish-purple

lymphocytes:

cytoplasm = light blue
nucleus = deep blue-violet

neutrophils:

granules = purple-to-lilac
cytoplasm = pale pink
nucleus = deep blue-violet

eosinophils:

granules = orange to pink

basophils:

granules = deep blue to violet

platelets:

central granules = red-purple surrounded by light blue

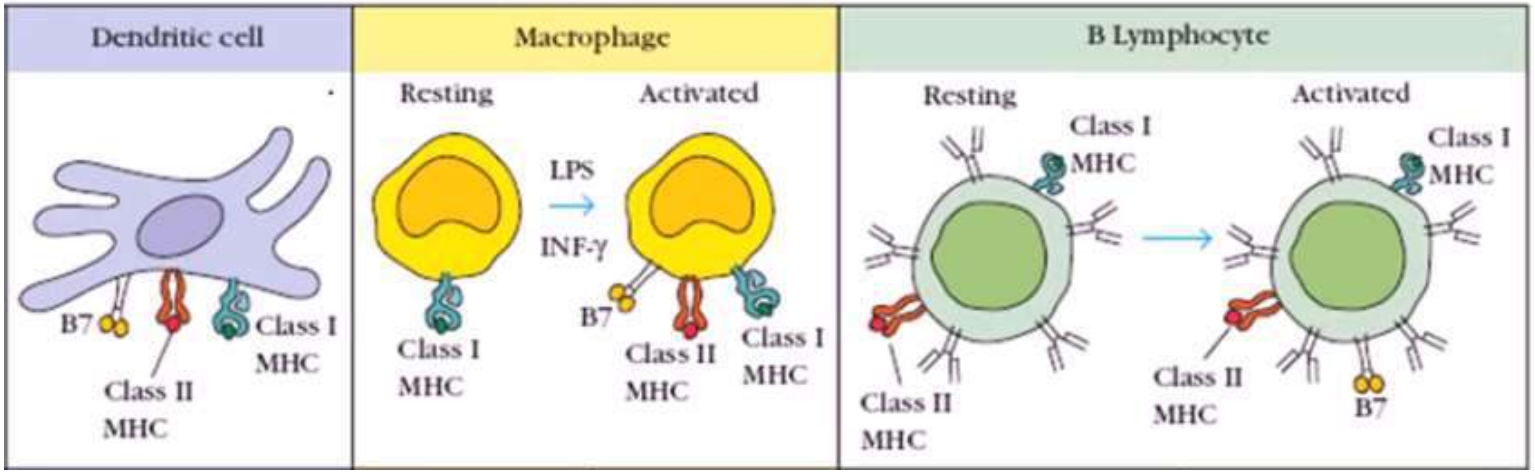
Types of cells

Antigen Presenting Cells (APCs)

- They cells which can present antigen to their cell surface.
- Almost all cells function as antigen presenting cells.

APCs

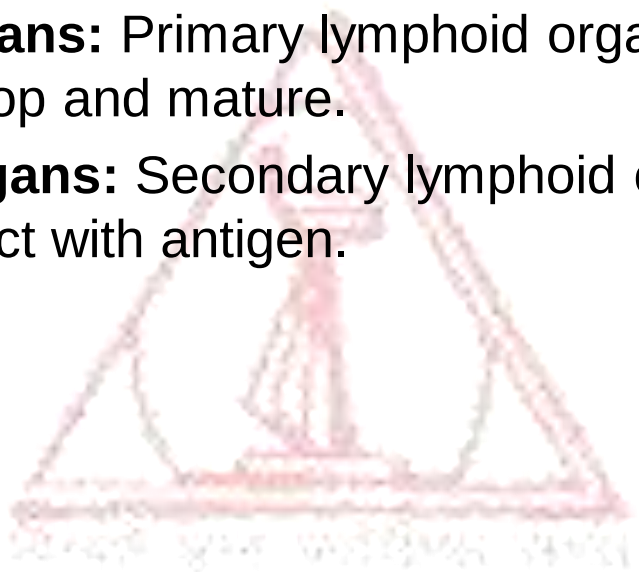
- **Non-professional APCs** → Cells that do not present antigen through MHCII, e.g. all cell other than professional APCs
- **Professional APCs** → Cells that present antigen also through MHCII, e.g. Macrophages, Dendritic cells and B cells.



