Organs and Cells of the Immune System

A Presentation by
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Objectives

- The **organs** and **tissues** of the immune system
- **Haematopoiesis** and formation of blood cells
- Immune cells **classes, functions and circulation**
- Immune cells **development and maturation**

Anatomy of the Immune System

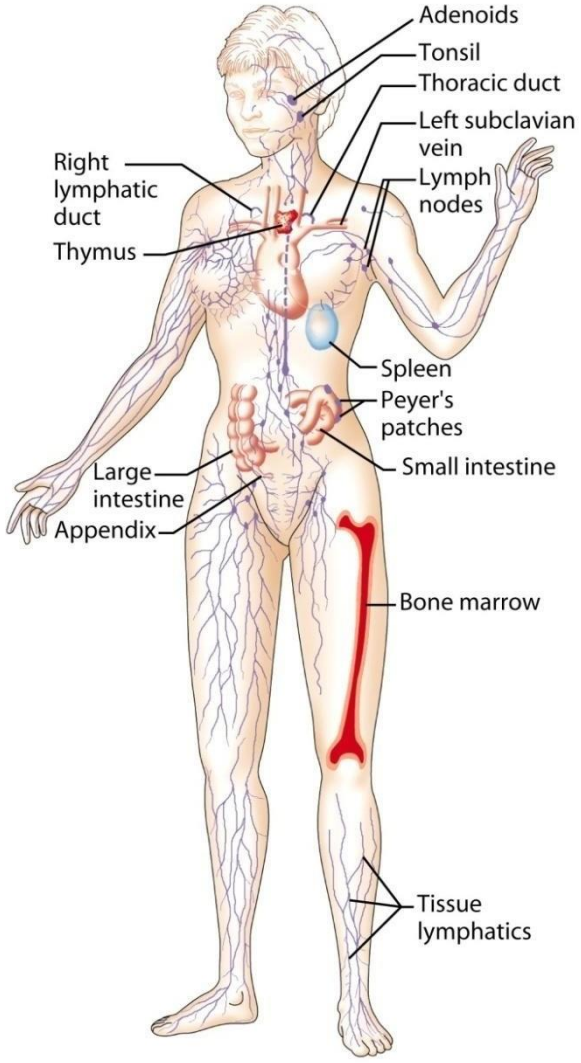
- **Lymphoid organs:**

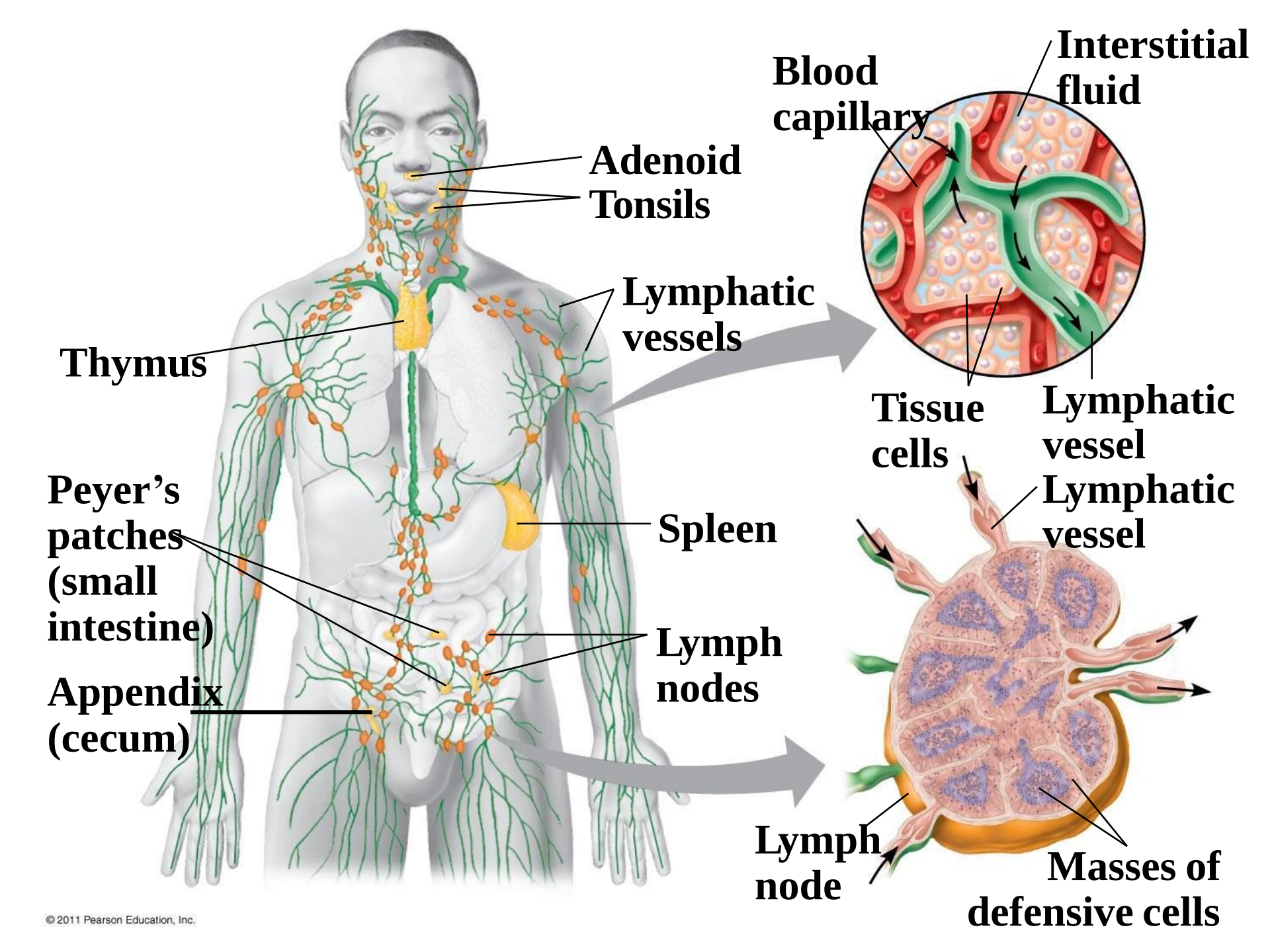
1. **Primary** or **central** lymphoid organs: bone marrow and thymus
2. **Secondary** or **peripheral** lymphoid organs: lymph nodes, spleen, mucosal, and cutaneous immune system

- **Blood cells in the immune sys:**

1. **Innate immune cells**: "phagocytes" macrophage, neutrophils, dendritic cells
2. **Adaptive immune cells**: "lymphocytes" T cells, B cells

