

Lymphatic System

Introduction

- The lymphatic system consists of a fluid called lymph flowing within lymphatic vessels, several structures and organs that contain lymphatic tissue, and red bone marrow which houses stem cells that develop into lymphocytes.
- The composition of the interstitial fluid and lymph are basically same.
- After fluid passes from interstitial spaces into lymphatic vessels, it is called lymph.
- Lymphatic tissue is a specialized type of conn. Tissue that contains large number of lymphocytes.

Functions of the Lymphatic System

- Draining interstitial fluid: lymphatic vessels drain excess interstitial fluid from tissue spaces.
- Transporting dietary lipids: lymphatic vessels transport the lipids and lipid-soluble vitamins (A,D, E, K) absorbed by the GI tract to the blood.
- Facilitating immune response: lymphatic tissue initiates highly specific responses directed against particular microbes or abnormal cells
- lymphocytes can recognize foreign cells, microbes, toxins and cancer cells. They respond in two ways.

Functions continued

- The T-lymphocytes or T-cells destroy the intruders by causing them to rupture or by releasing cytotoxic substances.
- The B-cells secrete antibodies which cause destruction of specific antigens.

Lymphatic Vessels and Lymph Circulation

- Lymphatic vessels begin as lymphatic capillaries.
- Lymphatic capillaries are found throughout the body except in avascular tissues, the CNS, portions of the spleen and red bone marrow.
- They are closed-ended tubes located in spaces between cells.
- These unite to form larger lymphatic vessels. They resemble veins but have thinner walls and more valves.
- At various intervals along the lymphatic vessels, lymph flows through structures called lymph nodes.
- In the skin, lymphatic vessels are in the subcutaneous tissue and in the viscera follow arteries, form plexuses.

Lymphatic Capillaries

- They are slightly larger than blood capillaries.
- The wall is made of endothelial cells. The margins of the cells overlap.
- When pressure is greater in the IF than in lymph, the cells separate and fluid enters the capillary.
- When pressure is greater in the capillary the cells adhere closer together, so lymph cannot flow back to IF.

Capillaries

- Anchoring filaments: attach lymphatic endothelial cells to surrounding tissues.
- When excess IF accumulates the filaments are pulled, to make the openings larger so fluid can enter the capillary.
- In the SI, the capillaries are called lacteals.
- These carry dietary lipids into lymphatic vessels and ultimately into blood.
- The presence of these lipids causes the lymph draining the SI to appear creamy white and is called chyle.

Lymph Trunks

- Lymph passes from lymphatic capillaries, through lymph vessels and then lymph nodes.
- The lymphatic vessels that exit nodes, pass lymph either toward another node or on to another group of nodes.
- From the most proximal group of each chain of nodes, the exiting vessel form lymph trunks.
- The principal trunks are lumbar, intestinal, bronchomediastinal, subclavian and jugular trunks.
- The principal trunks pass their lymph into two main channels, thoracic and right lymphatic duct. Lymph then passes into venous blood.

Lymphatic Ducts

- The thoracic (left lymphatic) duct-this is about 38-45 cm long. Begins as cisterna chyli ant to second lumbar vertebra. This receives lymph from the left side of the head, neck and chest, the left upper limb, and the entire body inferior to the ribs. This drains lymph into venous blood via the left subclavian vein.
- The cisterna chyli receives lymph from the right and left lumbar trunks and from the intestinal trunk.
- Lumbar trunk-from lower limbs, wall and viscera of pelvis, kidneys, adrenal glands.
- Intestinal trunk: from stomach, intestines, pancreas, spleen and part of liver.

Lymphatic Ducts

- In the neck the thoracic duct receives lymph from the left jugular. Left subclavian and left bronchomediastinal trunks.
- The right lymphatic duct is about 1.25 cm long and drains lymph from the upper right side of the body into venous blood via the right subclavian vein.
- Three lymphatic trunks drain into this duct-right jugular:right side of head and neck. Right subclavian:right upper limb. Right bronchomediastinal:right sides of thorax, lung heart and part of liver.

Formation and Flow of Lymph

- More fluid is filtered out of the capillaries than is reabsorbed.
- This excess filtered fluid-3L a day- drains into lymphatic vessels and becomes lymph.
- Function of lymphatic vessels is to return the lost plasma proteins back to blood.
- Ultimately, lymph drains into venous blood through the right lymphatic and thoracic duct at the junction of internal jugular and subclavian veins.

Relationship of lymphatic system to cardiovascular system

- Sequence of fluid flow is capillary (blood) ->interstitial spaces (IF)->lymphatic capillaries (lymph)->lymphatic vessels (lymph)->lymphatic ducts (lymph)->subclavian veins (blood).
- The skeletal muscle and respiratory pumps promote the flow of lymph from tissue spaces to the large lymphatic ducts to the subclavian veins.
- Lymphatic vessels posses one-way valves, similar to veins to prevent back flow.

Lymphatic Organs and Tissues

- The organs and tissues are classified into two groups based on the functions.
- Primary lymphatic organs: provide appropriate environment for stem cells to divide and mature into B cells and T cells. The organs are the red bone marrow (in flat bone and epiphysis of long bones of adults) and thymus gland.
- Secondary lymphatic organs: most immune responses occur. Include lymph nodes, spleen and lymphatic nodules.

Thymus Gland

- The thymus gland lies between the sternum and the two large blood vessels above the heart.
- It usually has two lobes. A connective tissue layer holds the two lobes together. A connective tissue capsule encloses each lobe separately.
- Lobes are divided into lobules.
- Each lobule made of an outer cortex: made of lymphocytes, epithelial cells and an inner medulla also of reticular epithelial cells. These produce thymic hormones aid in maturation of T cells. Thymic corpuscles.
- Thymus gland in infants=70 g and in adults=3 g.

Spleen

- The spleen is an oval shaped organ and is the largest mass of lymphatic tissue.
- It is located in the left hypochondriac region between the stomach and diaphragm.
- A capsule of dense connective tissue surrounds the spleen.
- The parenchyma of spleen consists of two diff. Kinds of tissues-white pulp and red pulp.

Spleen

- White pulp: lymphatic tissue, mostly lymphocytes and macrophages arranged around branches of the splenic artery called central arteries. Fn.-B and T cells carry out immune functions. Macrophages destroy blood-borne pathogens.
- Red pulp consists of venous sinuses filled with blood and cords called splenic cords. This consists of red blood cells, macrophages, lymphocytes, plasma cells and granulocytes. Fn.-removal by macrophages of worn out or defective RBC's and platelets. Storage of platelets and hemopoiesis during fetal life.
- Abdominal trauma-splenectomy to prevent shock. Red bone marrow and liver take over its function.

Lymph Nodes

- There are approx. 600 of these bean-shaped organs.
- Located along lymphatic vessels.
- Heavily concentrated near the mammary glands and in the axillae and groin.
- Are about 1-25mm long. Covered by a capsule of dense conn. Tissue.
- Capsular extensions called trabeculae divide it into compartments. Provide support and a route for blood vessels to pass.
- Internal to this is supporting network of reticular fibers and fibroblasts. The two form the stroma.

Lymph Nodes

- The parenchyma-a superficial cortex and an inner medulla.
- Outer cortex-B cells.
- Inner cortex-T cells.
- Medulla-B cells and plasma cells in strands called medullary cords.
- Lymph only flows in one direction.
- Only lymph nodes filter lymph. As lymph enters the foreign substances are trapped and destroyed. Filtered lymph leaves via the other end. plasma cells and T cells that have proliferated can also leave and go to other parts.

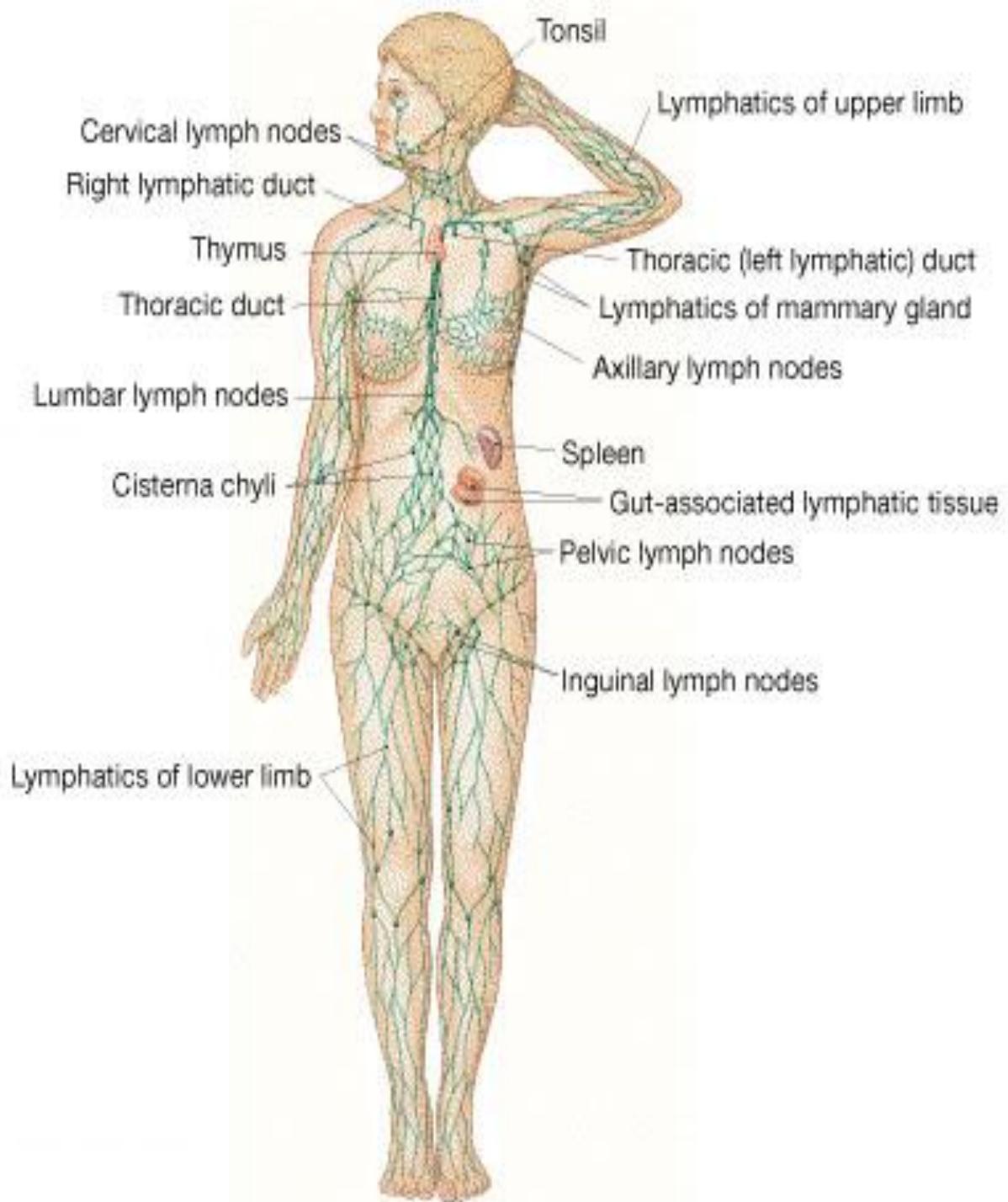
Lymph Nodules

- These are oval shaped concentrations of lymphatic tissue not surrounded by capsule.
- They are scattered through the lamina propria of mucous membranes and reproductive and respiratory tracts. Also referred to as MALT.
- Most are small and solitary. Some as aggregates-in tonsils, Peyer's patches in ileum of SI. Also in appendix.
- Five tonsils.-single pharangeal oe adenoid, two palatine tonsils(tonsilectomy) and the paired linguinal tonsils.

Lymphatic System

Introduction

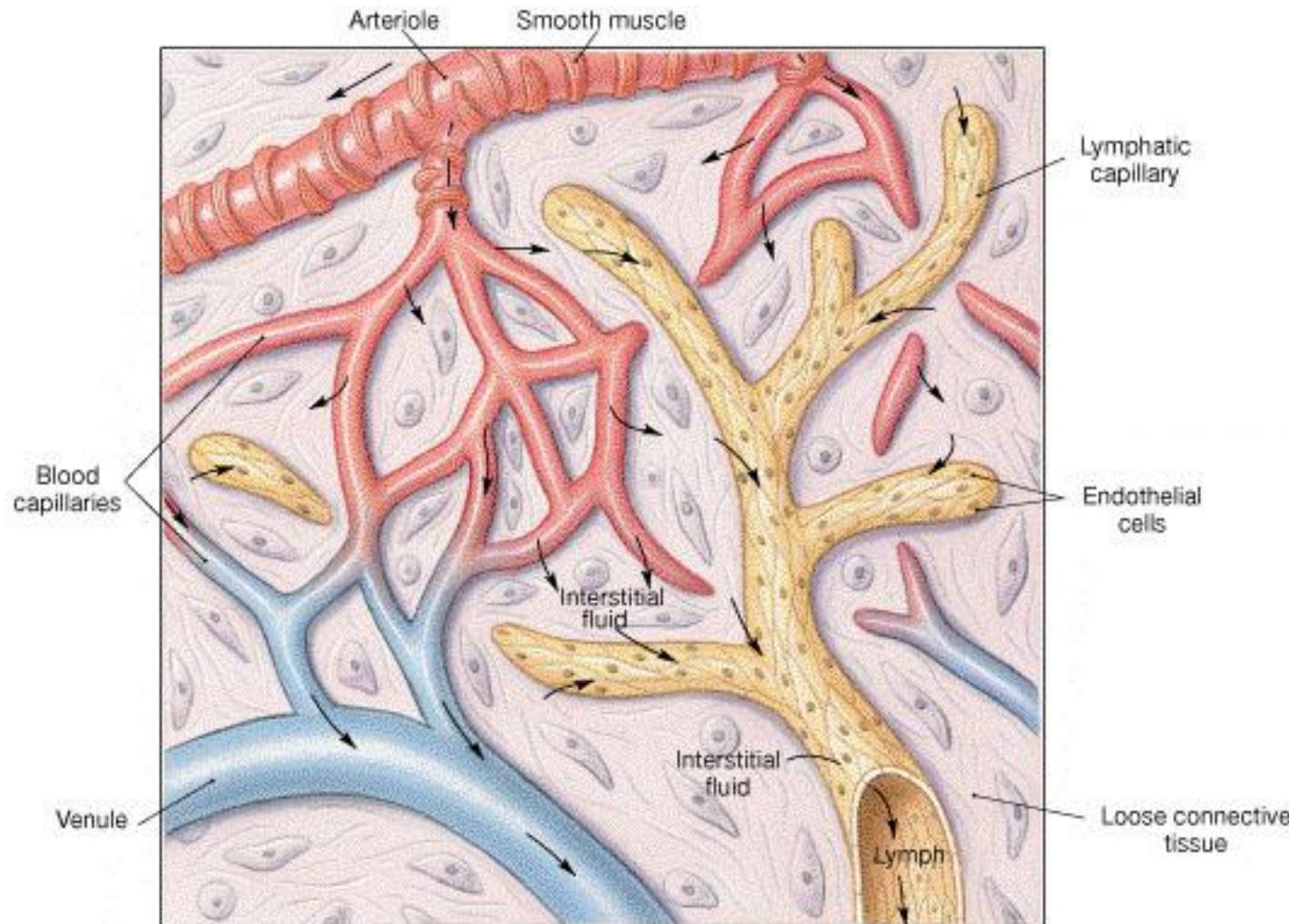
- Components
 - **Lymph** is the fluid
 - Vessels – **lymphatics**
 - Structures & organs
- Functions
 - Return tissue fluid to the bloodstream
 - Transport fats from the digestive tract to the bloodstream
 - Surveillance & defense



Lymphatics

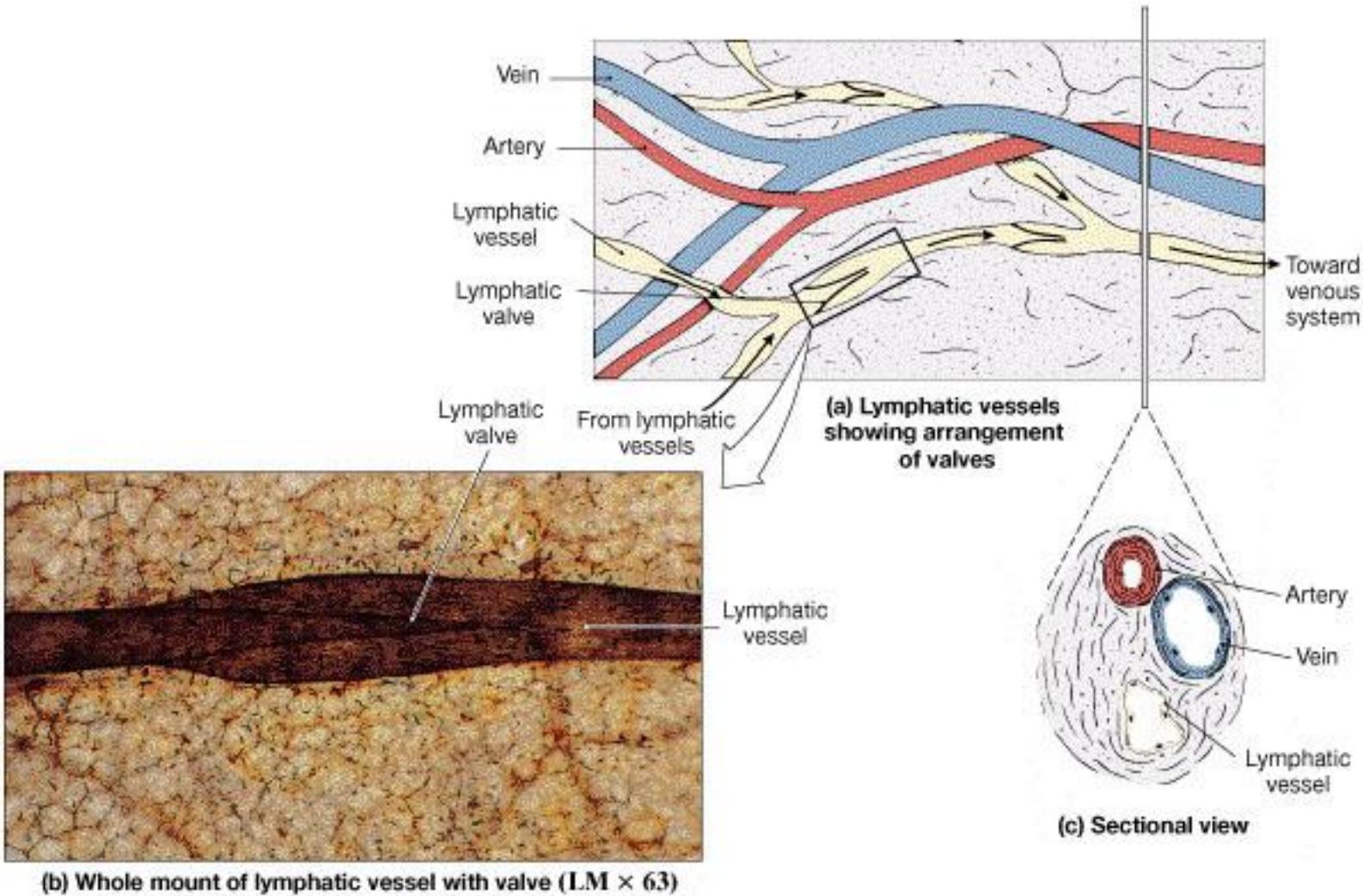
- Originate as lymph capillaries
- Capillaries unite to form larger vessels
 - Resemble veins in structure
 - Connect to lymph nodes at various intervals
- Lymphatics ultimately deliver lymph into 2 main channels
 - Right lymphatic duct
 - Drains right side of head & neck, right arm, right thorax
 - Empties into the right subclavian vein
 - Thoracic duct
 - Drains the rest of the body
 - Empties into the left subclavian vein

Lymph Capillaries

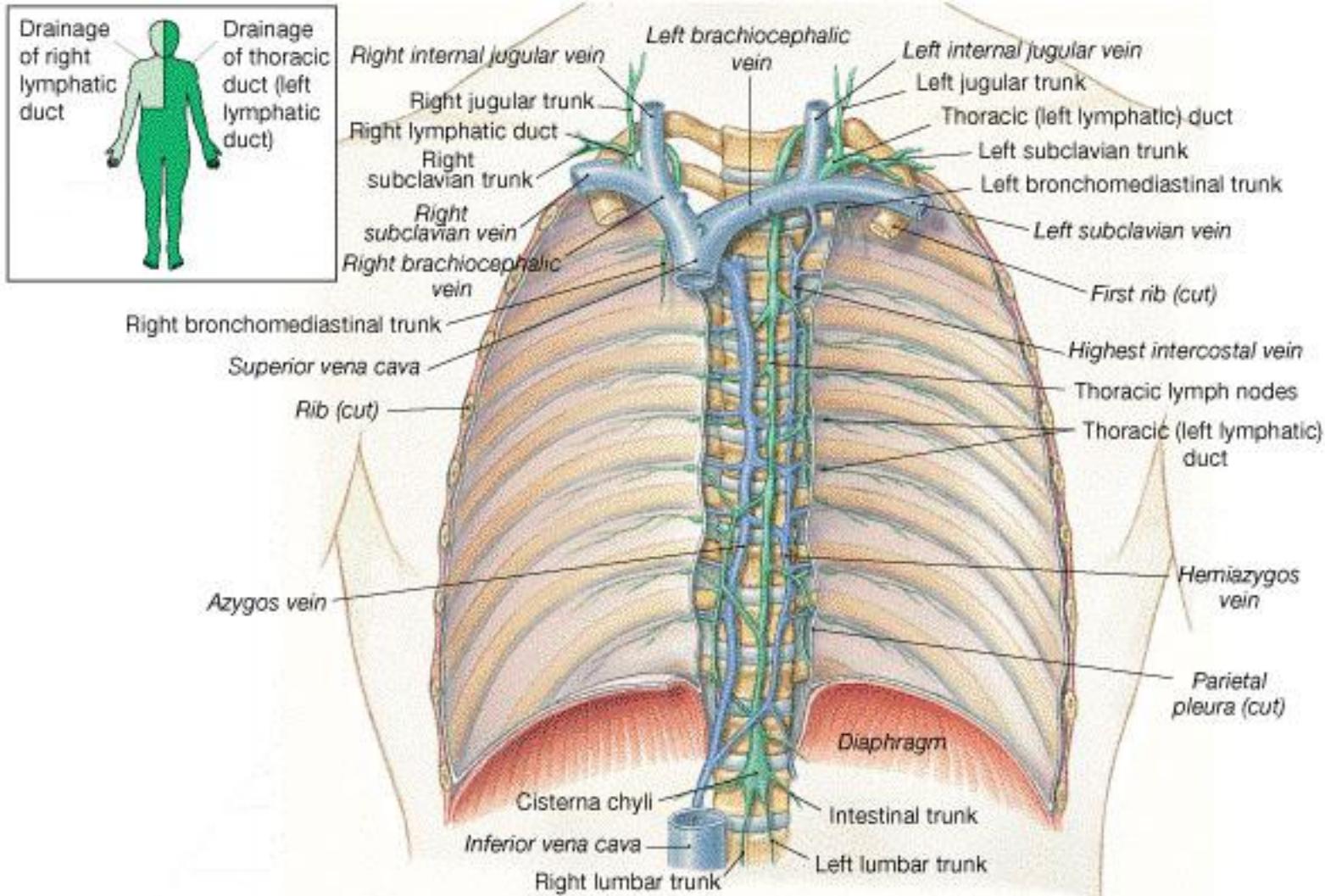


(a) Association of blood capillaries, tissue, and lymphatic capillaries

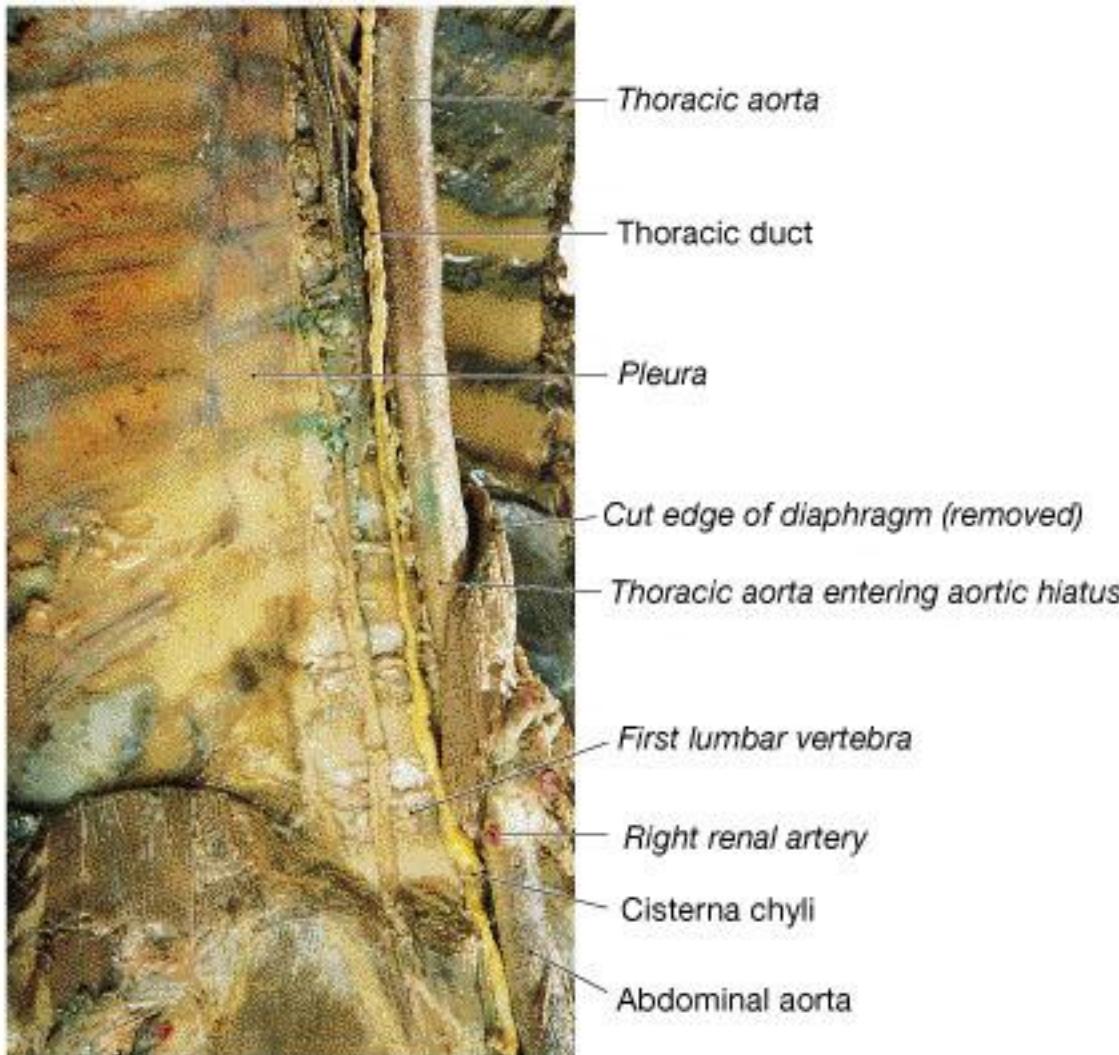
Lymphatic Vessels



Main Channels of Lymphatics



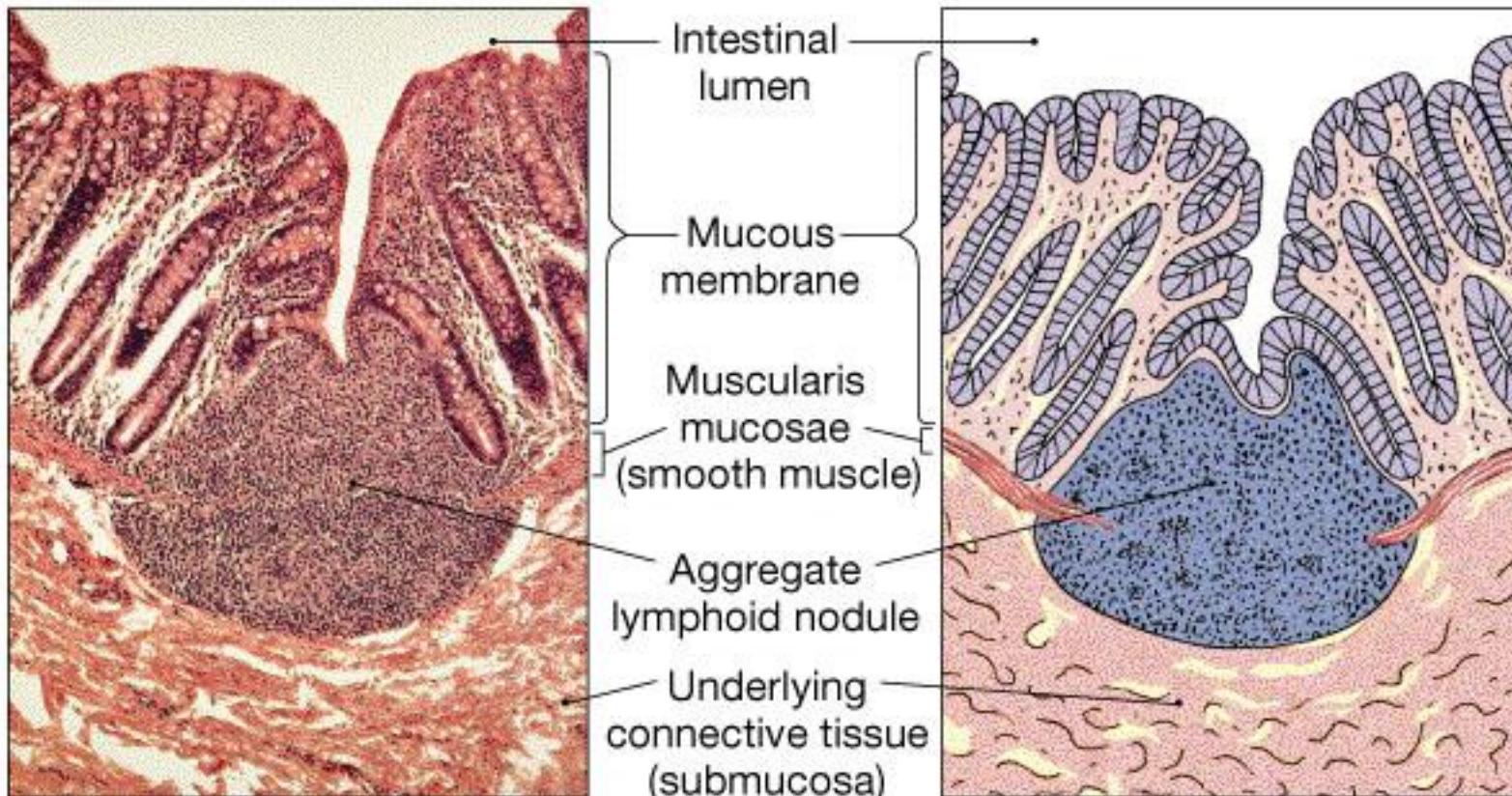
Major Lymphatic Vessels of the Trunk



Lymph Tissue

- 3 types
 - Diffuse lymphatic tissue
 - No capsule present
 - Found in connective tissue of almost all organs
 - Lymphatic nodules
 - No capsule present
 - Oval-shaped masses
 - Found singly or in clusters
 - Lymphatic organs
 - Capsule present
 - Lymph nodes, spleen, thymus gland

Lymph Nodules

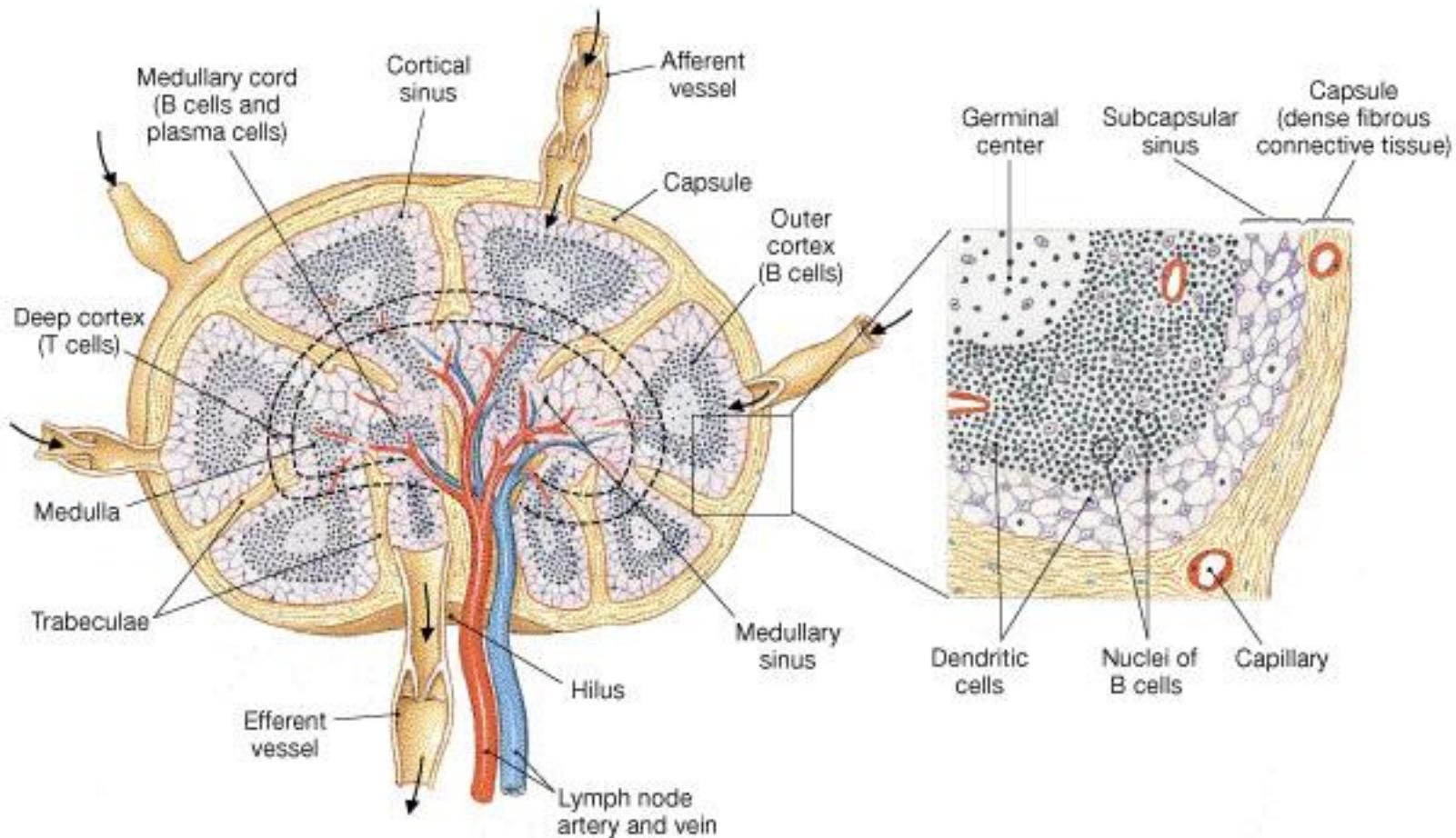


(a) Lymphoid nodule

Lymph Nodes

- Oval structures located along lymphatics
- Enclosed by a fibrous capsule
- Cortex = outer portion
 - Germinal centers produce lymphocytes
- Medulla = inner portion
 - Medullary cords
- Lymph enters nodes through afferent lymphatics, flows through sinuses, exits through efferent lymphatic

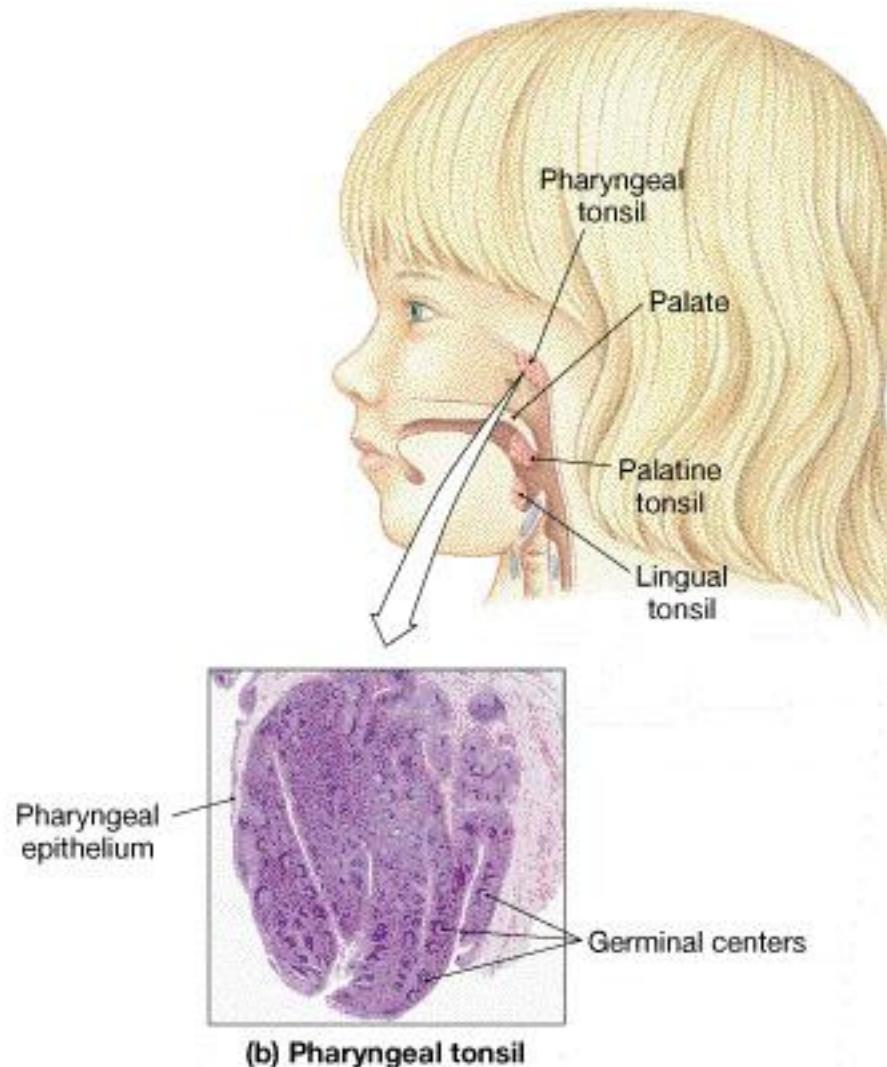
Lymph Node



Tonsils

- Multiple groups of large lymphatic nodules
- Location – mucous membrane of the oral and pharyngeal cavities
- Palatine tonsils
 - Posterior-lateral walls of the oropharynx
- Pharyngeal tonsil
 - Posterior wall of nasopharynx
- Lingual tonsils
 - Base of tongue

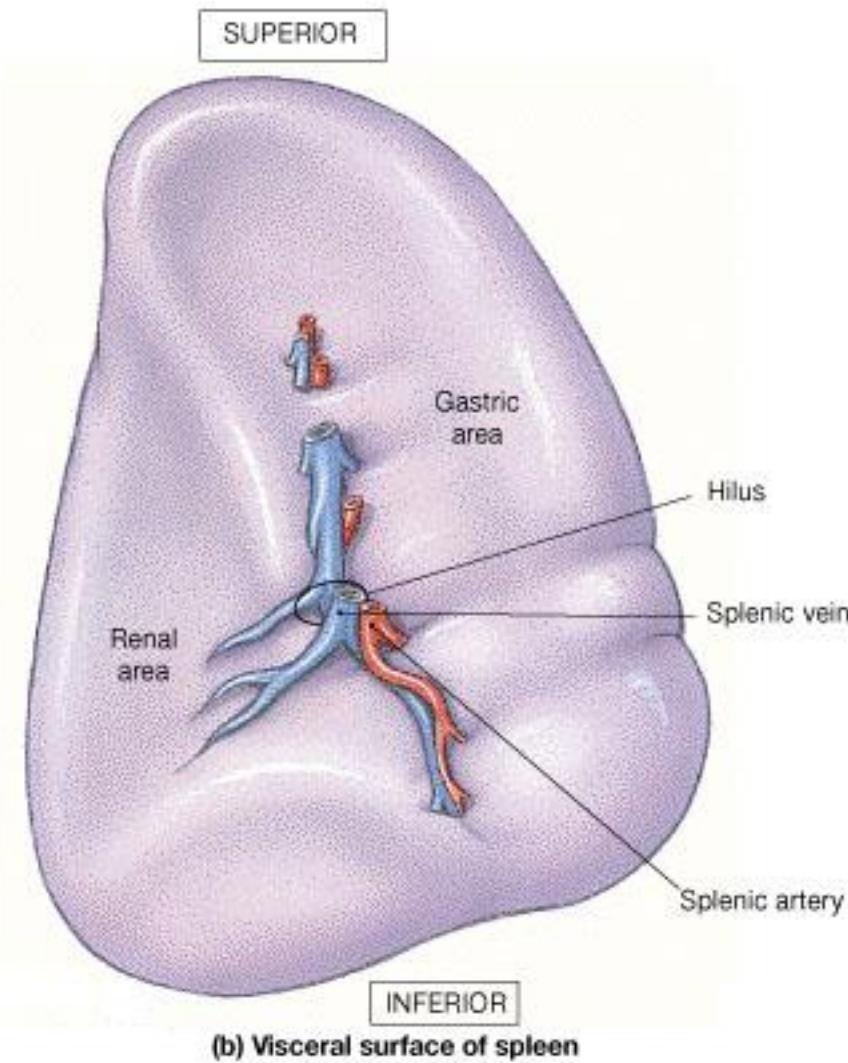
Tonsils



Spleen

- Largest lymphatic organ
- Located between the stomach & diaphragm
- Structure is similar to a node
 - Capsule present
 - But no afferent vessels or sinuses
- Histology
 - Red pulp contains all the components of circulating blood
 - White pulp is similar to lymphatic nodules
- Functions
 - Filters blood
 - Stores blood