Organs of the immune system

There are two major groups of the organs of the immune system

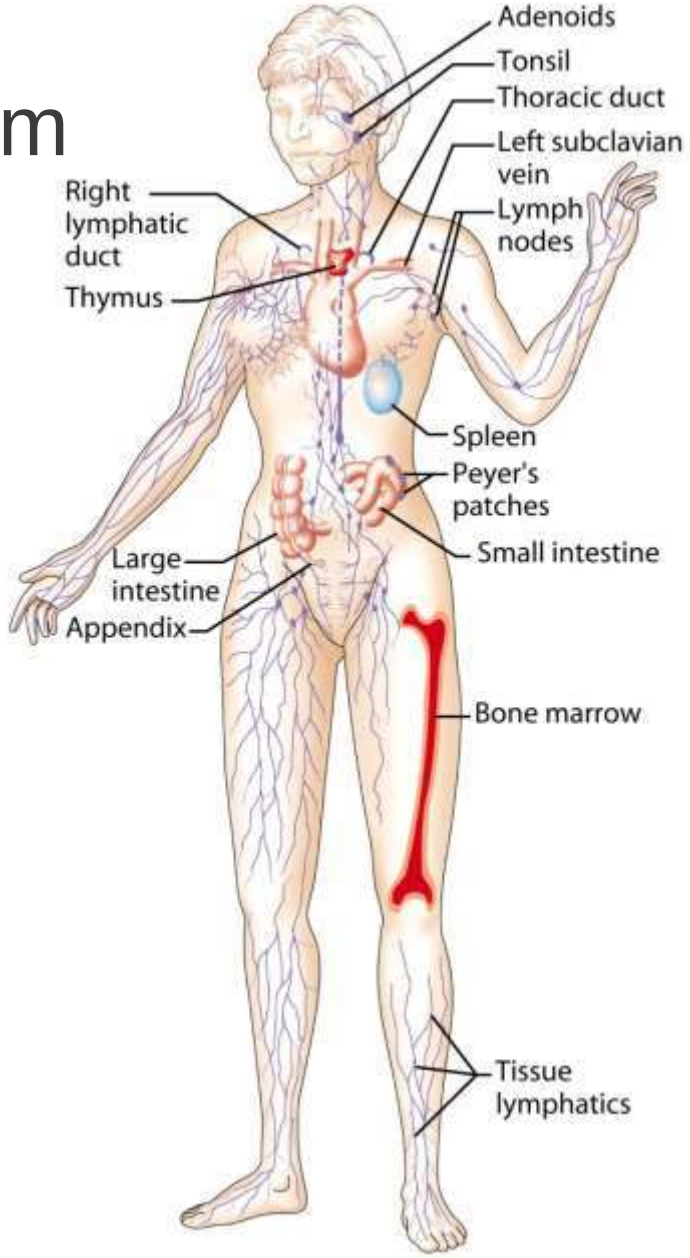
I. **I. 1º lymphoid organs:** Primary lymphoid organs where lymphocytes develop and mature.
II. **II. 2º lymphoid organs:** Secondary lymphoid organs where lymphocytes interact with antigen.



Organs of the immune system

Primary lymphoid organs (PLOs) are Bone marrow and Thymus

Secondary lymphoid organs (SLOs) are lymph nodes, spleen, Peyer's patches, and mucosal tissues such as the nasal-associated lymphoid tissue, adenoids, and tonsils.