- **Lymphatic and blood circulation**




Adenoid
Tonsils
Thymus
Lymphatic vessels
Peyer's patches (small intestine)
Appendix (cecum)
Spleen
Lymph nodes
Blood capillary
Interstitial fluid
Tissue cells
Lymphatic vessel
Lymphatic vessel
Lymph node
Masses of defensive cells
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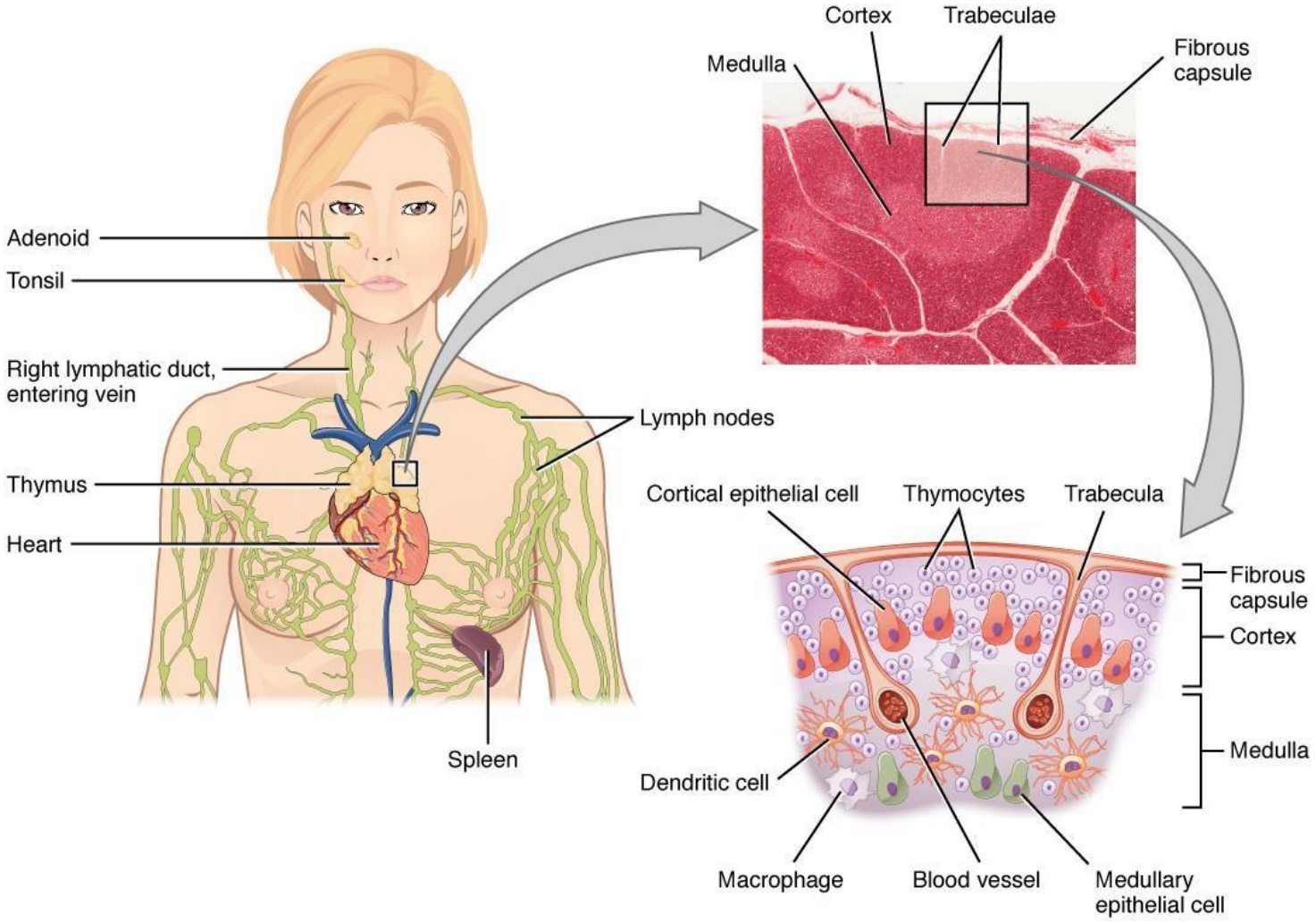
The Organs and Tissues of The Immune System

- The cells of the immune system spend much of their time in lymphoid organs.
- They develop (arise) in primary lymphoid organs, and they interact with antigens in secondary lymphoid organs.
  - **Thymus**: primary lymphoid organ for **T cell** development
  - **Bone marrow**: primary lymphoid organ for **B cell** development
  - **Lymph nodes**: collect **antigens** from **tissues**
  - **Spleen**: collects **antigens** from **blood stream**

Lymphoid Organs
1. Thymus

- Flat bilobed organ situated above the heart
- Each lobe is surrounded by a capsule and divided into lobules separated by connective tissues called **trabicula**
- The thymus reach its maximum size at **puberty** and then **atrophies**
- The thymus generation of **T cells** drop with time. By the age of 35 thymus generation of T cells drop to **20%** and by the age of 65 it drop to **2%** of newborn levels
- **Play critical role in formation and maturation of T cells**


Adenoid
Tonsil
Right lymphatic duct, entering vein
Thymus
Heart
Lymph nodes
Spleen
Cortex
Trabeculae
Medulla
Fibrous capsule
Cortical epithelial cell
Thymocytes
Trabecula
Fibrous capsule
Cortex
Medulla
Dendritic cell
Macrophage
Blood vessel
Medullary epithelial cell