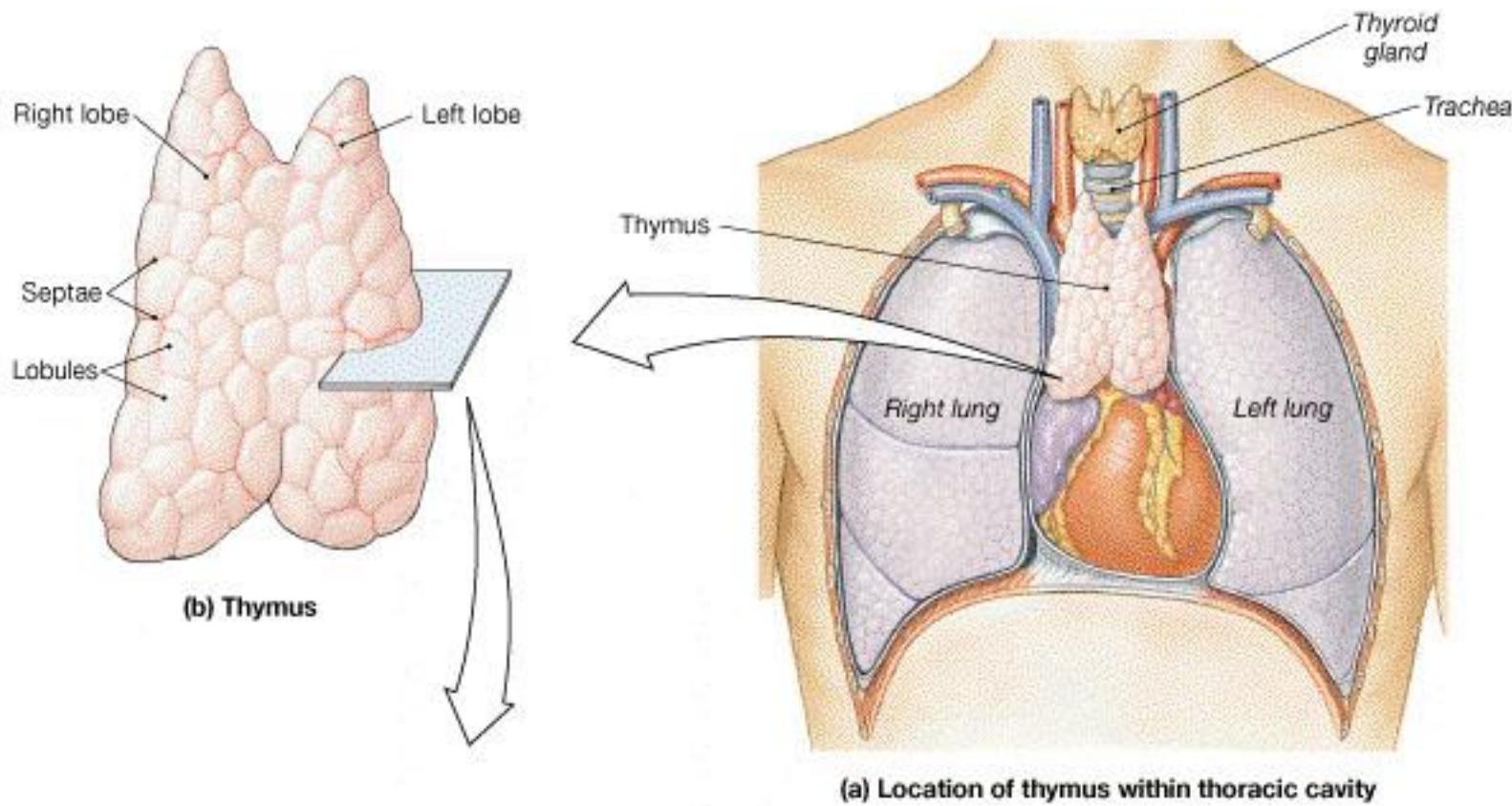
Spleen



Thymus Gland

- Location – behind the sternum in the mediastinum
- The capsule divides it into 2 lobes
- Development
 - Infant – conspicuous
 - Puberty – maximum size
 - Maturity – decreases in size
- Function
 - Differentiation and maturation of T cells

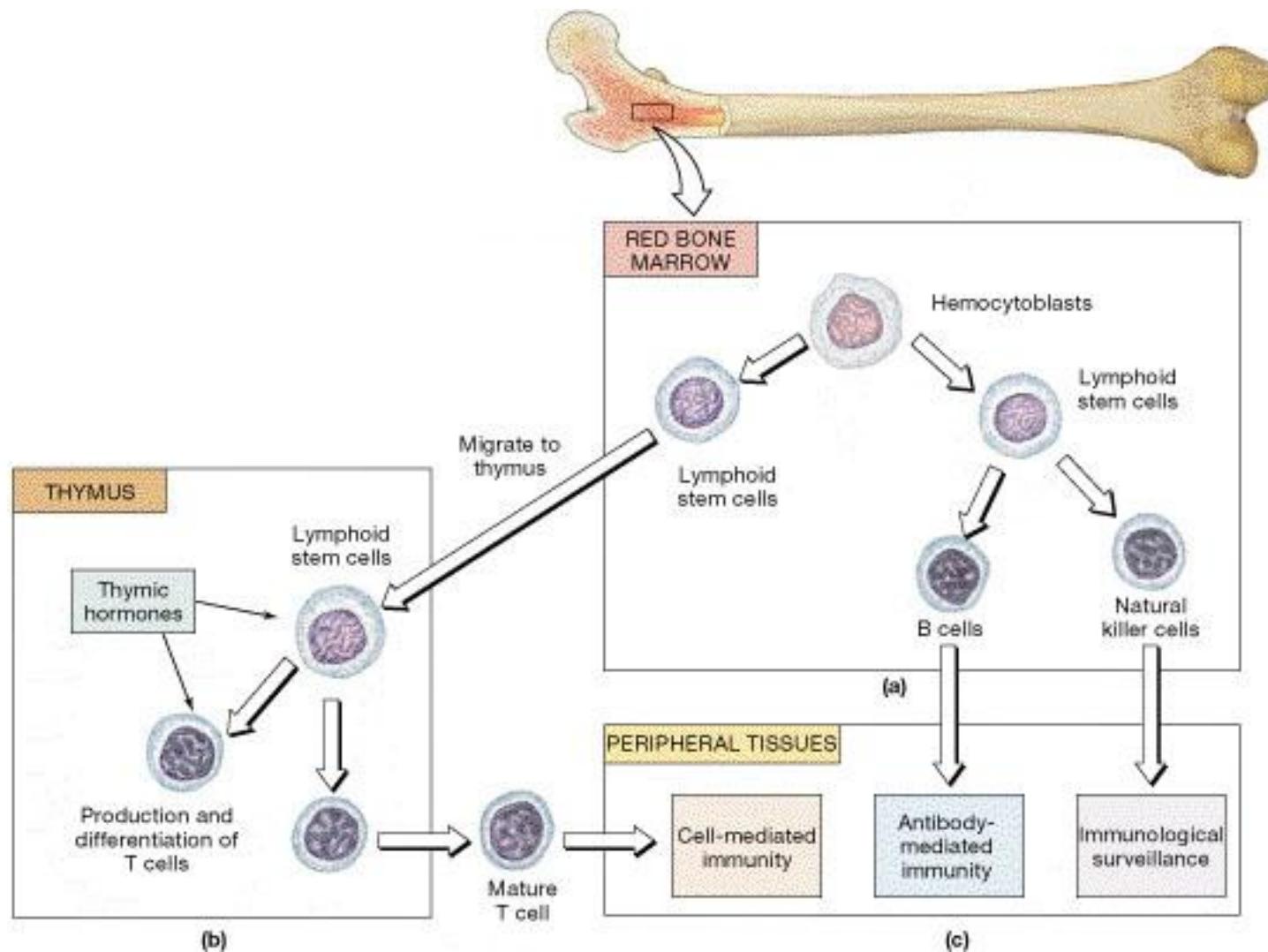
Thymus Gland



Function of the Lymphatic System

- Defense against harmful organisms and chemicals
- 2 types of defense
 - Nonspecific
 - Specific
- Specific defense = immunity
 - Humoral immunity involves B cells that become plasma cells which produce antibodies that bind with specific antigens.
 - Cell-mediated immunity involves T cells that directly destroy foreign cells

Derivation and Distribution of Lymphocytes



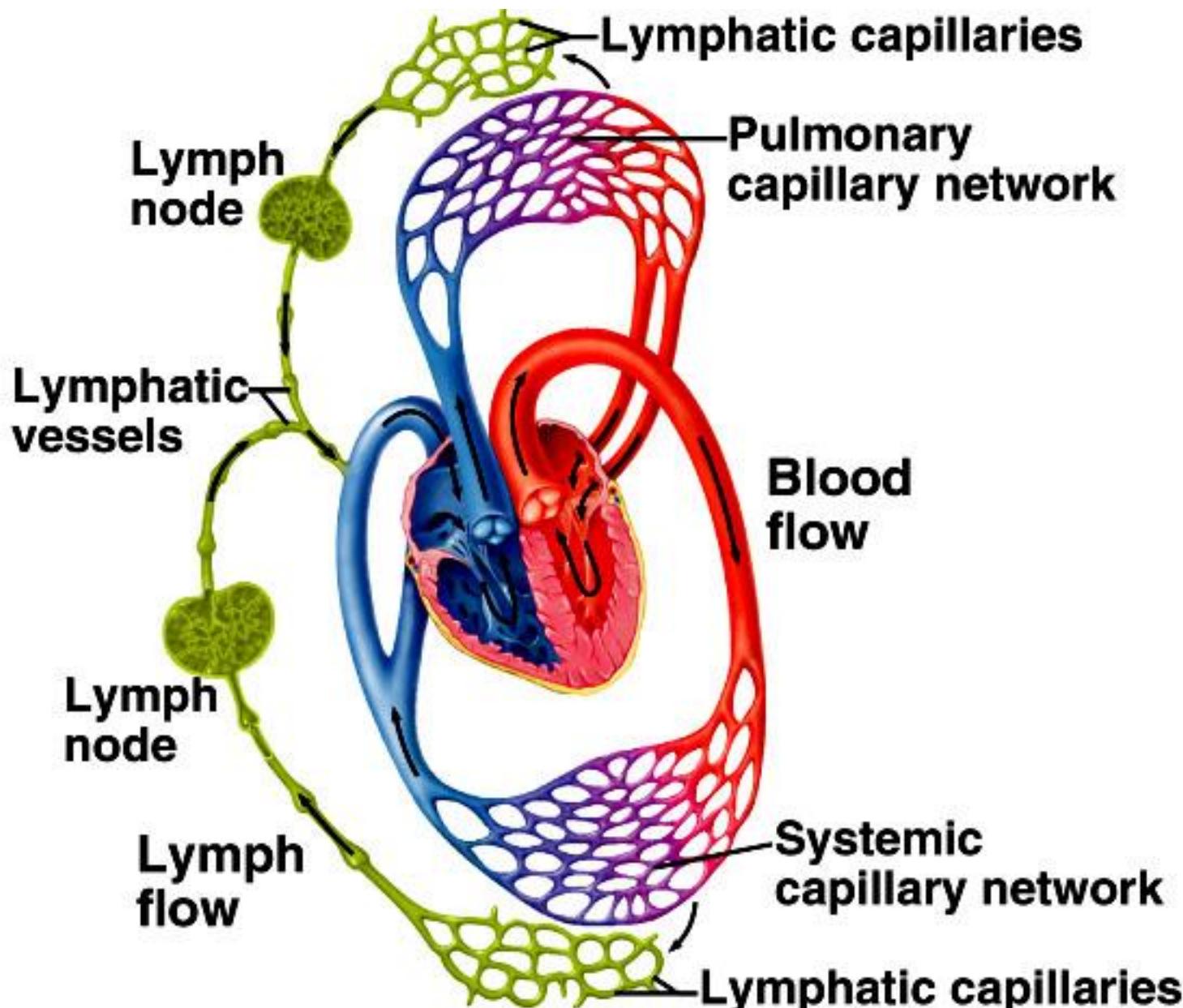
The lymphatic system and immunity

A circulatory system for fluids

returns fluid to the blood

removes antigens from the body

exposes antigens to the immune system



Lymphatic capillary



Lymphatic vessel



Lymph node



Lymphatic vessel



Lymphatic trunk



Collecting duct



Subclavian vein

How is fluid moved?

Contraction of skeletal muscles against lymphatic vessels

Smooth muscle contraction

Valves in lymphatic vessels

Breathing

Obstruction of system leads to edema

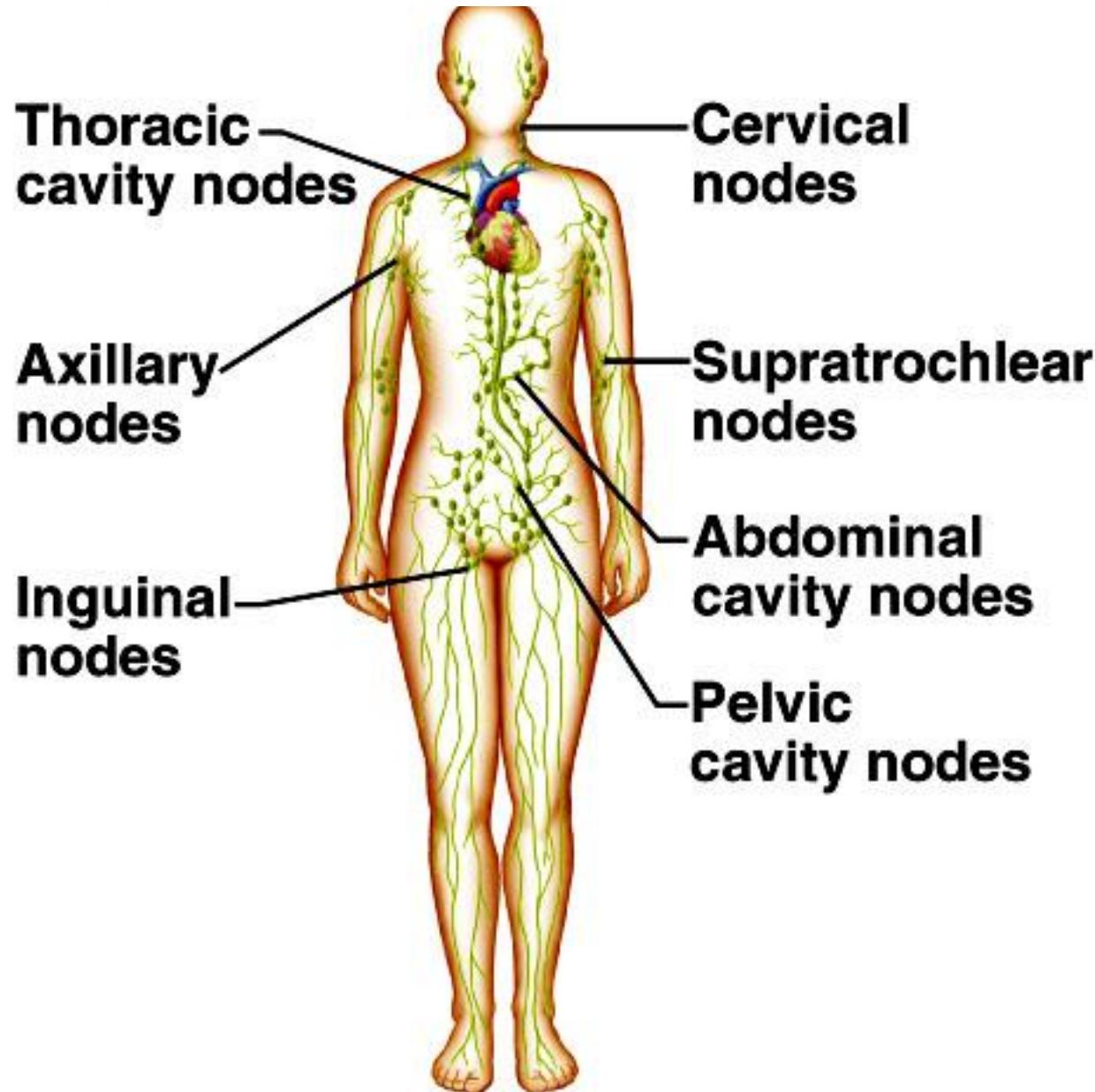
Lymph nodes

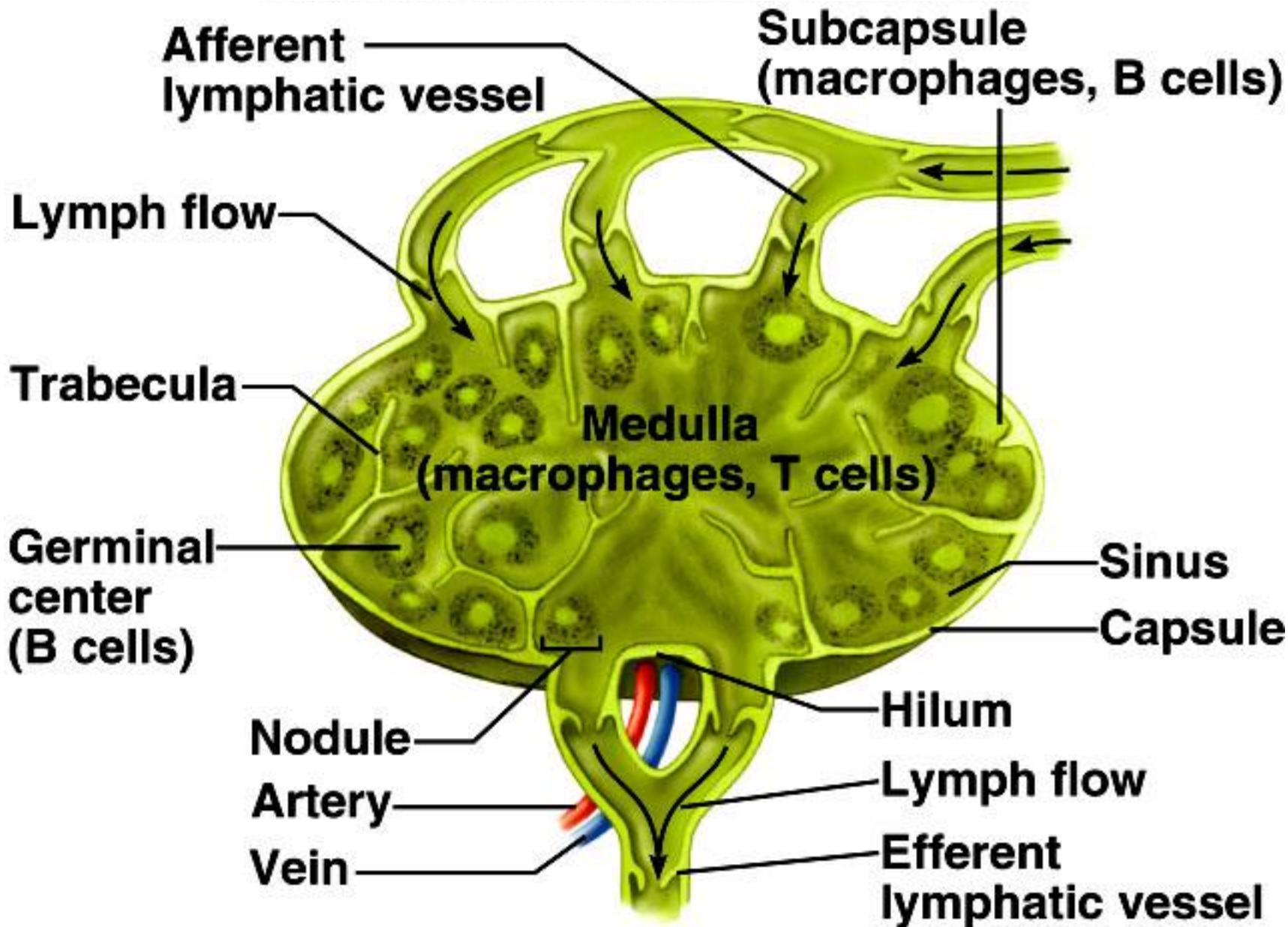
Grouped together at various parts of the body

Filtration

“Immune surveillance”

immune cells are concentrated there
(as is antigen)





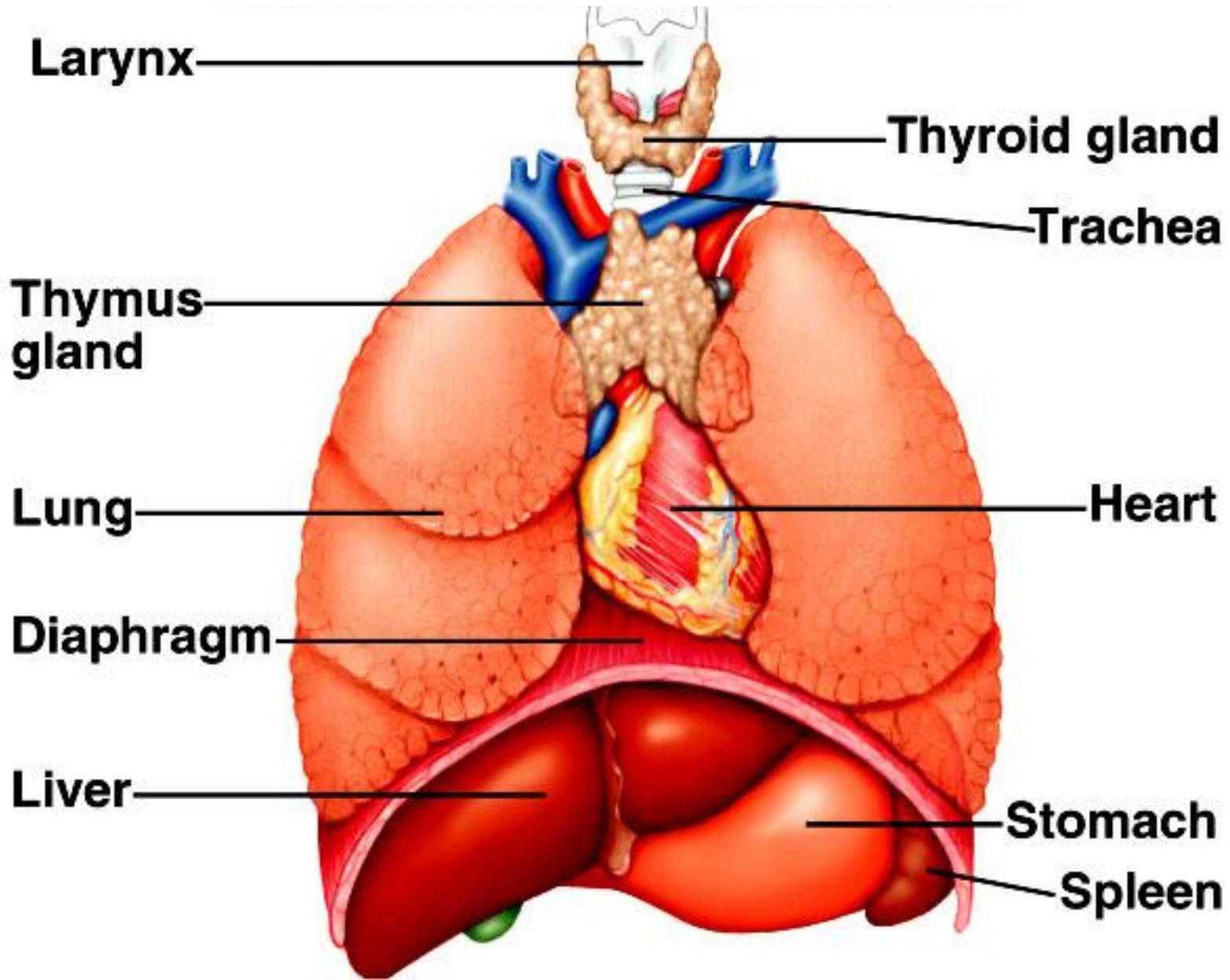
Lymphocytes develop in lymph nodes (after they are formed in the bone marrow)

T cells develop in the thymus and then enter the circulation

Macrophages and dendritic cells “present” antigen in the lymph nodes

What are the major organs/tissues of the lymphatic system?

How do the cells get there?



Thymus

T cell development: cells migrate from bone marrow and differentiate into T cells

T helper cells

Cytotoxic T cells

Thymus gets progressively smaller (and less active) through life

Spleen

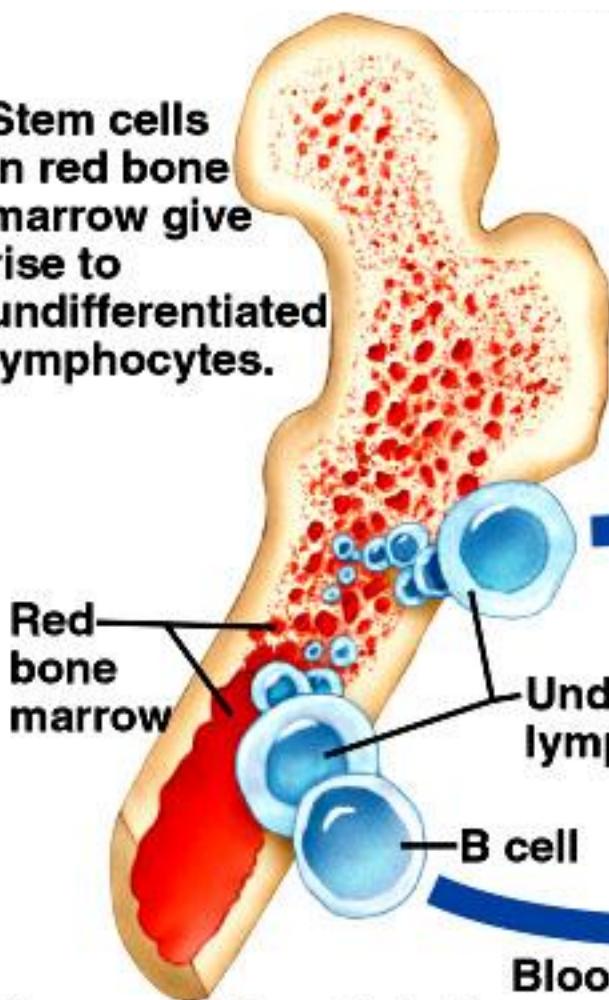
Filters blood, while lymph nodes filter lymph

White pulp- concentration of lymphocytes
(around arteries)

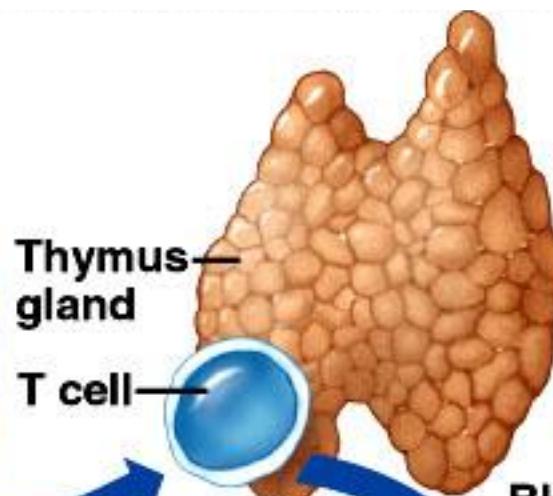
Red pulp- red cells are filtered too

Macrophages are plentiful throughout

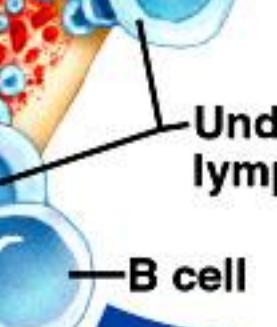
1 Stem cells in red bone marrow give rise to undifferentiated lymphocytes.



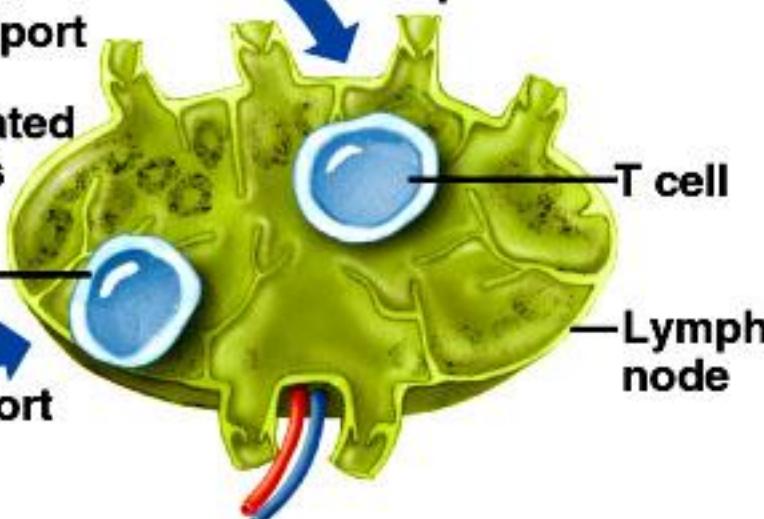
2 Some undifferentiated lymphocytes are processed in the thymus gland to become T cells.



3 Some undifferentiated lymphocytes are processed, probably within the bone marrow, to become B cells.



4 Both T cells and B cells are transported through the blood to lymphatic organs, such as the lymph nodes, lymphatic ducts, and spleen.



B and T lymphocytes confer “specific immunity”

Body also has “non-specific” responses to infection

Barriers- skin, mucosa, chemical barriers

**Inflammation
redness, swelling, heat, pain**

Phagocytes

Fever

Cells of inflammation

Neutrophils- leave blood and enter site of injury- kill and phagocytose microbes

Macrophages- also phagocytes

Mast cells- release inflammatory substances

Complement proteins- contribute to inflammation

Lymphocytes may be activated, too

What about specific immunity?

**Arises when barriers (first line of defense)
and inflammation (second line) do not
control the infection**

Is directed against specific antigens

What is an antigen?

What are the cells of specific immunity?

B lymphocytes (produce antibodies)

T lymphocytes (helper, cytotoxic)

Helper T cells regulate the immune response

Cytotoxic T cells kill altered cells
infected with viruses
tumor cells

What do these cells do, when exposed to antigen?

Proliferate (divide rapidly)

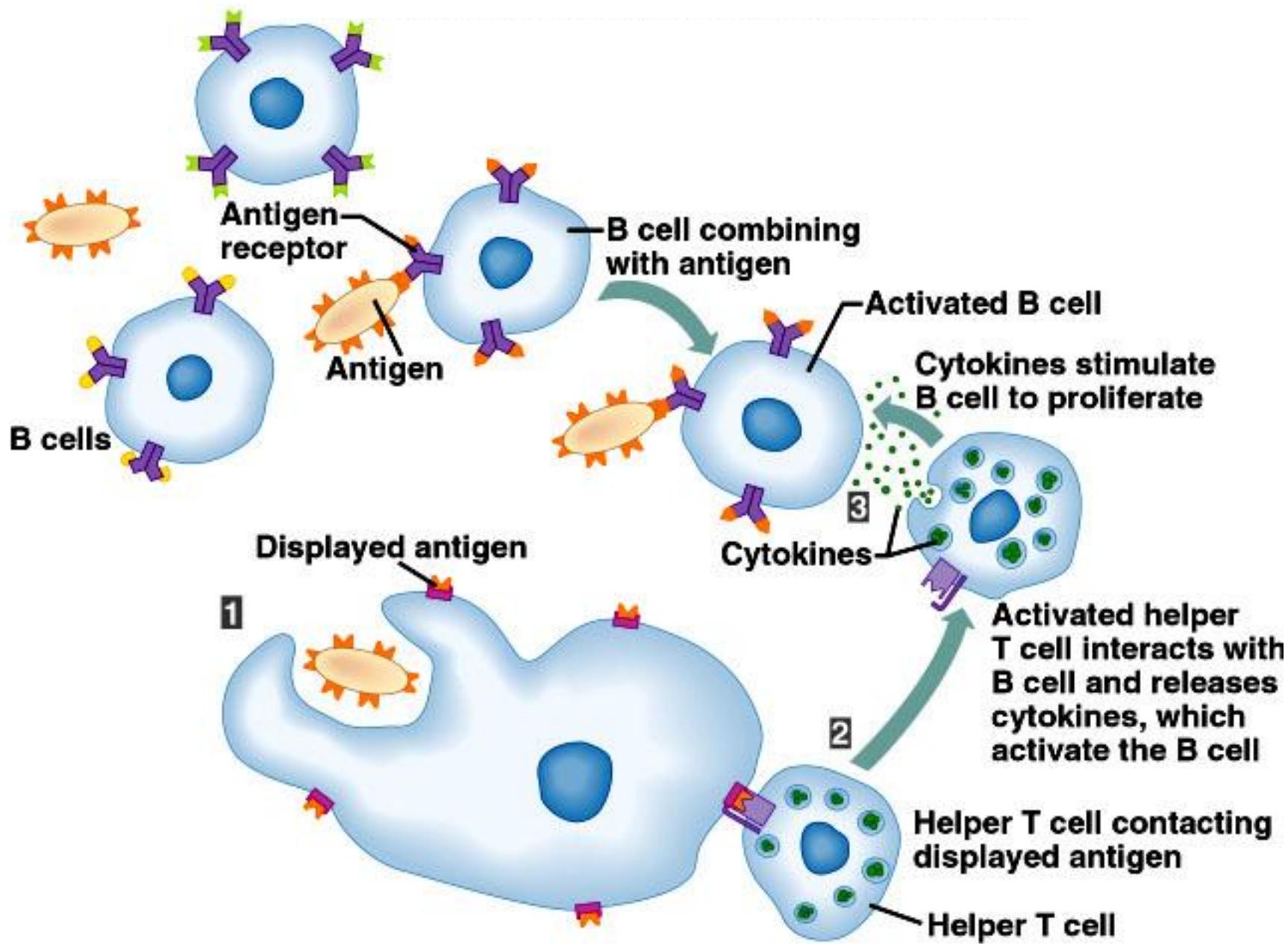
Produce “effector molecules”

B cells- antibodies

helper T cells- cytokines

cytotoxic T cells- cytotoxic granules

Macrophages, dendritic cells- present antigen to T cells



What do antibodies do? (five classes)

Ig (immunoglobulin) G- active in blood against bacteria and viruses

helps activate complement

helps phagocytes eliminate antigens

most common antibody in the blood

IgM- reacts with certain antigens, usually on first exposure

IgA- most common in mucosa

IgD and IgE are rare in blood

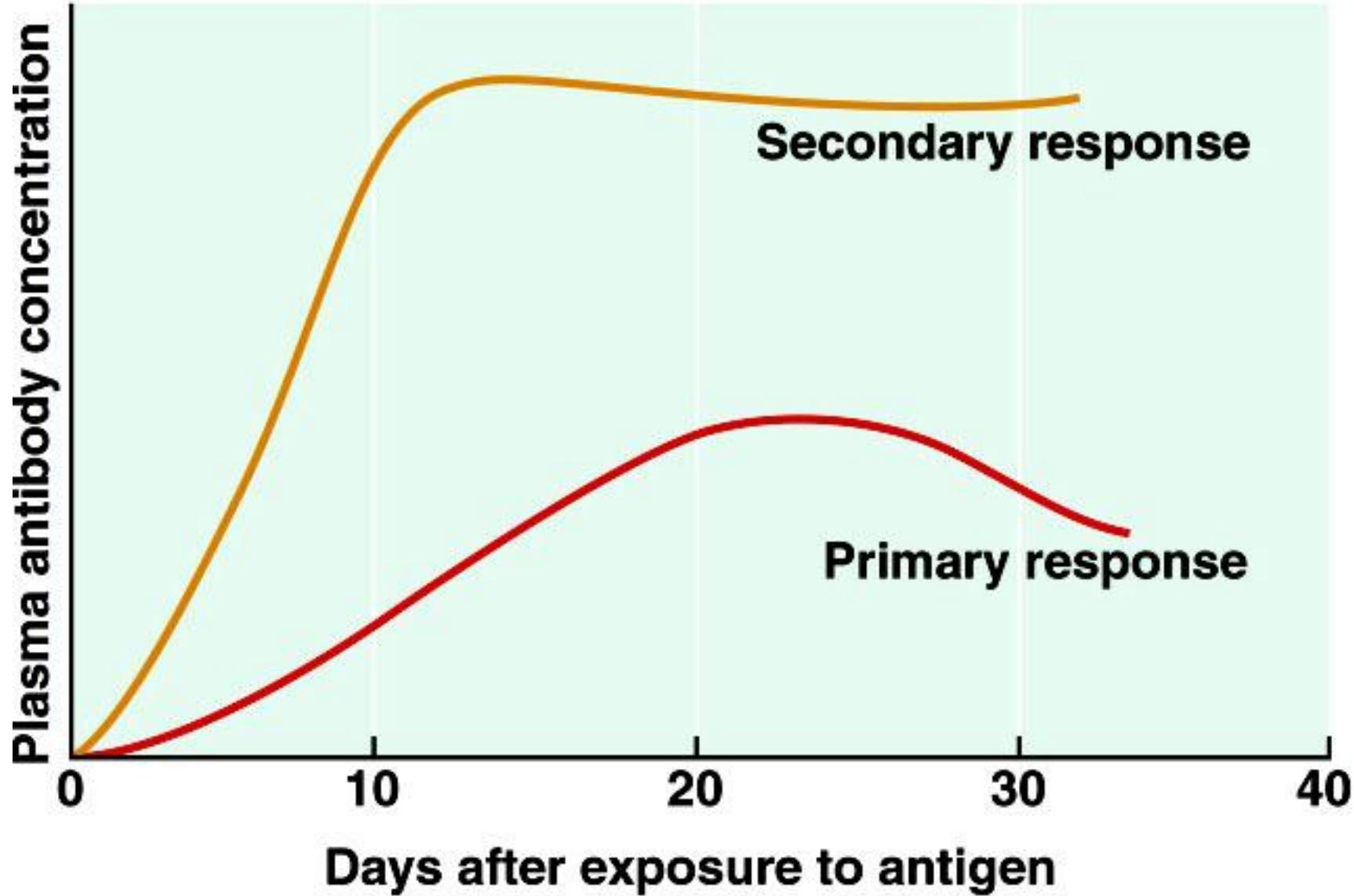
IgE is involved in allergic reactions
sticks to mast cells, which release
inflammatory substances

IgD is usually found on B cells (not released)
may be involved in B cell activation

When the body is exposed to an antigen for the first time, antibody production is slow and at low levels. Usually IgM

If exposed to the same antigen again, the antibody response is much more rapid and intense (IgG)

(Most antibody in the blood stream is IgG)



Vaccination

- Exposure to antigen will produce an immune response
- Repeated exposure will produce memory
- Vaccine-produce the memory response without getting the disease
- Why are vaccine produced to protect against some diseases but not others?

**Immune system protects against infection,
but also against other antigens**

Blood group antigens

Tissue antigens (i.e., graft rejection)

**For successful organ graft, immune system
must be suppressed**

**Transplanted tissue must be cleared of immune
cells, too**

**What if there is an immune response against
the “wrong” antigens?**

**Allergies- antigen that is otherwise harmless
(hypersensitivity)**

Immediate type is mediated by IgE

Delayed-type is caused by T cells

Autoimmunity

**Normally immune system does NOT react to
“self” antigens**

**Autoimmunity occurs when it does
disease can be localized (to kidneys,
joints, thyroid, etc.) or can be systemic
(lupus)**

**Treatment usually requires some form of
immunosuppression**

Immune deficiency

Primary- lack of development of all or part of the immune system

SCID- severe combined immune deficiency

DiGeorge syndrome- lack of a thymus, etc.

Secondary- due to disease

AIDS

can also be temporary

Summary

The lymphatic system helps maintain homeostasis of fluids, and also helps remove antigen from the body

The immune system consists of barriers (physical and chemical) and specific and nonspecific mechanisms to eliminate antigen

“Immune cells” are blood cells. Some circulate in the blood and can then migrate into tissues at site of injury. These include neutrophils and macrophages.

All blood cells arise in the bone marrow.

B lymphocytes initially develop in the bone marrow and then migrate to lymphoid tissues (esp. lymph nodes and spleen)

T lymphocytes develop in the thymus.

B cells produce antibodies, which interact with antigen to help eliminate it.

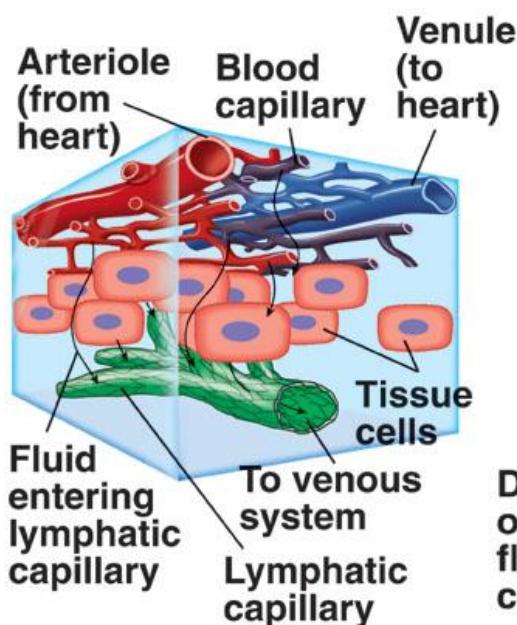
Helper T cells regulate the immune response; cytotoxic T cells kill virus-infected cells and probably tumor cells. (They also are responsible for transplant rejection.)