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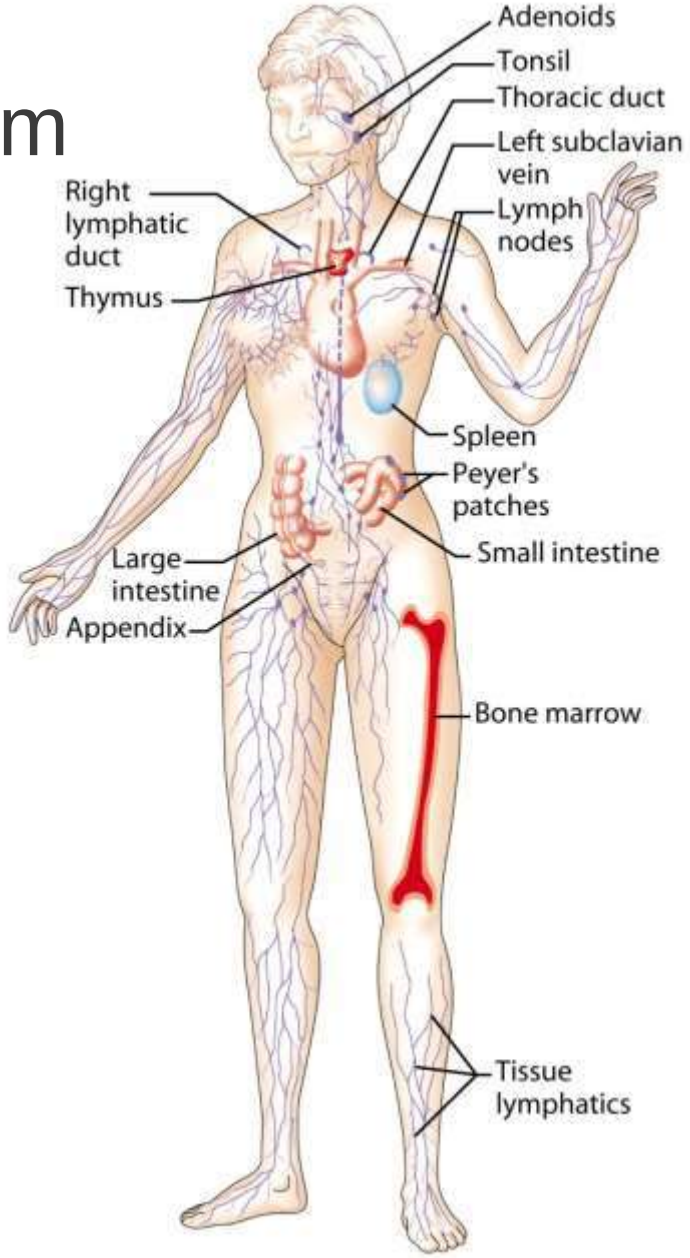
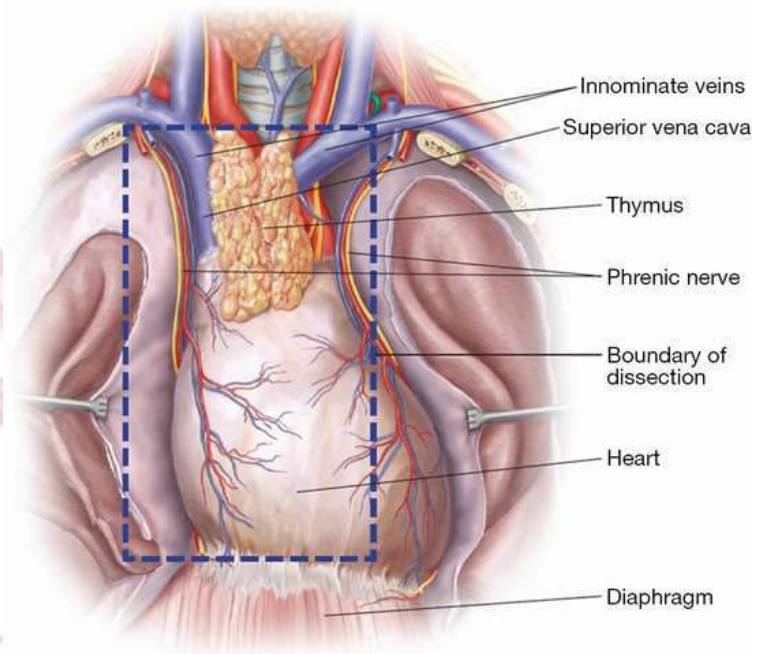
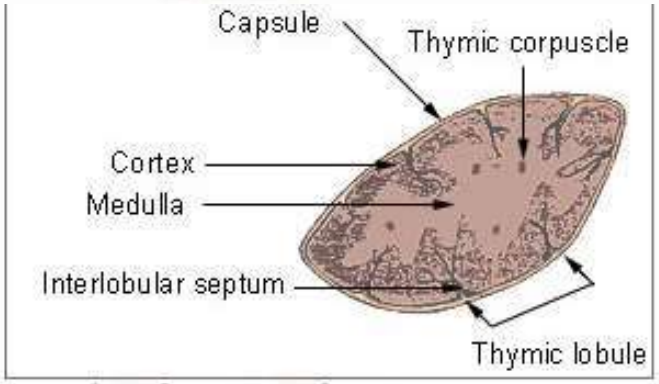


Organs of the immune system

Thymus

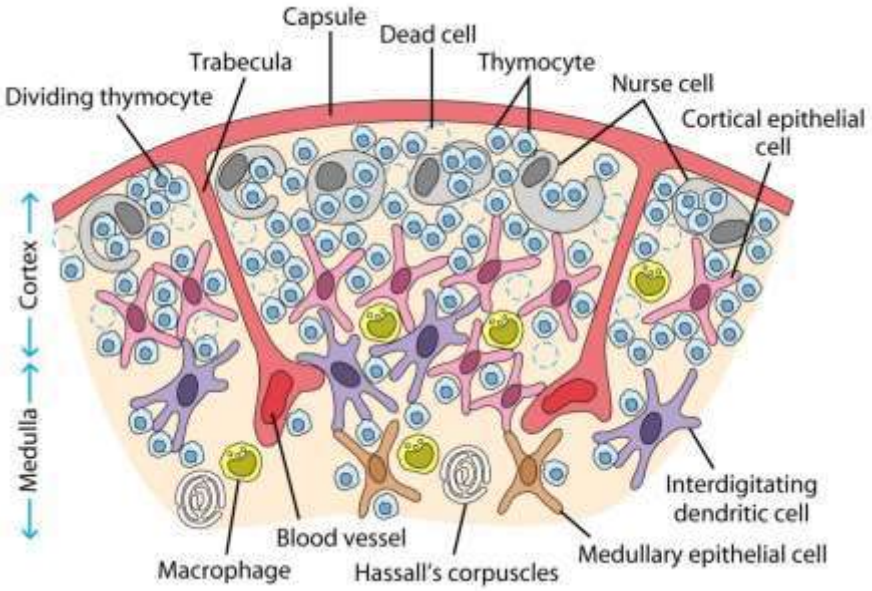
- Thymus (plural is thymi) is a bilobed organ on top of heart
- It has maximum size during Puberty
  - 70g infants, 3 g in adults
- 95-99% of T Cells Die in thymus
  - Due to self reactivity or no reactivity to Ag
- Consists of Cortex and Medulla
- Rat thymocytes are sensitive to glucorticoids.