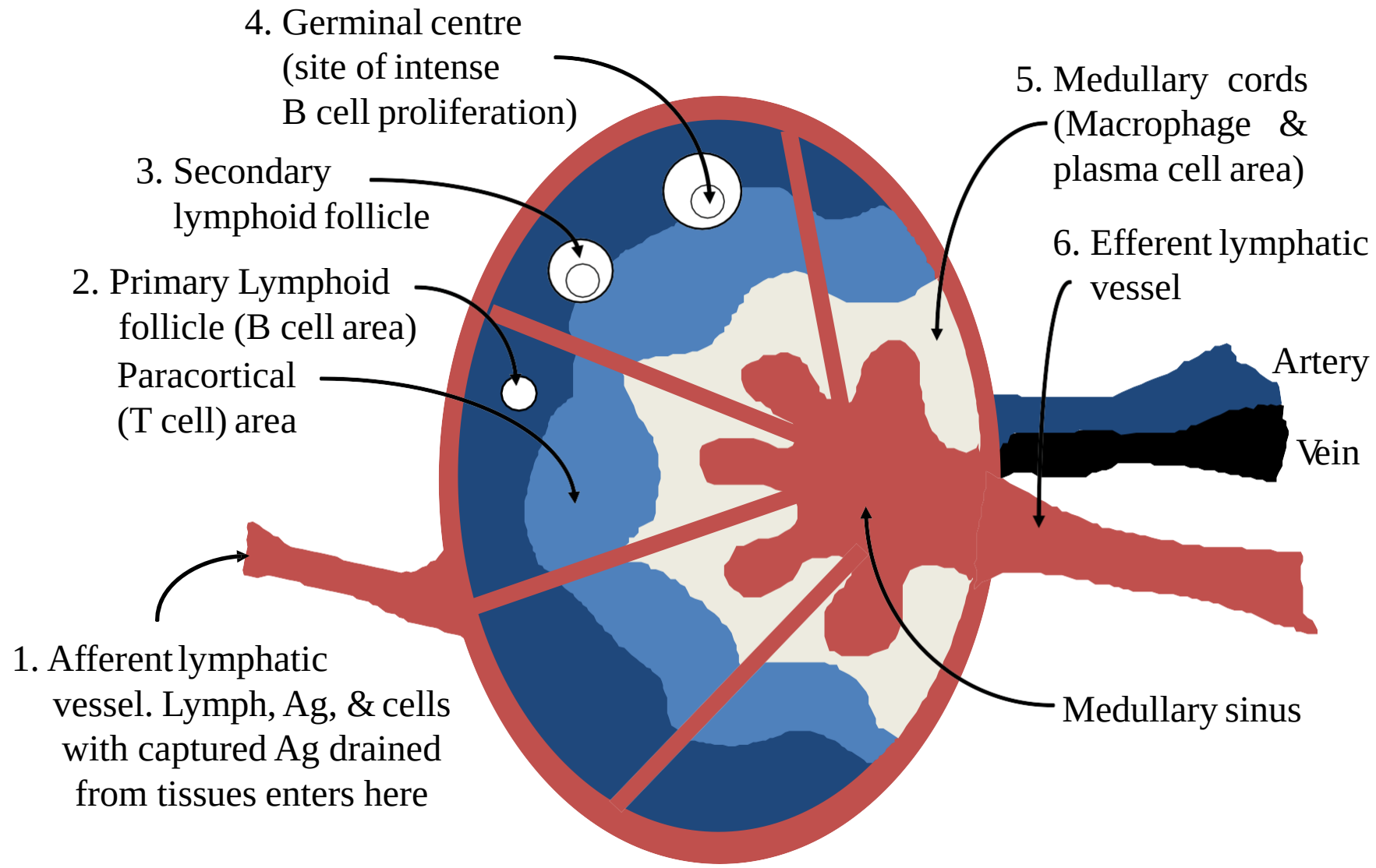
2. Bone Marrow

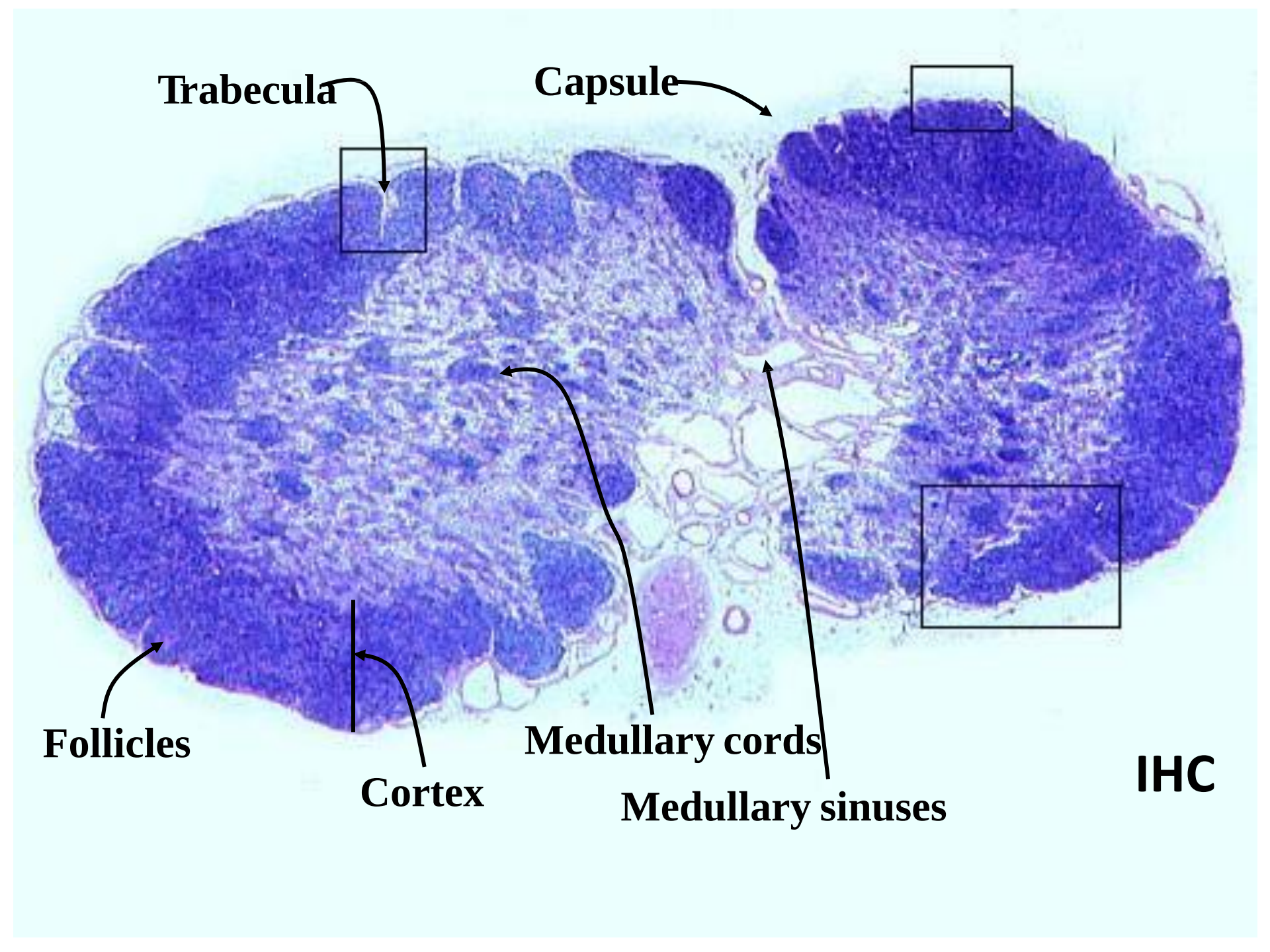
- Bone marrow is the flexible tissue in the interior of bones
- On average, bone marrow constitutes 4% of the total body mass of humans
- There are **two types** of bone marrow: **red marrow** (also known as myeloid tissue) and **yellow marrow**.
- Bone marrow is the site of **haematopoiesis** and the origin of **B cells** in human
- The hematopoietic component of bone marrow produces approximately **500 billion** blood cells per day

3. Lymph Nodes

- Lymph nodes are a **nodular aggregates** of lymphoid tissue located a long lymphatic channels through out the body
- As the lymph pass through the lymph nodes **immune cells** sample the **antigens** of microbes that might enter the body.
- **Antigens** that might enter the body became concentrated and captured in the lymph nodes

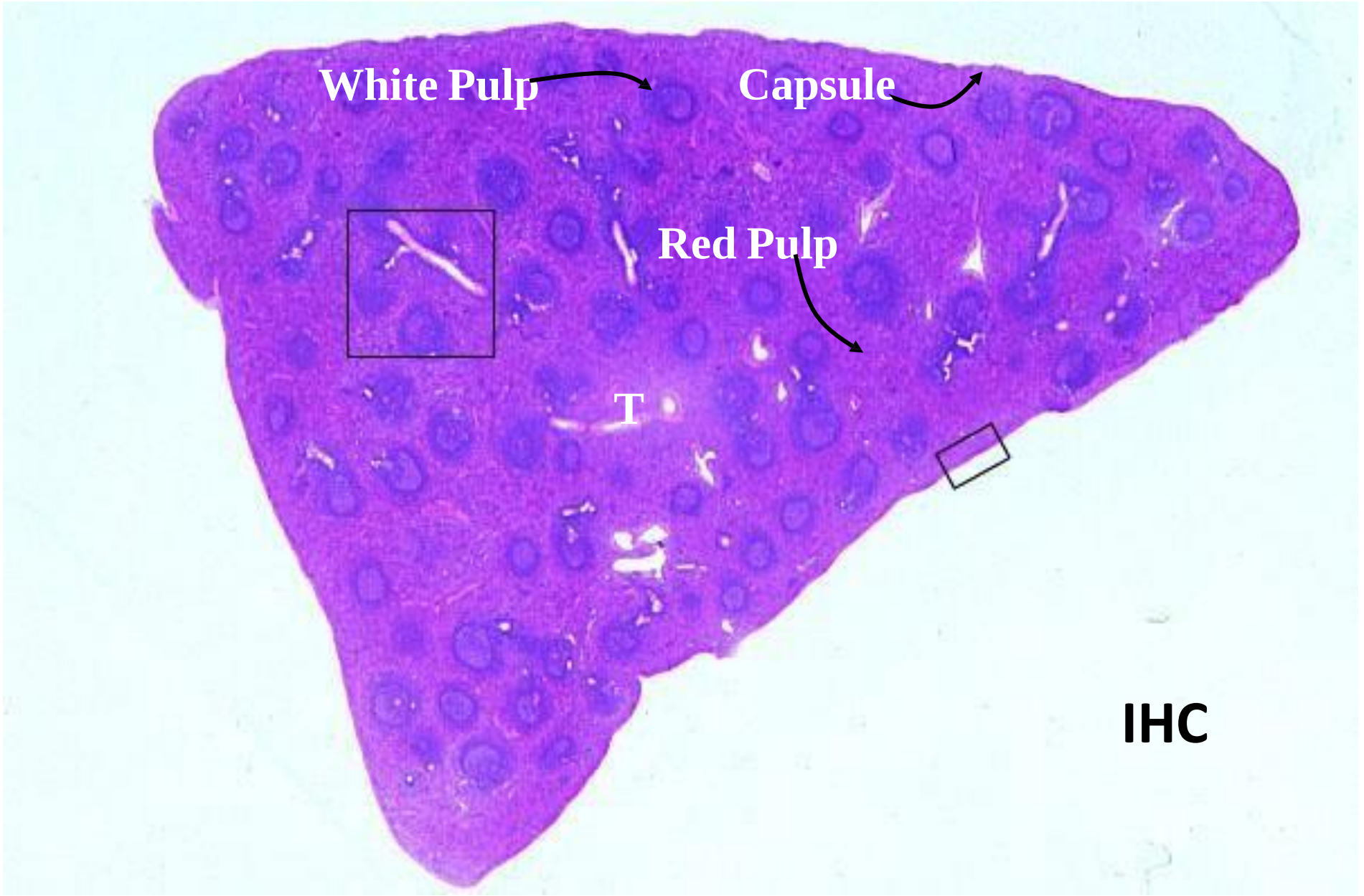
Lymph node


4. Germinal centre
(site of intense
B cell proliferation)
3. Secondary
lymphoid follicle
2. Primary Lymphoid
follicle (B cell area)
Paracortical
(T cell) area
1. Afferent lymphatic
vessel. Lymph, Ag, & cells
with captured Ag drained
from tissues enters here
5. Medullary cords
(Macrophage &
plasma cell area)
6. Efferent lymphatic
vessel
Artery
Vein
Medullary sinus