B and T cell response is antigen-specific and has “memory” (second response is faster and stronger than the first)

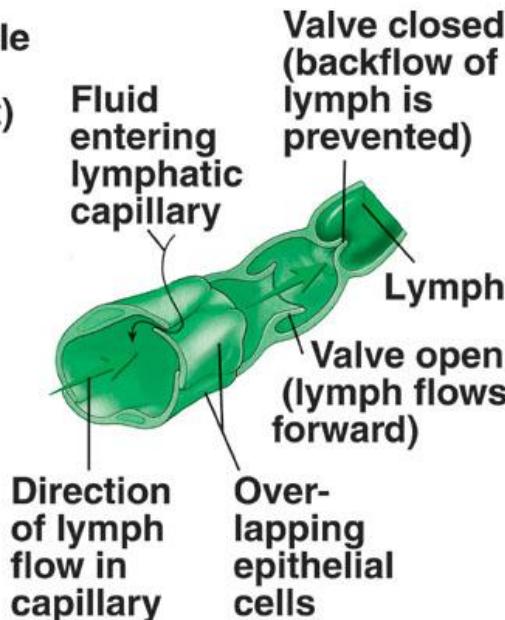
Immune system can be overly responsive to antigens (hypersensitivity/allergy) or can mistakenly be directed against self antigen (autoimmunity)

Immune deficiencies leave people vulnerable to infection

Lymphatic Vessels



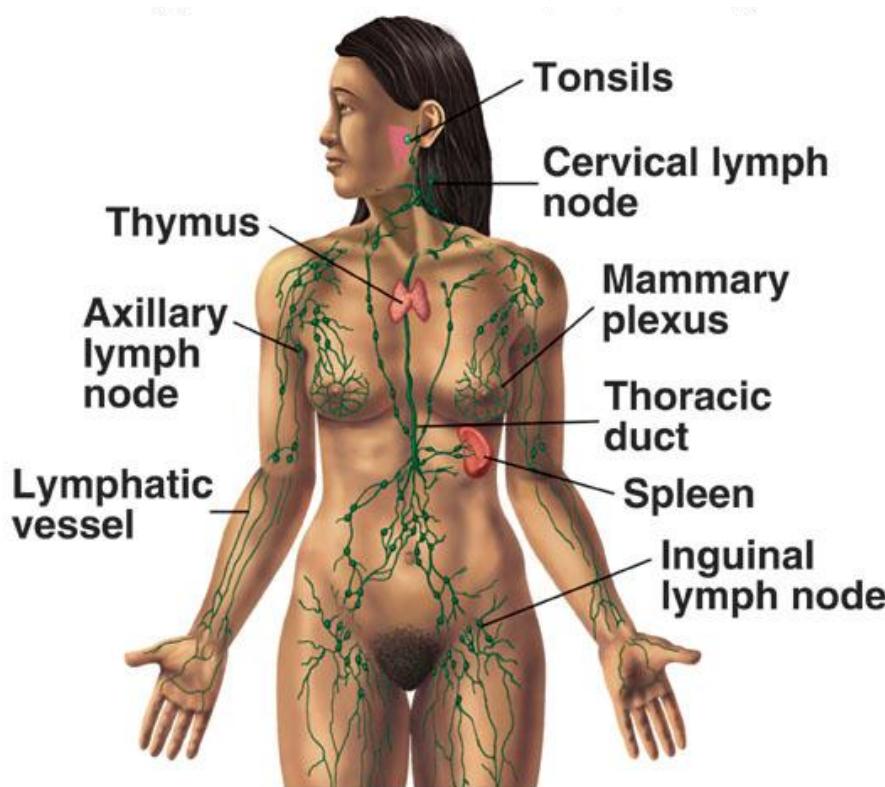
(a)



(b)

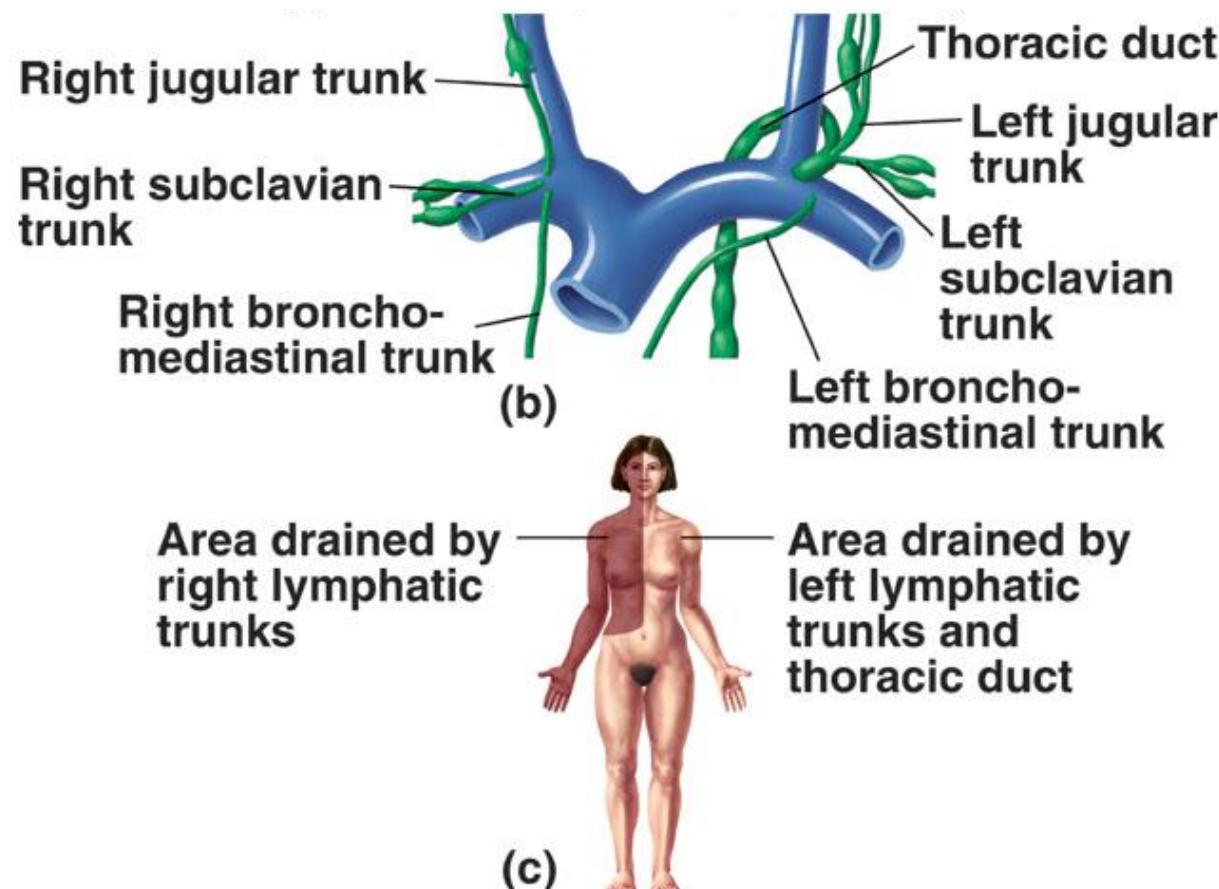
- Carry lymph away from tissues
- Lymphatic capillaries
 - More permeable than blood capillaries
 - Epithelium functions as series of one-way valves

Lymphatic System



- Lymph
- Lymphatic vessels
- Lymphatic tissue
- Lymphatic nodules
- Lymph nodes
- Tonsils
- Spleen
- Thymus

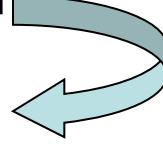
Lymphatic System and Immunity:



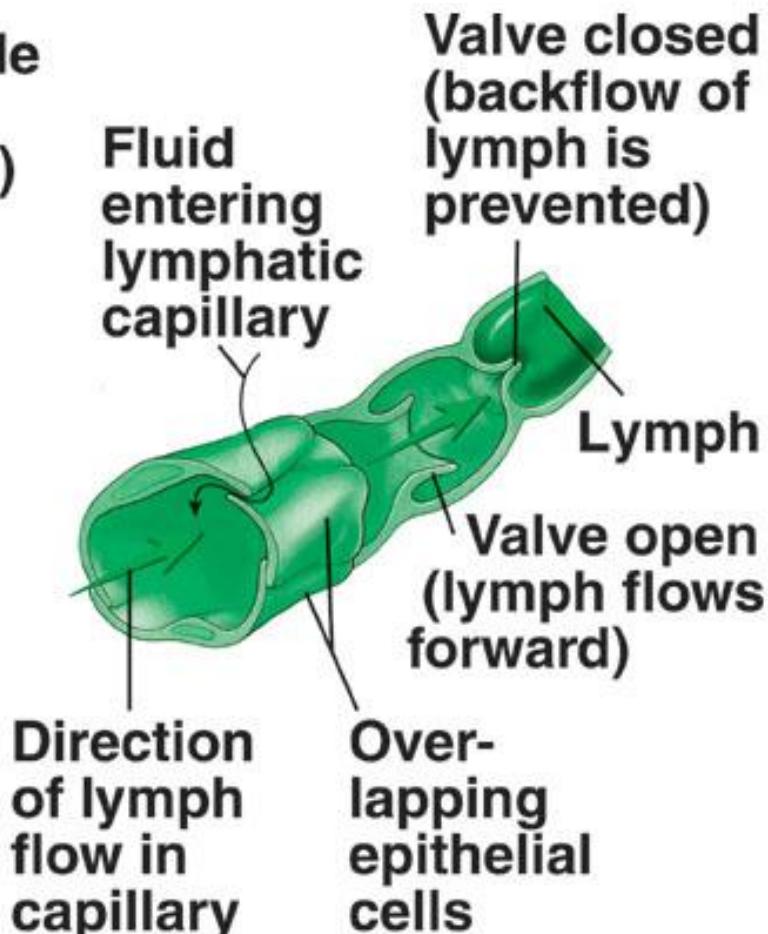
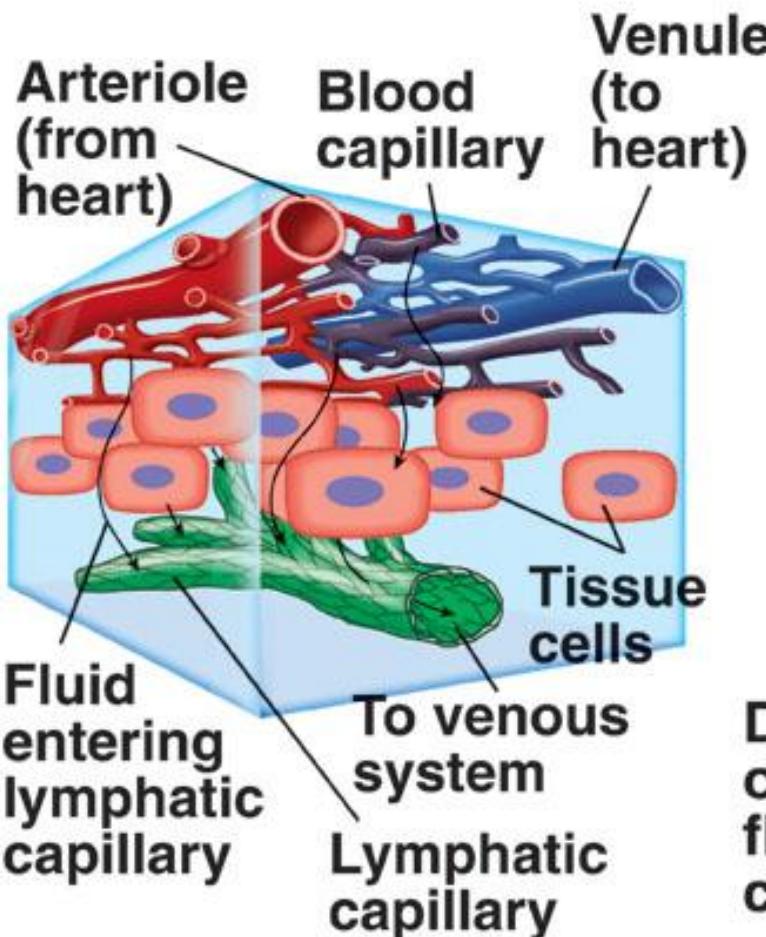
Functions of the Lymphatic System

- Fluid balance
 - Excess interstitial fluid enters lymphatic capillaries and becomes lymph
- Fat absorption
 - Absorption of fat and other substances from digestive tract
- Defense
 - Microorganisms and other foreign substances are filtered from lymph by lymph nodes and from blood by spleen

Lymphatic Vessels

- Lymphatic capillaries join to form
- Lymphatic vessels
 - Have valves that ensure one-way flow
- Lymph nodes: Distributed along vessels and filter lymph
- Lymphatic trunks: Jugular, subclavian, bronchomediastinal, intestinal, lumbar
- Lymphatic ducts: Right and thoracic which connect to large veins

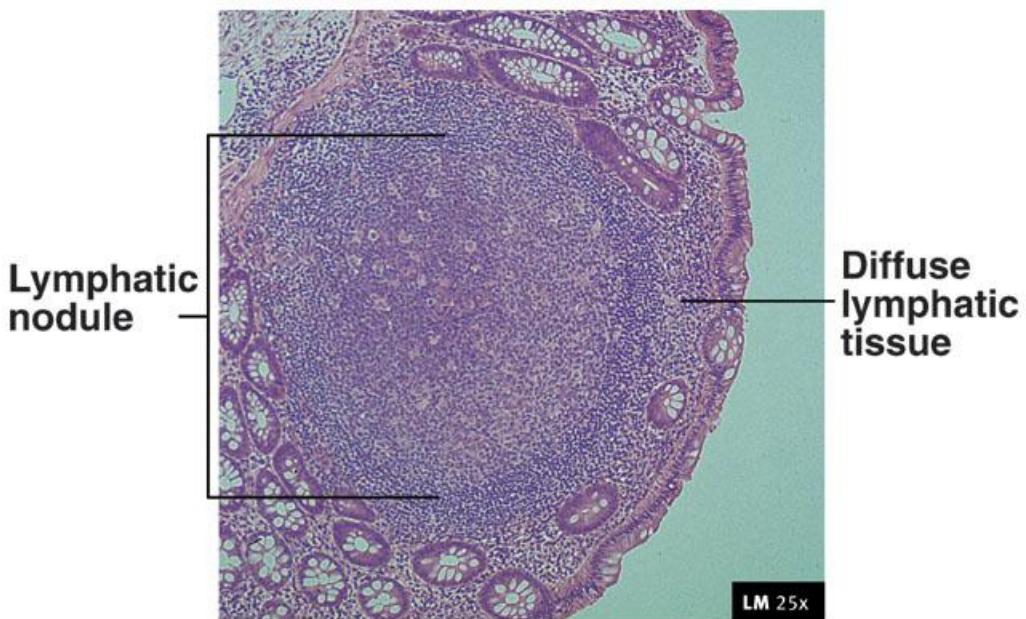
Lymph Drainage Into Veins



(a)

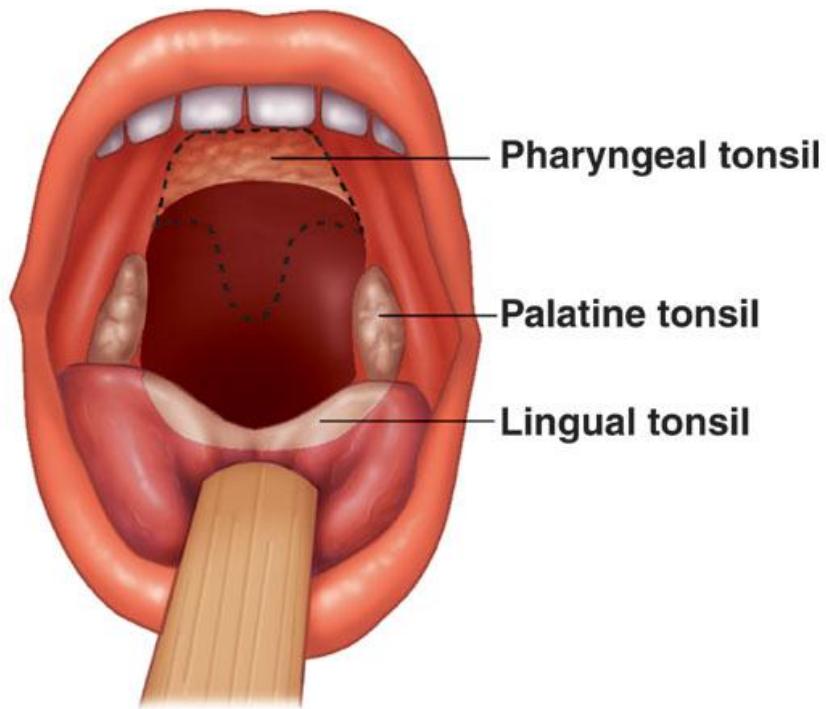
(b)

Lymphatic Tissue and Nodules



- Lymphatic tissue
 - Consists mainly of lymphocytes
 - Encapsulated or not
- Lymphatic nodules
 - Numerous in loose connective tissue of digestive (Peyer's patches), respiratory, urinary, reproductive systems

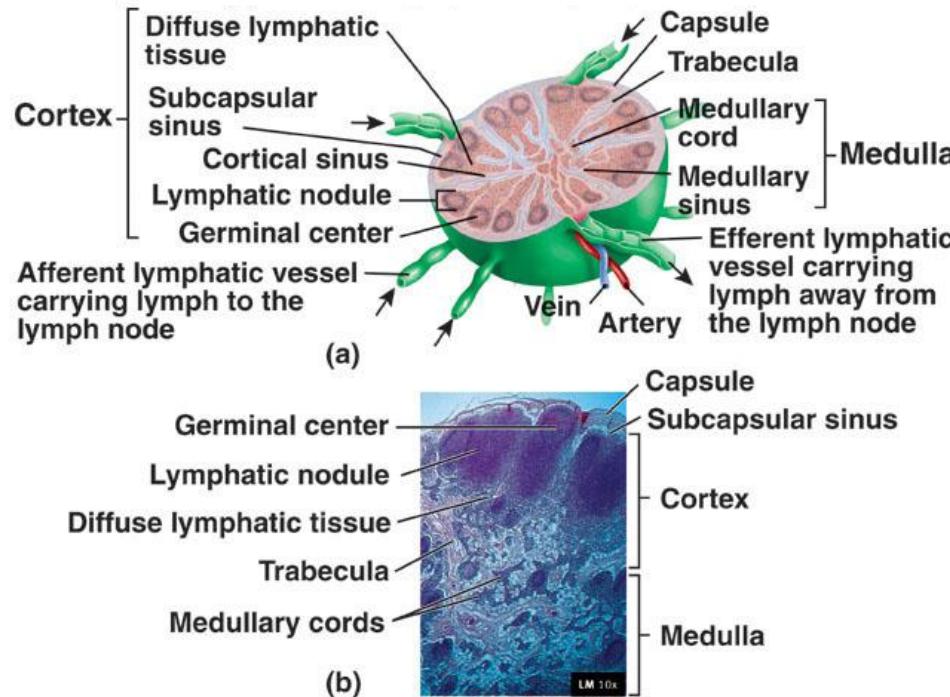
Tonsils



Large groups of lymphatic nodules in nasopharynx and oral cavity

- Provide protection against bacteria and other harmful material
- Groups
 - Palatine
 - Pharyngeal
 - Lingual

Lymph Nodes

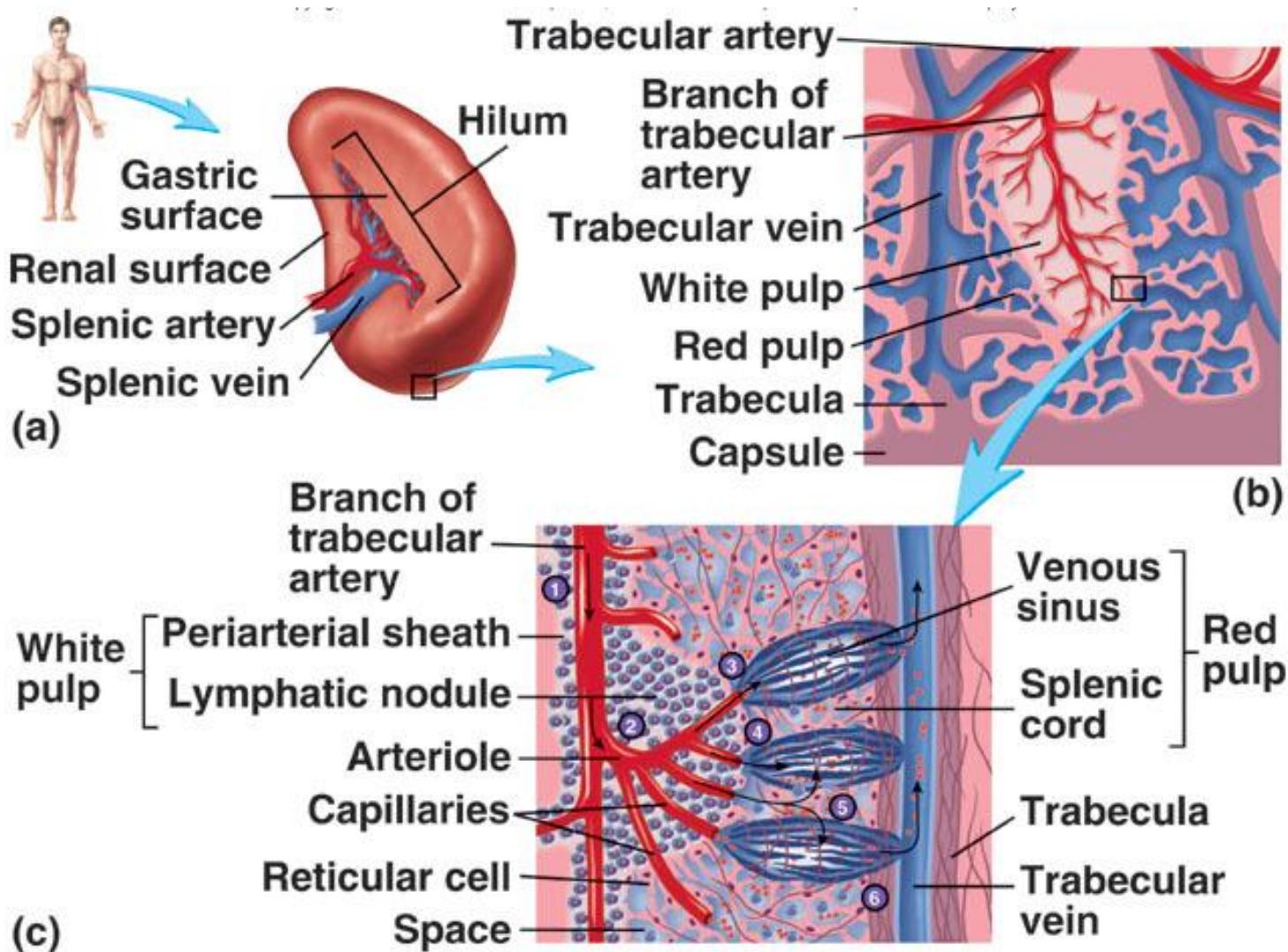


- Organized in cortex and medulla
- Substances removed by phagocytosis or stimulate lymphocytes or both
- Only structures to filter lymph
 - Afferent and efferent vessels

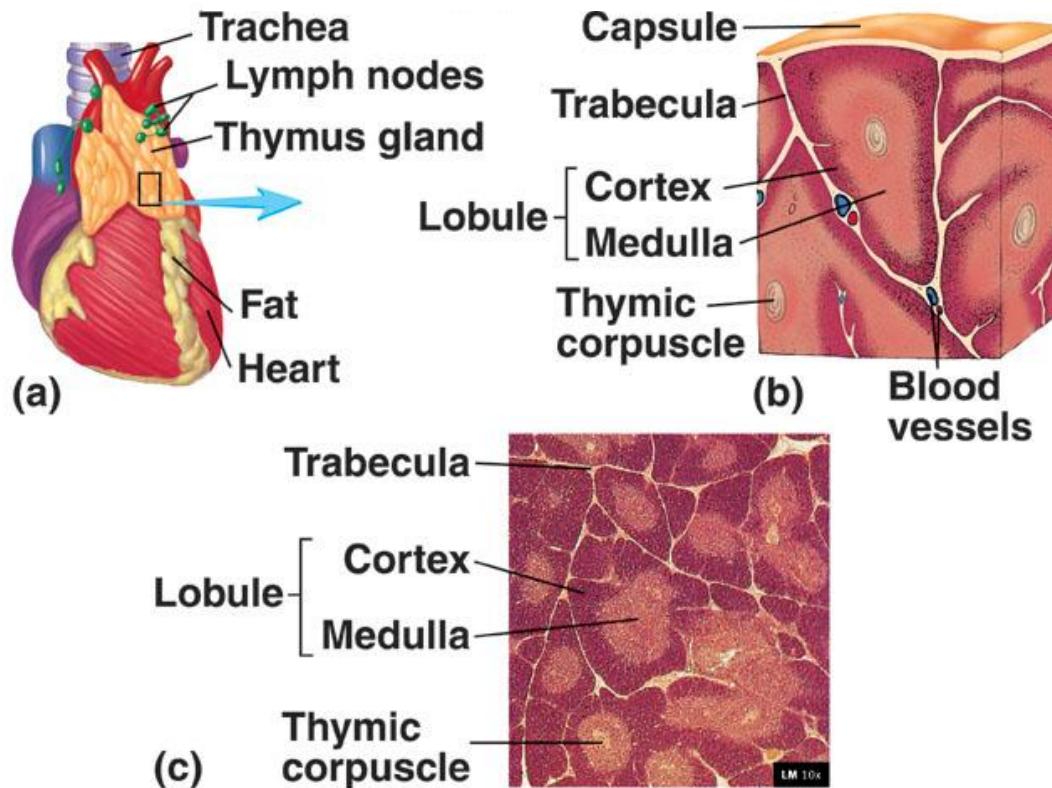
Spleen

- Located in left superior side of abdomen
 - Can be ruptured in traumatic abdominal injuries resulting in bleeding, shock, death
- Blood flows through at 3 different rates
 - Fast (most), slow, intermediate
- Functions
 - Destroys defective RBCs
 - Detects and responds to foreign substances
 - Limited reservoir for blood

Spleen



Thymus



- Located in superior mediastinum
- Divisions: Cortex and medulla
- Site of maturation of T cells

Immunity

- Ability to resist damage from foreign substances as microorganisms and harmful chemicals
- Categories
 - Innate or nonspecific resistance
 - Mechanical mechanisms: Prevent entry or remove microbes
 - Chemical mediators: Promote phagocytosis and inflammation
 - Cells: Involved in phagocytosis and production of chemicals
 - Adaptive or specific immunity
 - Specificity: Ability to recognize a particular substance
 - Memory: Ability to remember previous encounters with a particular substance and respond rapidly

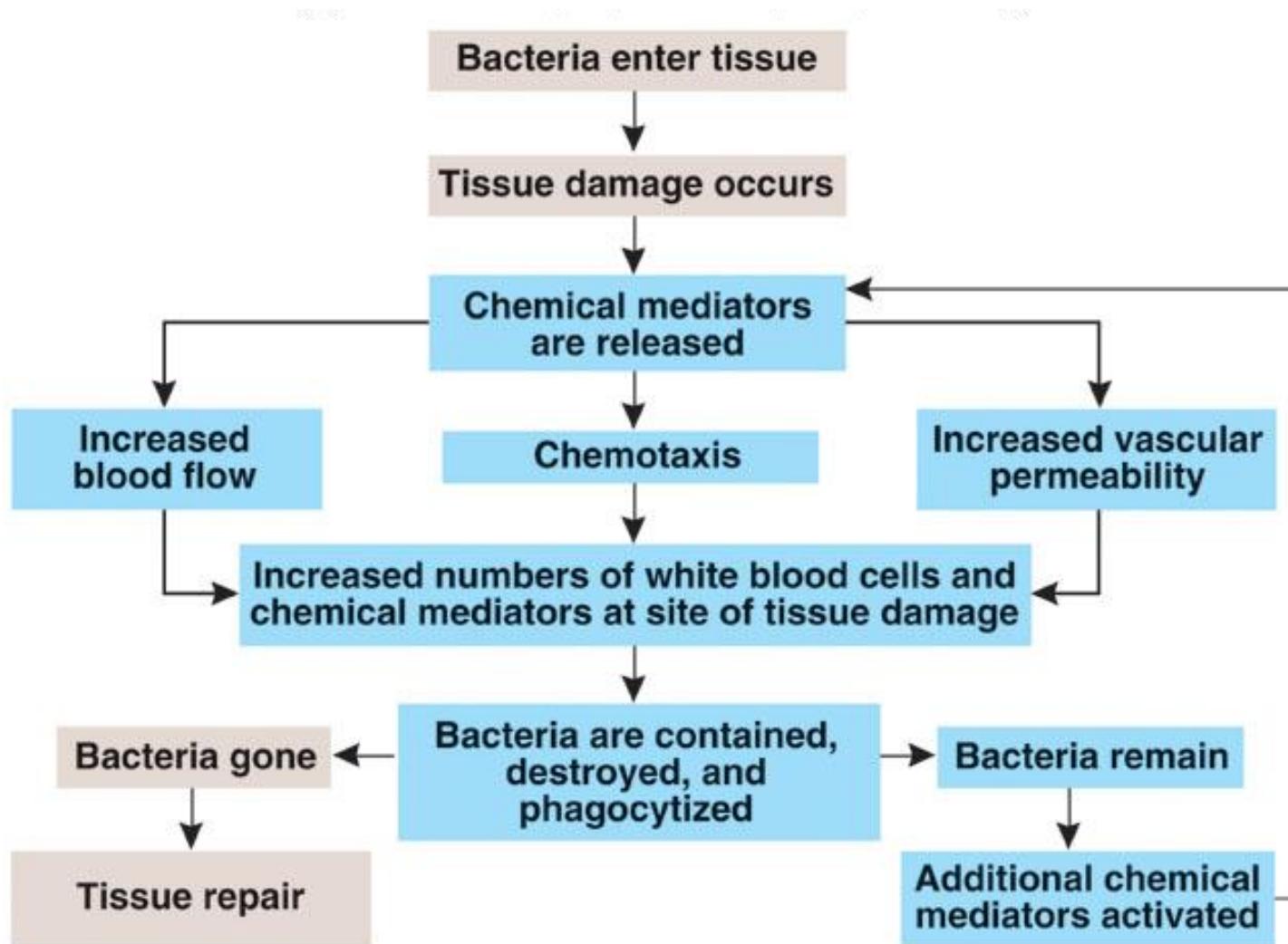
Innate Immunity: Cells

- White blood cells
 - Most important cellular components of immune system
 - Methods
 - Chemotaxis
 - Phagocytosis
- Neutrophils
 - Phagocytic and first cells to enter infected tissue
- Macrophages
 - Monocytes that leave blood, enter tissues
 - Large phagocytic cells
- Basophils and mast cells
 - Promote inflammation
- Eosinophils
 - Reduce inflammation
- Natural killer cells
 - Lyse tumor and virus-infected cells

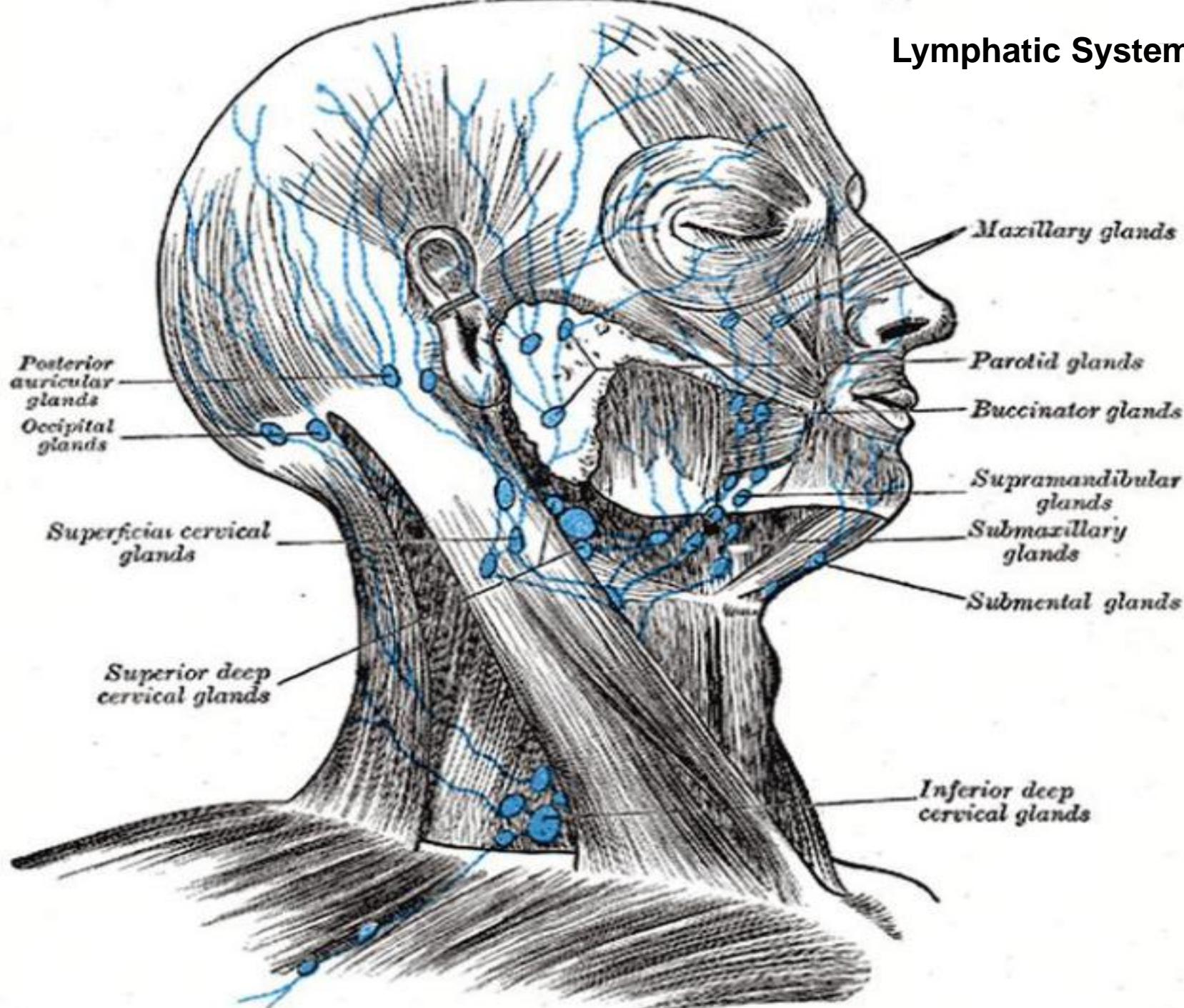
Inflammatory Response

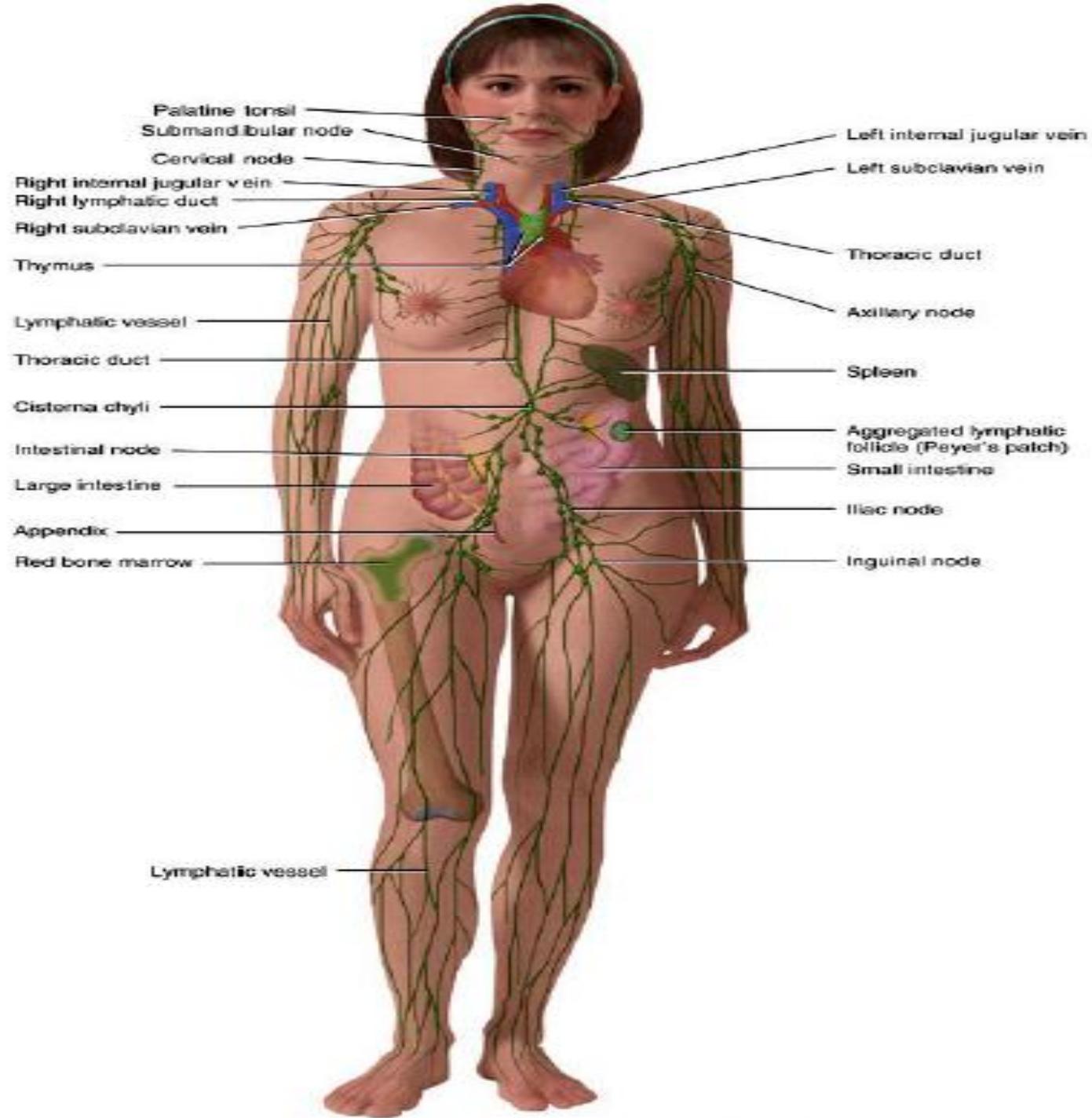
- Tissue injury regardless of type can cause inflammation
- Response initiated by chemical mediators that produce vasodilation, chemotactic attraction, increased vascular permeability
- Types
 - Local: Symptoms are redness, heat, swelling, pain, loss of function
 - Systemic: Symptoms are increase in neutrophil numbers, fever and shock

Inflammatory Response



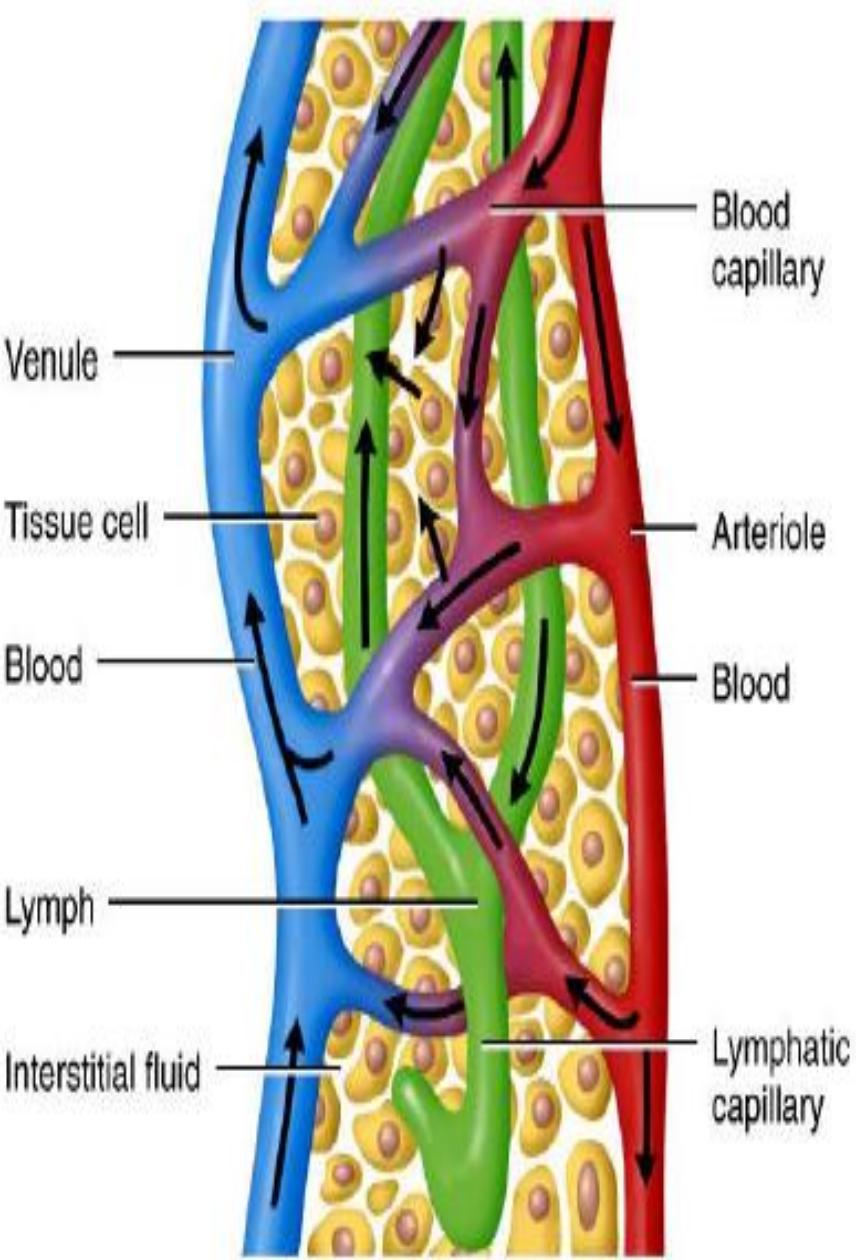
Lymphatic System



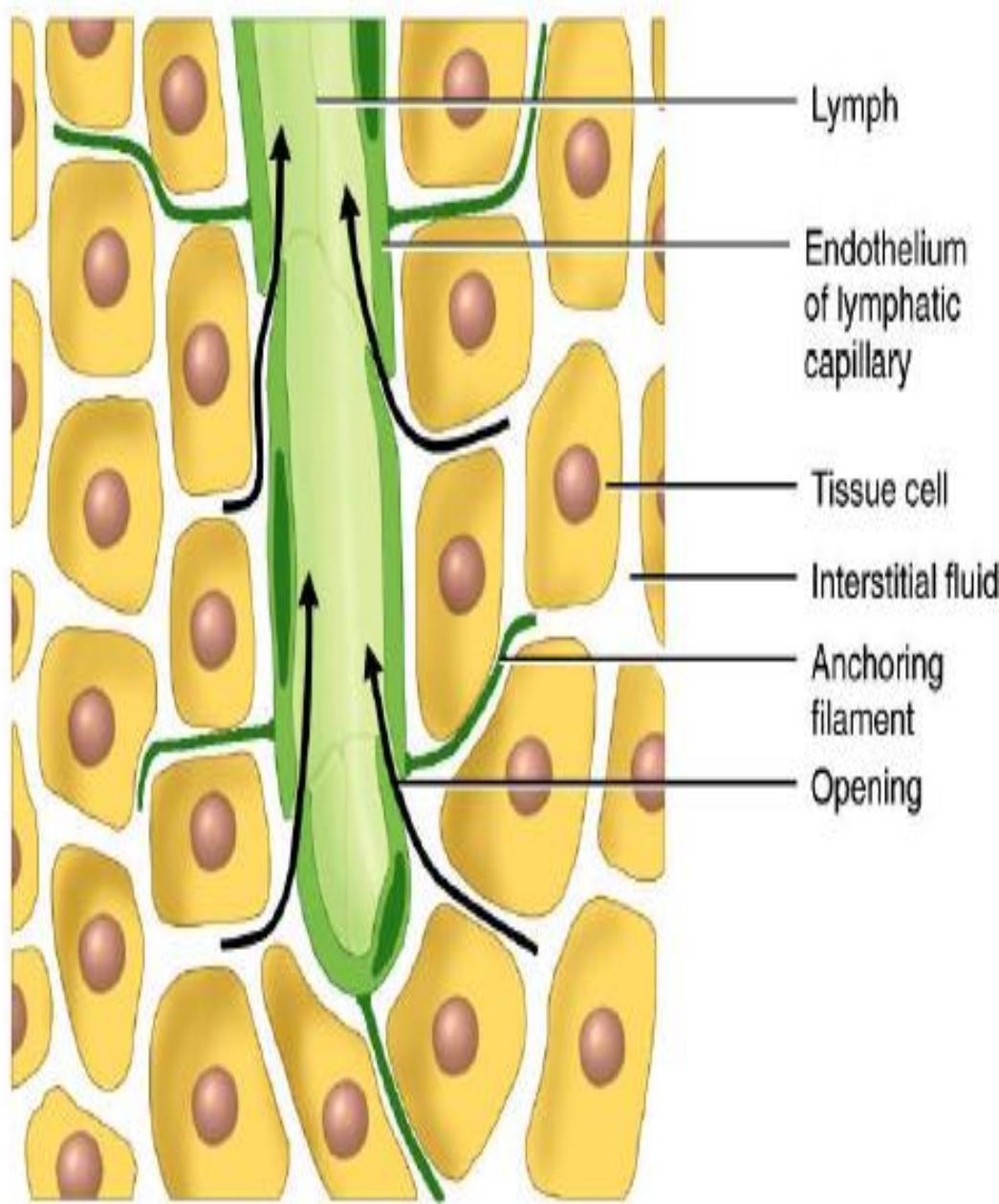


(b) Areas drained by right lymphatic and thoracic ducts

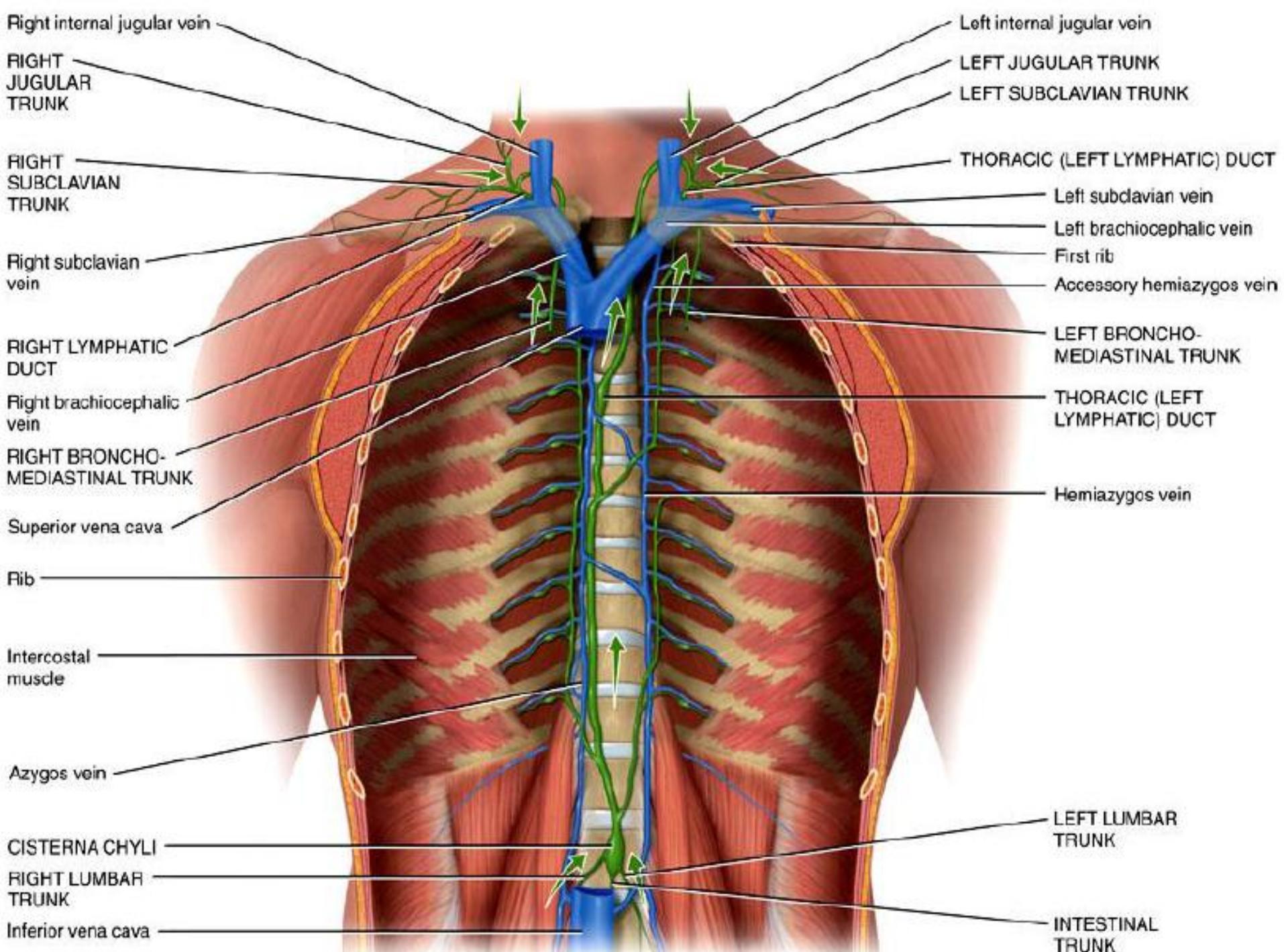
Area drained by right lymphatic duct
Area drained by thoracic duct