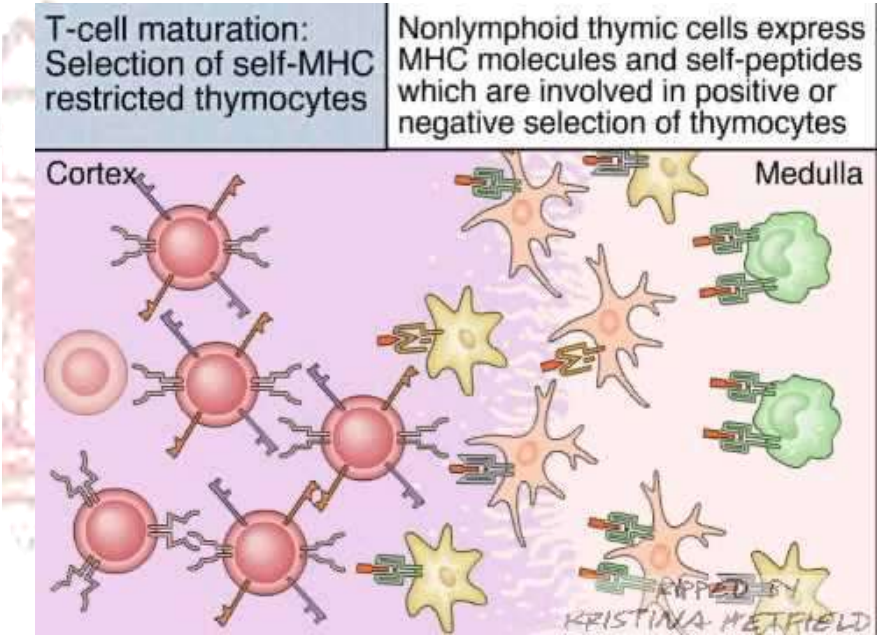


Organs of the immune system

Thymus



Transverse section of thymus

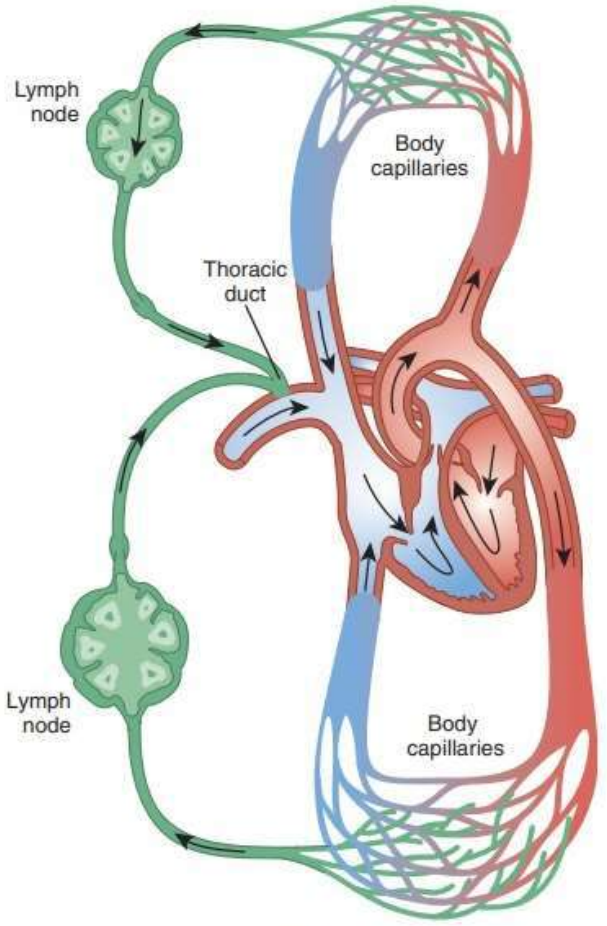


Maturation of T lymphocytes in thymus

Organs of the immune system

Lymphatic system

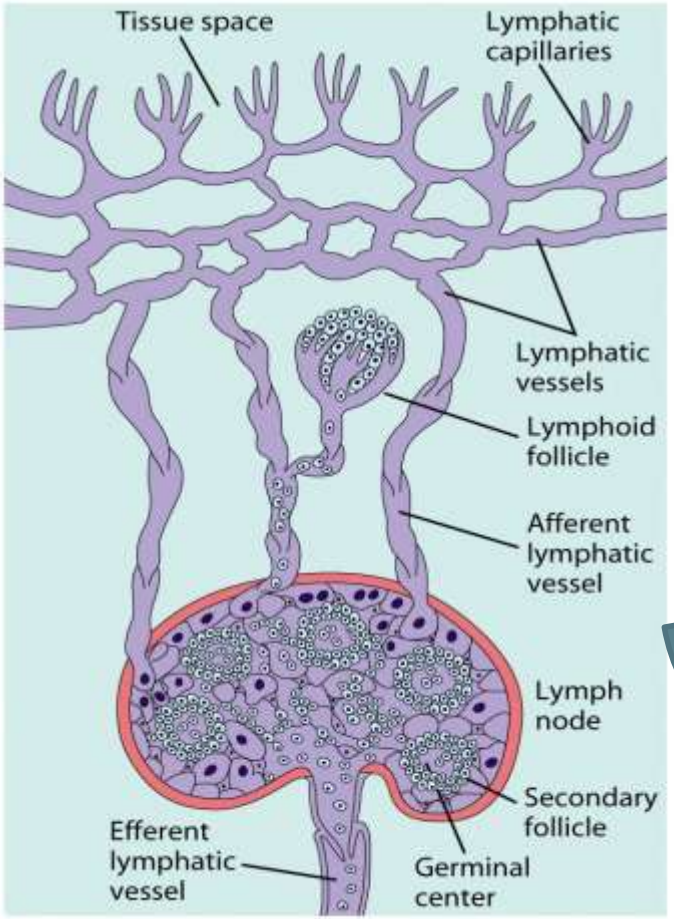
- Plasma from blood seeps into tissue
- Interstitial fluid either goes back or becomes Lymph