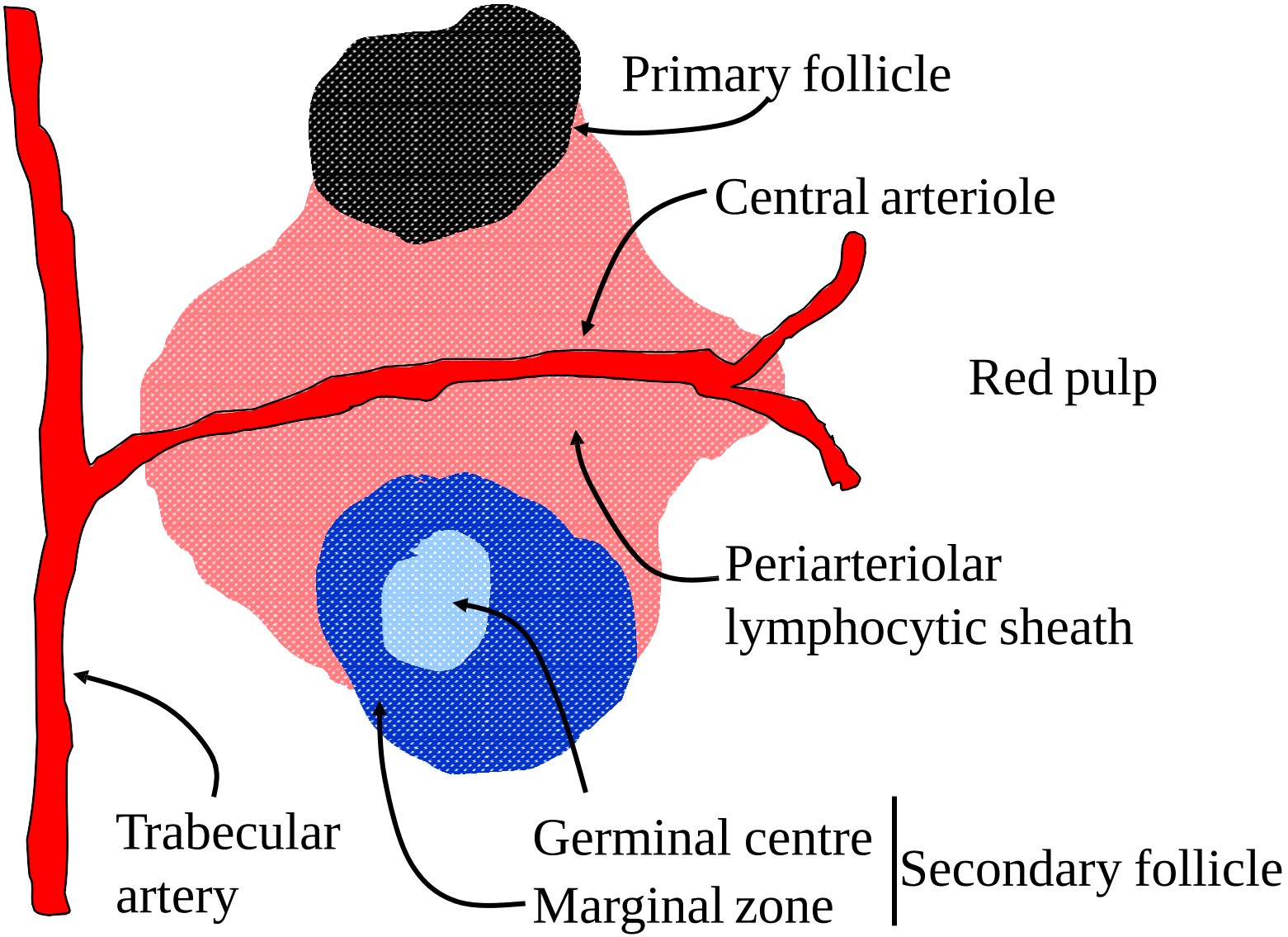

Trabecula
Capsule
Follicles
Cortex
Medullary cords
Medullary sinuses
IHC

4. Spleen

- Abdominal organ that serve as a **big lymph node**
- Unlike the lymph nodes the spleen is **not** supplied by lymphatic vessels
- The spleen had **two** main compartments the **red pulp** and the **white pulp** separated by diffuse marginal zone
- **Blood** enter the spleen through a network of channels called **sinusoids**
- **Blood**-borne antigen are trapped and concentrated in the **spleen**
- Immune cells in the spleen identify, ingest and destroy microbes


White Pulp
Capsule
Red Pulp
T
IHC

Spleen

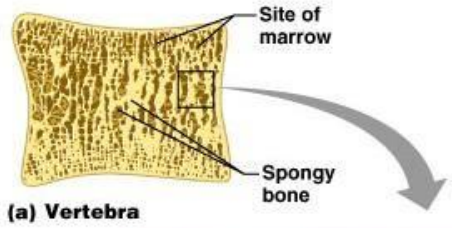

Primary follicle
Central arteriole
Red pulp
Periarteriolar
lymphocytic sheath
Trabecular
artery
Germinal centre
Marginal zone
Secondary follicle

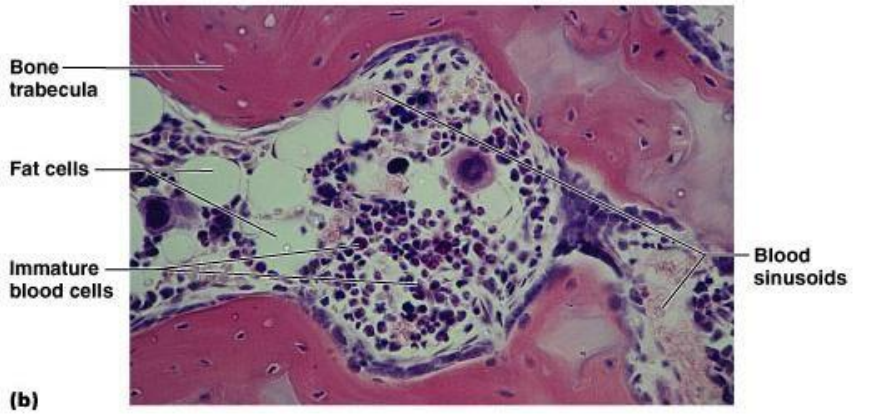
5. Cutaneous and Mucosal Lymphoid Organs

- **Located** under the epithelia of the skin, GIT and respiratory tracts.
- **It includes**: pharyngeal tonsils, adenoids, appendix and peyer's patch
- Sites of immune response to microorganisms that breach **epithelia**