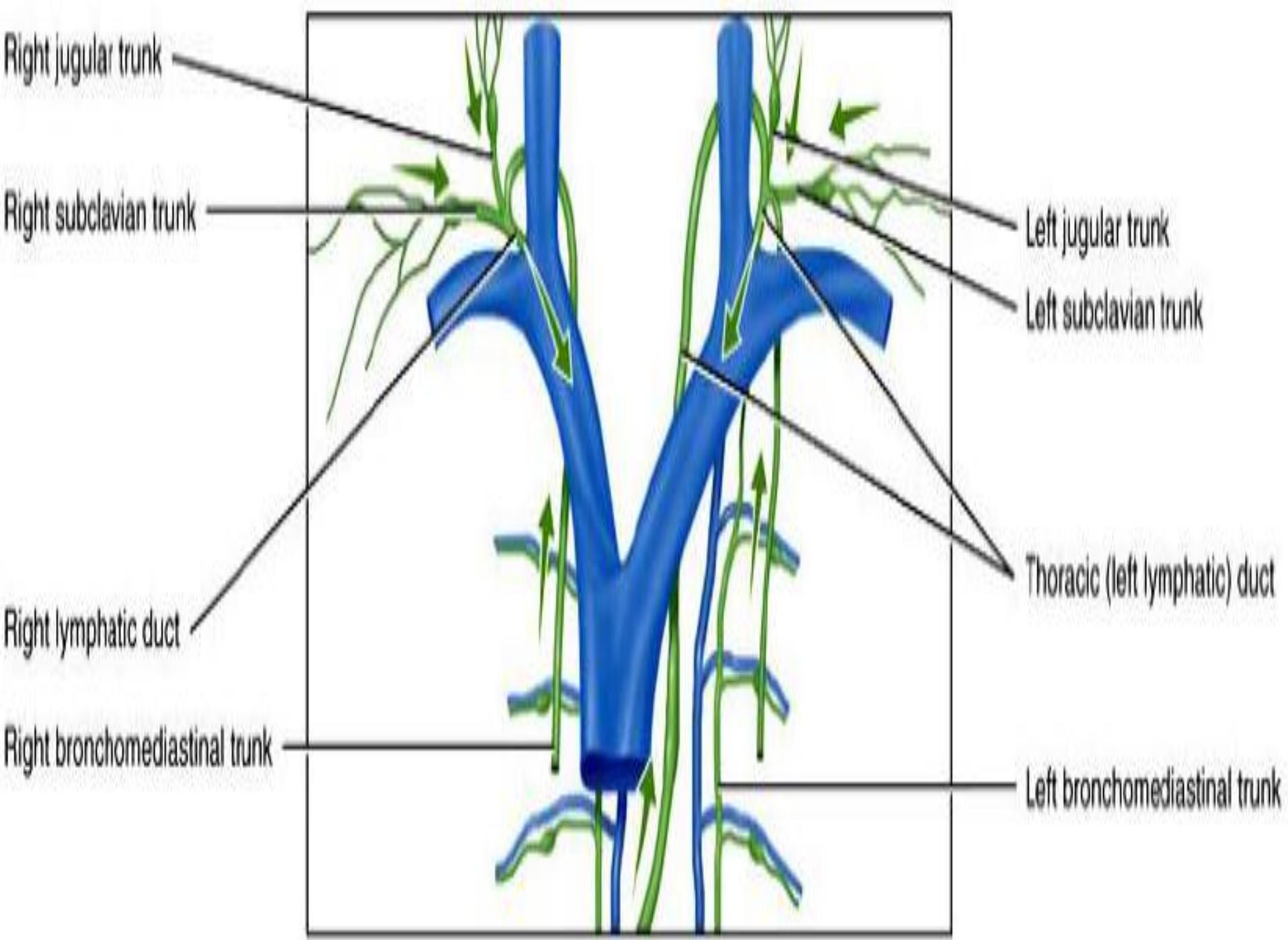


(a) Relationship of lymphatic capillaries
to tissue cells and blood capillaries



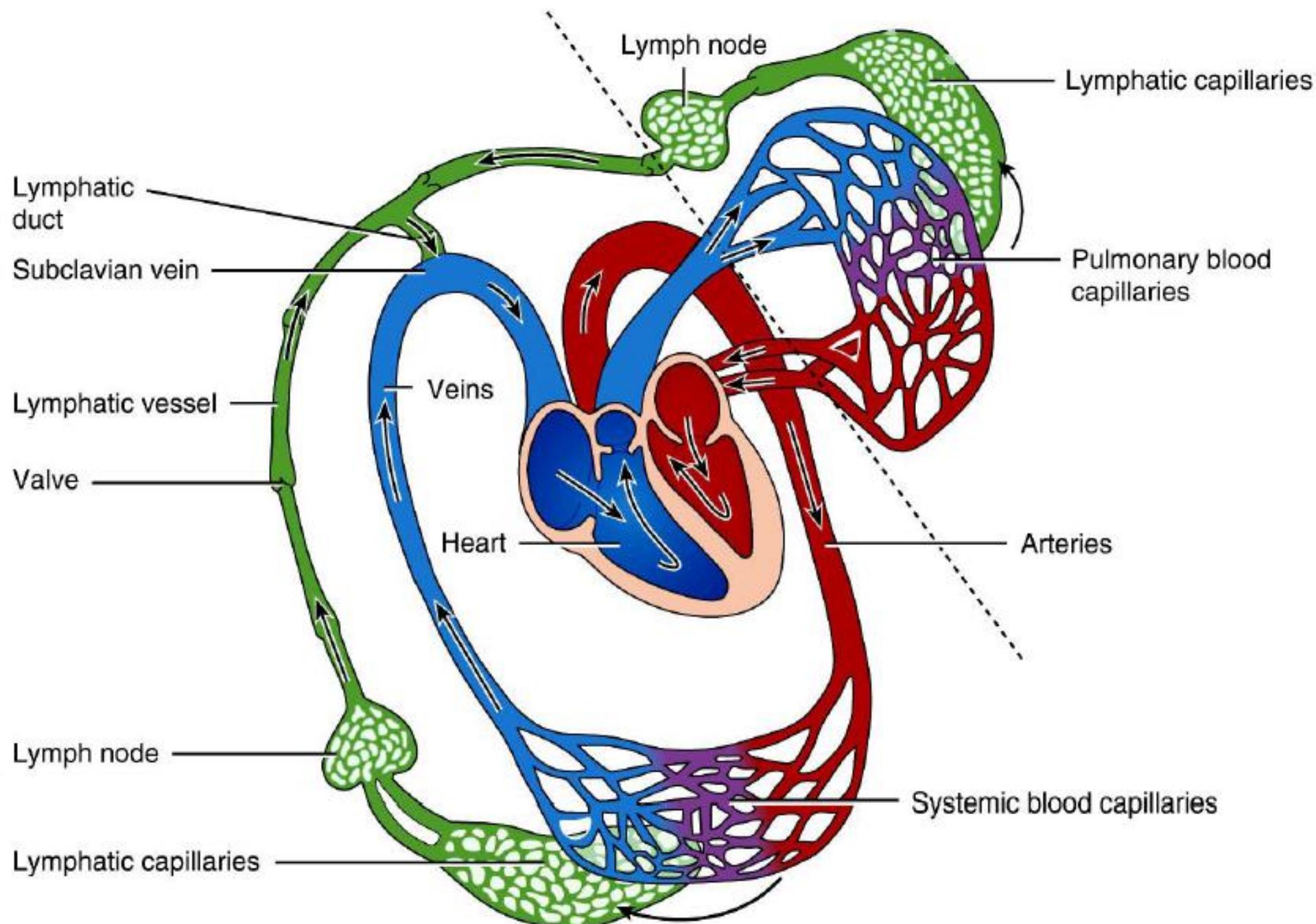
(b) Details of a lymphatic capillary

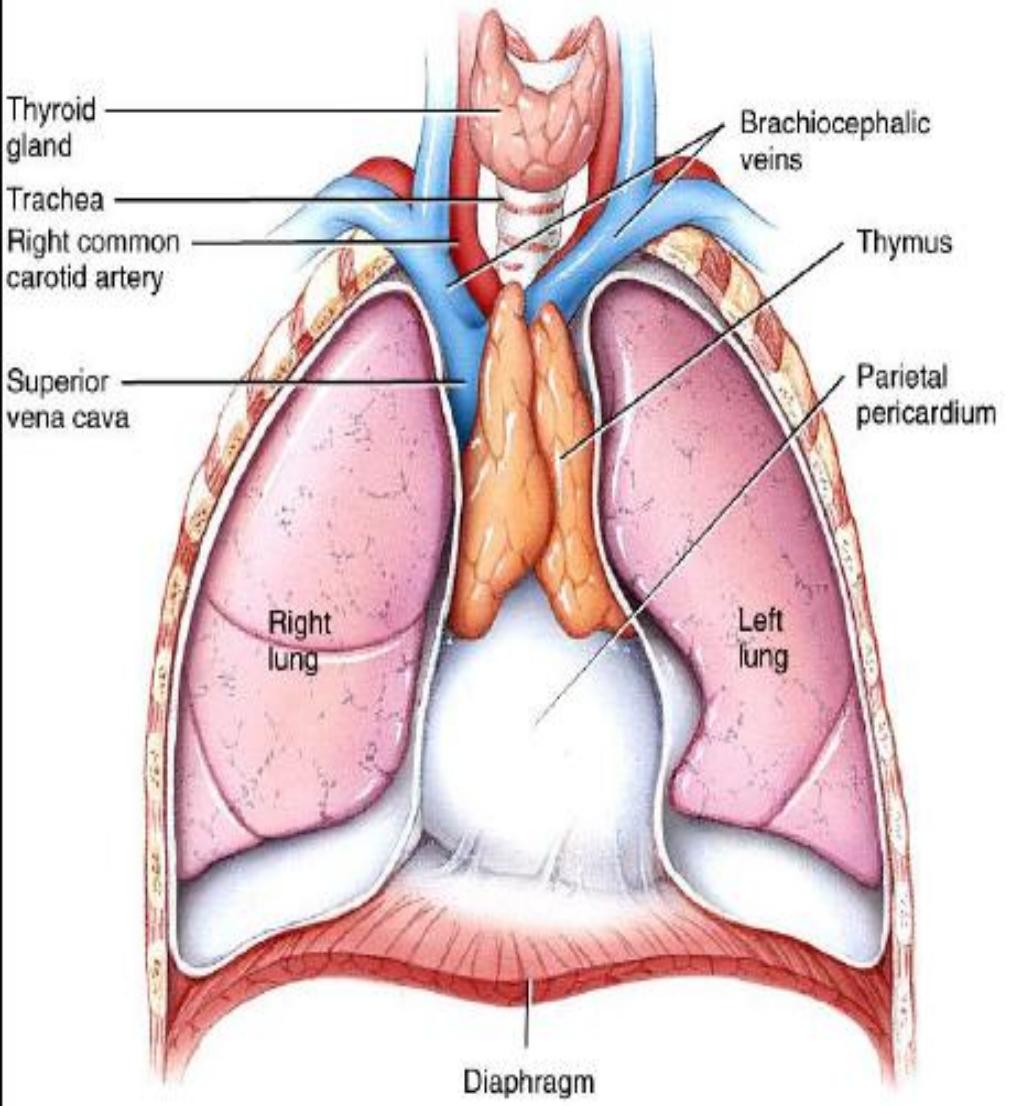




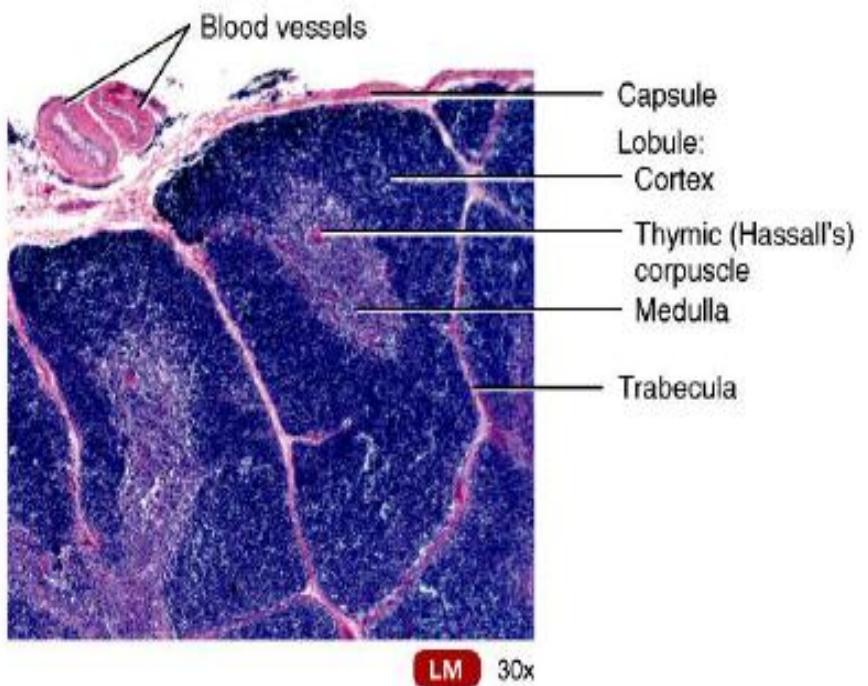
SYSTEMIC CIRCULATION

PULMONARY CIRCULATION

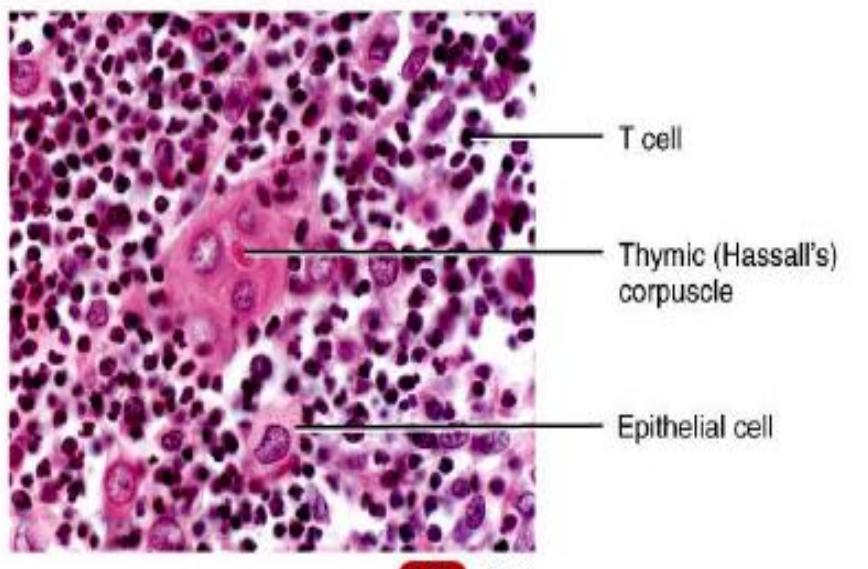




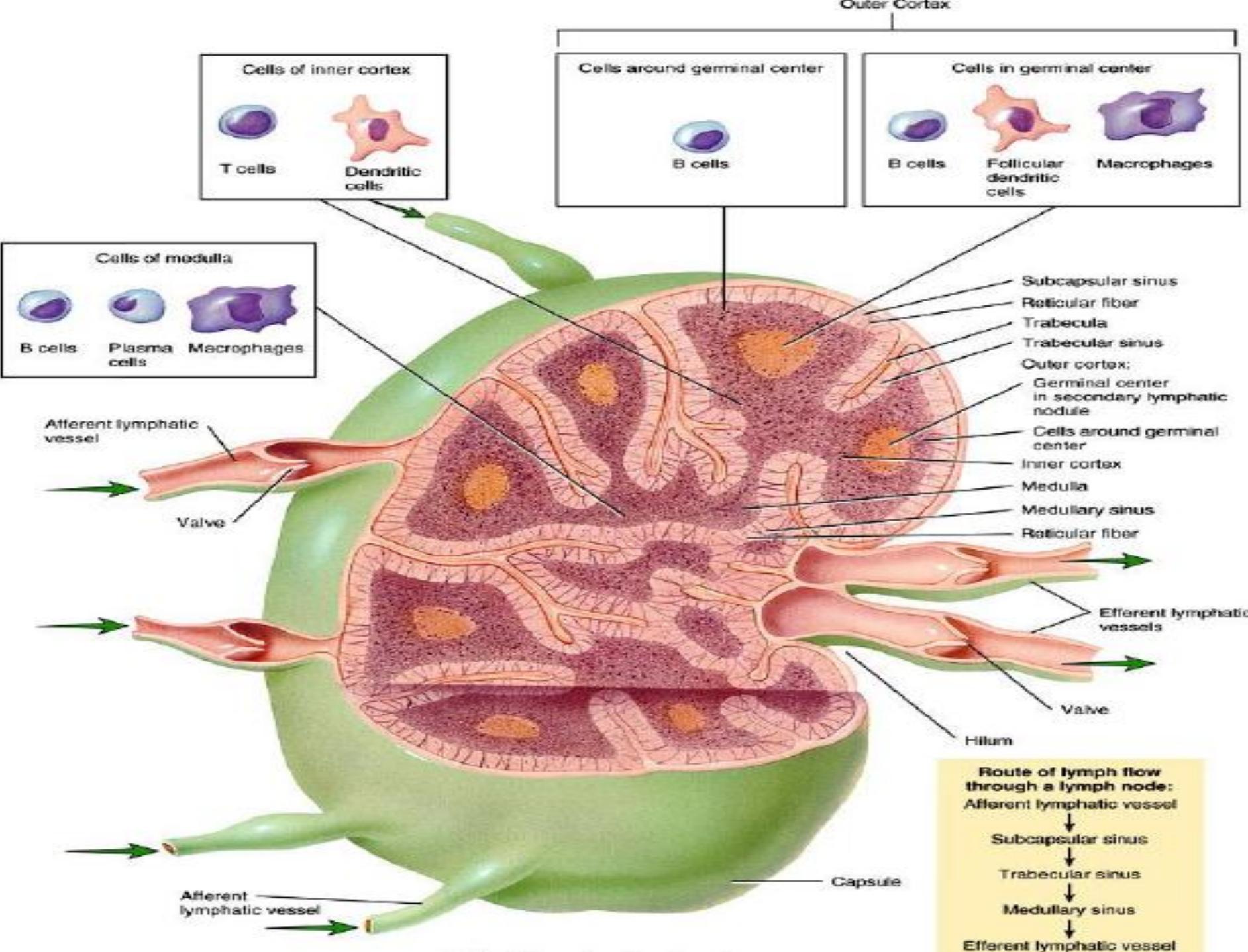
(a) Thymus of adolescent

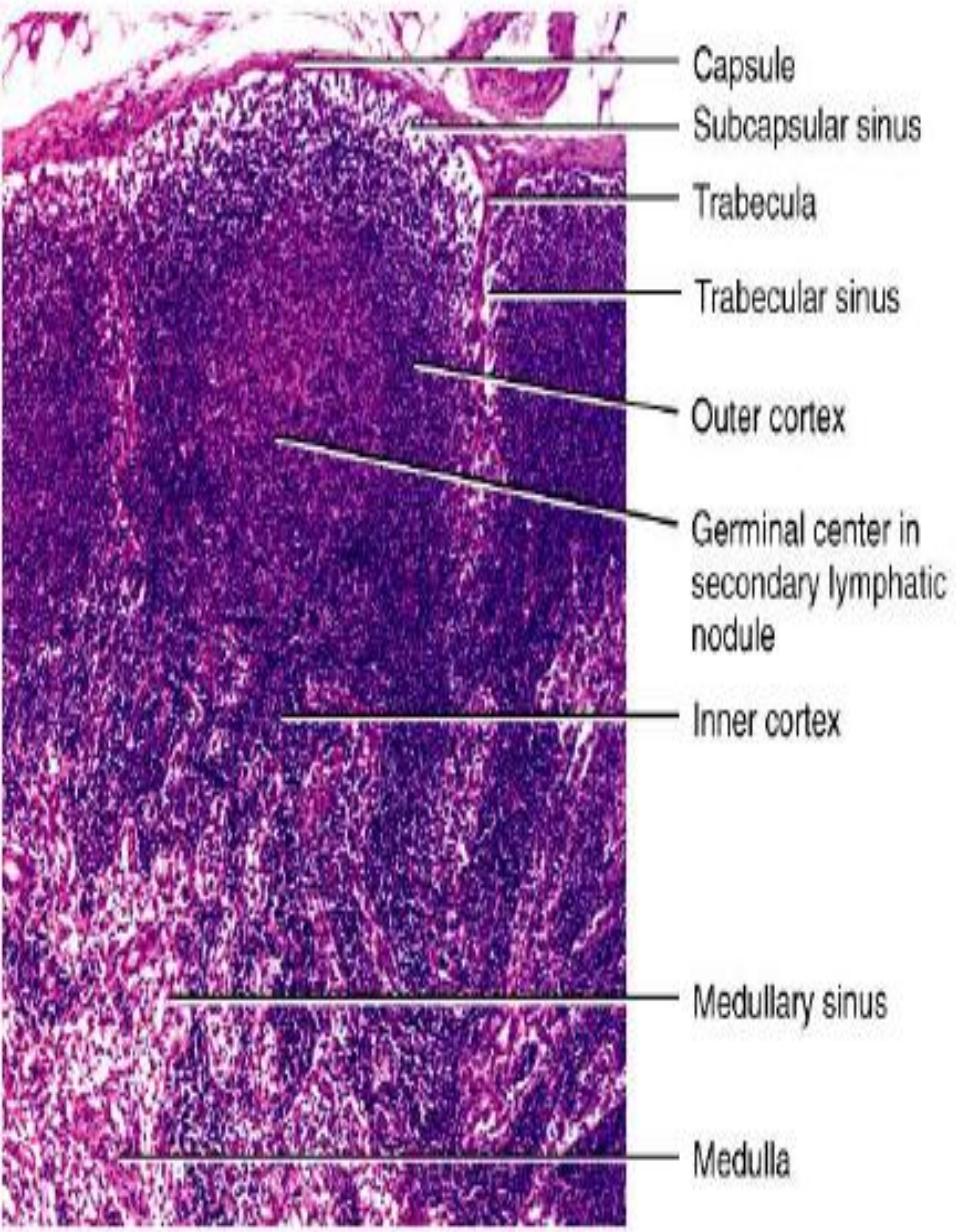


(b) Thymic lobules



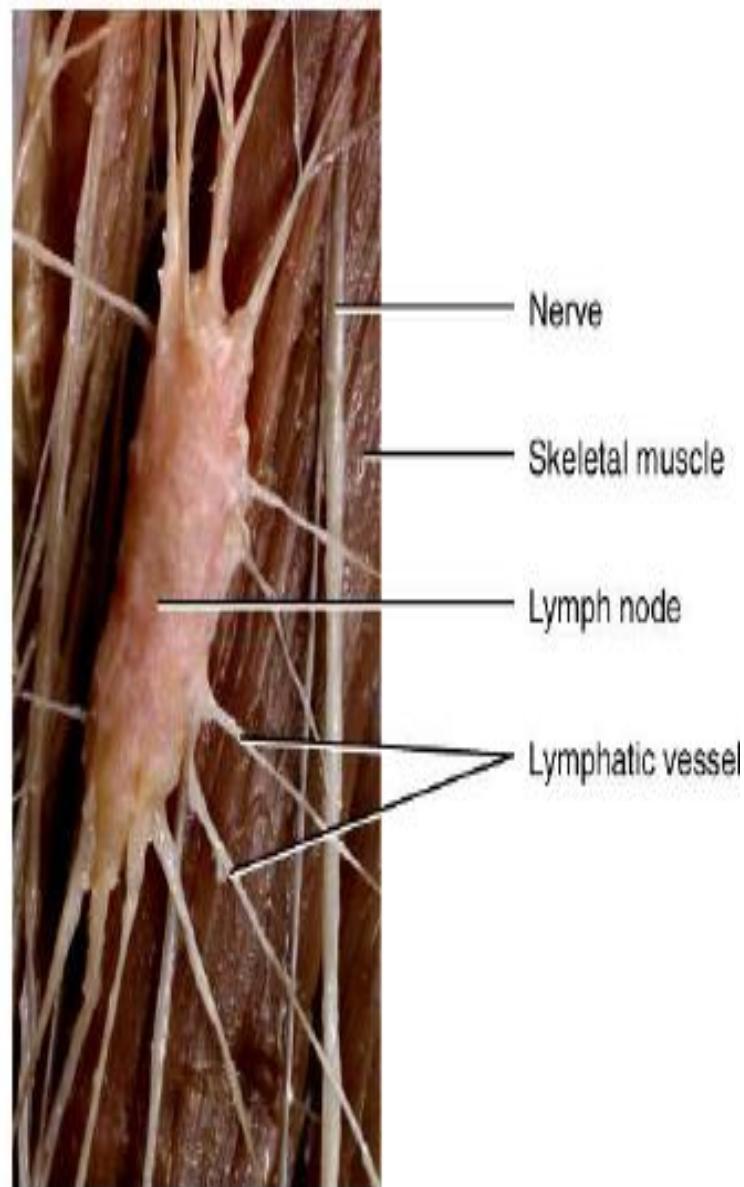
(c) Details of the thymic medulla



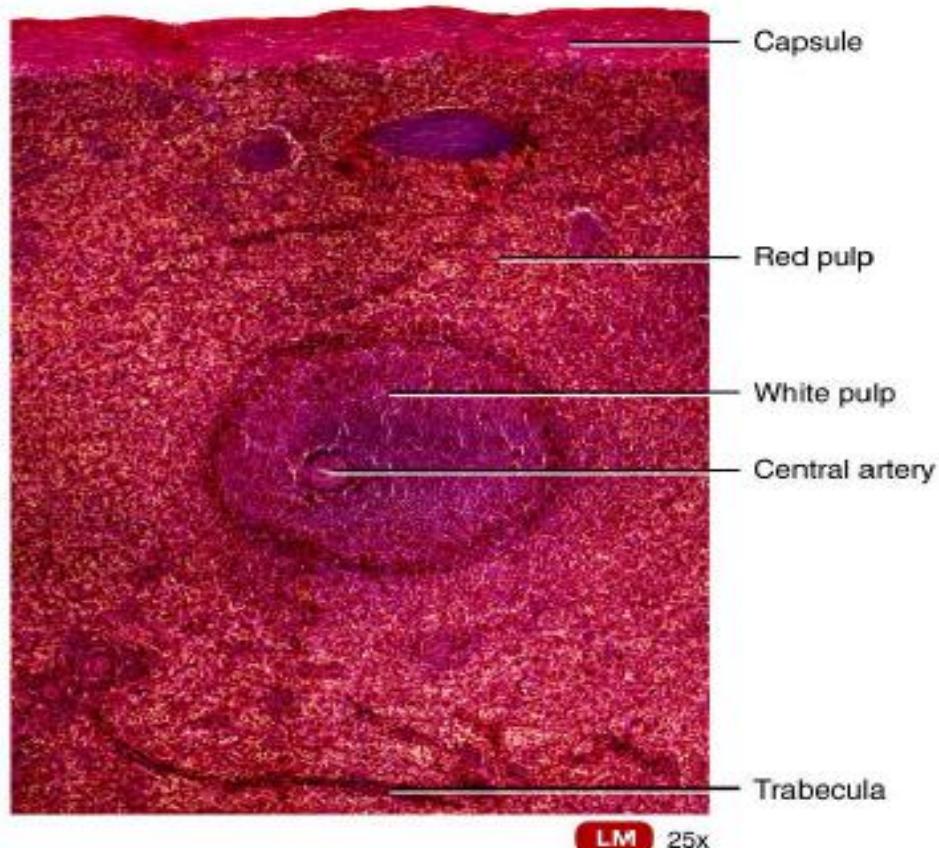
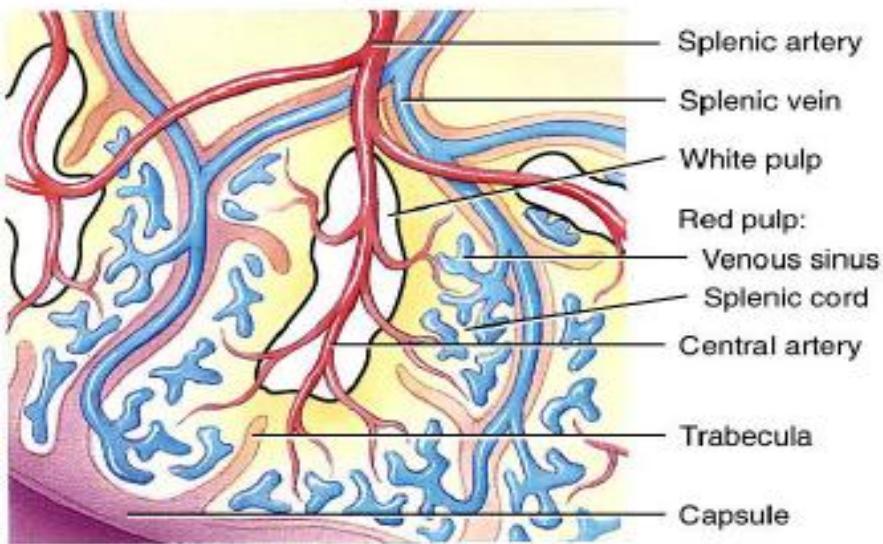
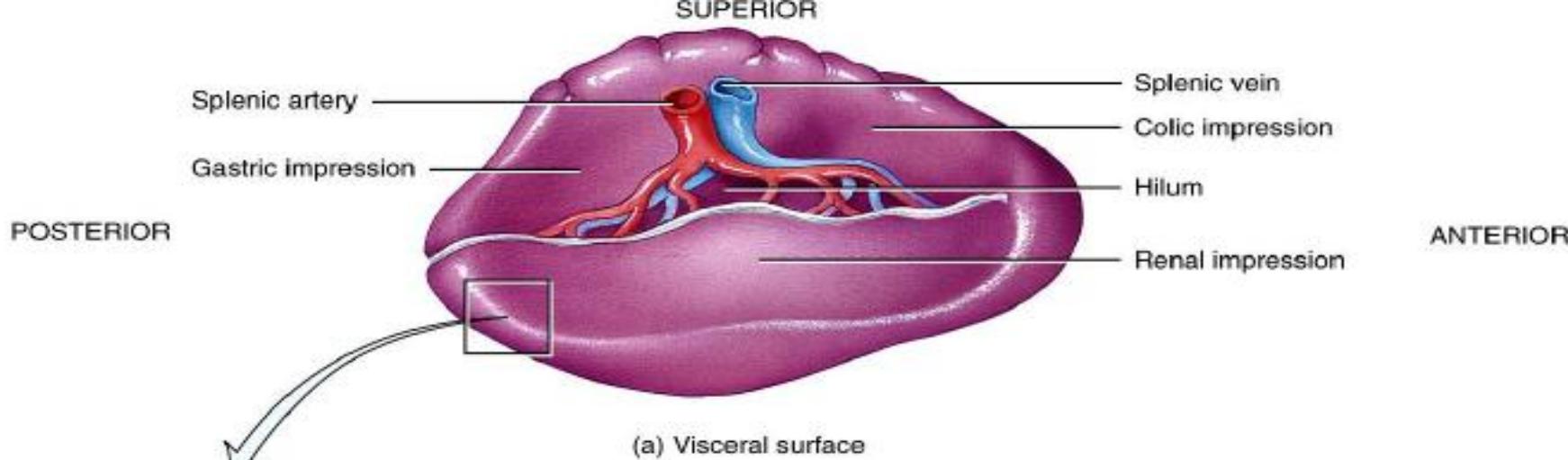