- Lymph enters lymphatic vessels
- Composed of lymphatic vessels and lymph nodes
- Thoracic duct is largest vessel empties into left subclavian Vein
- Lymphatic vessel depends on muscle contractions for movement
- One way valves ensure one direction
- Lymph nodes act as filters for antigens

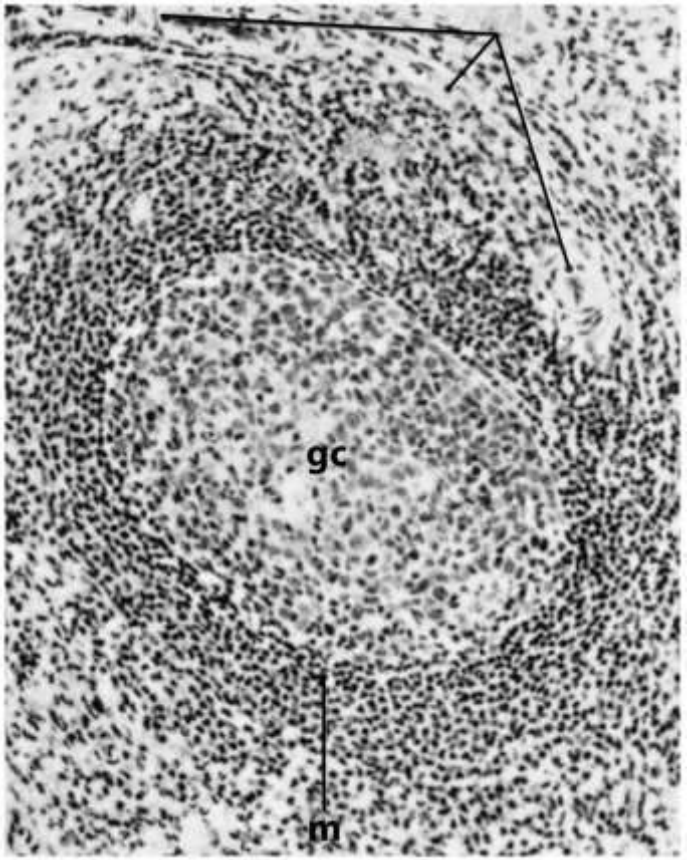


The lymphatic system transports fluids through a network of vessels.