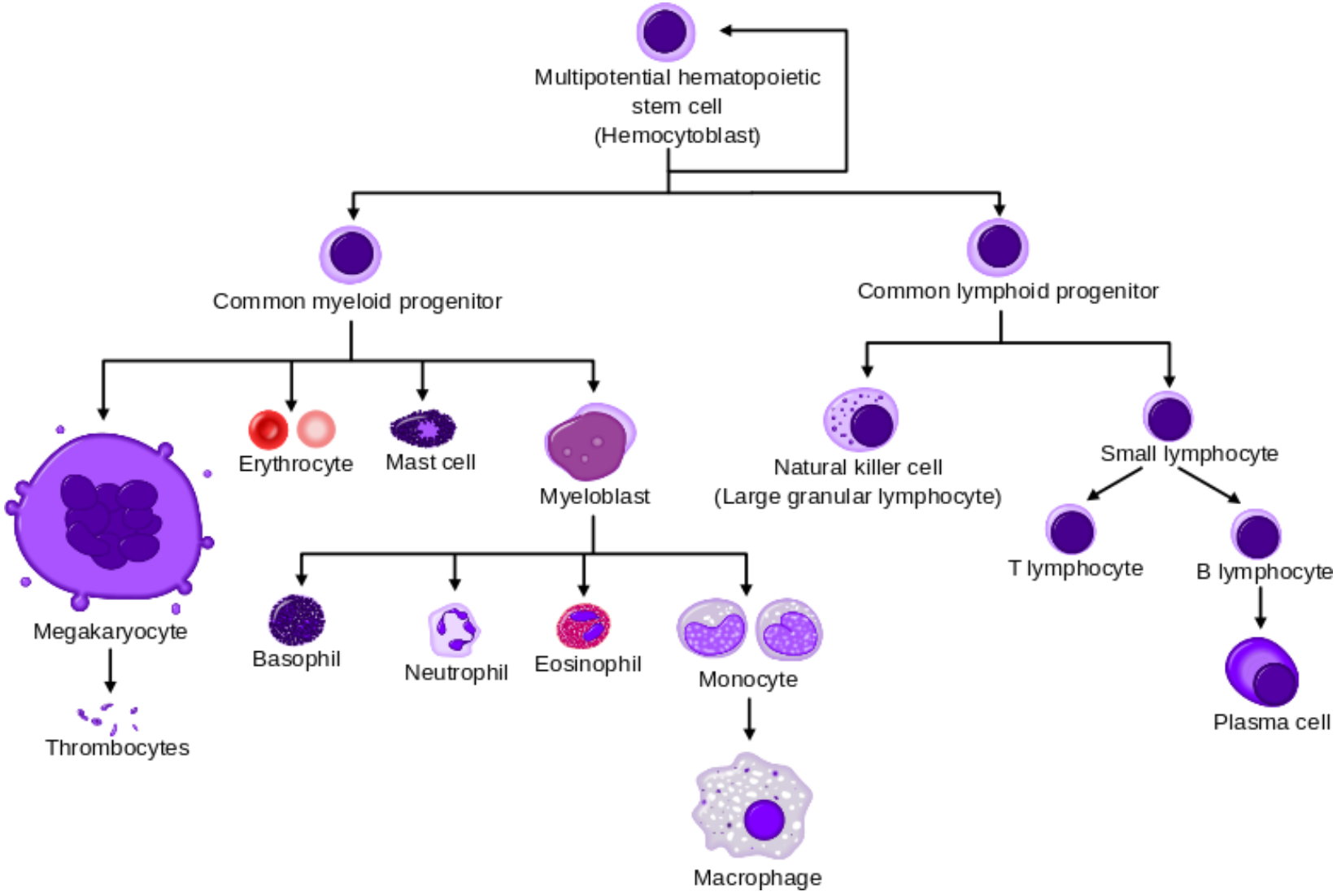
Hematopoiesis

- **Formation of blood cells**
- Occurs mostly in **red bone marrow**
- All cells arise from same **blood stem cell** (**pluripotent hematopoietic stem cells**)

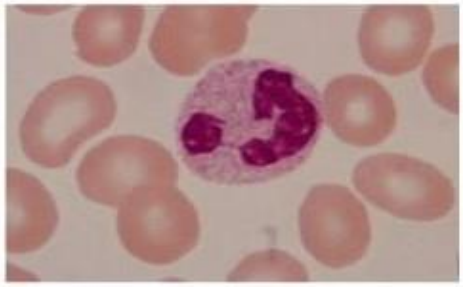




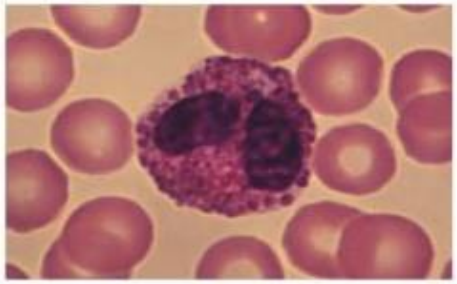
Formation of Blood Cells



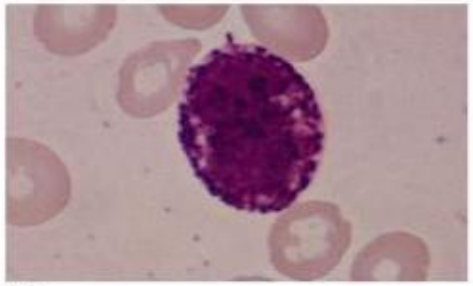
Leukocytes



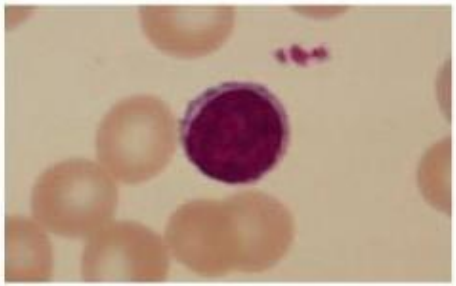
(a) neutrophil



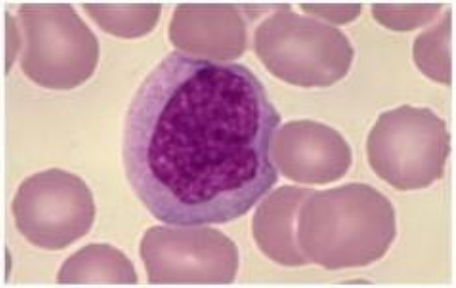
(b) eosinophil



(c) basophil



(d) small lymphocyte

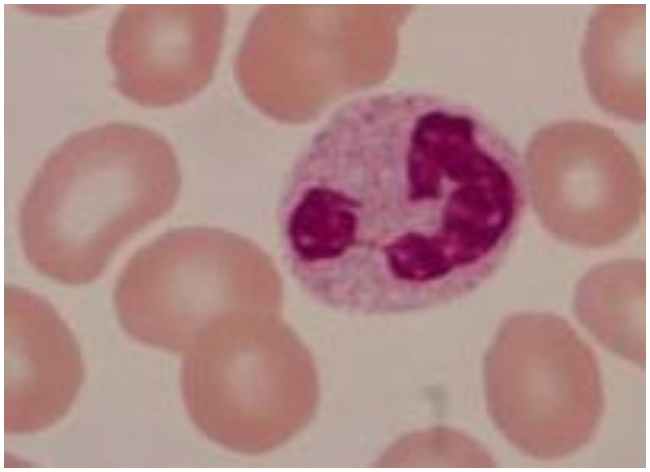


(e) monocyte

Leukocyte Types

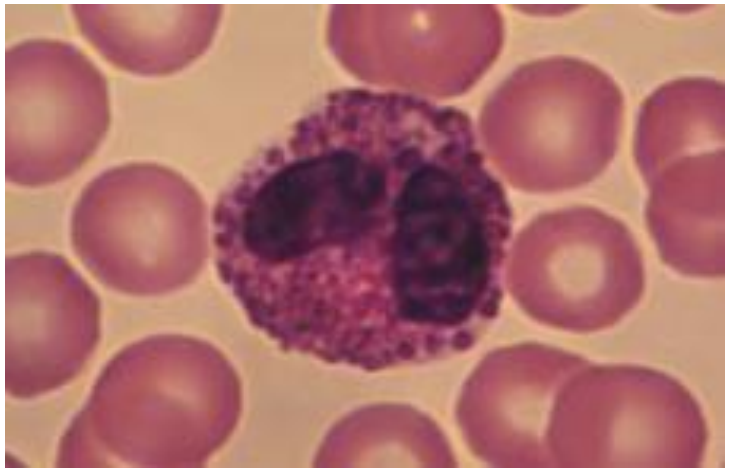
- Divided into granulocytes and agranulocytes
- **Granulocytes**: neutrophils, eosinophils, basophils (according to how stain)
  - Granules
  - Lobed nuclei
  - All are phagocytic
- **Agranulocytes**: lymphocytes, monocytes

1. Neutrophils

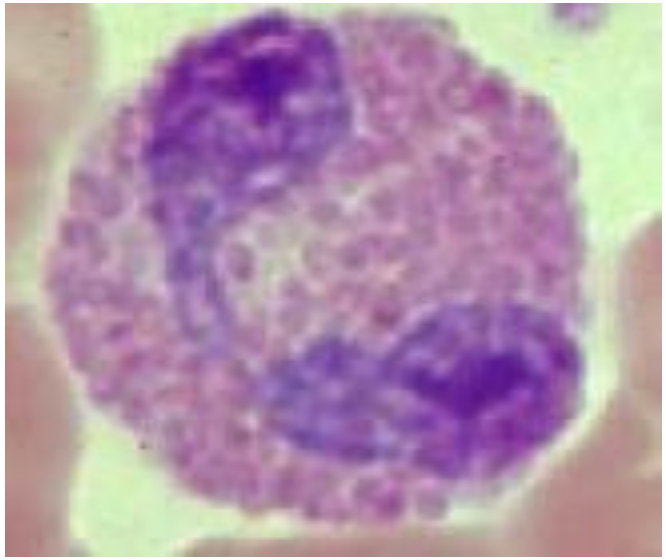


- **60%** of all WBCs
- **Other name**: Polymorphonuclear cells (PMNs)
- **Appearance**: pink granules in cytoplasm, nucleus has 3-5 lobes
- Function: **Phagocytosis** of **bacteria**
  - Granules have **enzymes**
  - Can damage tissue if severe or prolonged
  - Form pus