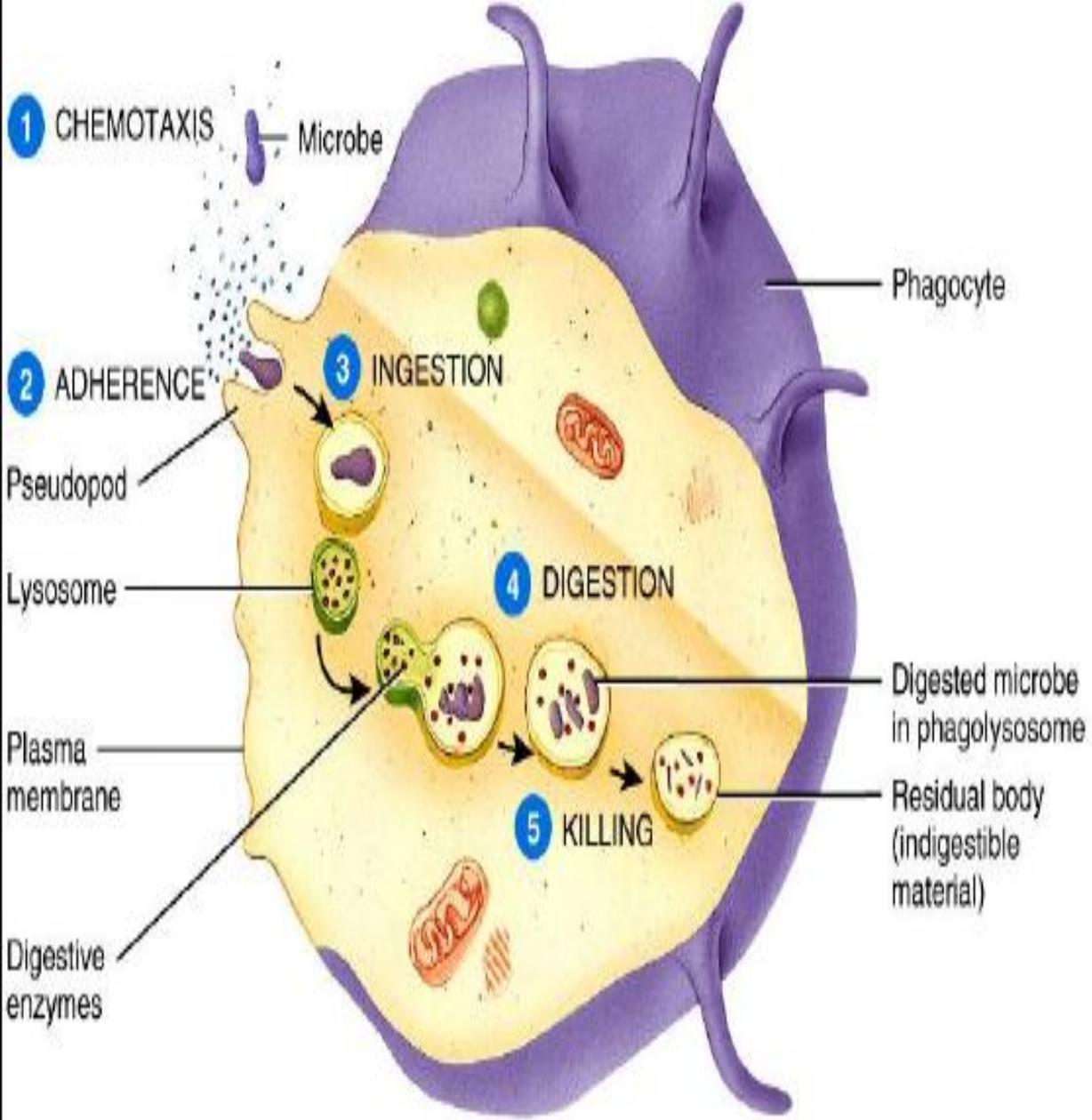
LM 55x

(b) Portion of a lymph node



(c) Anterior view of an inguinal lymph node



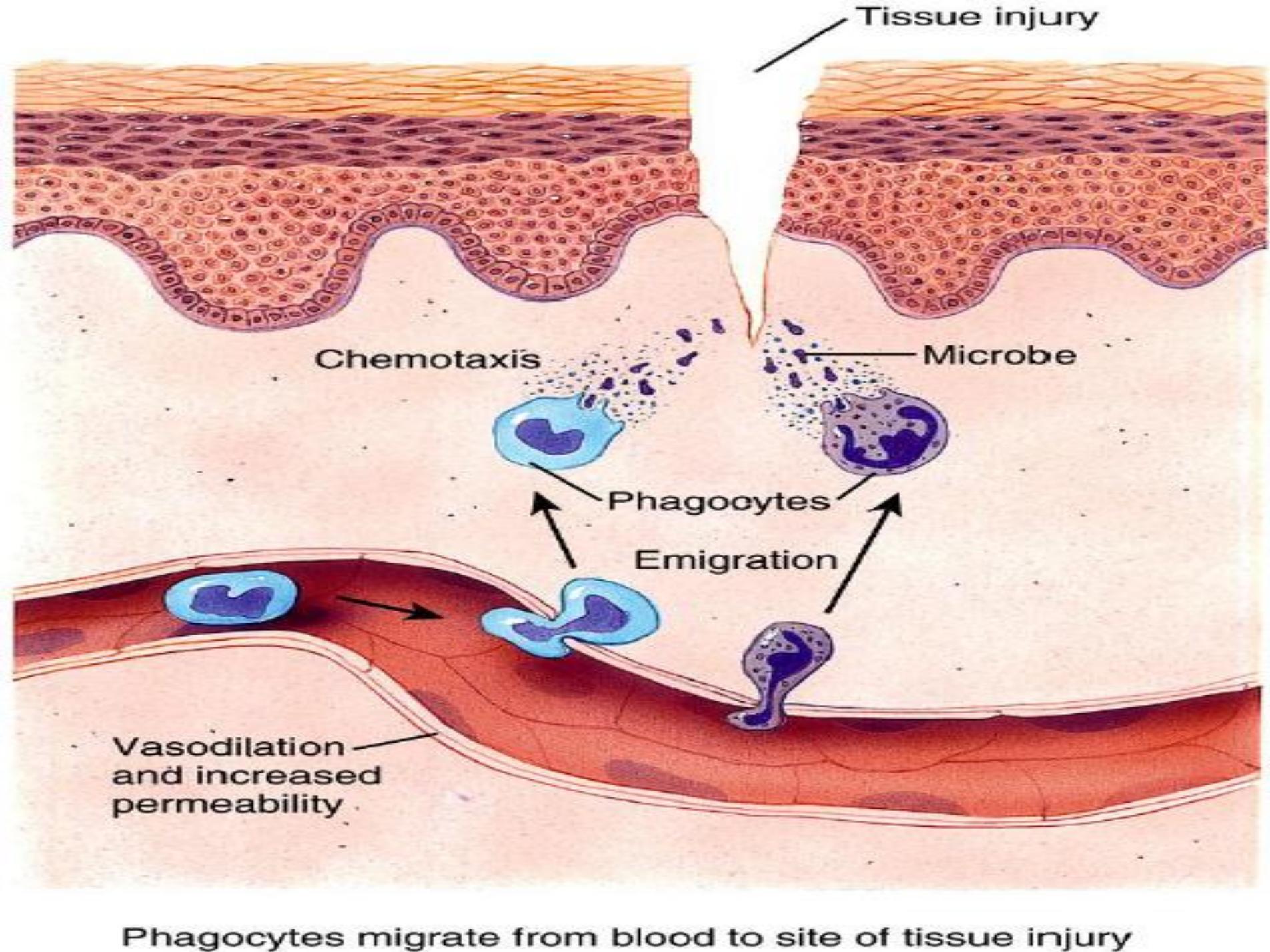


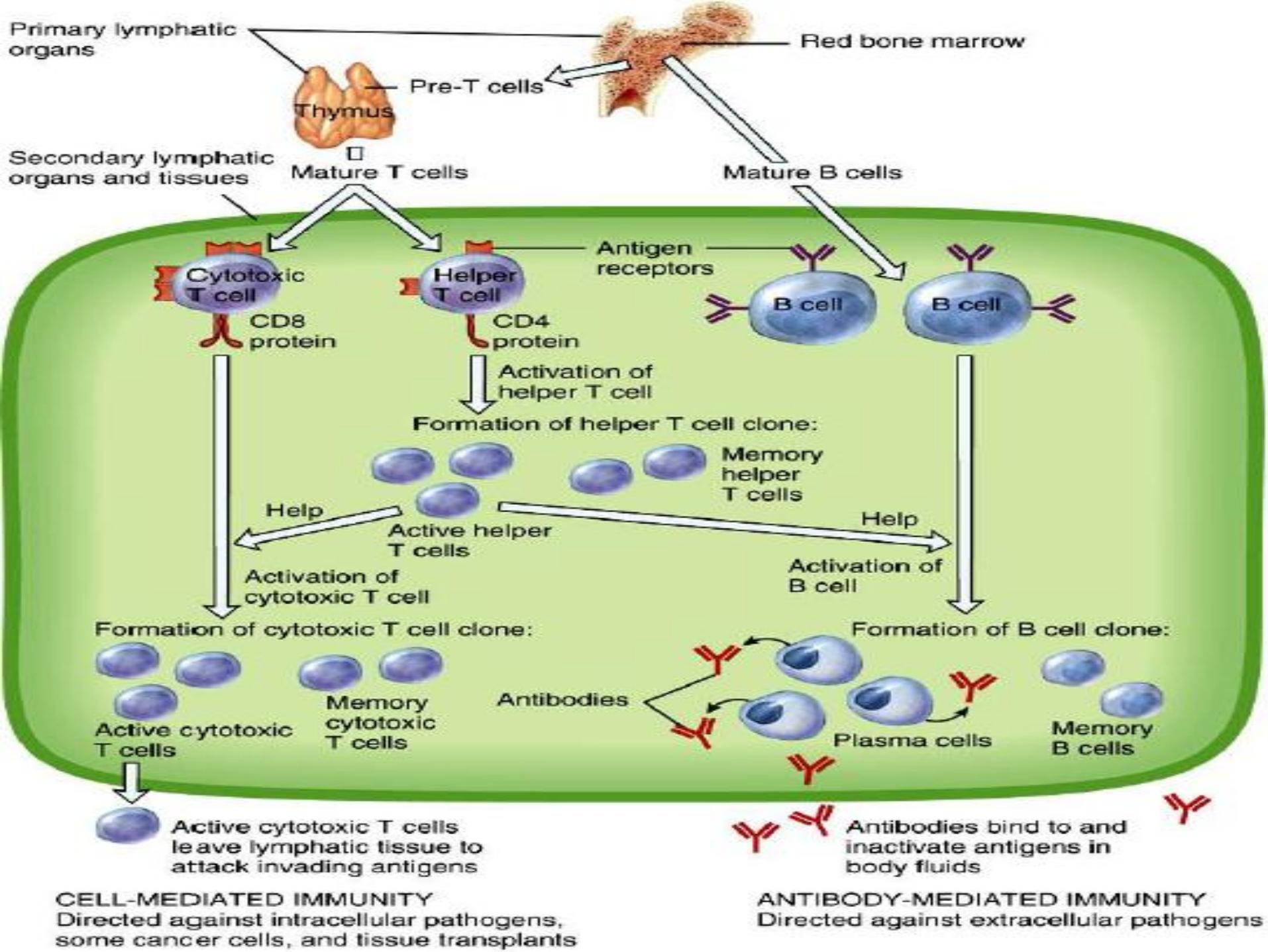
(a) Phases of phagocytosis

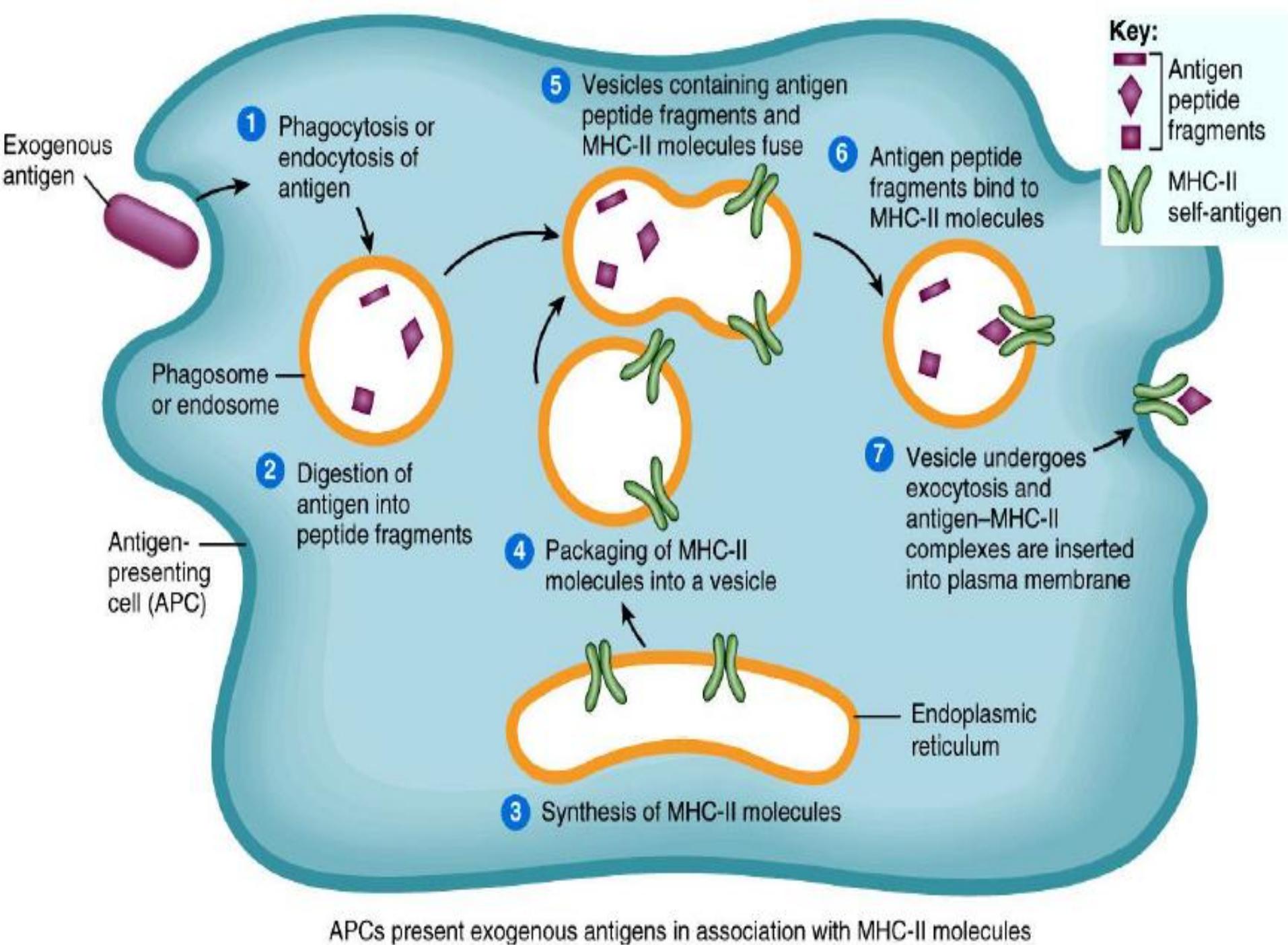


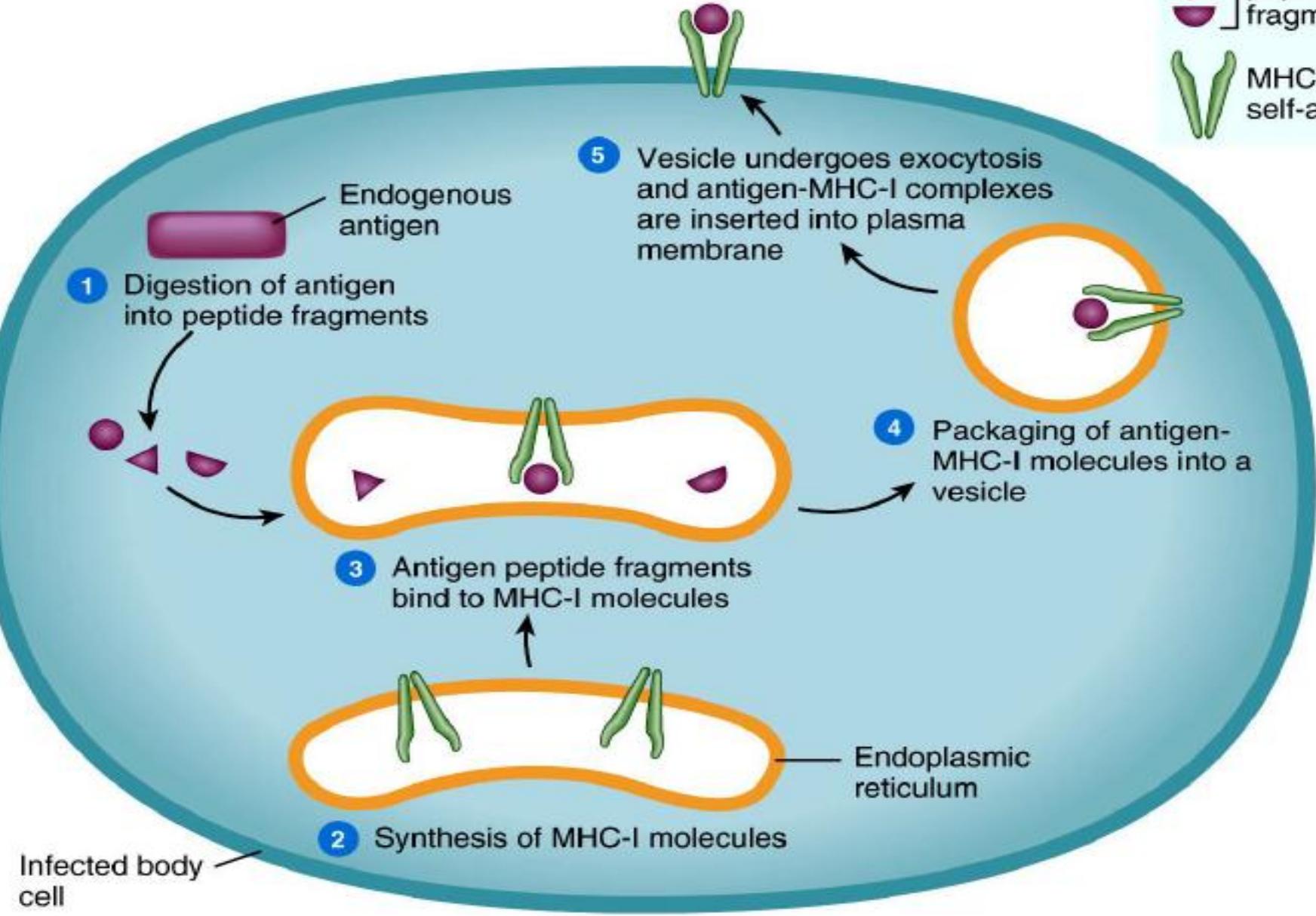
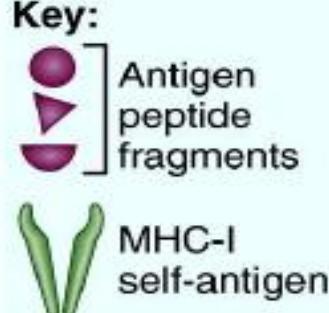
(b) Phagocyte (white blood cell) engulfing a microbe.

SEM 1800x



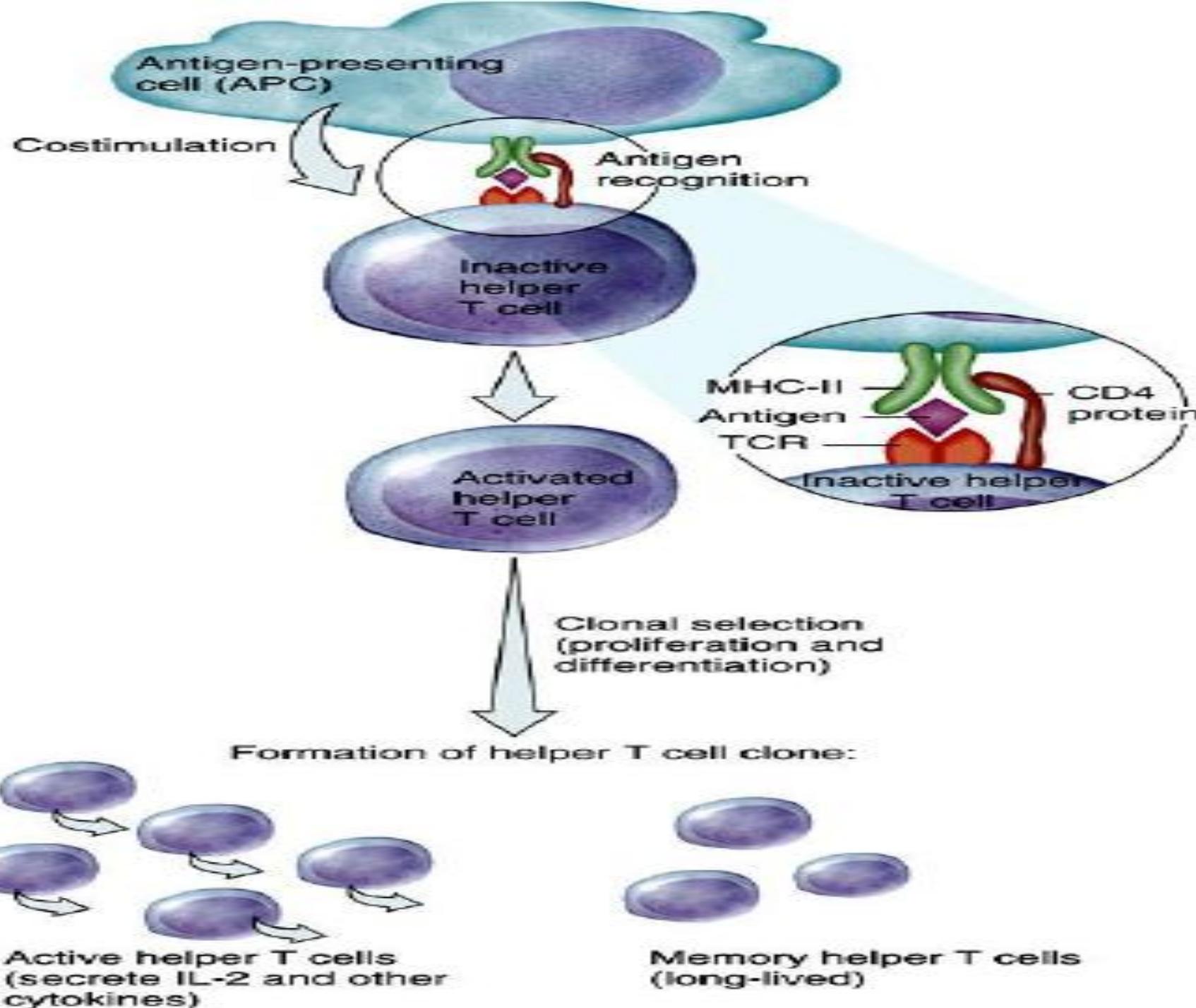


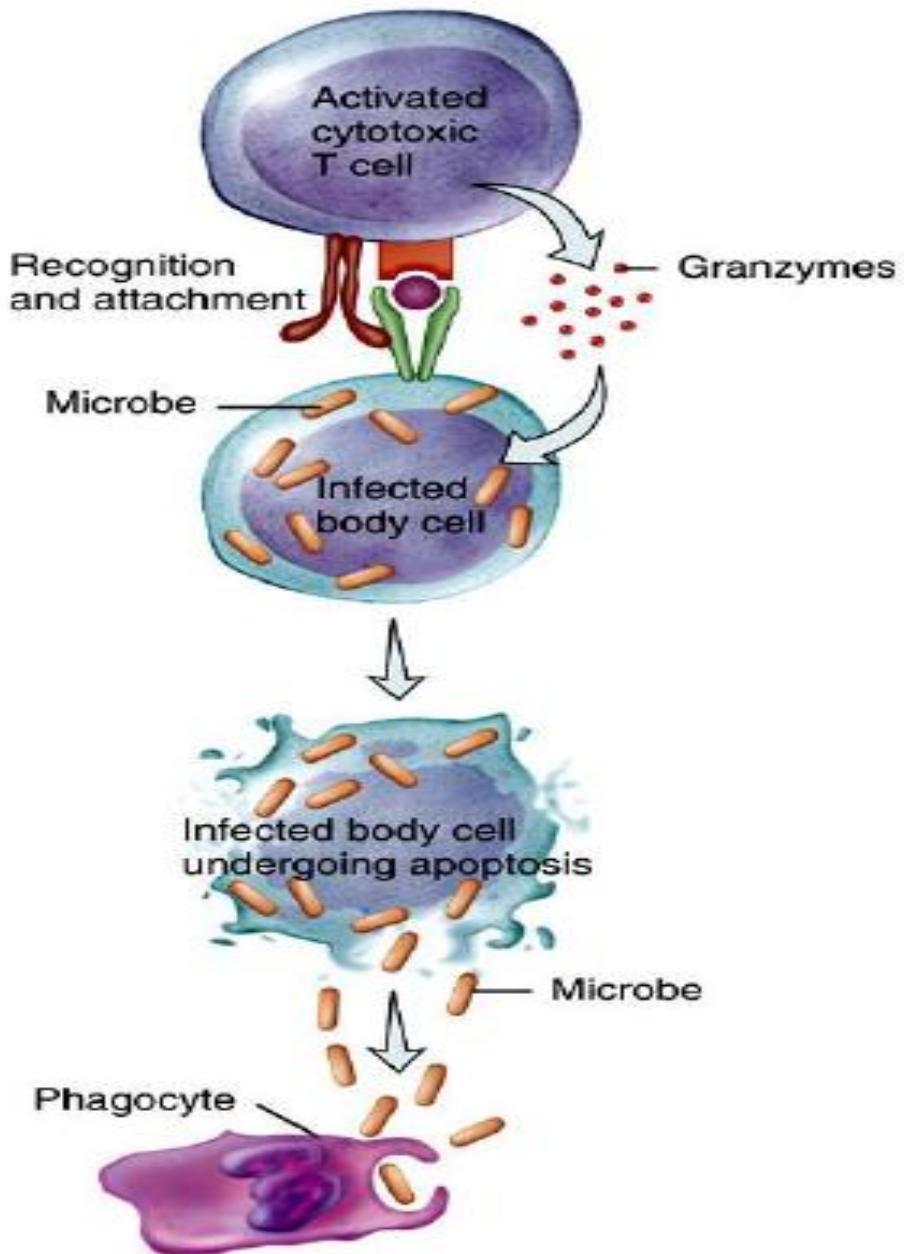




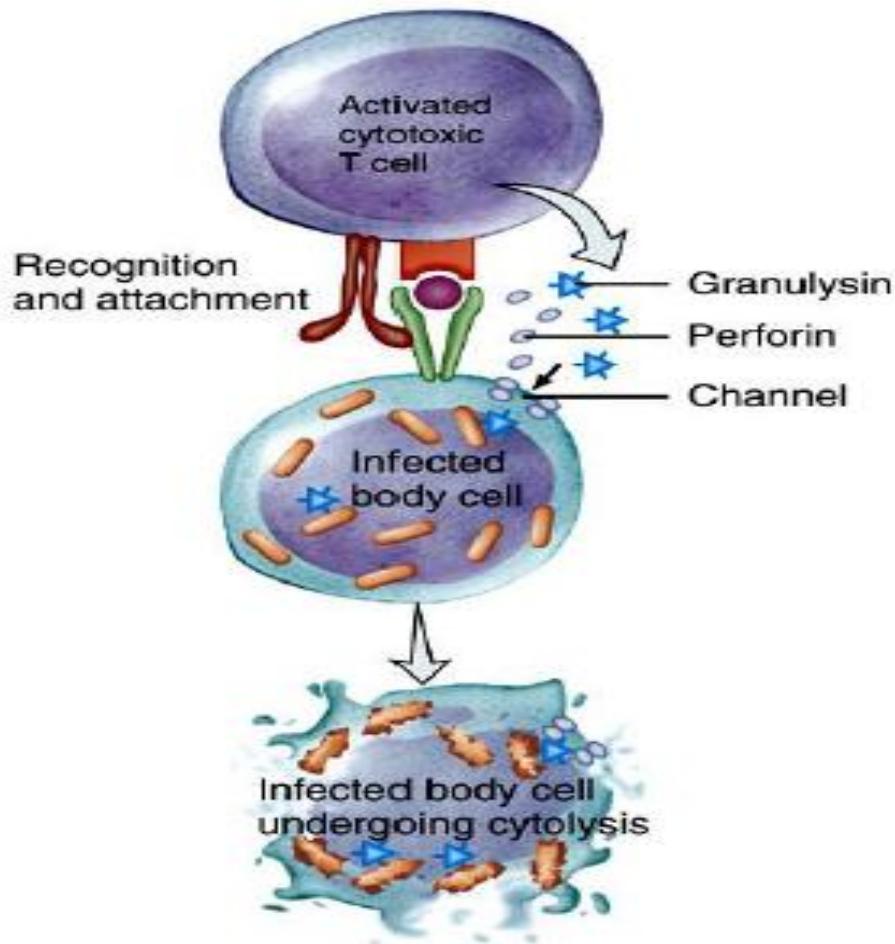
Infected body cells present endogenous antigens in association with MHC-I molecules

Fig.





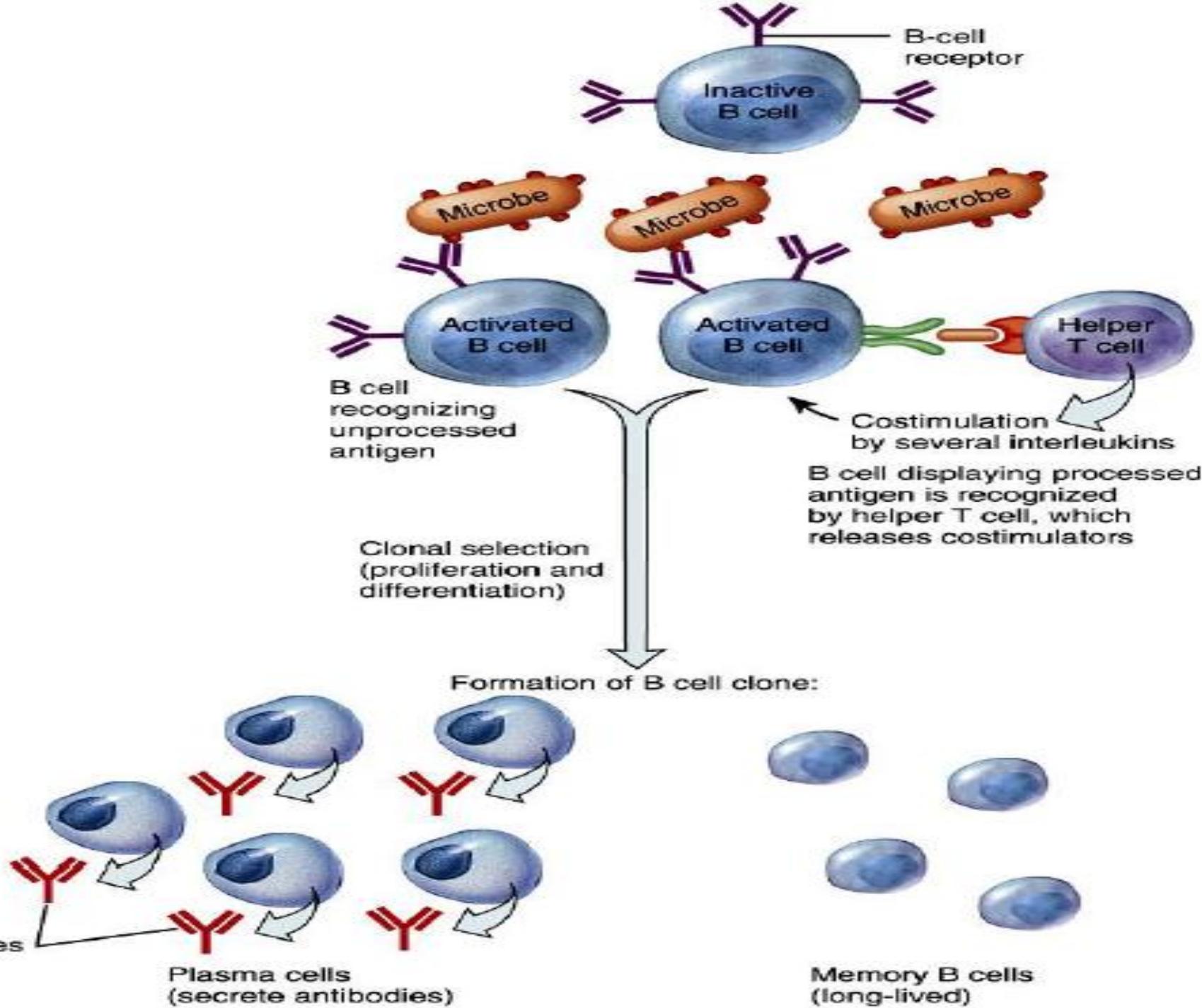
(a) Cytotoxic T cell destruction of infected cell by release of granzymes that cause apoptosis; released microbes are destroyed by phagocyte.

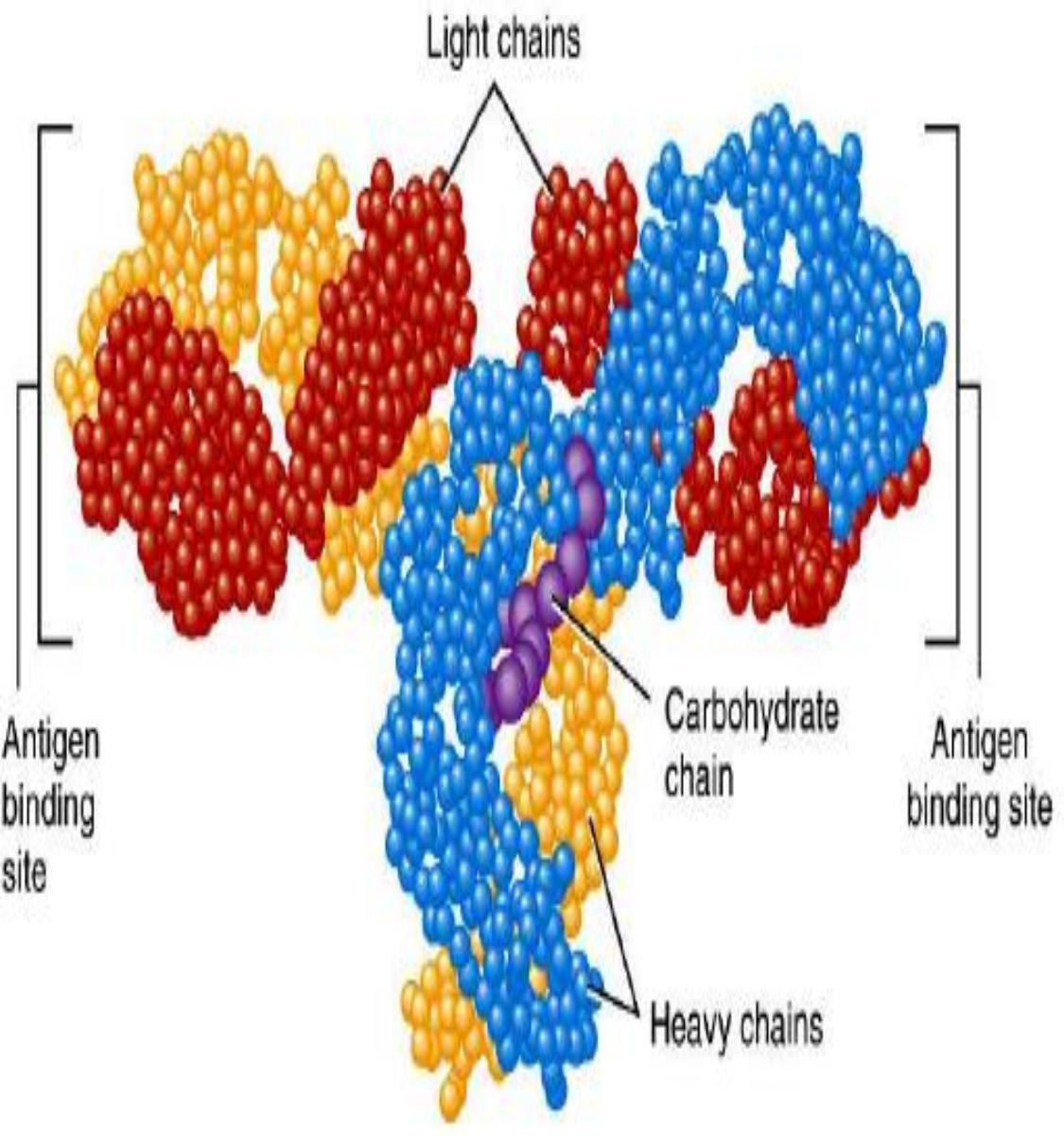


(b) Cytotoxic T cell destruction of infected cell by release of perforins that cause cytolysis; microbes are destroyed by granulysin.

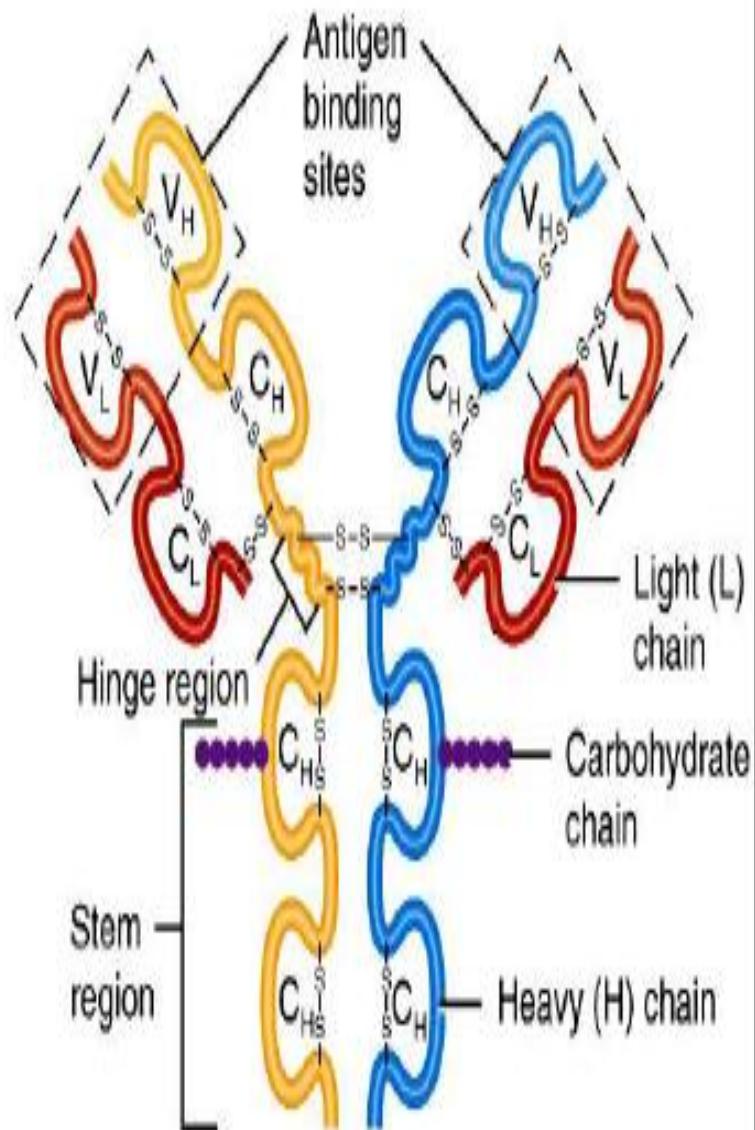
Key:

- TCR
- CD8 protein
- Antigen-MHC-I complex

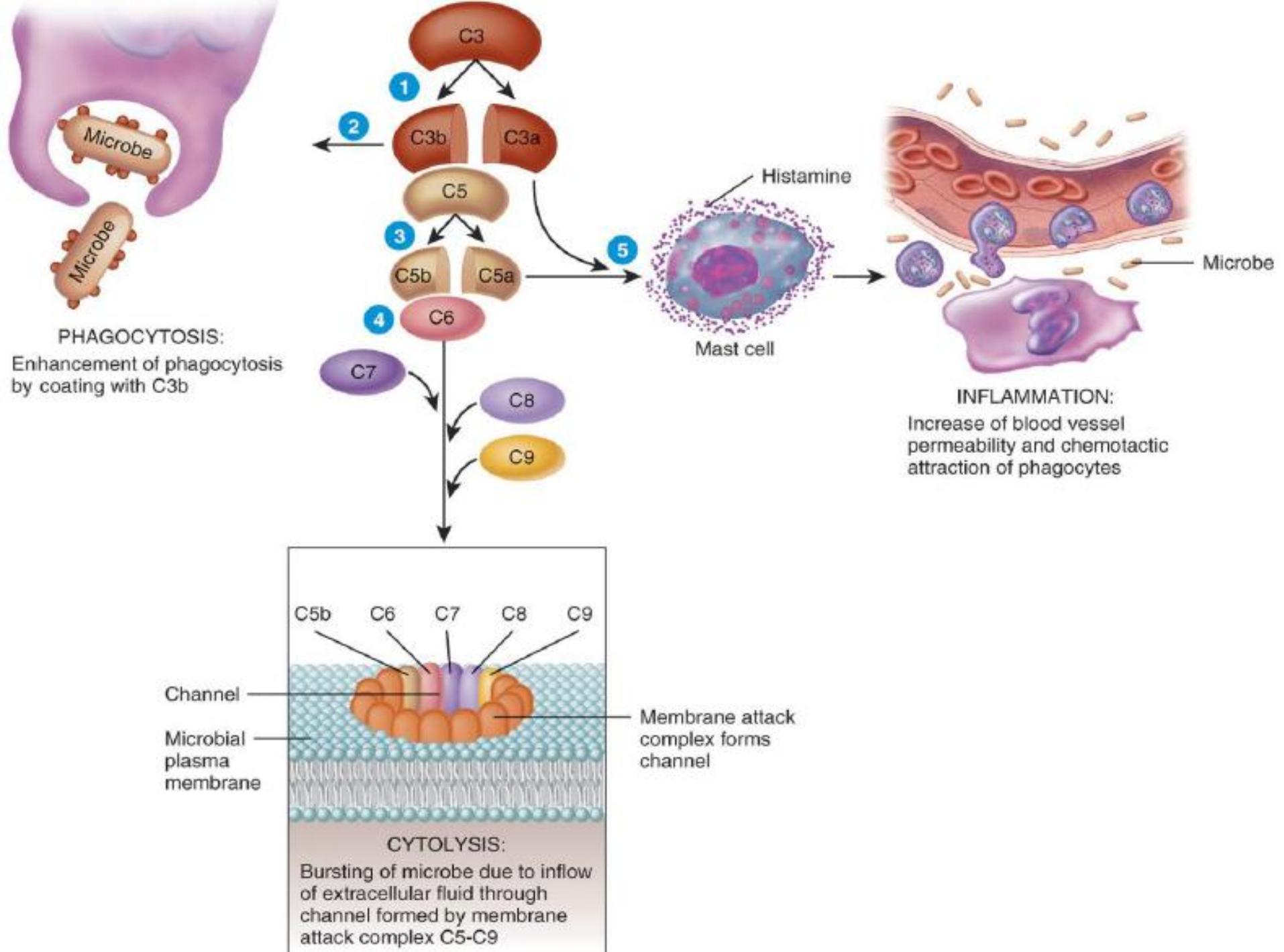




(a) Model of IgG molecule



(b) Diagram of IgG heavy and light chains



LYMPHATIC SYSTEMS

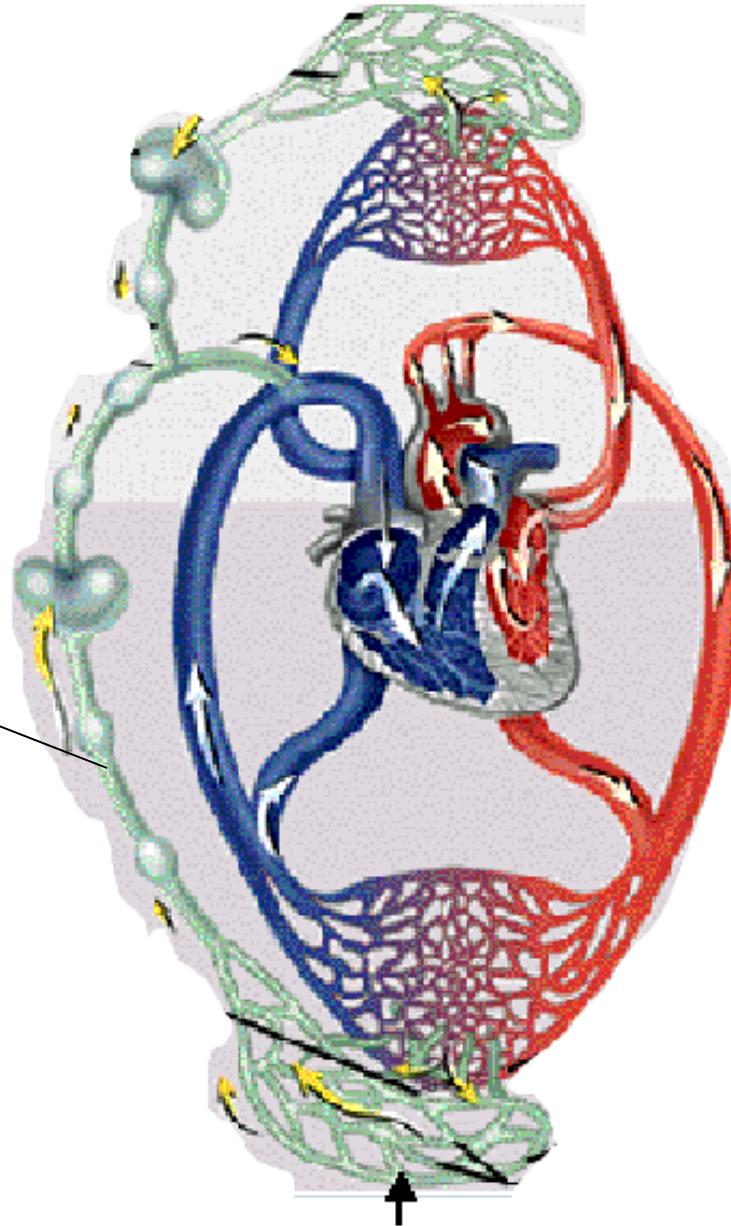
consists of:

- 1) *lymphatic vessels*
- 2) *lymphoid tissues* and
lymphoid organs



travel along with blood vessels.