Organs of the immune system

Lymphatic system – Lymphatic vessels & Lymph node





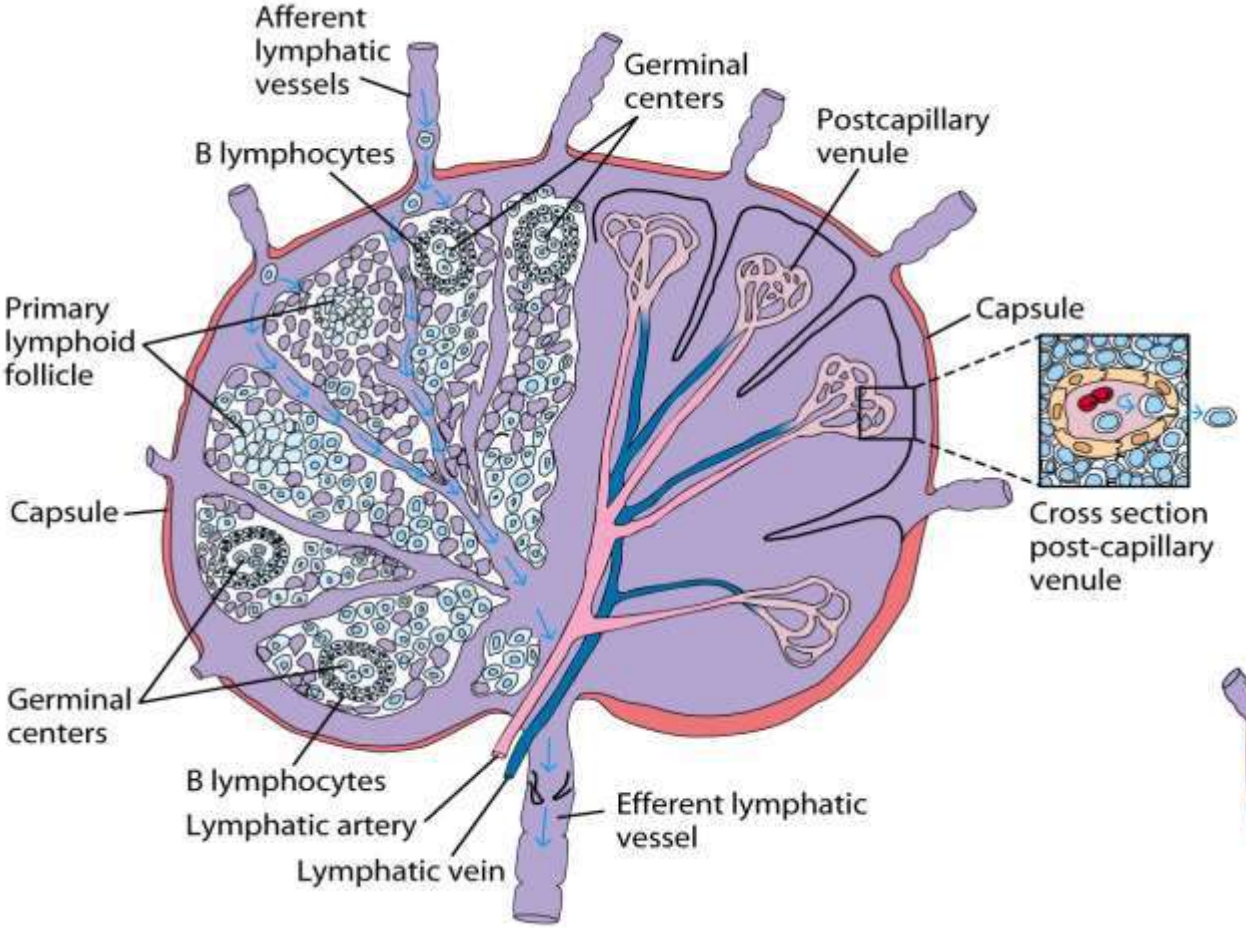
Organs of the immune system

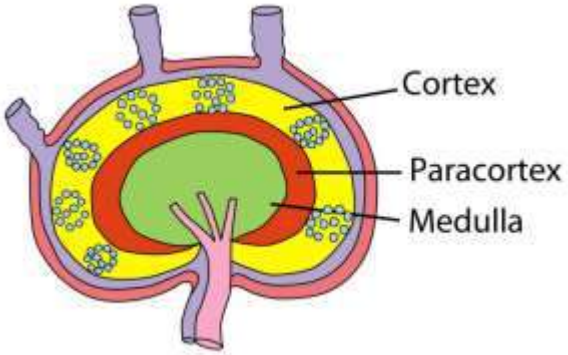
<u>Lymphatic system</u> – Lymph node

- Multiple afferent lymphatics – enters lymph
- Cortex
  - B-cells, Follicular DCs, MΦ, GCs, Primary follicles
- Paracortex
  - T_h, MΦ, DCs
- Medulla
  - Plasma Cells
- Post capillary venule
  - Allow lymphocyte migration from circulation into lymph node
- One efferent lymphatic
  - Lymph come out

Organs of the immune system

Lymphatic system – Lymph node





Organs of the immune system

Mucosal Associated Lymphoid Tissue (MALT)