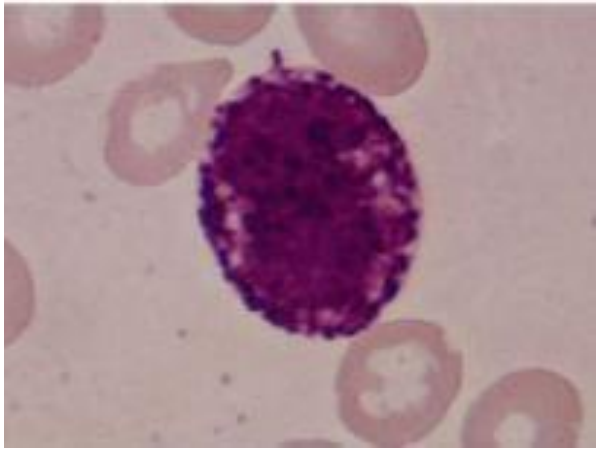
2. Eosinophils



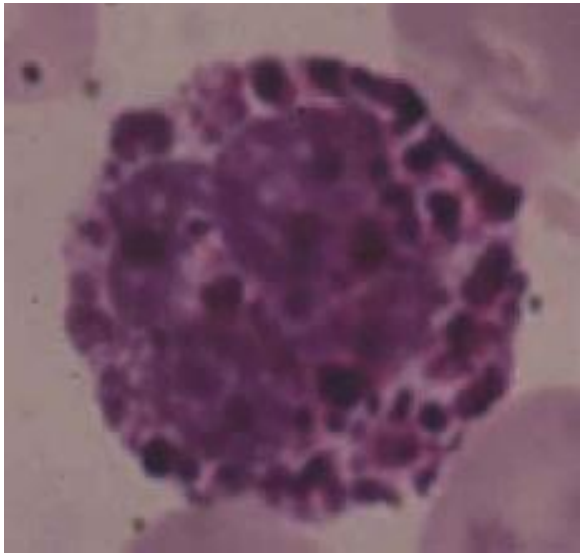
- **1-4** % of leukocytes
- **Bilobed** and contain eosinophilic granules which have **digestive enzymes**
- Role in ending **allergic reactions** and in fighting **parasitic** infections



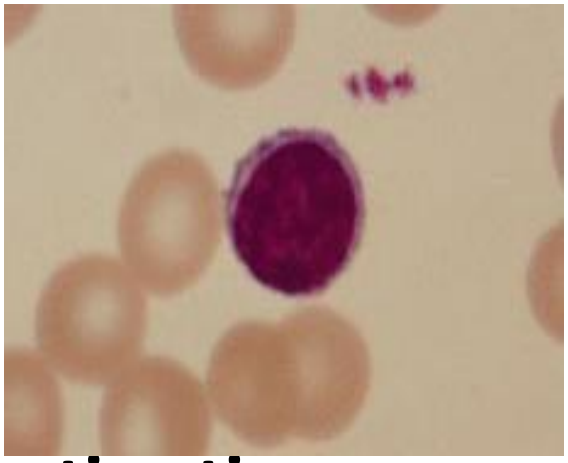
3. Basophils



- **Rarest** WBC, **<1%** WBC
- **Bilobed** nucleus
- Dark purple granules (**basophilic granules**)
- Granules contain: **histamine and heparin**
- IgE receptors - Involved in **allergy**



4. Lymphocytes



- Most important WBC **20-45**%
- **Small** (same size as **RBCs**)
- Mostly present in **lymphoid connective tissue**, e.g. **lymph nodes**, **tonsils**, **spleen**
- Nucleus occupies most of the cell volume (little visible cytoplasm) and no specific granules
- **Two main types** attack antigens in different ways

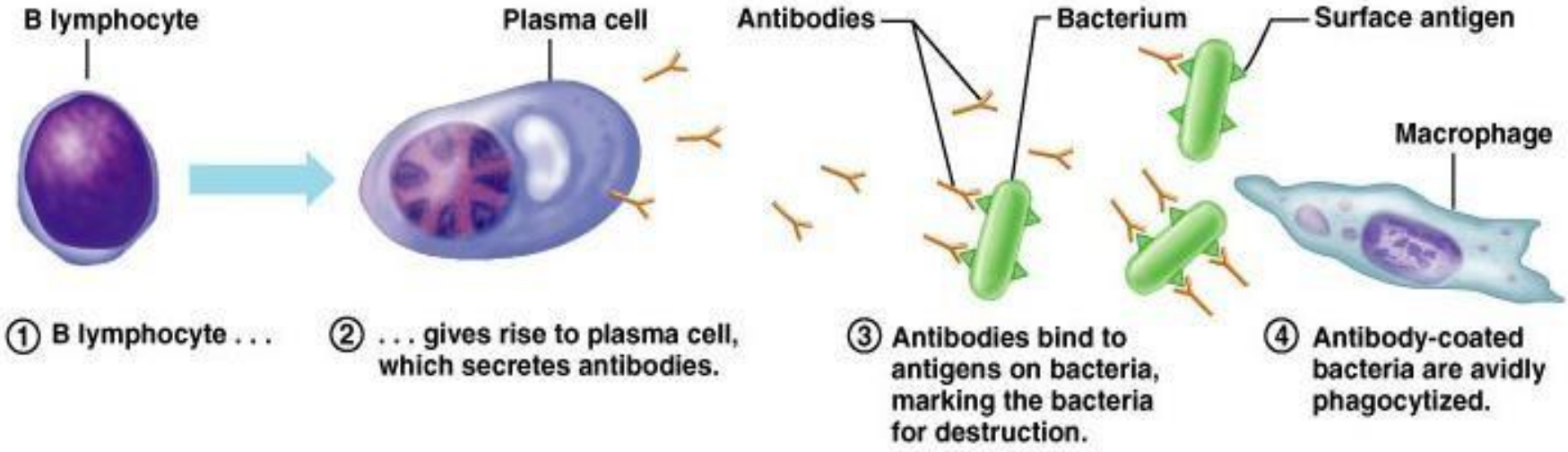
1. **T cells**
2. **B cells**

plus “natural killer cells”

B cells

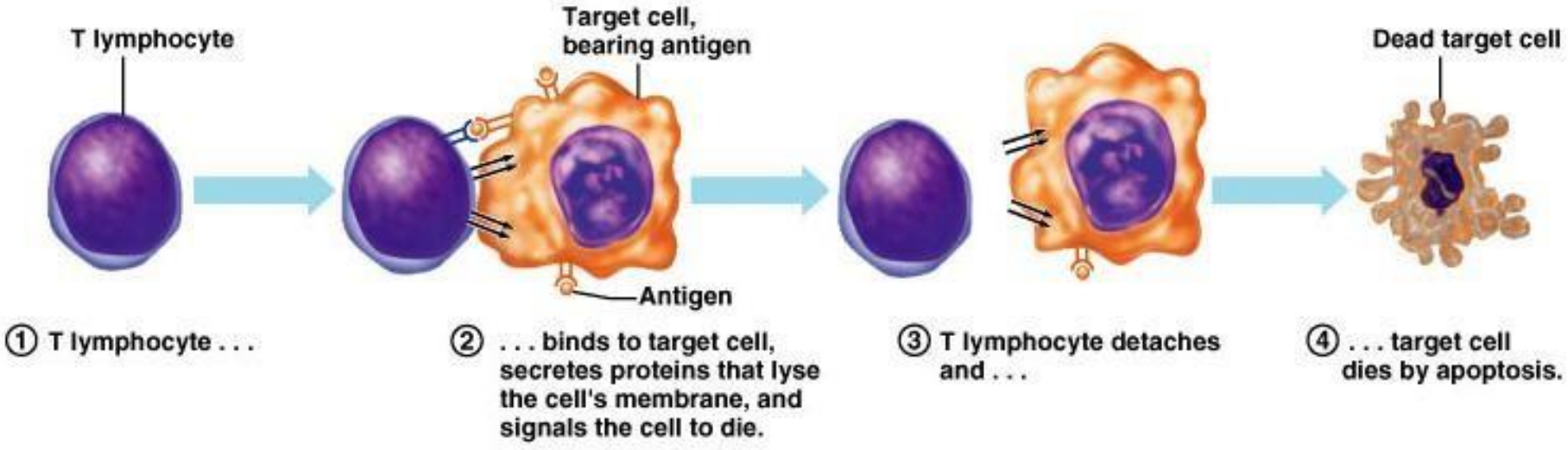
- Formed and mature in **bone marrow** in mammals.
- **Differentiate** into **plasma cells** that secrete antibodies or become a **memory cells** that live longer
- B cells also **display antibodies** on **their membrane**
- **Antibodies flag cells** for destruction by macrophages