1) *lymphatic vessels*

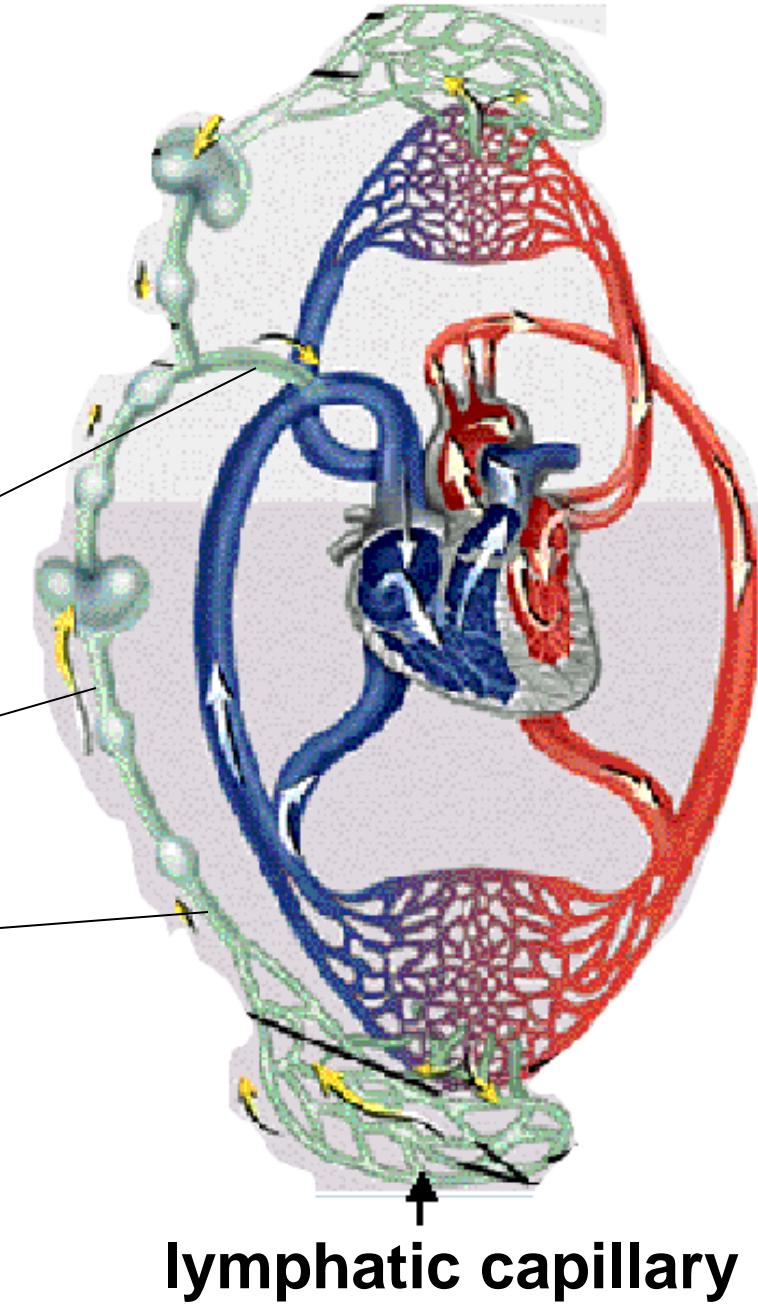


Lymphatic vessels start with lymphatic capillaries

lymphatic ducts

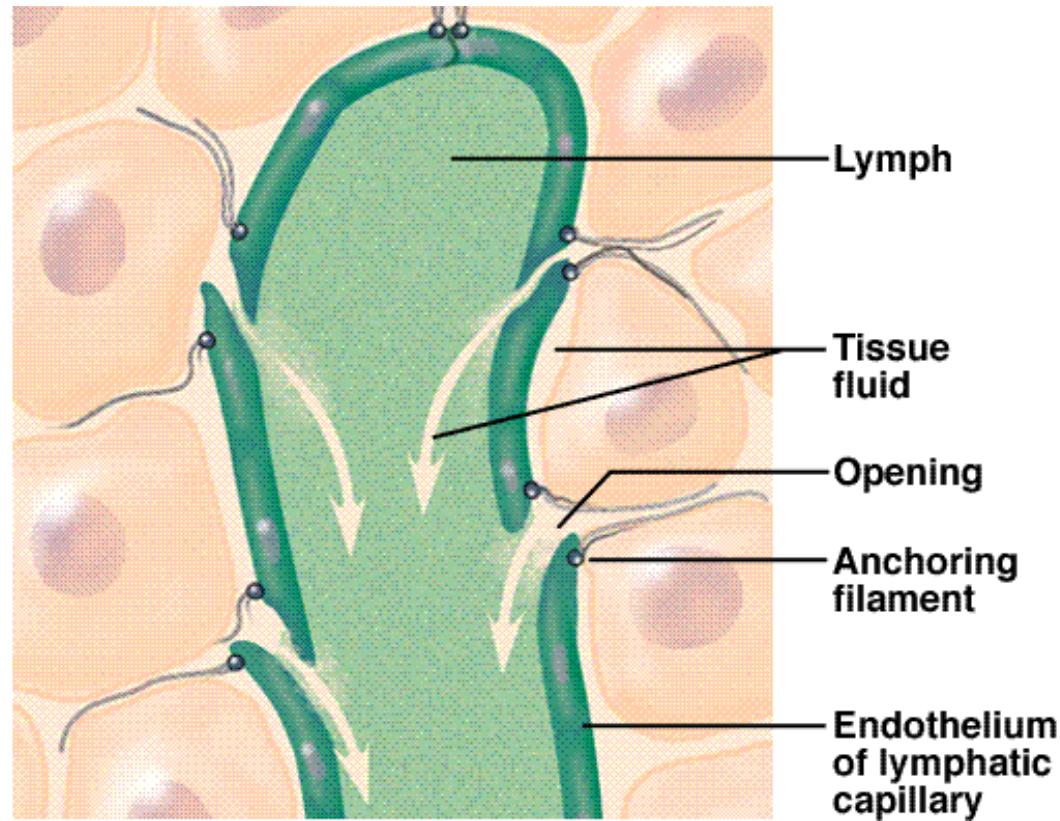
lymphatic trunks

lymphatic collecting vessels



lymphatic capillary

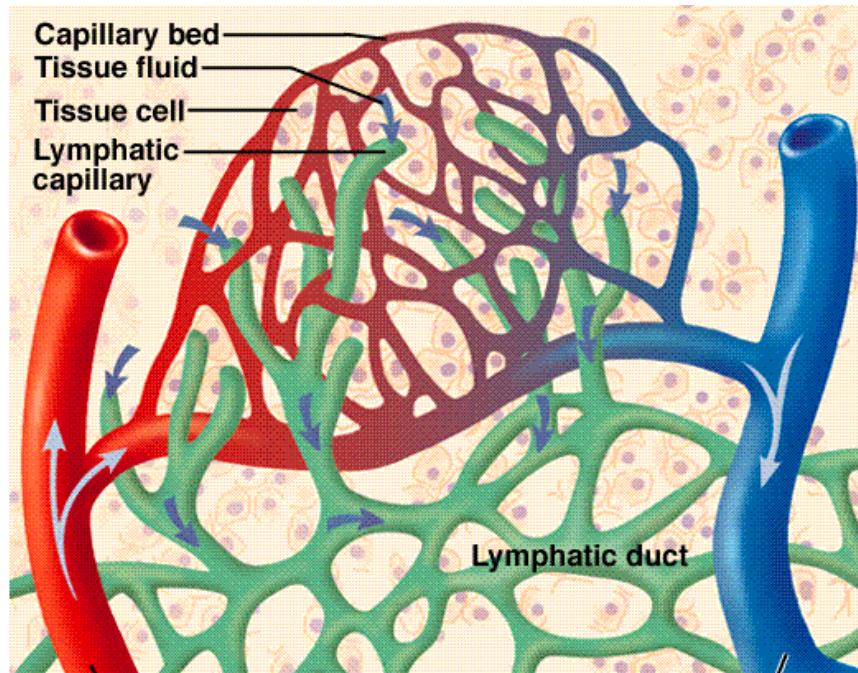
- blind ended vessels
- permeable to ***proteins*** even ***cells***



The main function

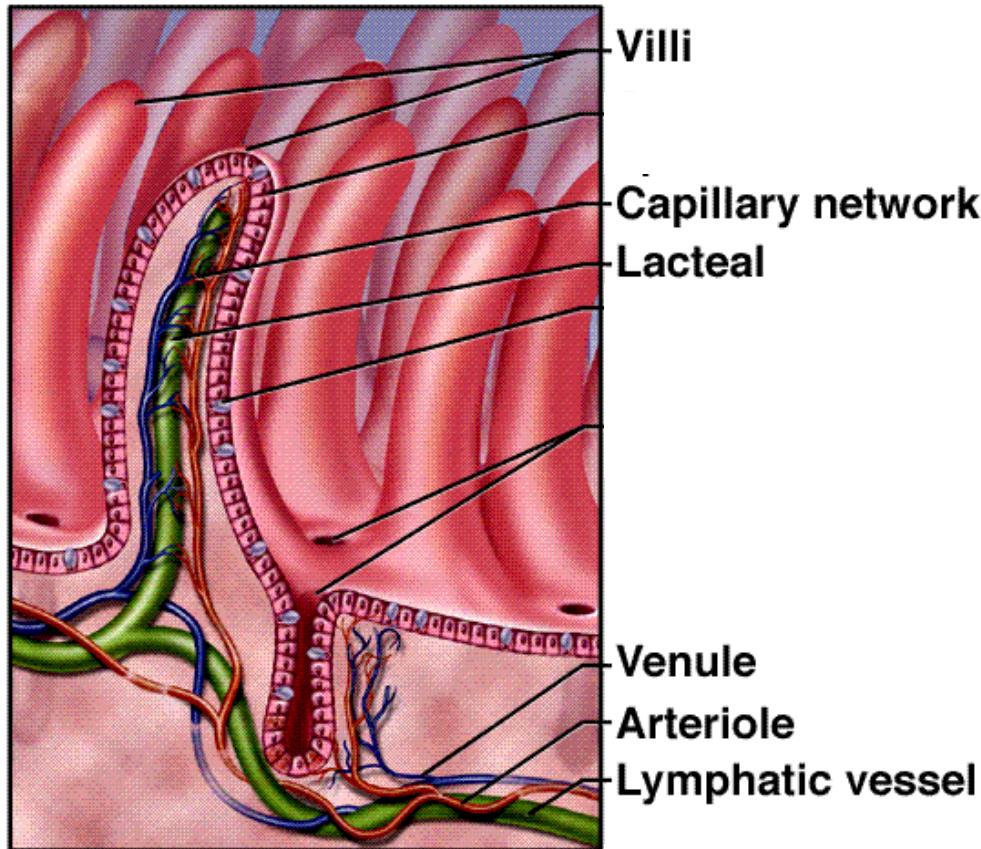
- collect excess large particles and tissue fluid

lymph

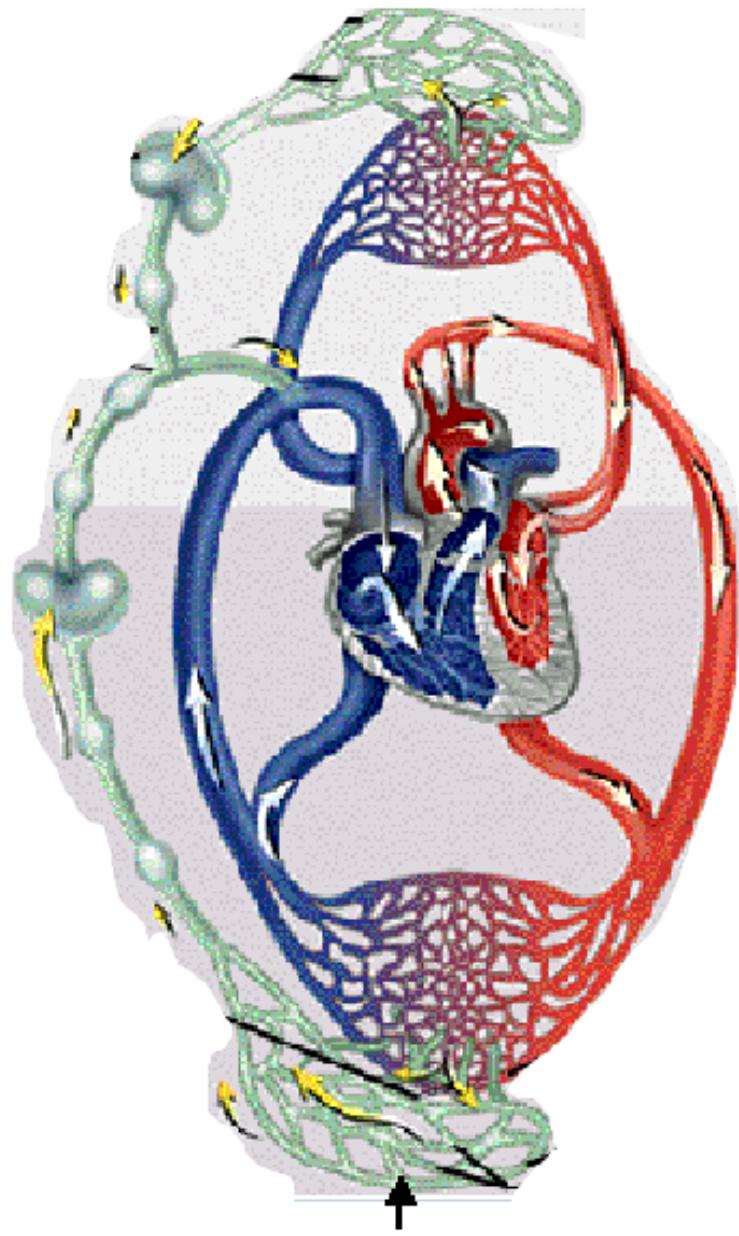


Special lymph capillaries --- **Lacteals**

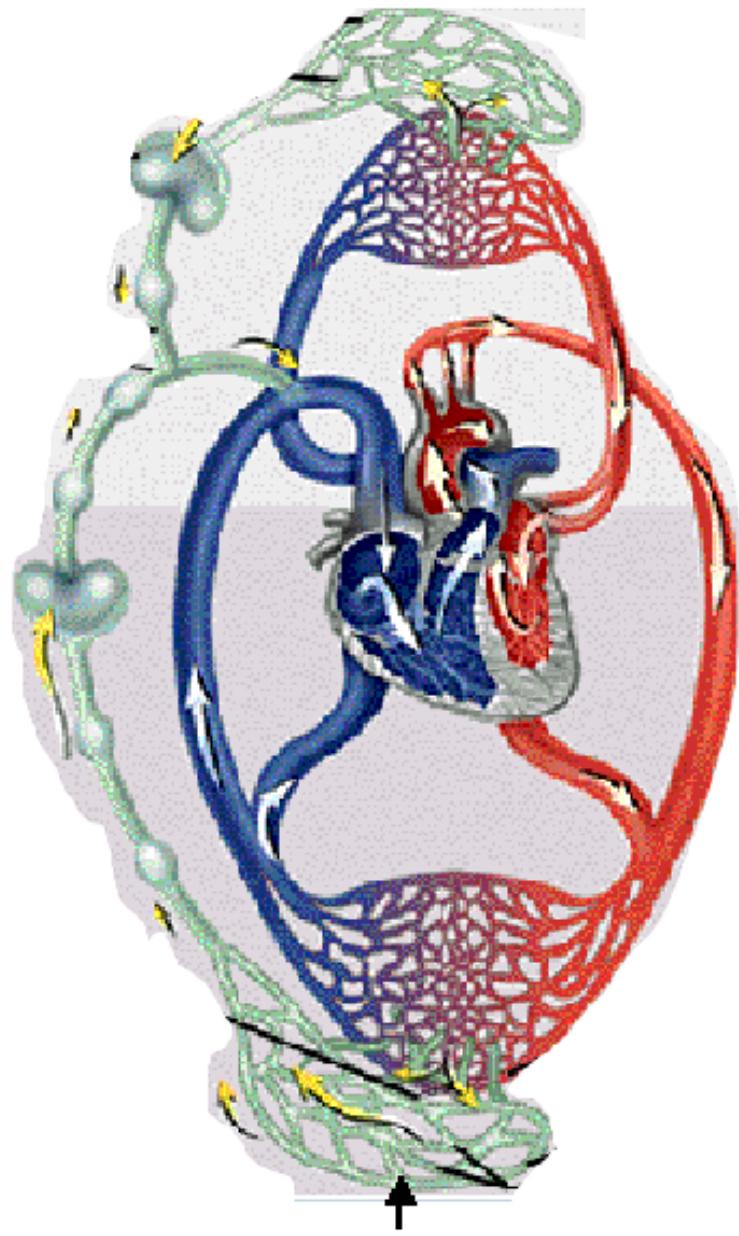
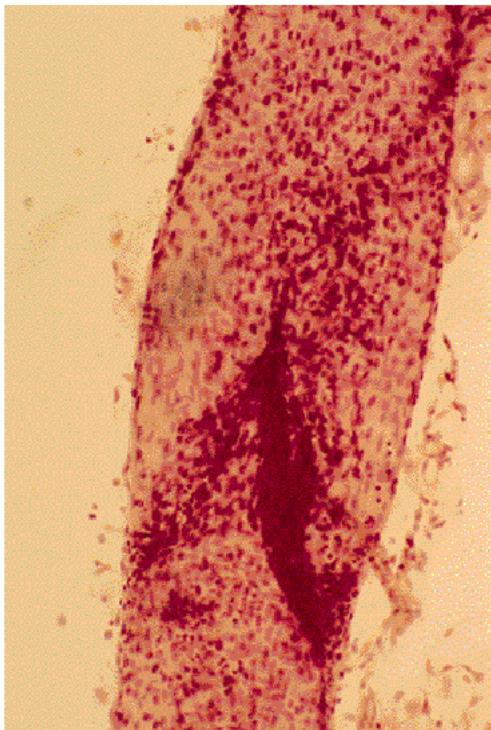
- collect digested fats (in chylomicrons)



Valves are present to prevent backflow.

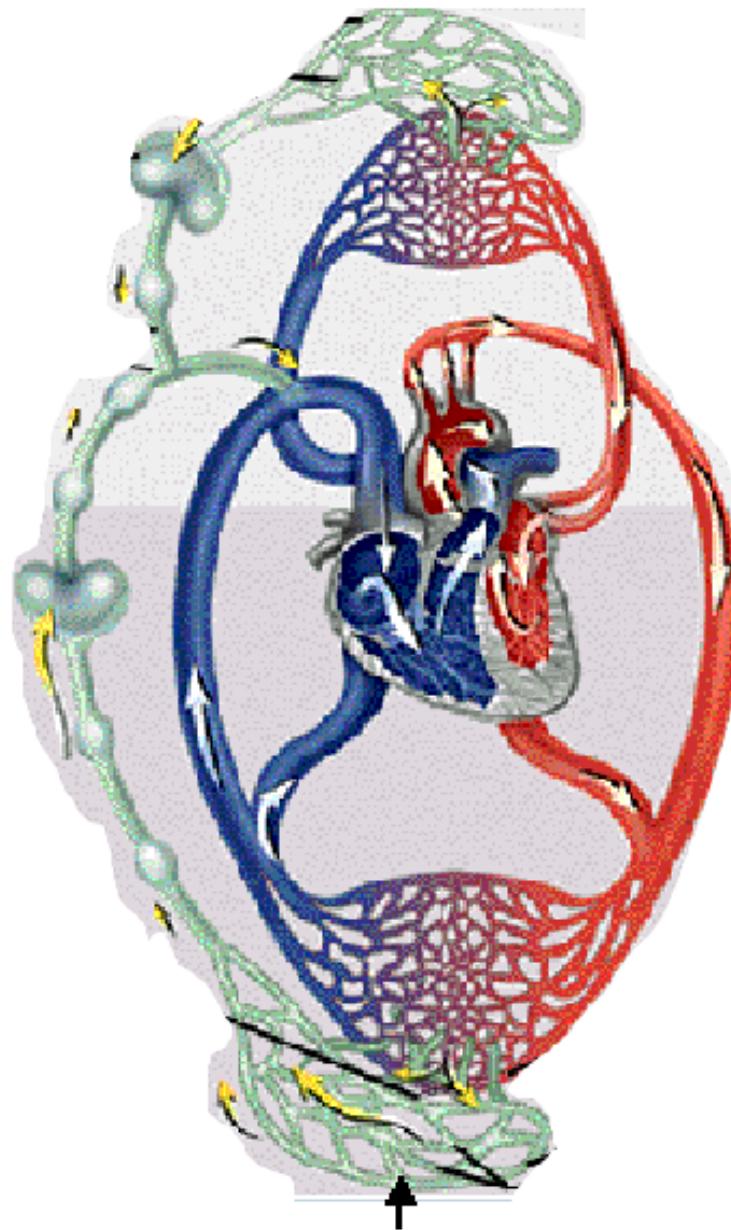
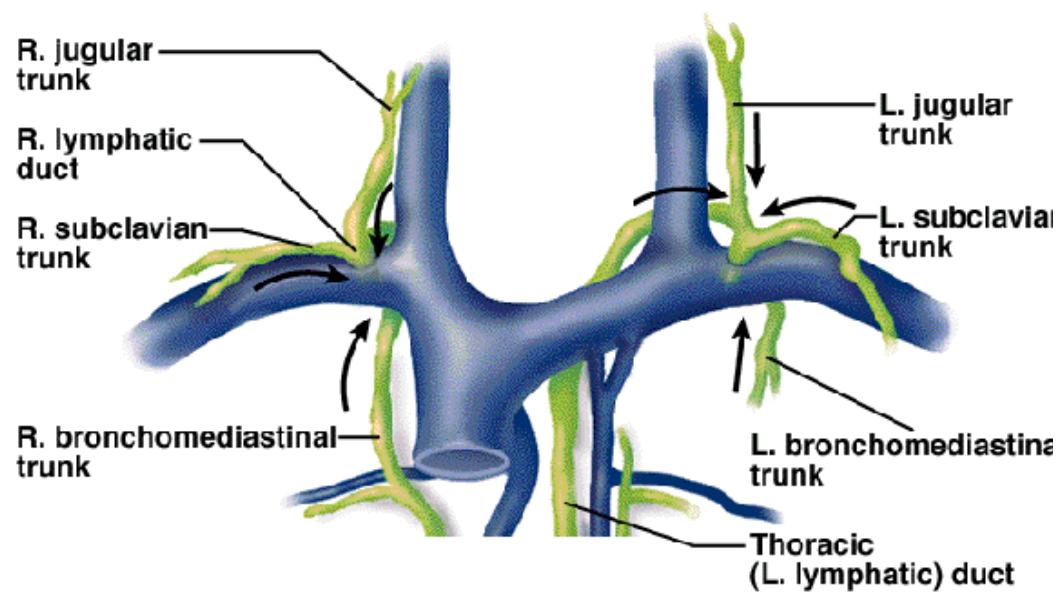


Valves are present to prevent backflow.



connection to the veins

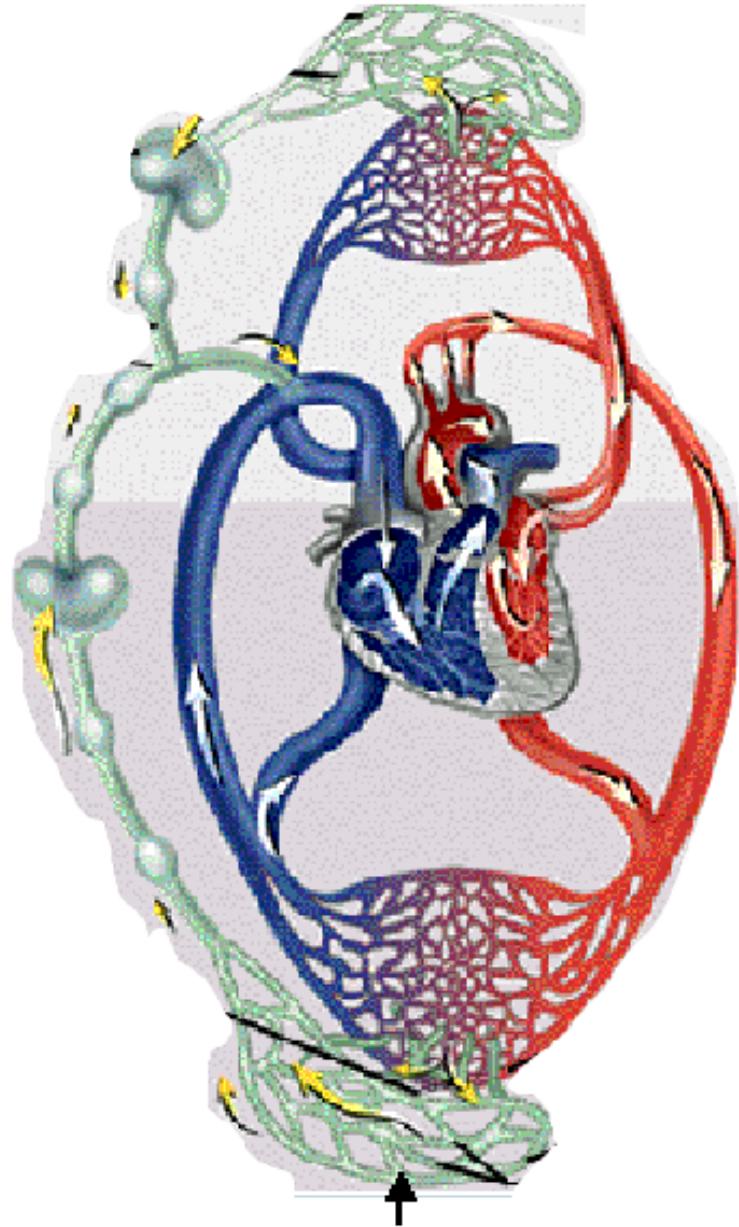
Thoracic Lymphatic Drainage (4)



blockage of lymph drainage

Lymphedema

- swelling in tissues
- due to tumor pressure, parasites, or surgery

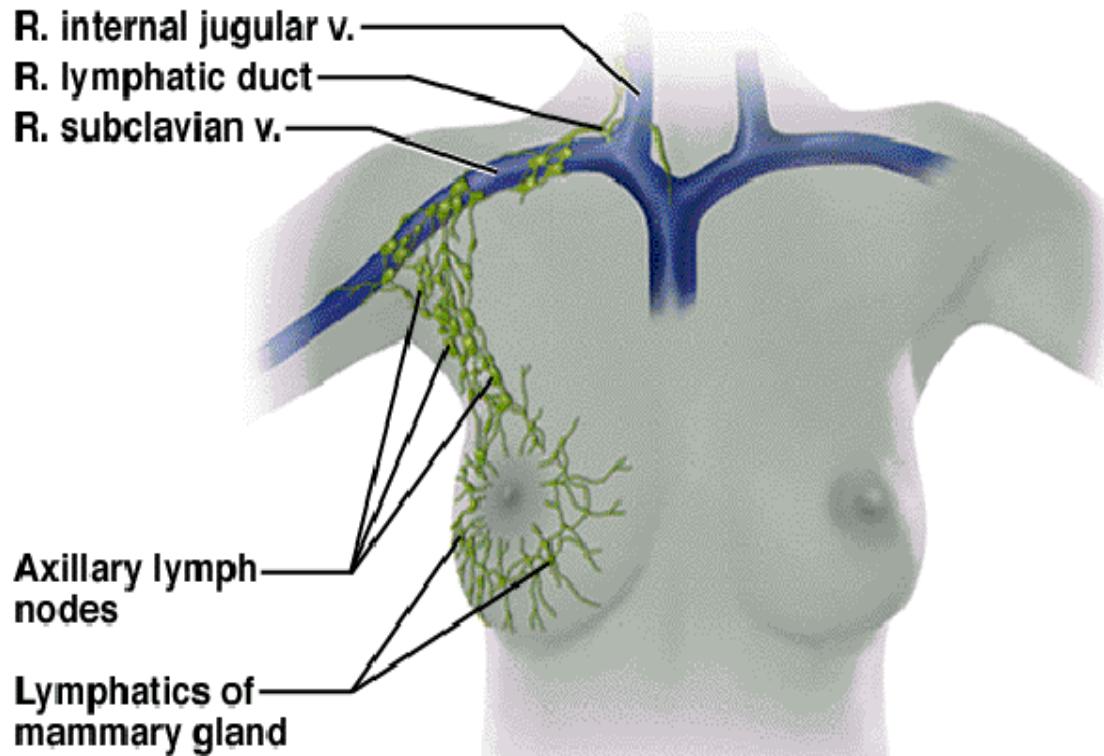
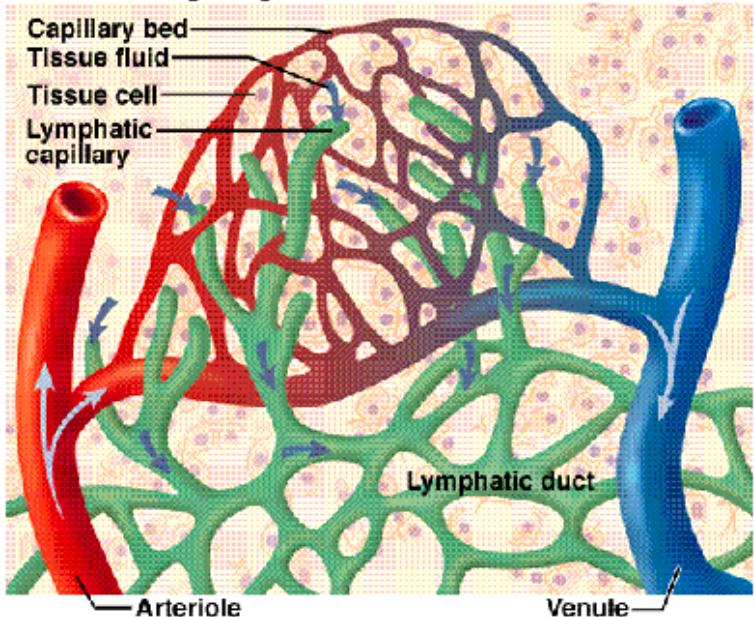


Elephantiasis

- blockage by parasitic worms



Role of Lymph Vessels in *Metastasis*



LYMPHATIC SYSTEMS

consists of:

- 1) *lymphatic vessels*
- 2) *lymphoid tissues* and
lymphoid organs



LYMPHOID TISSUE

- diffusely located throughout body in all organs
- contains ***germinal centers*** with dense population of B lymphocytes
- houses ***macrophages***
- Function: host defense

LYMPHATIC SYSTEMS

consists of:

- 1) *lymphatic vessels*
- 2) *lymphoid tissues* and
lymphoid organs



lymphoid organs

Include: *Lymph Nodes*

Spleen

Thymus

Tonsils

Function:

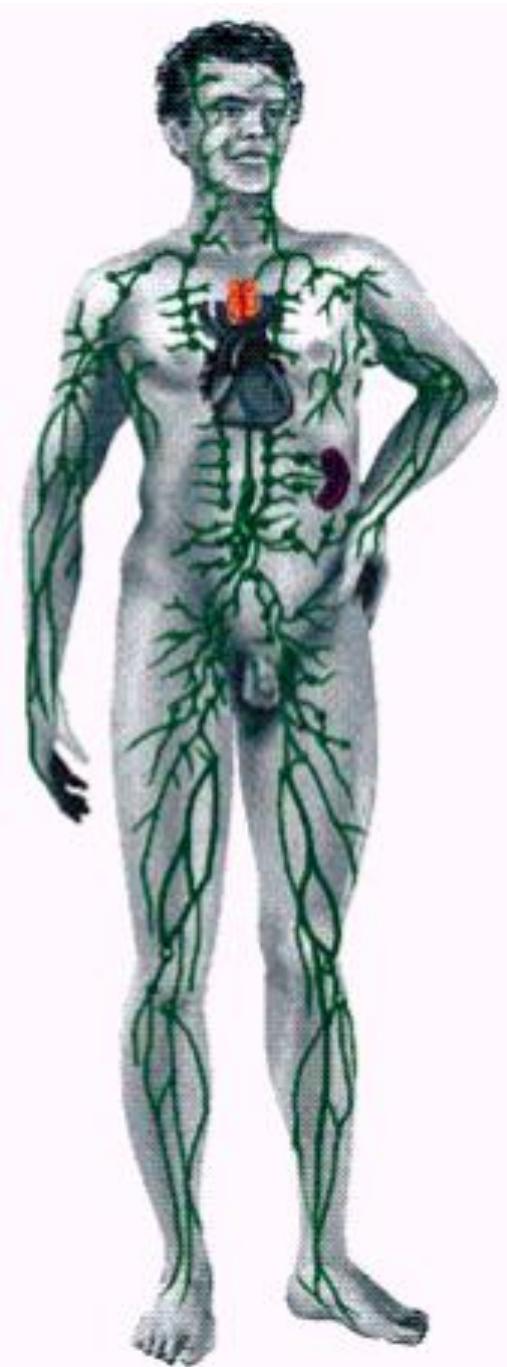
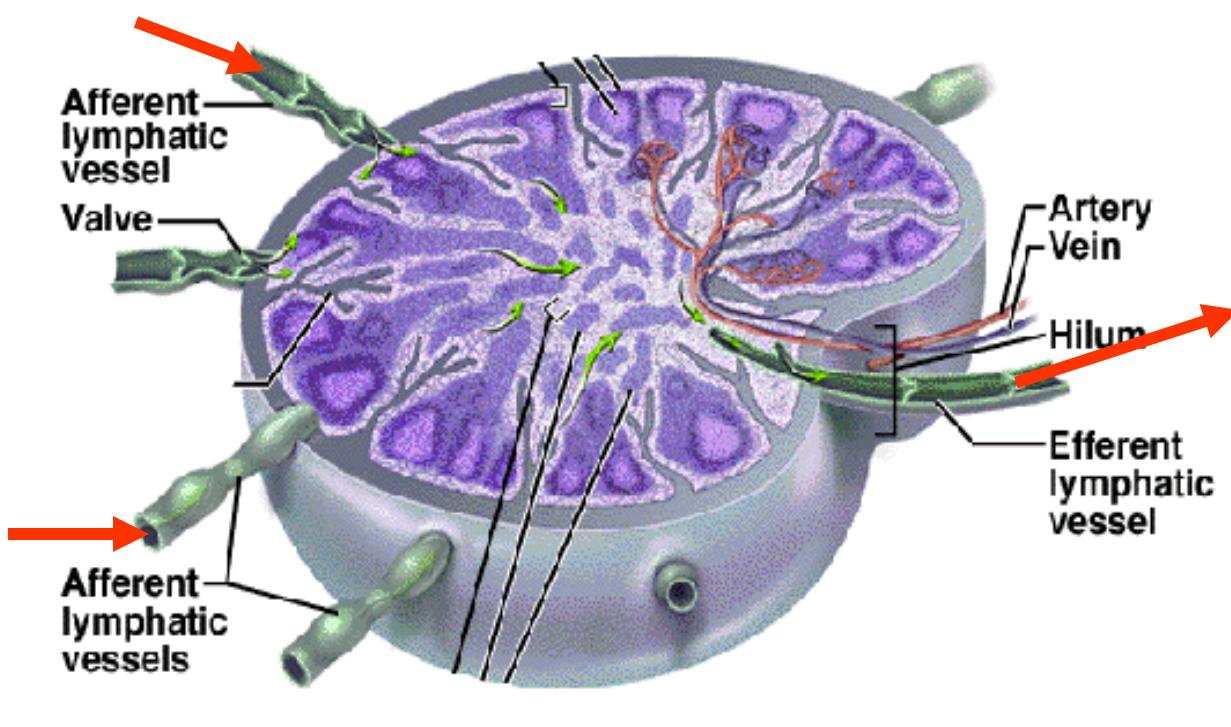
host defense

eliminates abnormal (sick, aged, or cancerous)
cells and pathogens

lymphoid organs

Lymph Nodes

Swollen lymph nodes is caused by expansion in the number of lymphocytes

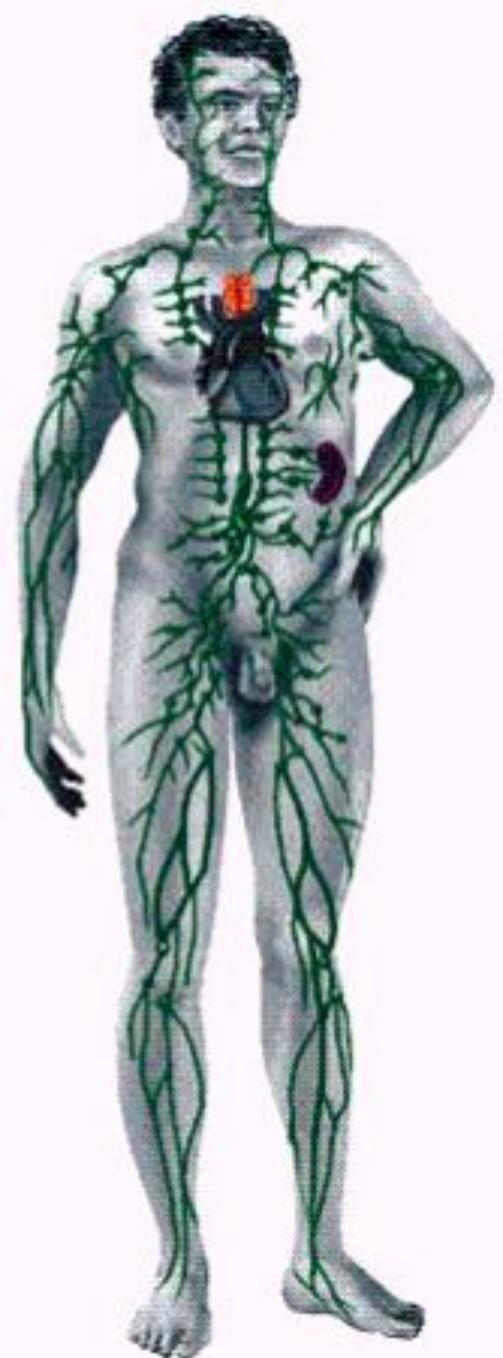


lymphoid organs

Lymph Nodes

Spleen

- site for immune surveillance and response
- removes debris, foreign matter, toxins, bacteria, viruses, old blood cells
- readily subject to rupture from mechanical trauma



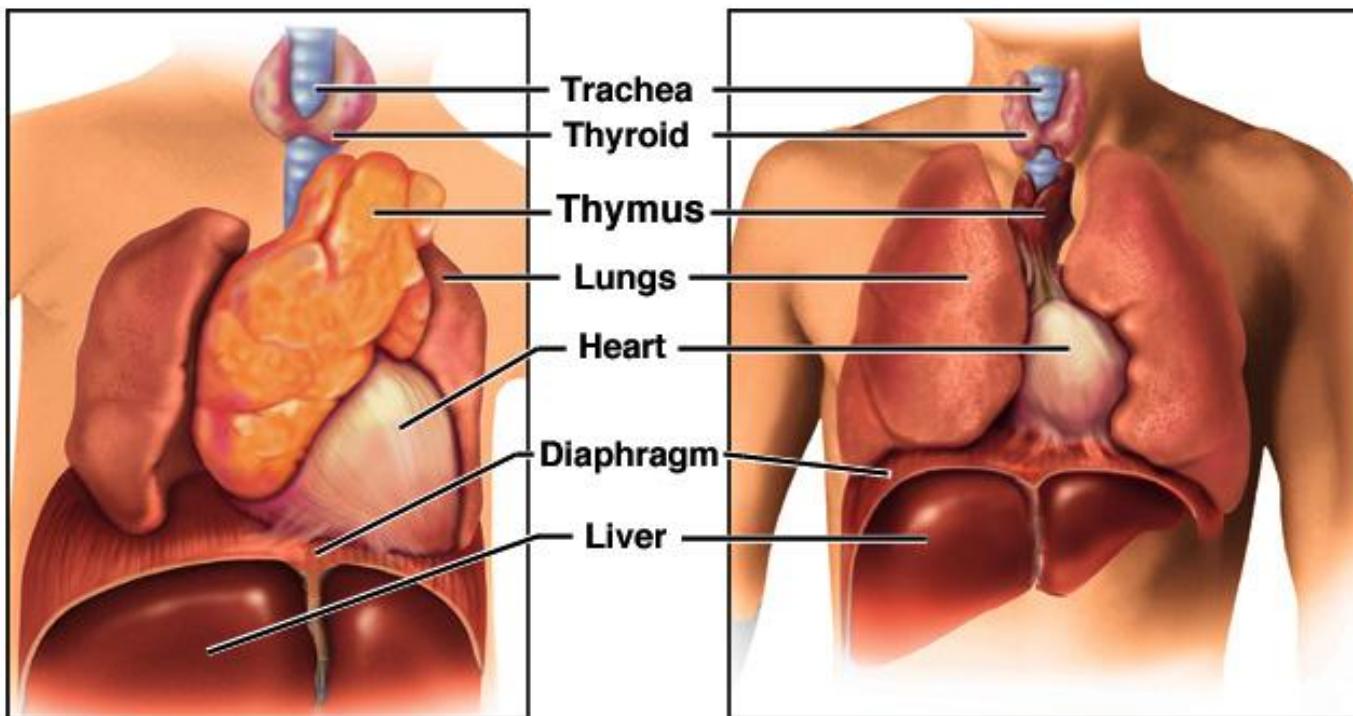
lymphoid organs

Lymph Nodes

Spleen

Thymus

- site of maturation of T lymphocytes
- secretes hormones (thymopoietin and thymosins)
- critical role in childhood



lymphoid organs

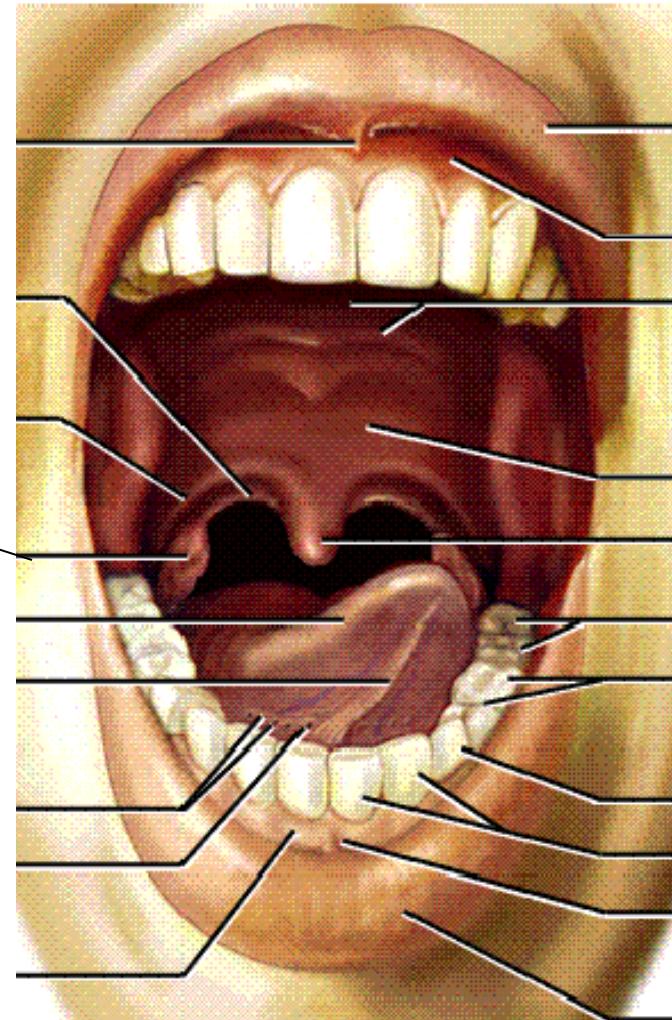
Lymph Nodes

Spleen

Thymus

Tonsils

- trap and destroy bacteria



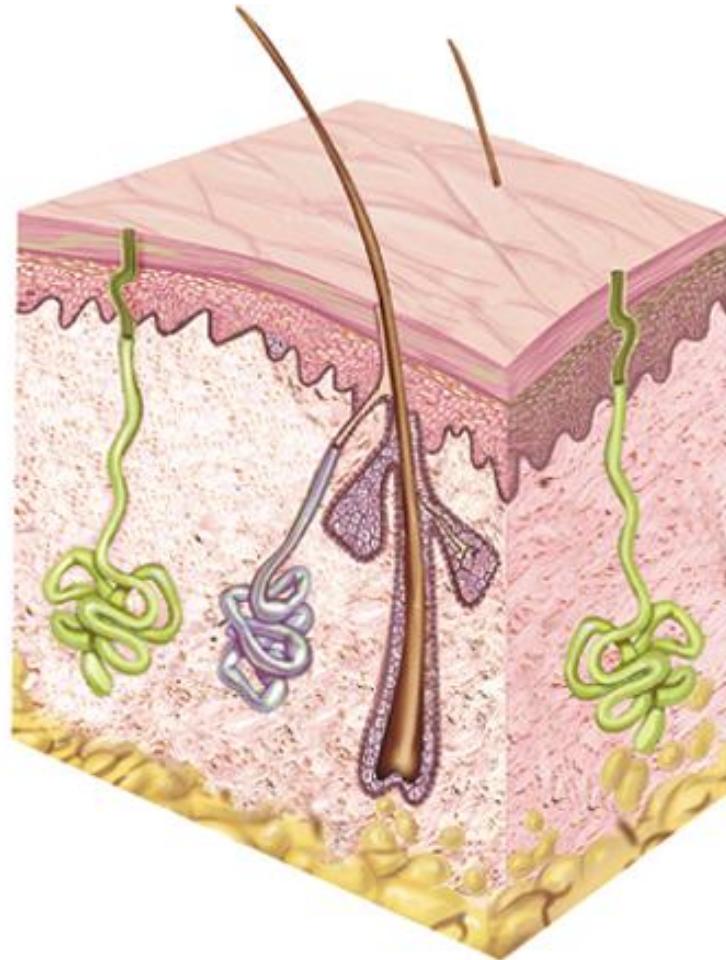
Defenses Against Pathogens

- 1) Nonspecific defenses - broadly effective, no prior exposure
 - 1) external barriers
 - 2) inflammation
 - 3) fever
- 2) Specific defense - results from prior exposure, protects against only a particular pathogen
 - immune system

1) External Barriers

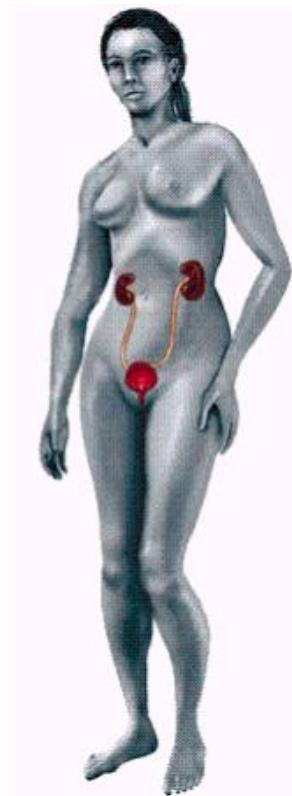
- Subepithelial areolar tissue

- tissue gel: viscous barrier of hyaluronic acid
 - hyaluronidase: enzyme used by pathogens (snake bites and bacterial toxins)



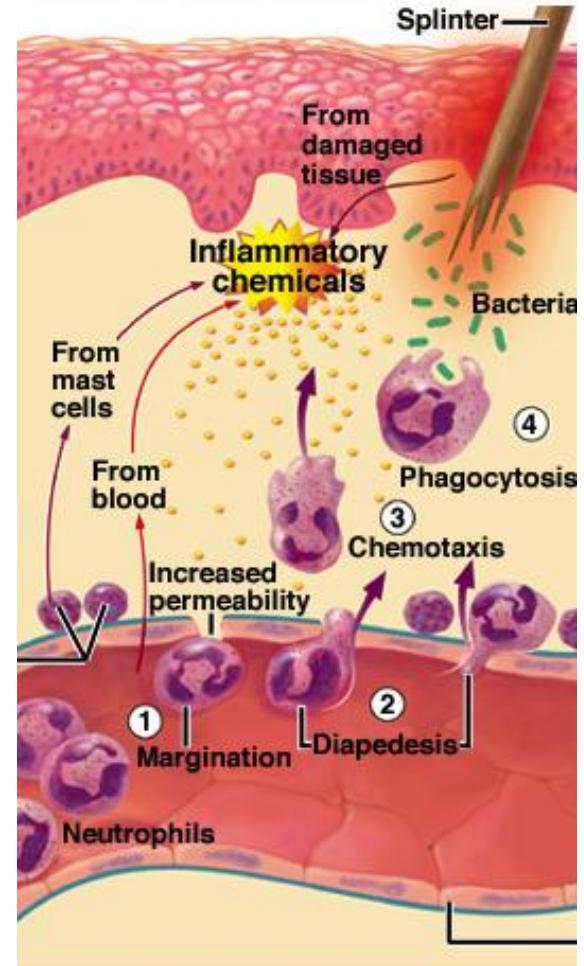
1) External Barriers

- Mucous membranes
 - stickiness of mucus
 - lysozyme: enzyme destroys bacterial cell walls



2) Non Specific Immunity - Inflammation

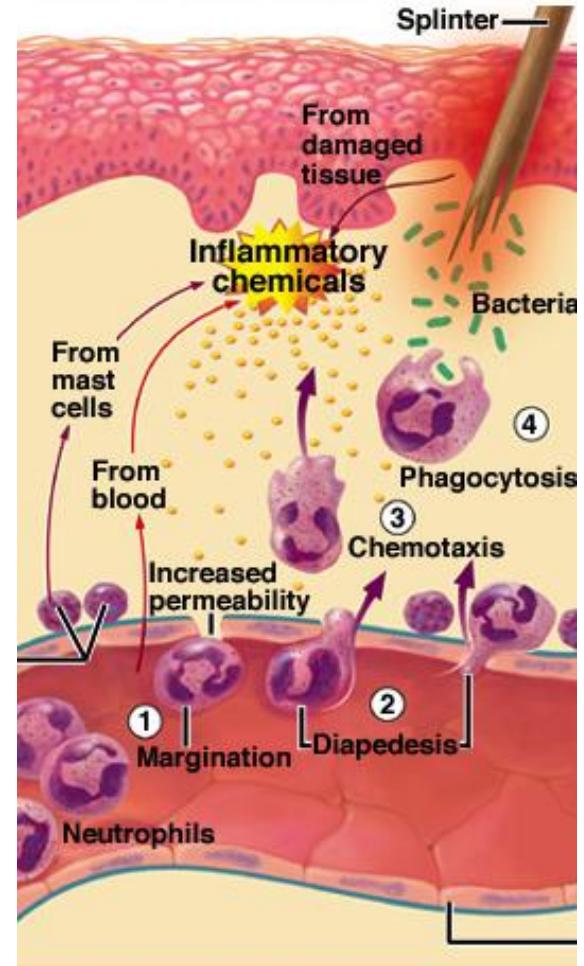
- **Defensive response to tissue injury**
 - limits spread of pathogens, then destroys them; removes debris, initiates tissue repair
 - suffix *-itis* denotes inflammation of specific organs



2) Inflammation

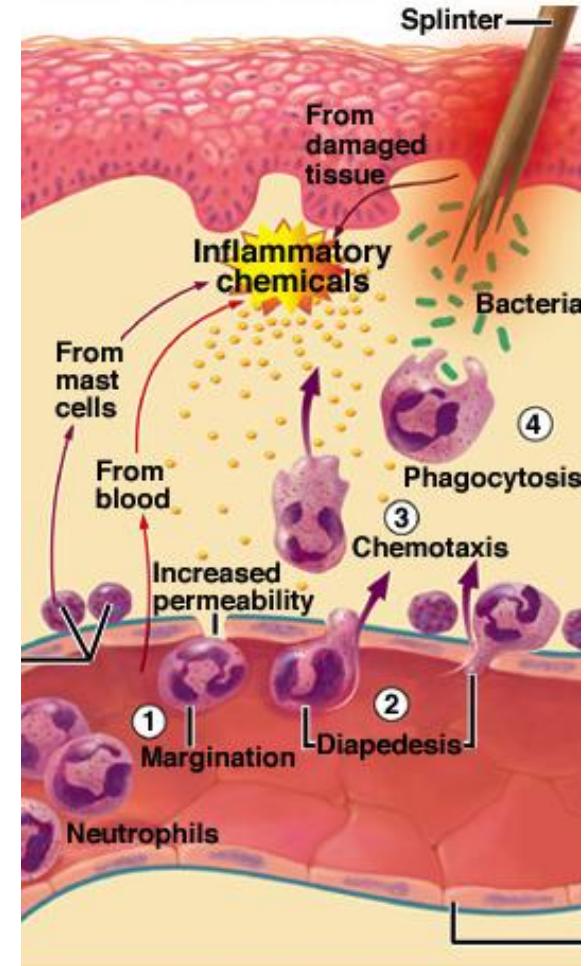
- Cardinal signs

- **redness** (erythema) caused by hyperemia (\uparrow blood flow)
- **swelling** (edema) caused by \uparrow capillary permeability and filtration
- **heat** caused by hyperemia
- **pain** caused by inflammatory chemicals and pressure on nerves



2) Inflammation

- **Inflammatory chemicals**
 - bradykinin, histamine, and leukotrienes
 - secreted by damaged cells, mast cells, basophils, lymphocytes, macrophages and platelets
 - stimulates vasodilation, increases capillary permeability, and induces pain.