- Mucous membranes – Surface area = 400m^2
- Mucous membrane – Most common pathogen entry site
- Mucous membrane is protected by MALT
- Organization varies (most organized Payer's Patches, Tonsils, appendix, etc.)
- Gastro-intestinal (GI) tract, Intra-epithelial lining (IEL) - Unique $\gamma\delta$ TCRs
- Lamina propria (below epithelium) - MΦ, B cells, T_H
- M Cell allows Ag entry because of its unique architecture

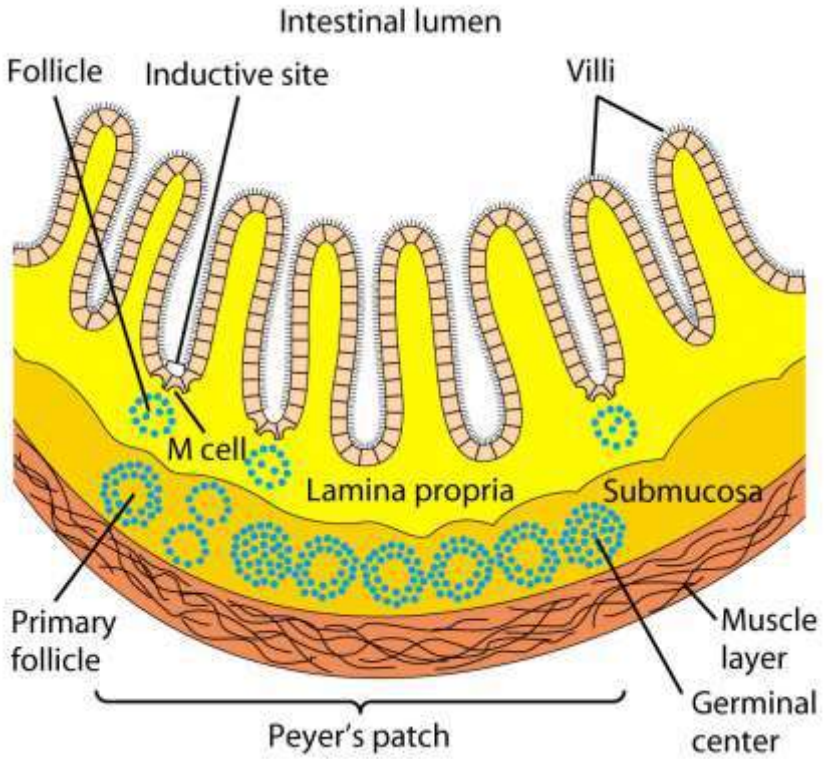
Functions of M cells

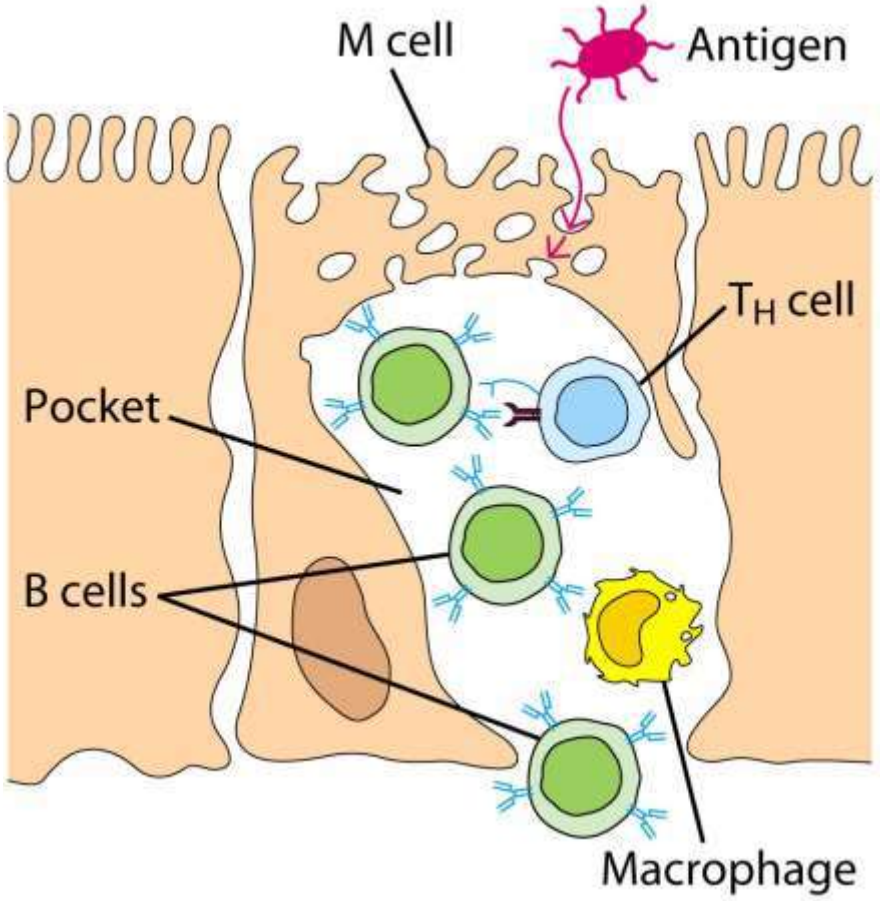
- Selective endocytosis of antigens.
- Transportation of Ag to intraepithelial macrophages and lymphocytes.