B cells

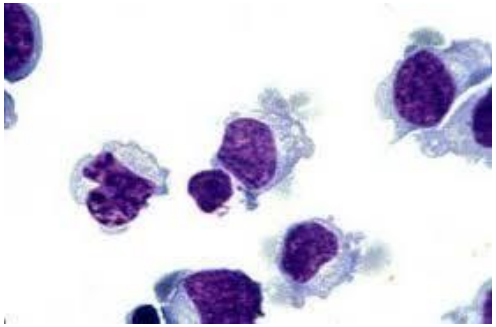

B lymphocyte
Plasma cell
Antibodies
Bacterium
Surface antigen
Macrophage
① B lymphocyte . . .
② . . . gives rise to plasma cell, which secretes antibodies.
③ Antibodies bind to antigens on bacteria, marking the bacteria for destruction.
④ Antibody-coated bacteria are avidly phagocytized.

T cells

- **T lymphocyte** maturates in **thymus**
- T cells antigen binding molecule called **T cell receptor**
- T cells are subdivided into **3 main groups**: **Helper T cells**, **Cytotoxic T cells**, and **regulatory T cells**

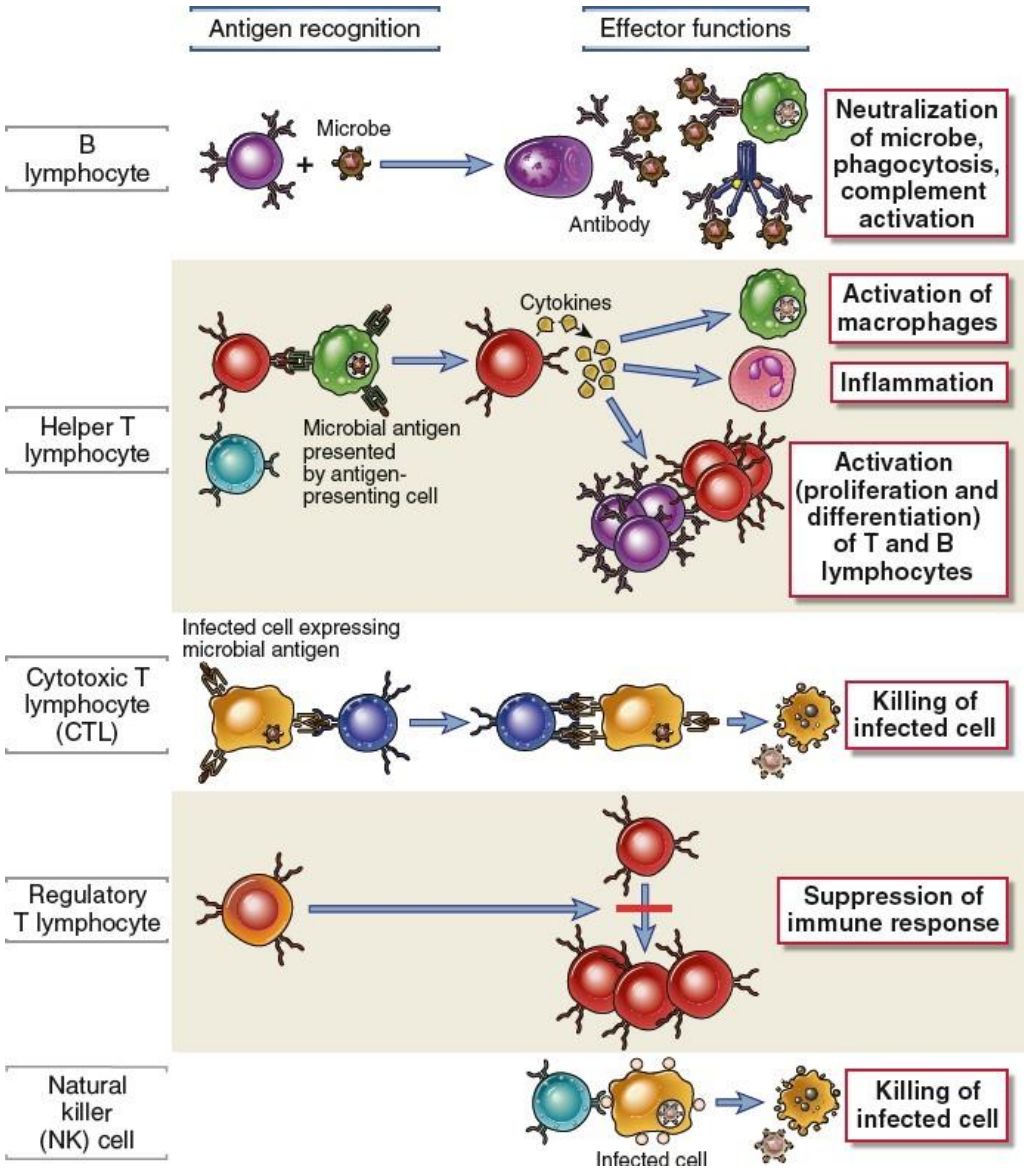


5. Natural Killer Cells (NK)



- Constitute **5-10%** of human lymphocyte are **large** and **granular cells**
- Display **cytotoxic activity** against **tumor cells** and cells infected with **viruses**
- These cells **don not** have **specific receptors** for **antigens** on their surface and considered **part of innate immunity**
- **NK** cells have **receptors** for **antibodies** and can **destroy targeted cells** through a process known as **antibody-dependent cells mediated toxicity**

Classes of Lymphocytes



6. Monocytes/ Macrophages

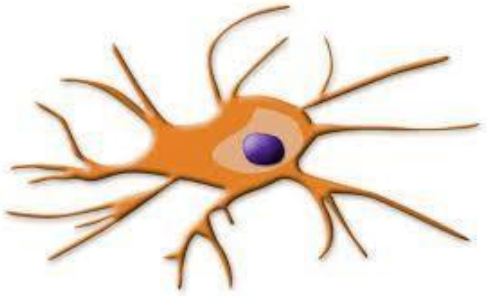
Monocyte

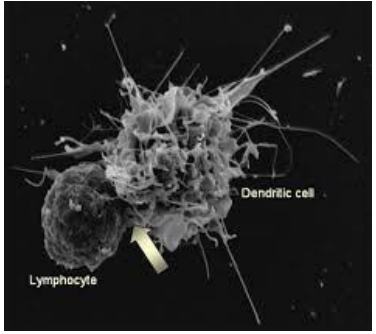
- **3-8%** WBC
- Monocytes circulate in blood for about **8 hours** then it enlarge and **migrate** into **tissues and differentiate** into specific tissue **macrophage**
- Recruited to sites of inflammation

Macrophages

- Macrophage play role in **phagocytosis**, **bacterial killing**, and **antigen presentation**
- Some macrophages move through the body and remain as **free macrophage** and some **reside** in particular tissue and become **fixed macrophage** like:
  - Peritoneal cavity: peritoneal macrophages
  - Lung: alveolar macrophages
  - Spleen: splenic macrophages
  - Liver: Kupffer cells
  - Intestinal macrophage
  - Microglial cells in brain
  - Histocytes in connective tissue

7. Dandritic Cells





- Acquired its name because it is covered with long **membrane extensions** that resemble the dandrites of nerve cells
- Dandritic cells have **4 main classes**:
  - **Langerhans DCs**
  - **Interstitial DCs**
  - **Monocyte-derived DCs**
  - **Plasmacytoid-derived DCs**
- DCs **main functions** are monitoring of body pathogen invasion and presentations of antigens for T cells

Stages of Lymphocyte Activation

- **Naïve lymphocytes**
  - Mature lymphocytes that have not previously encountered antigen; function -- **antigen recognition**
  - Preferential migration to peripheral lymphoid organs (**lymph nodes**), the sites where antigens are concentrated, and immune responses start

Stages of Lymphocyte Activation

- **Effector lymphocytes**
  - **Activated** lymphocytes capable of performing the functions required to **eliminate** microbes (effector functions)
  - **Effector T lymphocytes**: cytokine secretion (helper cells), killing of infected cells (CTLs)
  - **B lymphocytes**: antibody-secreting cells (e.g. plasma cells)
- **Memory lymphocytes**
  - Long-lived, functionally silent cells; mount rapid responses to antigen challenge (secondary responses)

Function of Immune Cells

- **Lymphocytes of the adaptive immune system**
  1. **T helper cells**: regulate other immune cells
  2. **T cytotoxic (killer) cells**: kill infected cells
  3. **B cells**: produce antibodies (immunoglobulin)

- **Dendritic cells and macrophage**:

➢ directly kill microbes by phagocytosis and other mechanisms.