Pain

- Causes
 - Direct injury to nerve endings
 - Inflammatory chemicals
 - Tissue swelling
- Brandykinin, Prostaglandins, and bacterial toxins can induce pain.
- Brandykinin, produced from a plasma protien, is released from basophils and mast cells
- Pain is an important signal to tissue repair, as it signals the body to rest and not further injury itself.

3) Fever

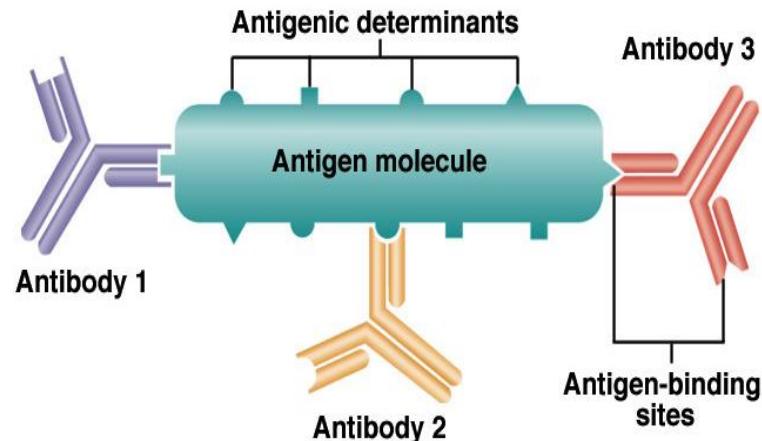
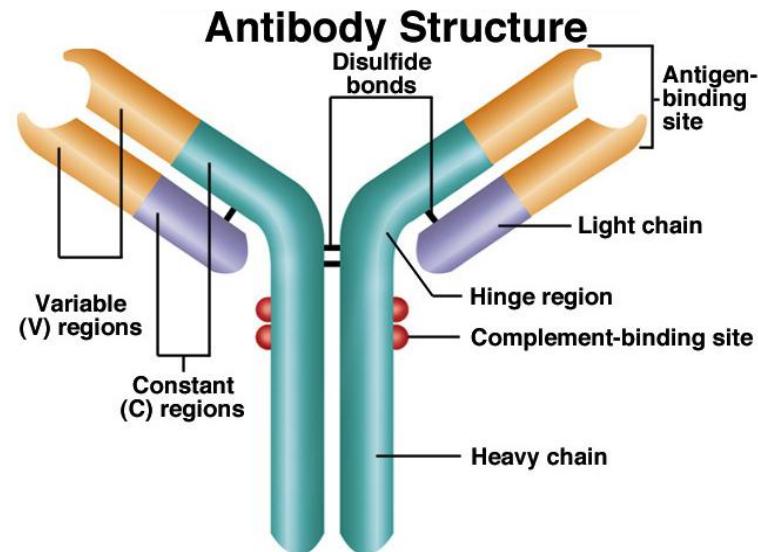
- Defense mechanism: can do more good than harm
 - promotes interferon activity
 - accelerating metabolic rate and tissue repair
 - inhibiting pathogen reproduction
- Pyrogen (fever-producing agent):
 - secreted by macrophages (endogenous) and microorganisms (exogenous)
 - stimulates anterior hypothalamus to secrete prostaglandin E which resets body thermostat higher

Specific Immunity

- 1) Humoral Immunity – based on B-cells and antibodies
 - 1) Recognition
 - 2) Attack
 - 3) Memory
- 2) Cellular Immunity – uses 4 types of T cells to promote immunity, regulate attack, attack, and remember.
 - Recognition
 - Attack
 - Memory

Antibodies and Antigens

- 1) **Antibody** – Y-shaped immunoglobins created to bind to various antigen-binding sites
- 2) **Antigen** – any molecule that triggers an immune response. Generally large and complex, making it distinguishable from self.



Humeral Immunity – Clonal Selection

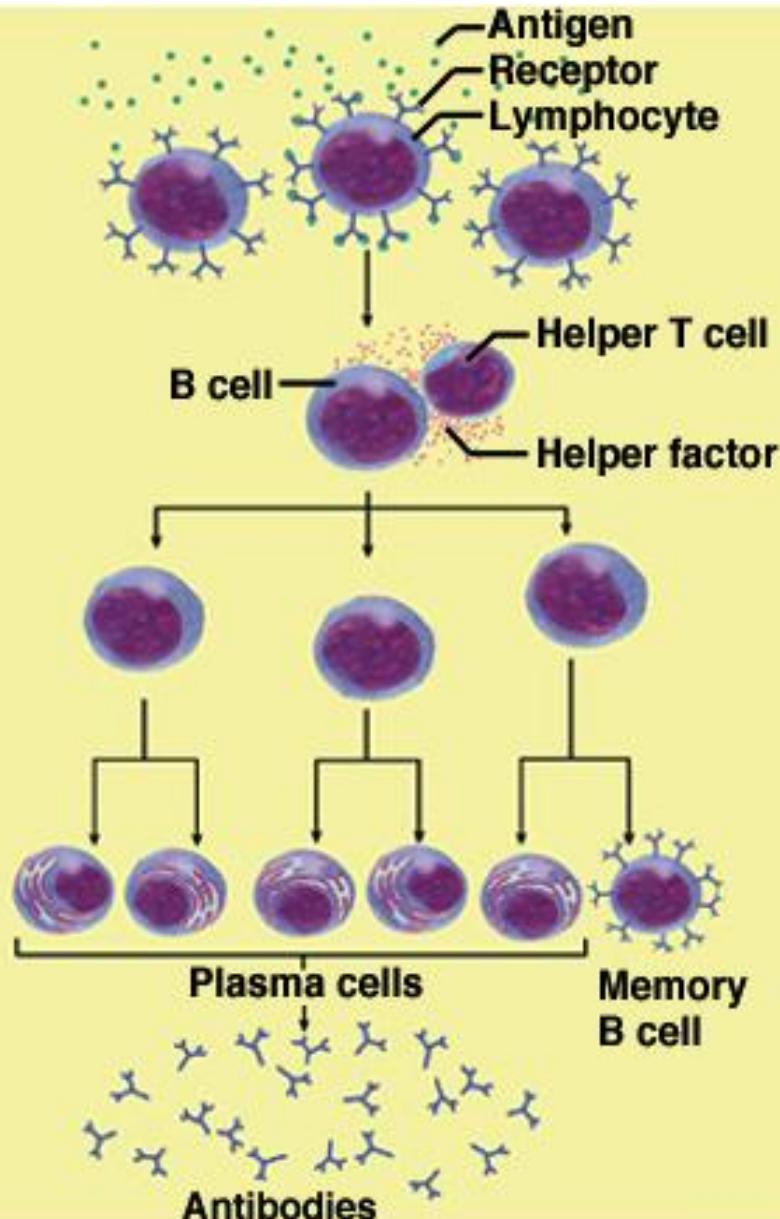
1. Immunocompetent B cells exposed to antigen. Antigen binds only to B cells with complementary receptors.

2. B cell displays processed antigen fragments. Helper T cell binds to B cell and secretes helper factor.

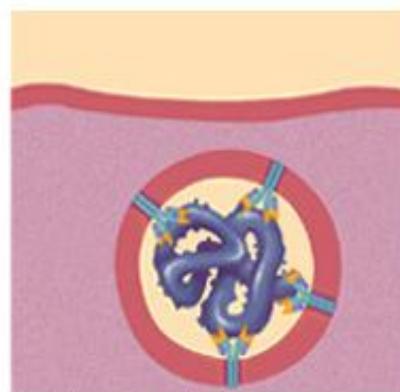
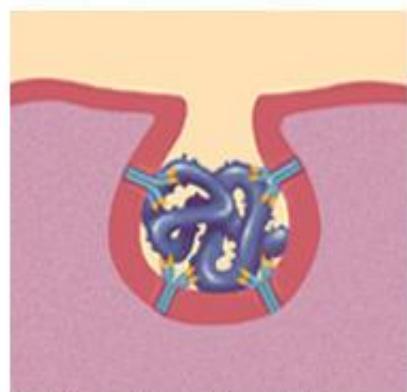
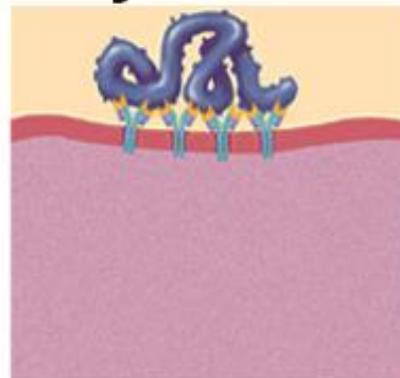
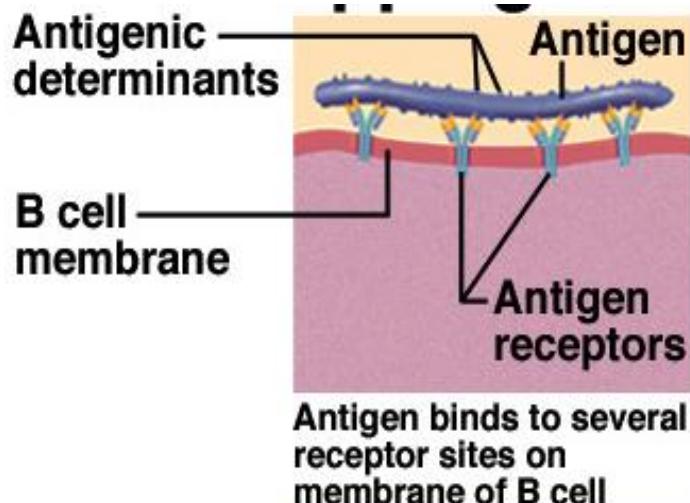
3. Helper factor stimulates B cell to divide repeatedly and form a clone.

4. Some cells of the clone become memory B cells. Most differentiate into plasma cells.

5. Plasma cells synthesize and secrete antibody.



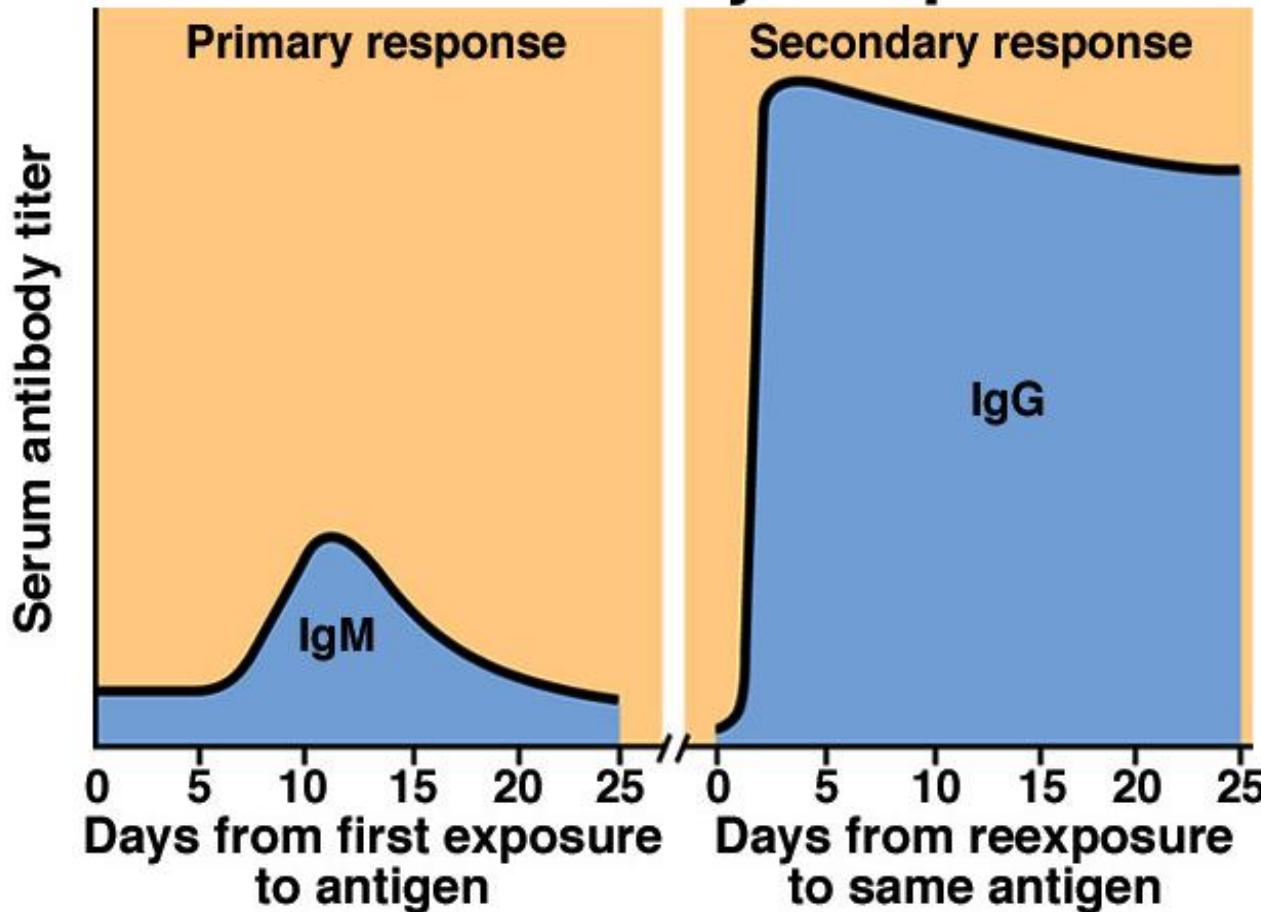
Humeral Immunity



B-cells are capable of identifying antigens through capping and endocytosis.

Long-term Immunity

Humoral Immunity Responses



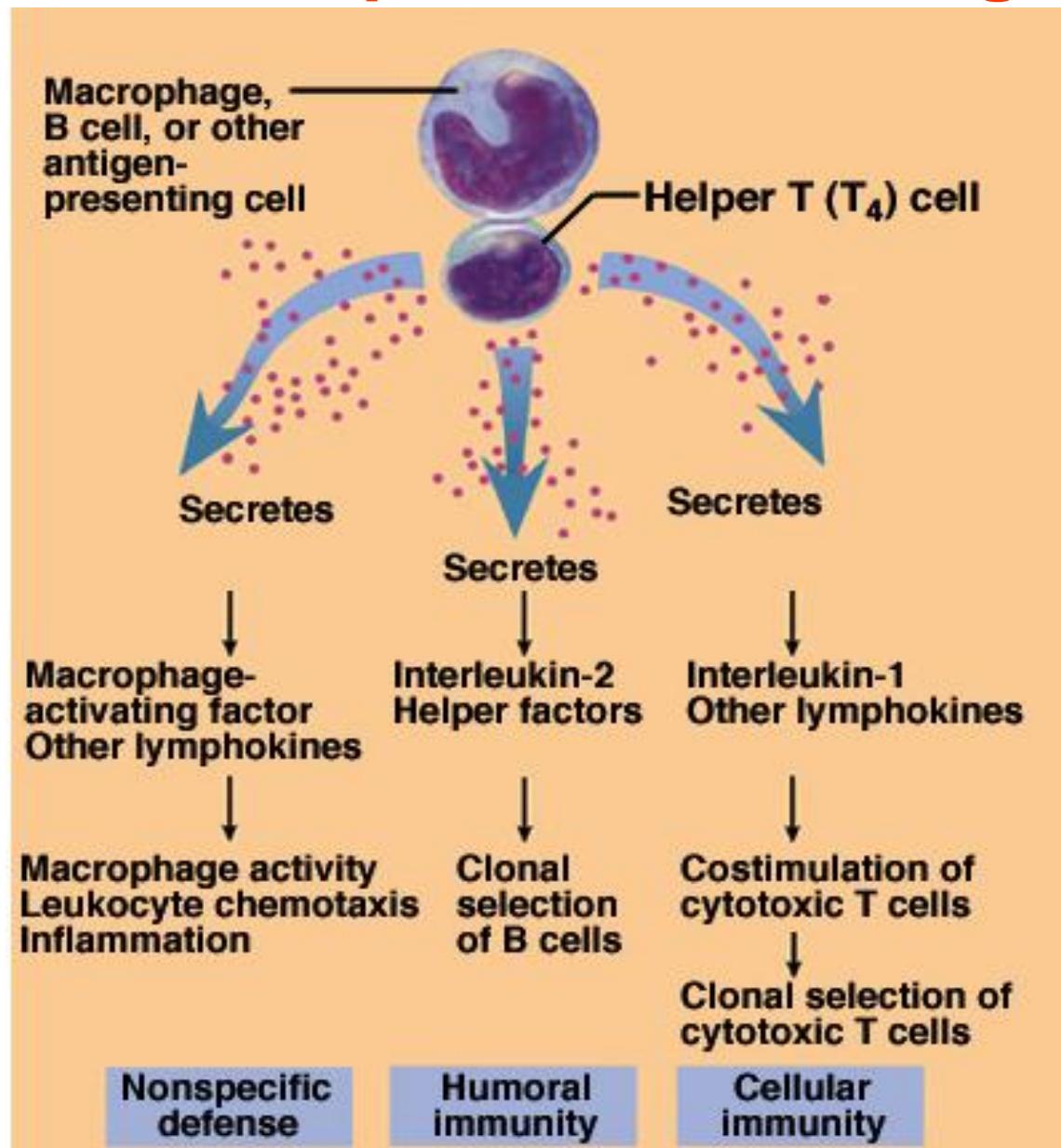
Ability to mount a large, aggressive response to repeat infections.

Cellular Immunity

- Types of T cells
 - 1) helper T cells (CD4)
 - 2) cytotoxic T cells (CD8)
 - 3) suppressor T cells
 - 4) memory T cells

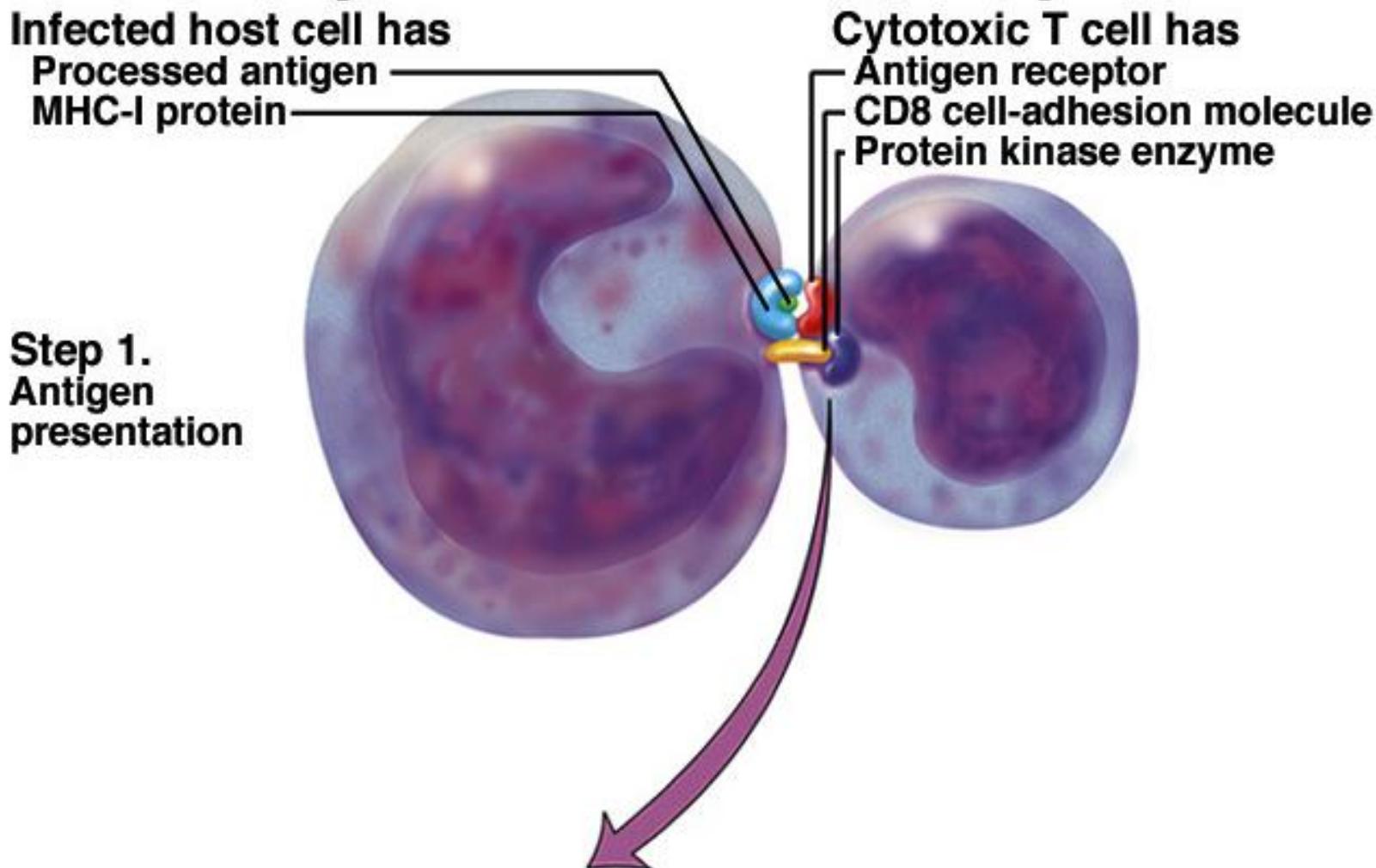
Helper T cells are involved in most aspects of immunity

Role of the helper T cell - Recognition



Cellular Immunity

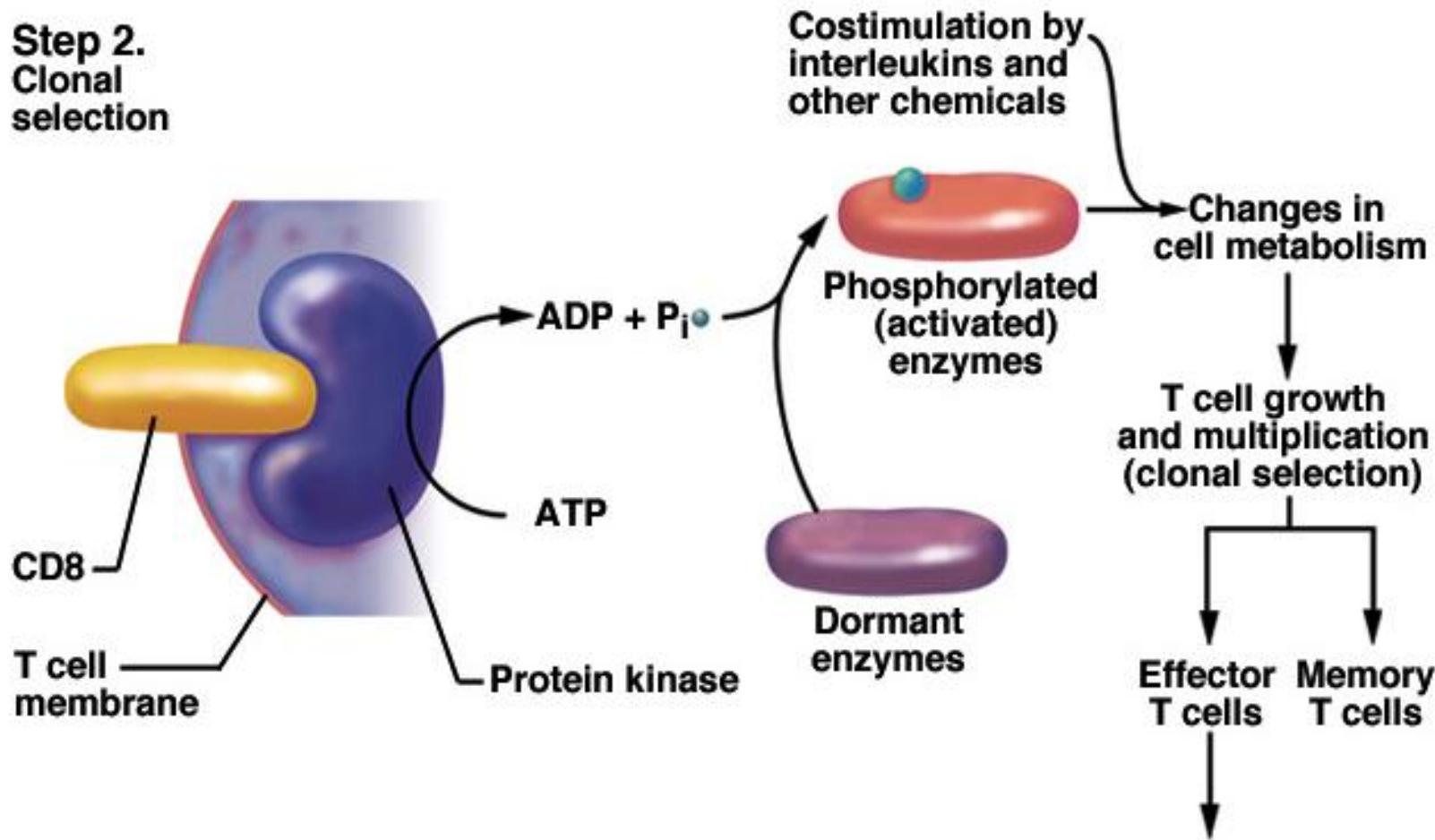
Activation and Attack of Cytotoxic T Cell, Step 1



Cellular Immunity

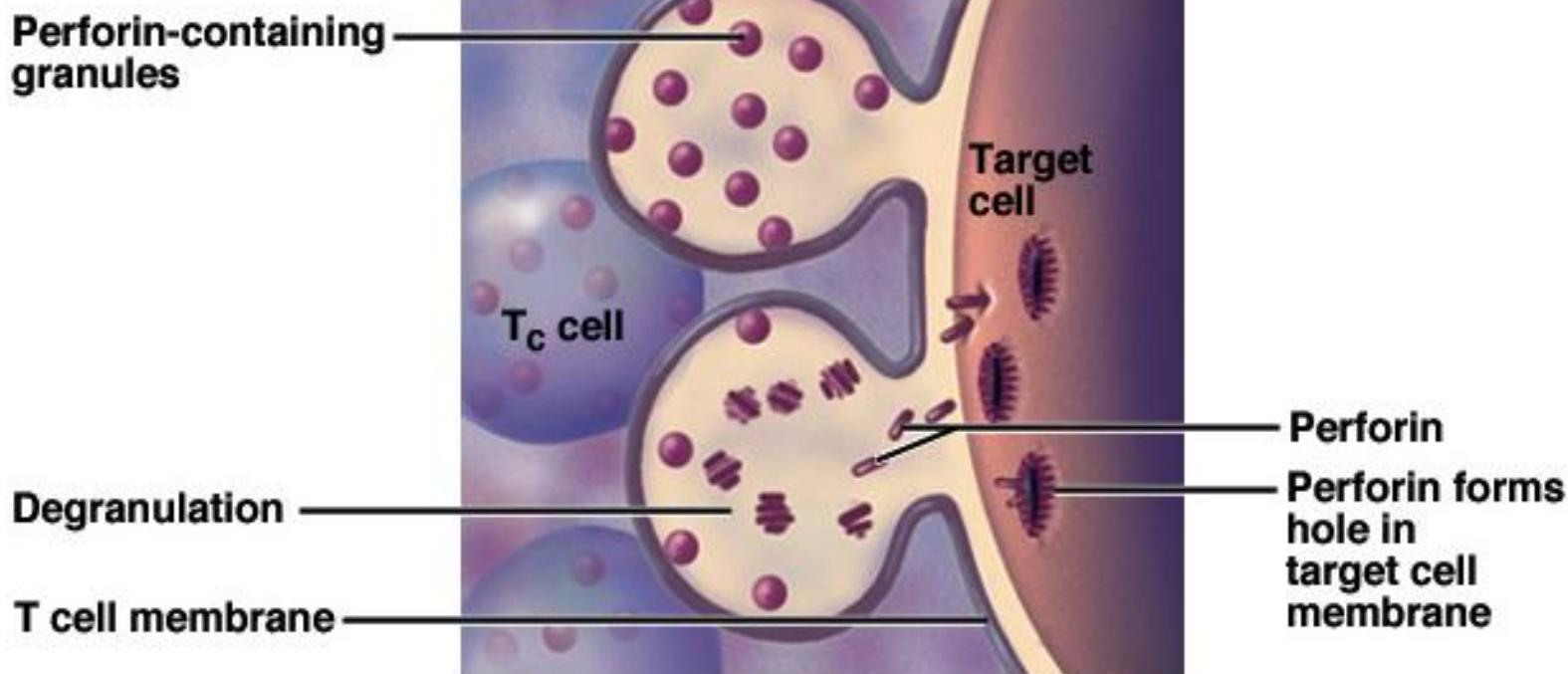
Activation and Attack of Cytotoxic T Cell, Step 2

Step 2.
Clonal selection



Cellular Immunity

Activation and Attack of Cytotoxic T Cell, Step 3



Step 3.
Lethal hit

Macrophage-activating factor
Migration-inhibiting factor
Tumor necrosis factor
Lymphotoxin
Interferons
Perforin

Cellular Immunity

- Cytotoxic T cells – attack enemy cells
 - 1) Perforin to punch holes in cell membrane
 - 2) Lymphotoxin attacks target cell's DNA
 - 3) Tumor necrosis kills tumor cells
- Suppressor T cells – release lymphokine that inhibit T and B cell activity, prevents the immune system from damaging self.
- Memory T cell – some T cells become memory after first attack. Second defense is faster like the second humeral response. Called the T cell recall response.

Immune System Disorders

- Hypersensitivity
- Autoimmune Disease
- Immunodeficiency Diseases

Hypersensitivity

Production of antibodies to substances most tolerate, ie allergies.

- **Type I (acute)** - Most common, starts within seconds and most often ends within 30 minutes.
 - Anaphylaxis – causes edema, mucus, and congestion
 - Asthma – reaction to inhaled allergen.
 - Causes massive release of histamine and spasmatic contraction of the bronchioles.
 - Anaphylactic shock – systemic response to an injected allergen.
 - Can cause bronchiolar constriction, circulatory shock, and possible death.
- **Type II (antibody-dependant cytotoxic)**- as in transfusion reaction.
- **Type III (immune complex)**- large antibody-antigen complexes that get trapped under the tunic interna of blood vessels and cause inflammation.
- **Type IV (delayed)**- occur 12 to 72 hours after exposure. Delay commonly associated with travel time to lymph nodes. Cosmetics and poison ivy hapten commonly do this.

Autoimmune Diseases

Failure of the immune system to distinguish self from foreign antigens.

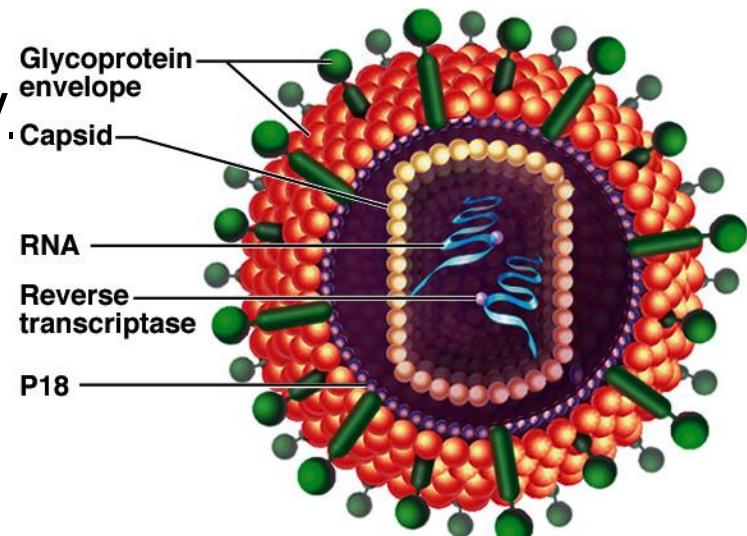
Immune systems produces antibodies against bodies own tissues.

Causes:

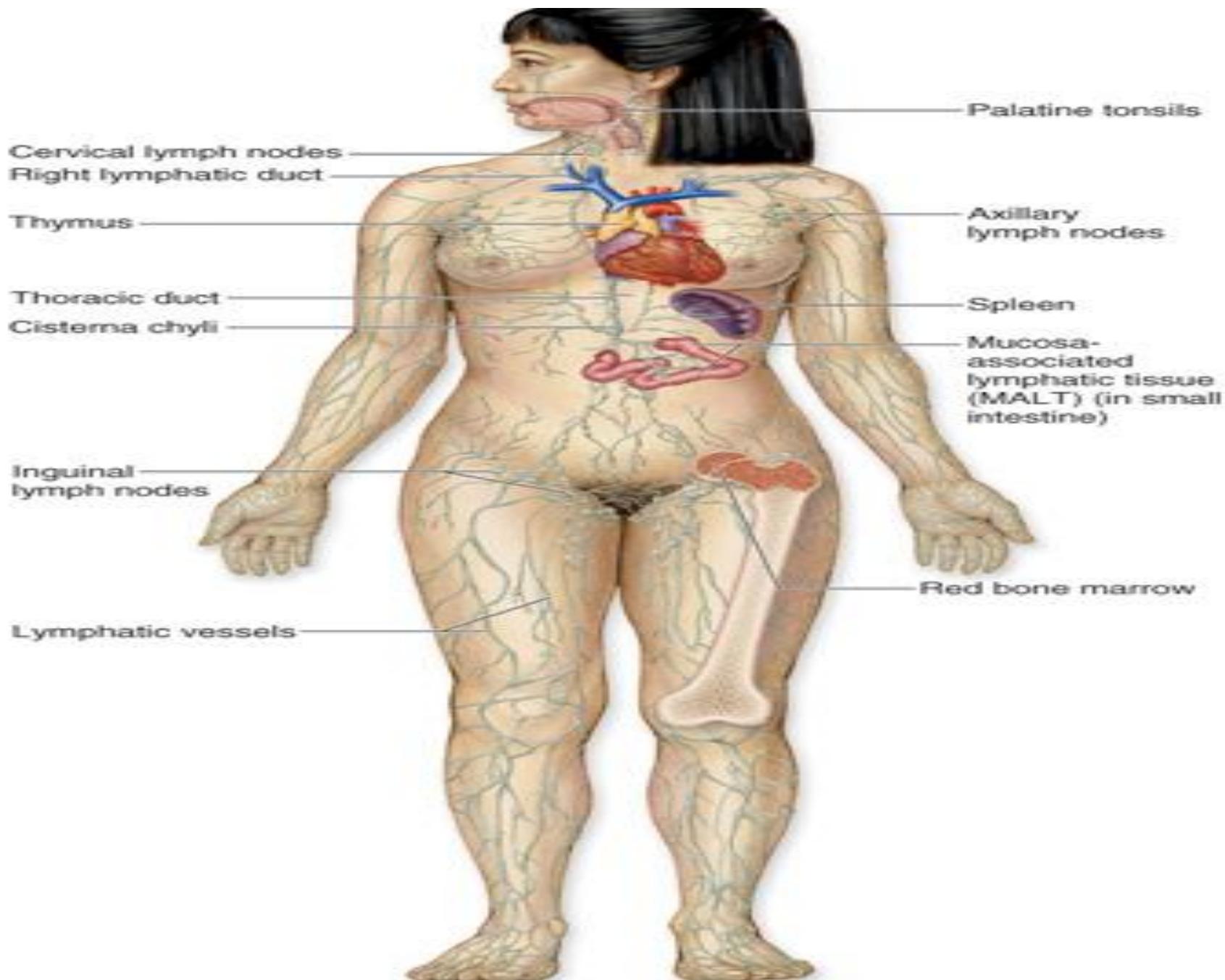
- Cross reactivity – fight against a foreign antigen leads to antibodies that attack self.
- Abnormal exposure to self-antigens in the blood
- Changes in the structure of self-antigens

Immunodeficiency Diseases

- **SCID** – Severe combined immunodeficiency disease
 - congenital deficiency of both T and B cells.
 - susceptible to opportunistic infections.
 - “Bubble babies”
- **AIDS** – Acquired Immunodeficiency diseases
 - Acquired after birth, like HIV.
 - HIV targets helper T cells
 - Without these cells, all 3 immune responses are hampered.
 - Most patients with AIDS die of opportunistic infections.



HIV virus



Lymphatic System

- Assists the cardiovascular system by transporting excess interstitial fluid (**lymph**) through lymphatic vessels.
- Lymph is filtered and checked for foreign or pathologic material, such as cancer cells and bacteria.
- Lymphatic structures contain certain cells that initiate an **immune response** to abnormal materials and perform other functions essential to **homeostasis** and survival.
- Without the **primary immune response** by the lymphatic system, the body would be unable to **fight infection** and keep itself healthy.