Ag migrate to lymph nodes where an immune response can be initiated.

Organs of the immune system

Mucosal Associated Lymphoid Tissue (MALT)





Organs of the immune system

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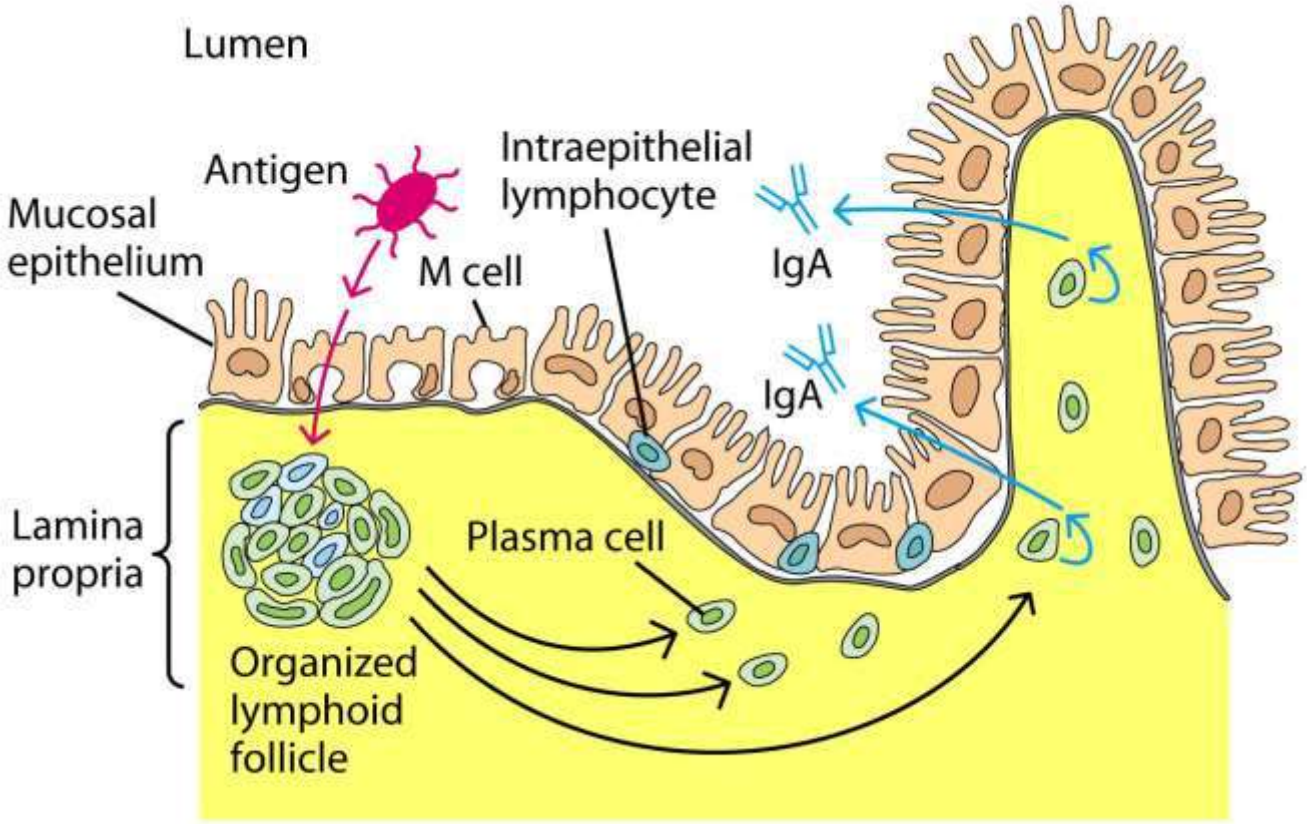

Further reading

- Abbas A.K. & Andrew H. 2001. Basic Immunology. Saunders Publication, Philadelphia, USA.
- Abbas A.K., Litchman A.H., Pillai S. 2022. Cellular and Molecular Immunology 10th Edition. Elsevier Inc., Philadelphia, USA.
- Punt J., Stanfor S., Jones P., Owen J. 2019. Kuby Immunology 8th Edition. W. H. Freeman, New York, USA.
- Cellular and Molecular Immunology, 10th Edition.
- Murphy K. & Weaver C. 2022. Janeway's Immunobiology 9th Edition. Garland Science, New York, USA.