➢ They also help to activate T cells (connection between innate and adaptive immunity)

- Dendritic cells and other Antigen presenting cells (APCs) also play role in capturing microbes and then process and display antigens
- **NK cells** are lymphocytes: Recognizes and kill abnormal cells like **tumour cells**, and **virus infected cells**

Lymphocyte Circulation

- Lymphocytes constantlycirculates between tissues in such a awaythat

1. **Naïve** lymphocytes **traverse** the peripheral lymphoid organs where immune responseare initiated.
2. The **effectors** lymphocytes **migrates** to sites of infections to eliminates microbes

- **Lymph**: Fluids from all epithelia, connective tissues and paranchymal organs is drained by lymphatic's

THE LYMPHOCYTE RECIRCULATION

- Mature naive lymphocytes leave the central lymphoid organs to travel to the sites of activation: the secondary lymphoid organs/tissues (SLO)
- They enter the different SLOs randomly via the process called ‚HOMING'
- They either **GET ACTIVATED** after recognizing an antigen and differentiate to effector cells or they **LEAVE VIA THE EFFERENT LYMPHATIC VESSELS**
- The lymph is collected by lymph nodes, the lymphocytes pass many of them, and in every node they may get activated
- Eventually all the lymph is flowing into the **THORACIC DUCT** and get back to the circulation, so the lymphocytes can reach another **SLO**
- They do their recirculation until they find an antigen or until the end of their lifespan

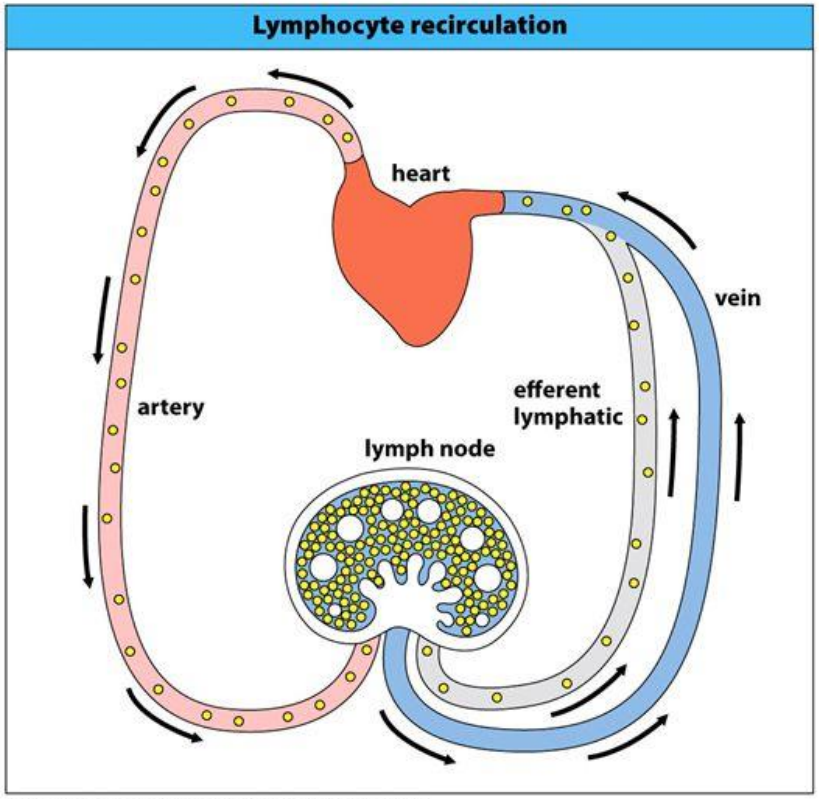


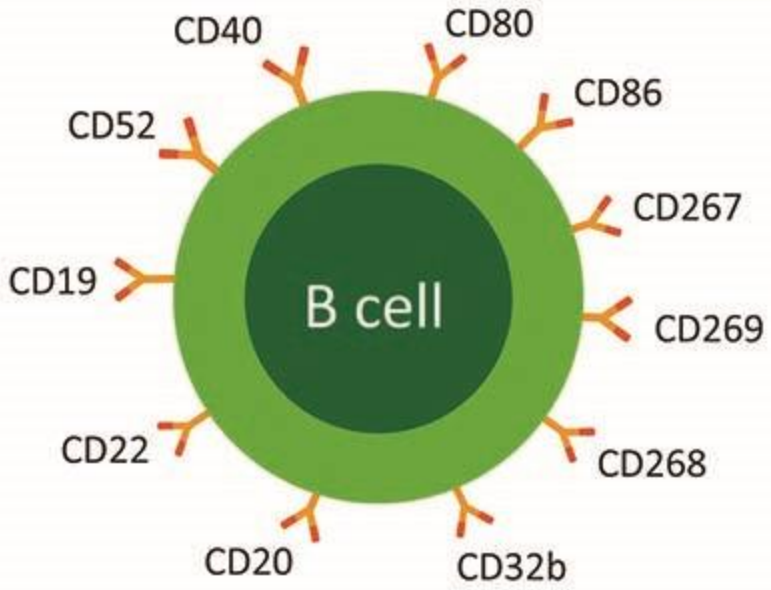
Figure 1.19 The Immune System, 3ed. (© Garland Science 2009)

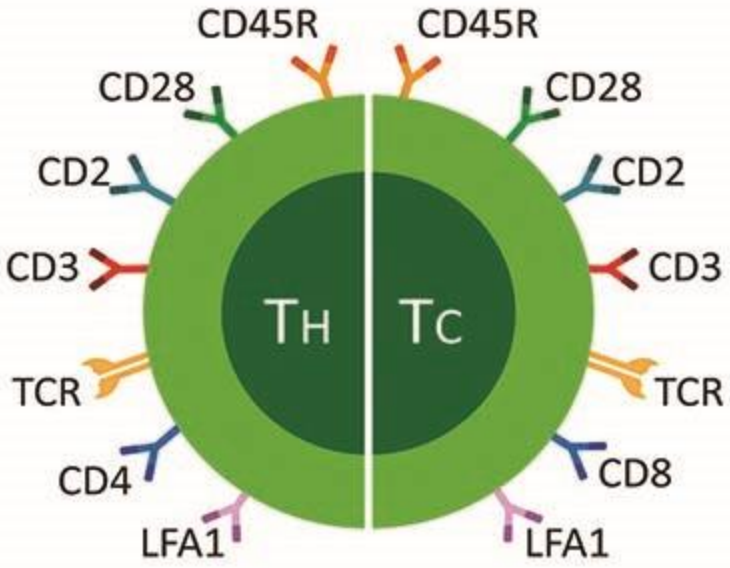
The CD Nomenclature

- The **cluster of differentiation** (also known as **cluster** of designation or classification determinant and often abbreviated as **CD**) **is a protocol used for the identification and investigation of cell surface molecules providing targets for immunophenotyping of cells.**

- Used to classify leukocytes into functionally distinct subpopulations, e.g. **helper T cells are CD4+, Cytotoxic T cells are CD8+**, and **Regulatory T cells are CD4+ and CD25+**
- Often involved in leukocyte functions
- Antibodies against various CD molecules are used to:
  1. Identify and isolate leukocyte subpopulations
  2. Study functions of leukocytes
  3. Eliminate particular cell populations

B-Cells VS T-Cells





SUCCESS IS NO ACCIDENT.
IT IS HARD WORK,
PERSEVERANCE, LEARNING,
STUDYING, SACRIFICE
AND MOST OF ALL, LOVE
OF WHAT YOU ARE DOING
OR LEARNING TO DO.