Functions of the Lymphatic System

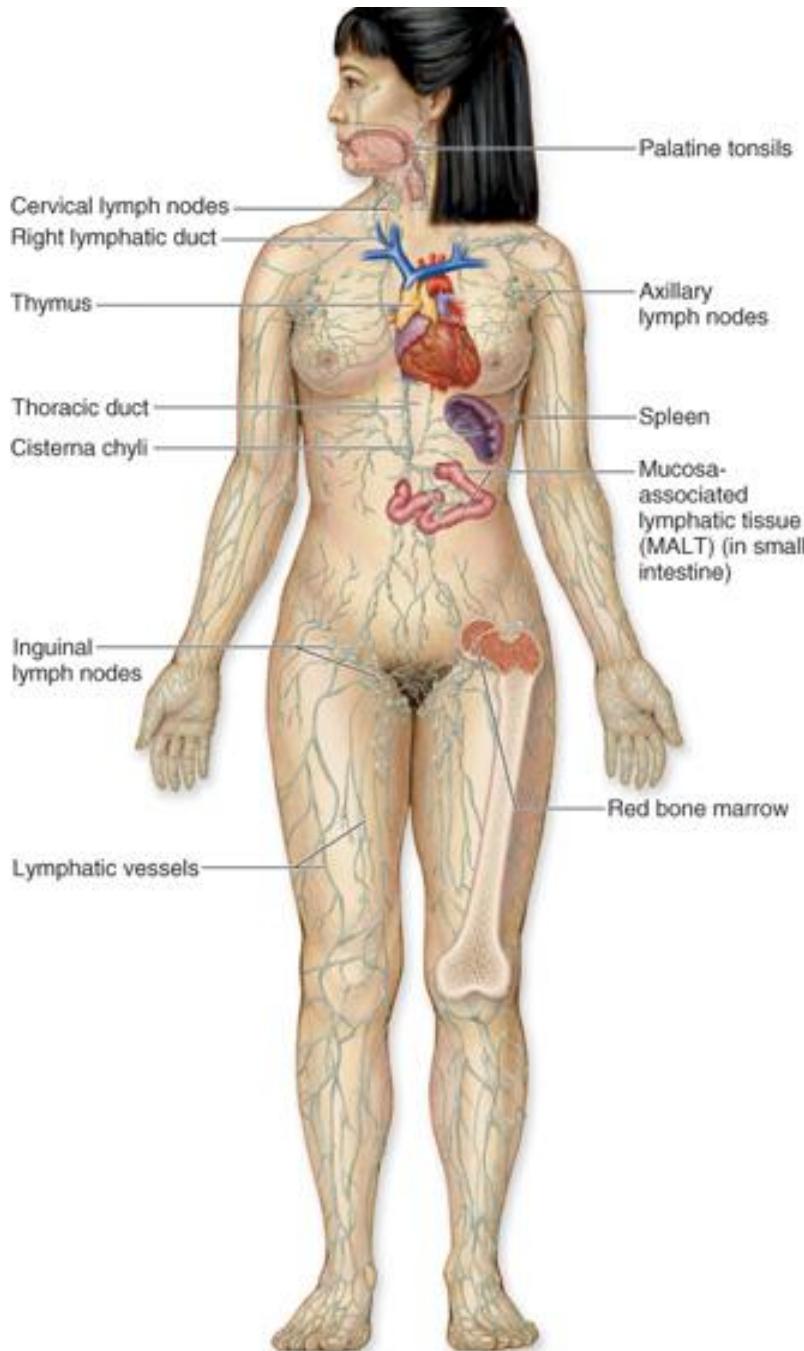
- Fluid and nutrient transport, lymphocyte development, and the immune response.
- Reabsorbs excess interstitial fluid:
 - returns it to the venous circulation
 - maintain blood volume levels
 - prevent interstitial fluid levels from rising out of control.
- Transport dietary lipids:
 - transported through lacteals
 - drain into larger lymphatic vessels
 - eventually into the bloodstream.

Immune Response

- Some cells (B lymphocytes) produce soluble proteins called **antibodies**.
 - bind to and immobilize the foreign or abnormal agent
 - damaging it or identifying it to other elements of the immune system
- Other cells (T lymphocytes) **attack** and destroy the antigen **directly**.
- Other cells become **memory cells** (B and T):
 - remember the past antigen encounters
 - initiate an even **faster** and more powerful response should the same antigen appear again

Components of the Lymphatic System

- Lymph
- Lymphatic Vessels
 - Lymphatic Capillaries
 - Lymphatic Vessels
 - Lymphatic Trunks
 - Lymphatic Ducts
- Lymphatic Organs
 - Thymus
 - Lymph Nodes
 - Spleen



Lymphatic Capillaries

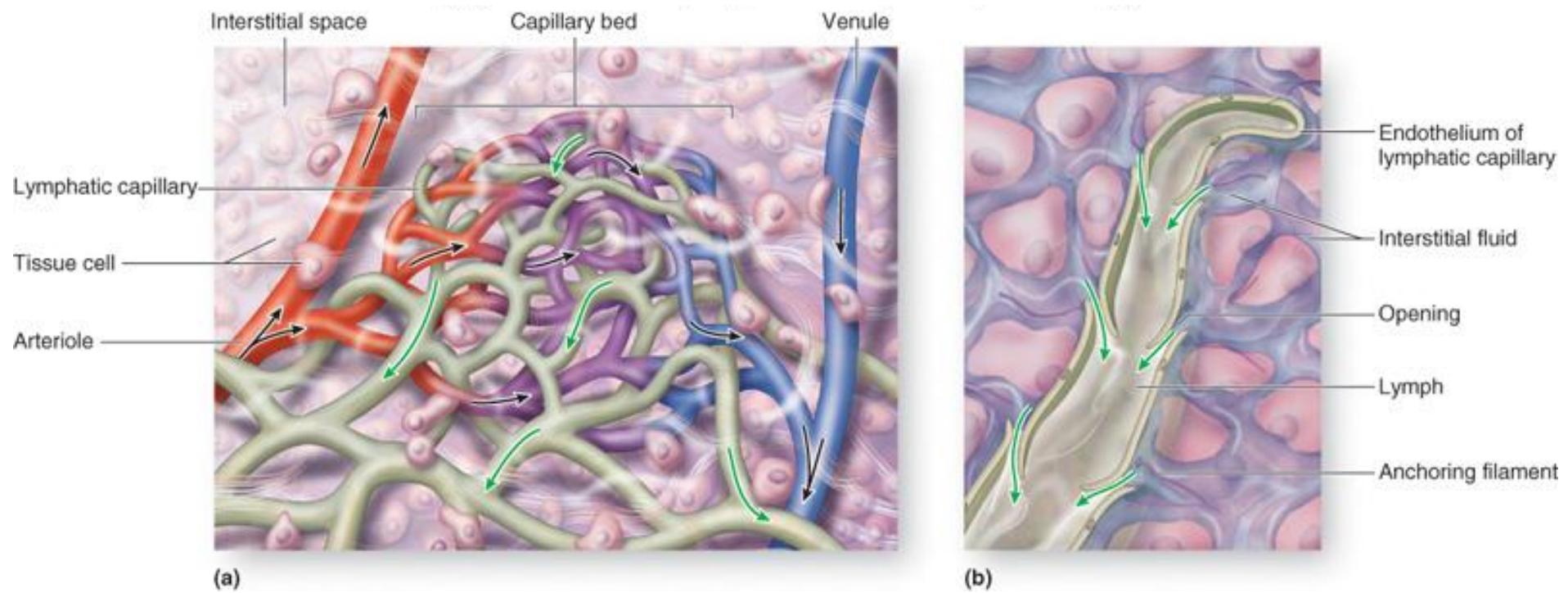
- The lymphatic network begins with microscopic vessels called lymphatic capillaries.
 - closed-ended tubes that are found in most blood capillary networks
 - similar to a blood capillary in that its wall is an endothelium
 - tend to be larger in diameter, lack a basement membrane, and have overlapping endothelial cells
 - anchoring filaments help hold these endothelial cells to the nearby tissues

Lymphatic Capillaries

- Act as one-way valves.
 - when interstitial fluid pressure rises, the margins of the endothelial cell walls push into the lymphatic capillary lumen and allow interstitial fluid to enter
 - when the pressure increases in the lymphatic capillary, the cell wall margin pushes back into place next to the adjacent endothelial cell
 - fluid “trapped” in the lymph capillary cannot be released back into the tissues

Lymphatic Capillaries – Lacteals

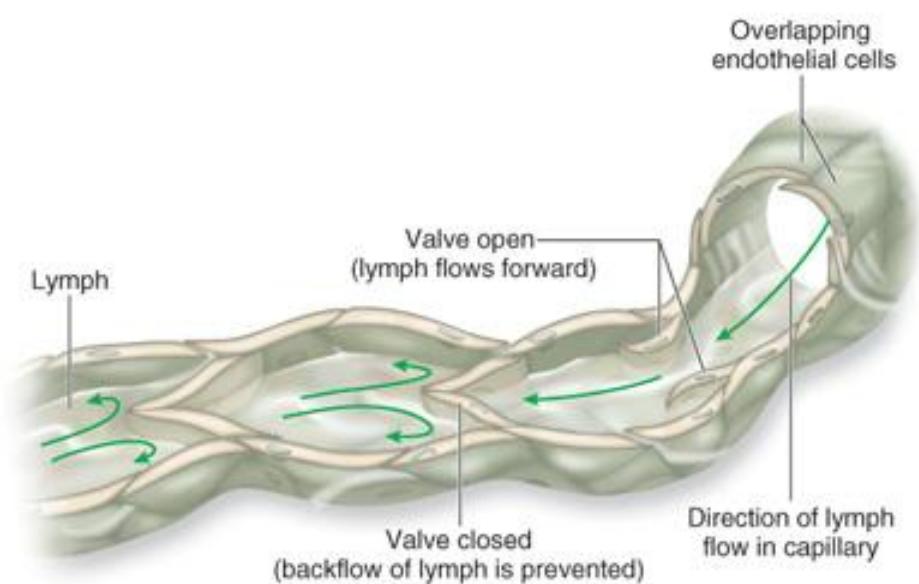
- The **small intestine** contains special types of lymphatic capillaries called lacteals.
- **Lacteals** pick up not only interstitial fluid, but also dietary lipids and lipid-soluble vitamins.
- The lymph of this area has a milky color due to the lipid and is also called **chyle**.



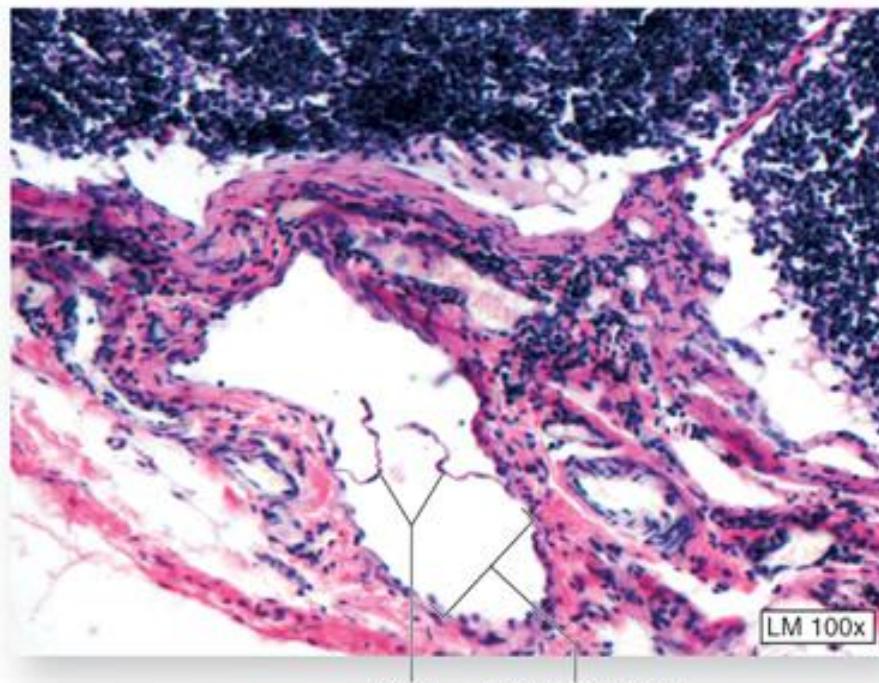
Lymphatic Vessels

- Lymphatic capillaries merge to form larger structures.
- Lymphatic vessels **resemble small veins**.
 - both contain three tunics and both have valves
- Some vessels connect directly to lymphatic organs called **lymph nodes**.
- Afferent lymphatic vessels bring lymph to a lymph node where it is examined for foreign or pathogenic material.
- Once filtered, the lymph exits the lymph node via **efferent** lymphatic vessels.
- Lymph nodes are often found in **clusters**.
 - lymph is **repeatedly examined** for the presence of foreign or pathogenic materials

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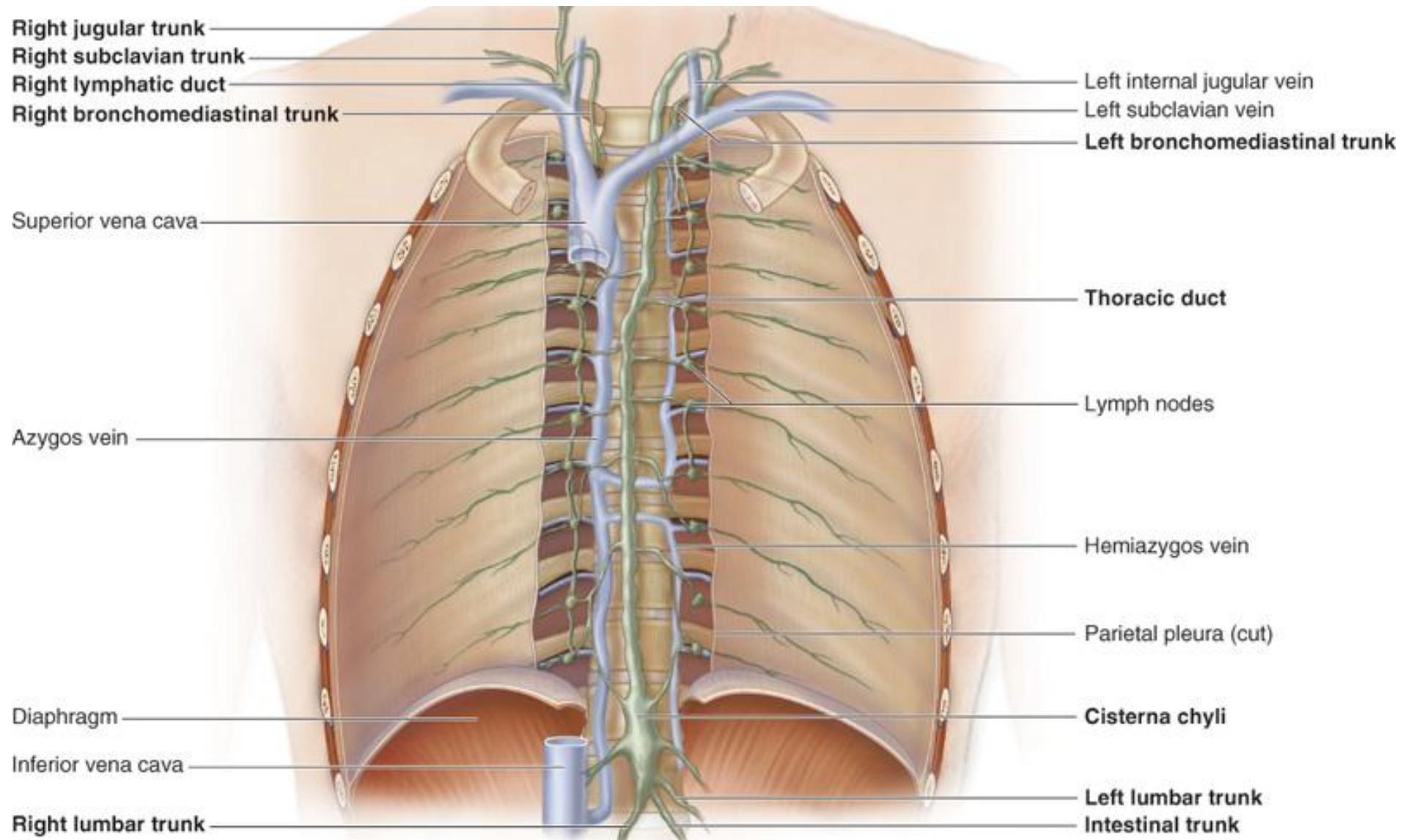
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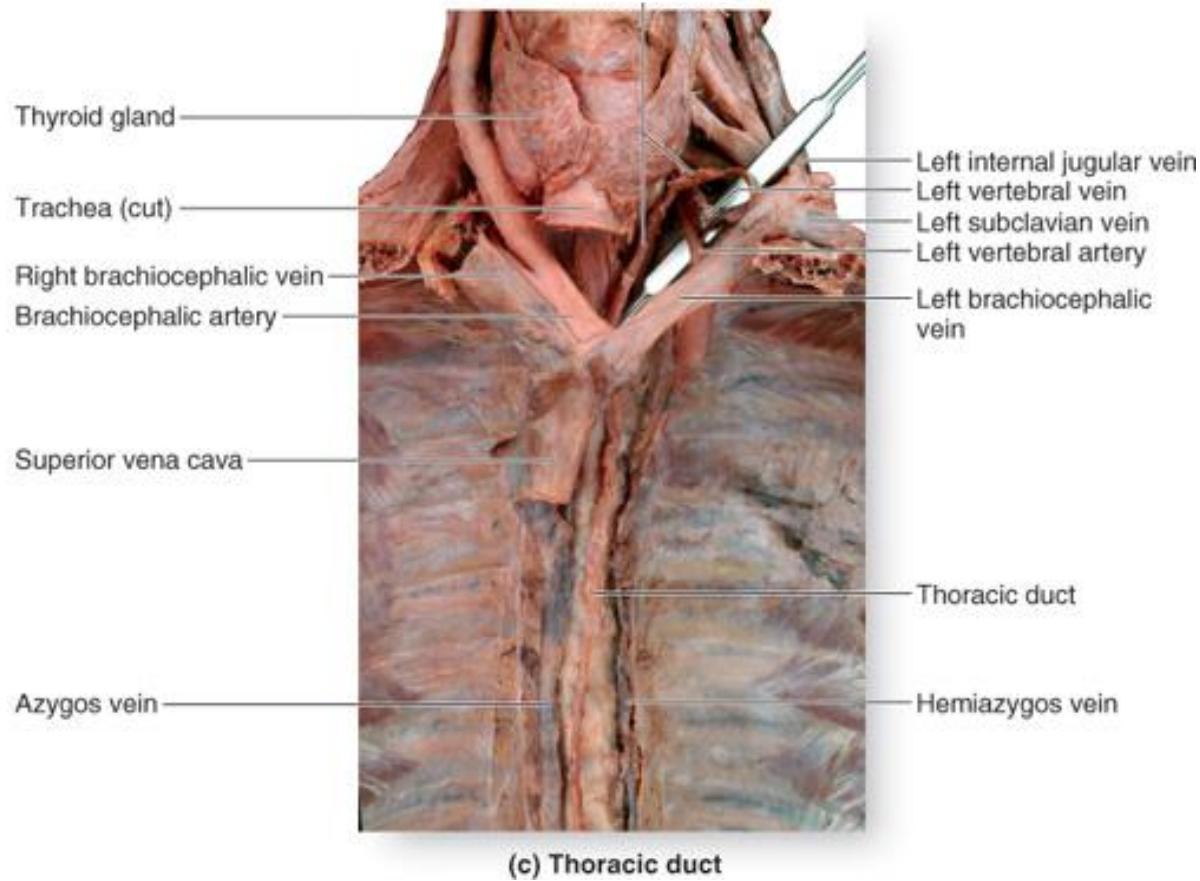
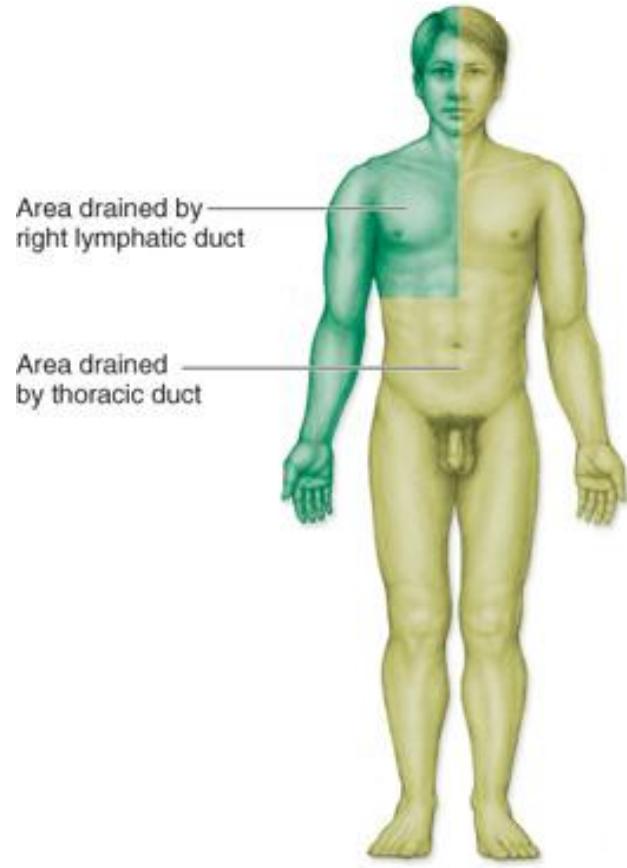
(b)

Trunks and Ducts

- Trunks:
 - Jugular
 - Subclavian
 - Bronchomediastinal
 - Intestinal
 - Lumbar
- Ducts:
 - Right Lymphatic Duct
 - Into right subclavian vein/right internal jugular junction
 - Thoracic Duct:
 - Into left subclavian vein/left internal jugular junction
 - Cisterna chyli
 - Drains most of the body



(a) Posterior thoracic wall, anterior view



Lymphatic Cells

- Also called lymphoid cells.
- Located in both the lymphatic system and the cardiovascular system.
- Work together to elicit an immune response.
- Types of lymphatic cells are:
 - macrophages
 - epithelial cells
 - dendritic cells
 - lymphocytes

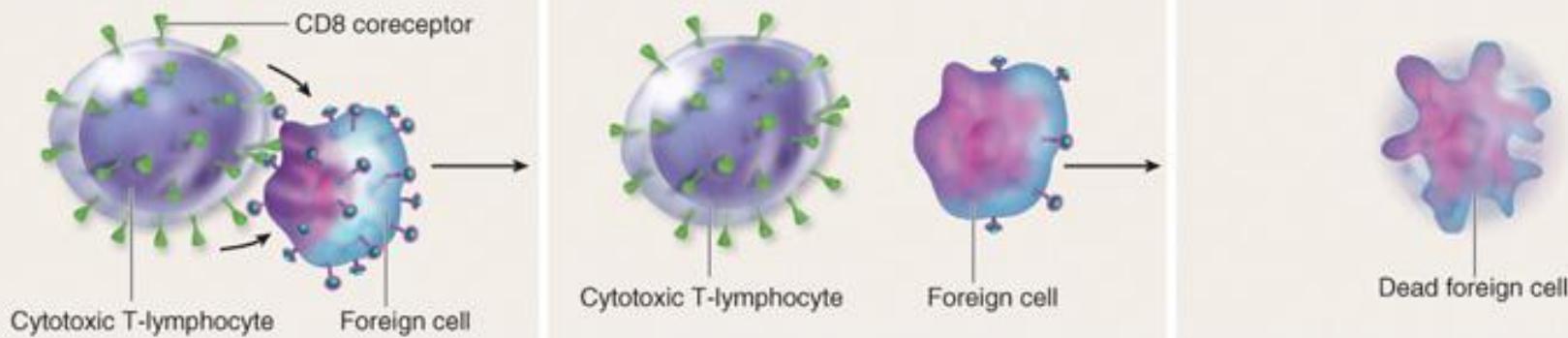
Types and Functions of Lymphocytes

- T-lymphocytes (also called T-cells).
- B-lymphocytes (also called B-cells).
- NK cells.
- Migrate through the lymphatic tissues and monitor them for the presence of antigens.
- Identified according to the tissue or organ where they mature:
 - T-lymphocytes mature in the Thymus
 - B-lymphocytes mature in the Bone marrow

Types and Functions of Lymphocytes – T-lymphocytes

- Make up about 70–85% of body lymphocytes.
- Plasma membrane contains a coreceptor that can recognize a particular antigen.
- There are several types of T-lymphocytes, each with a particular kind of coreceptor.
 - helper T-lymphocytes
 - cytotoxic T-lymphocytes

(b) Cytotoxic T-lymphocyte



① In response to a signal from a helper T-lymphocyte, CD8 coreceptors in cytotoxic T-lymphocyte attach to a foreign cell and initiate processes for cell death.

② Cytotoxic T-lymphocyte detaches from foreign cell.

③ Foreign cell dies.

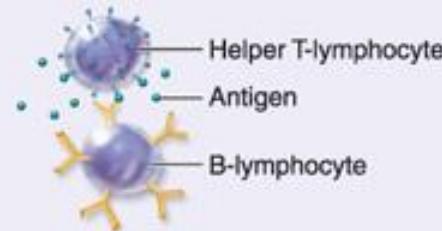
B-Lymphocytes

- Make up about 15–30% of the lymphocytes in the body.
- Contain antigen receptors that respond to one particular antigen and cause the production of immunoglobulins (Ig), or antibodies, that respond to that particular antigen.
 - the five main classes of immunoglobulins are called IgG, IgA, IgD, IgM, and IgE.
 - these immunoglobulins are released by the specific B-lymphocytes to immobilize or neutralize specific antigens

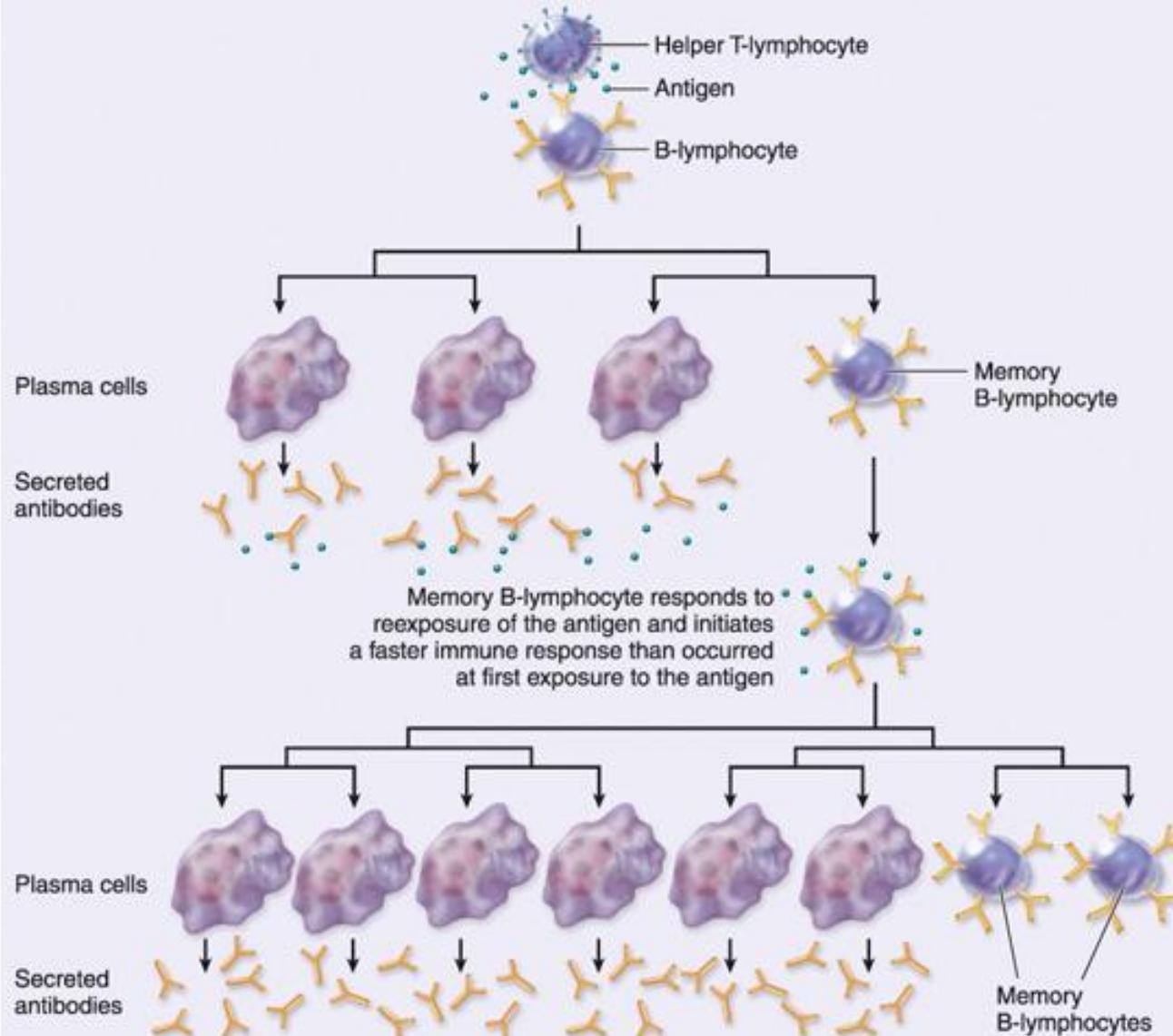
Vaccines

- Some vaccines introduce milder or dead forms of an antigen.
- The body can fight and eliminate the illness before any symptoms ever develop.
- Depending upon the life span of the particular memory B-lymphocytes:
 - vaccine may provide lifelong immunity, or
 - periodic booster shots may be needed

1 Helper T-lymphocyte secretes cytokines and presents an antigen to a B-lymphocyte.



2 B-lymphocyte divides, differentiating into plasma cells and memory B-lymphocytes.



3 Plasma cells secrete antibodies that immobilize the antigen, and then die in 4 to 5 days. Memory B-lymphocytes remain to protect against future attacks by the same antigen.

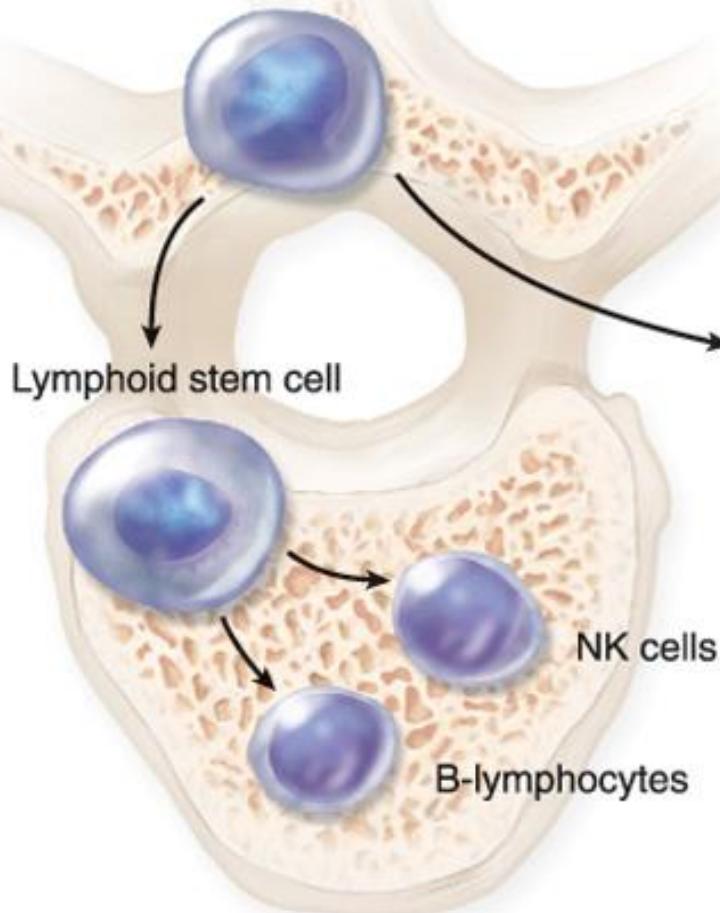
4 If the same antigen enters the body at a later time, the memory B-lymphocytes divide to make more plasma cells and memory cells.

NK Cells

- Also called large granular lymphocytes.
- Make up the remaining small percentage of body lymphocytes.
- NK cells tend to have CD16 receptors.
- NK cells can kill a wide variety of infected cells and some cancerous cells.

Red Bone Marrow

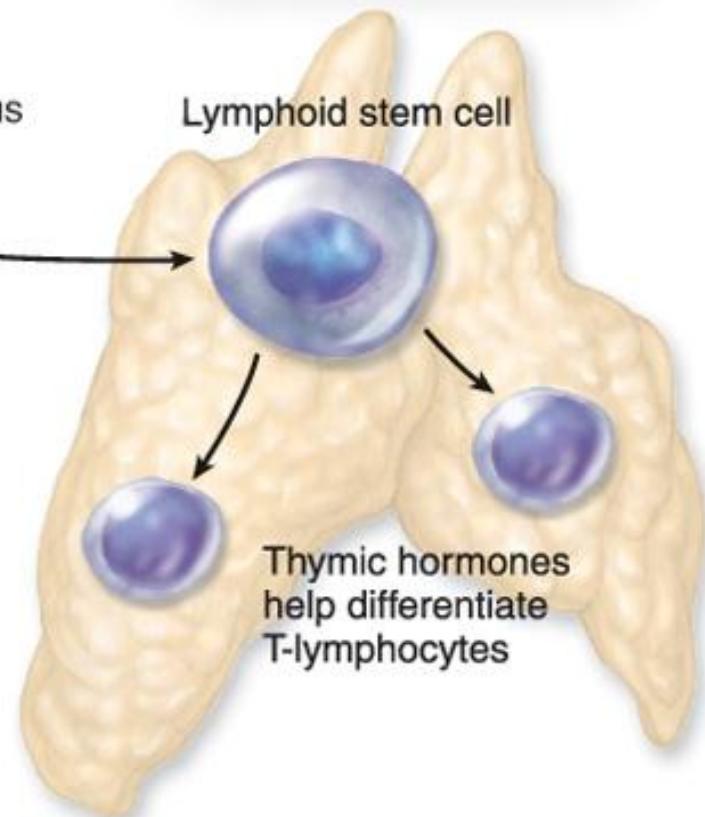
Hemopoietic stem cell



(a) B-lymphocyte and NK cell maturation
(in red bone marrow)

Thymus

Lymphoid stem cell



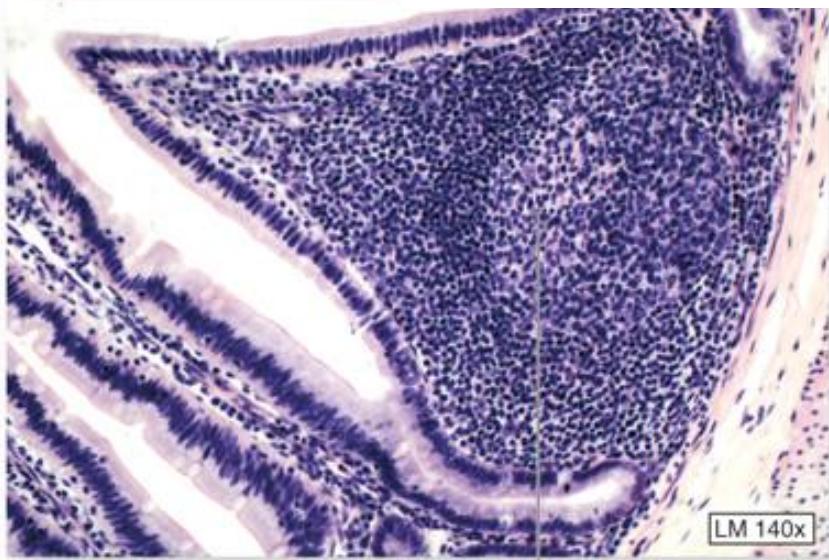
(b) T-lymphocyte maturation
(in thymus)

Lymphatic Nodules

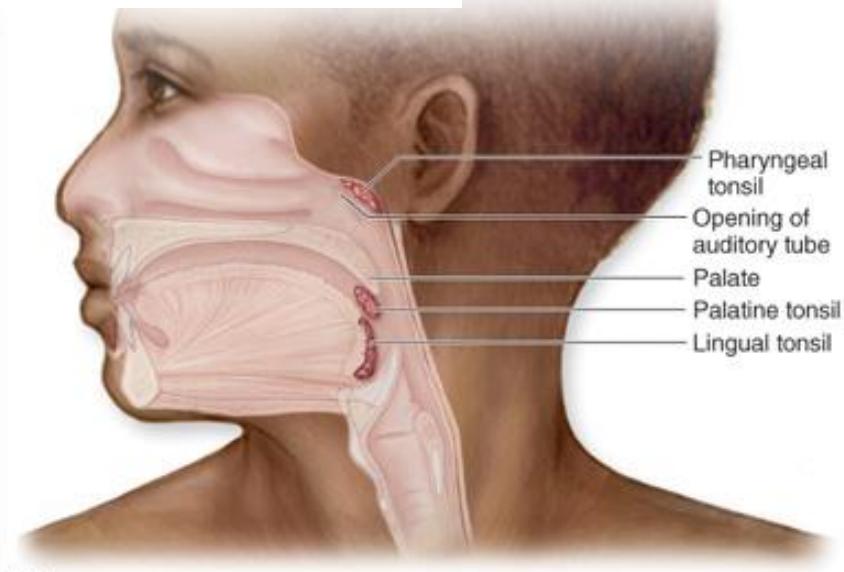
- Oval clusters of lymphatic cells with some extracellular matrix that are not surrounded by a connective tissue capsule.
- Contains proliferating B-lymphocytes and some macrophages.
- T-lymphocytes are located outside the germinal center.
- Filter and attack antigens.
- In some areas of the body, many lymphatic nodules group together to form larger structures.
 - mucosa-associated lymphatic tissue (MALT) or tonsils
 - MALT detect antigens and initiate an immune response
 - very prominent in the mucosa of the small intestine, primarily in the ileum
 - Peyer patches
 - also prevalent in the appendix

Tonsils

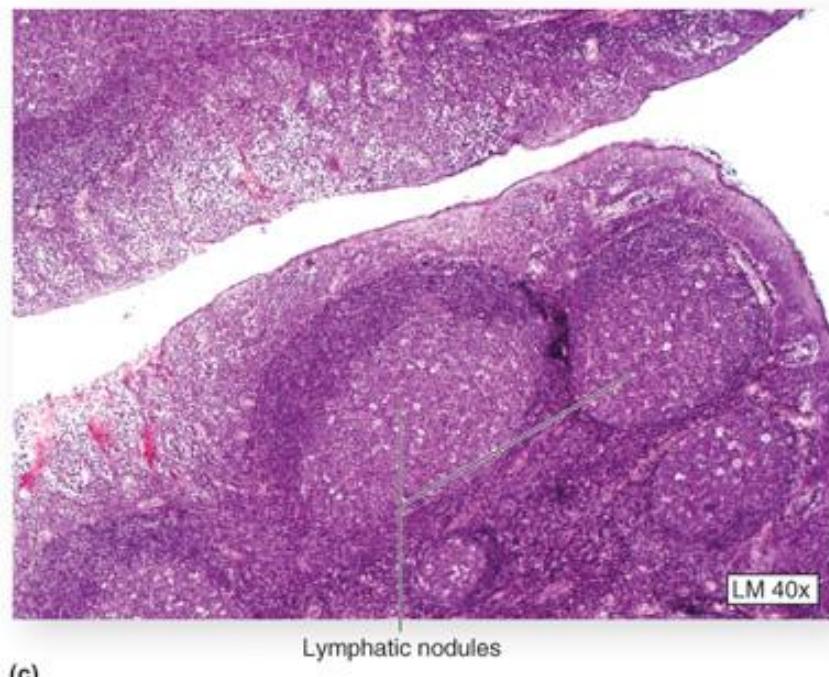
- Large clusters of lymphatic cells and extracellular matrix that are not completely surrounded by a connective tissue capsule.
- Consist of multiple germinal centers and have invaginated outer edges called crypts.
 - crypts help trap material and facilitate its identification by lymphocytes
- Several groups of tonsils form a protective ring around the pharynx.
 - pharyngeal tonsils (or adenoids) are in the posterior wall of the nasopharynx
 - palatine tonsils are in the posterolateral region of the oral cavity
 - lingual tonsils are along the posterior one-third of the tongue



(a)



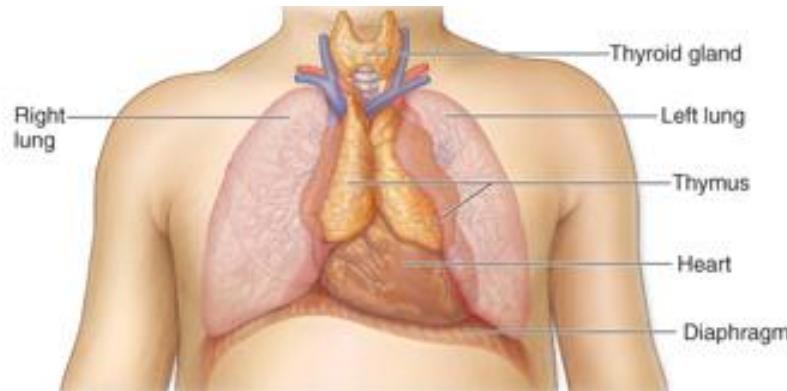
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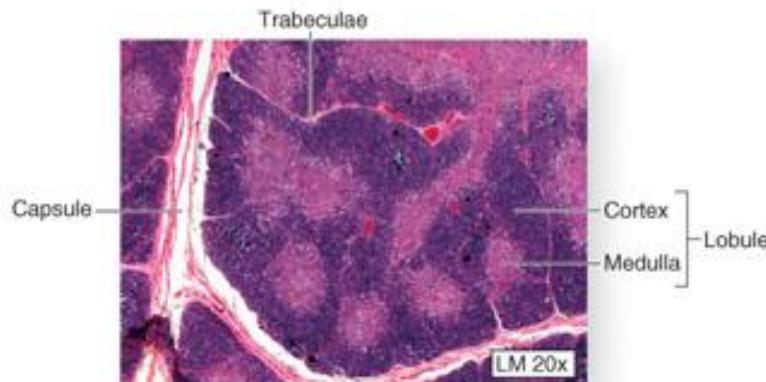
(c)

Lymphatic Organs

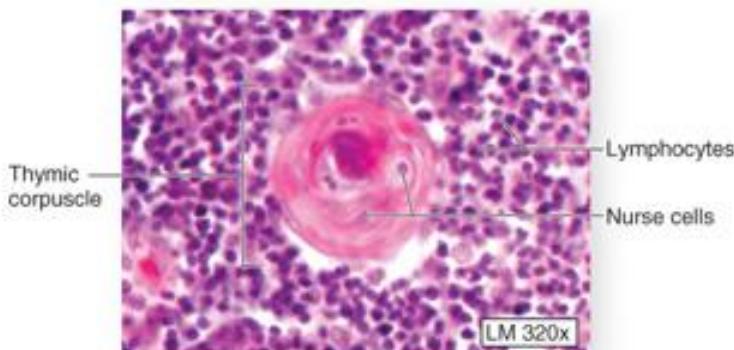
- Consist of lymphatic cells and extracellular matrix, and are completely surrounded by a connective tissue capsule.
 - lymph nodes
 - spleen
 - thymus
 - a bilobed organ located in the anterior mediastinum
 - in infants and young children, it is quite large and extends into the superior mediastinum as well
 - continues to grow until puberty, when it reaches a maximum weight of 30–50 grams
 - cells of the thymus regress, and it is eventually replaced by adipose connective tissue
 - in adults, it atrophies and becomes almost nonfunctional



(a)



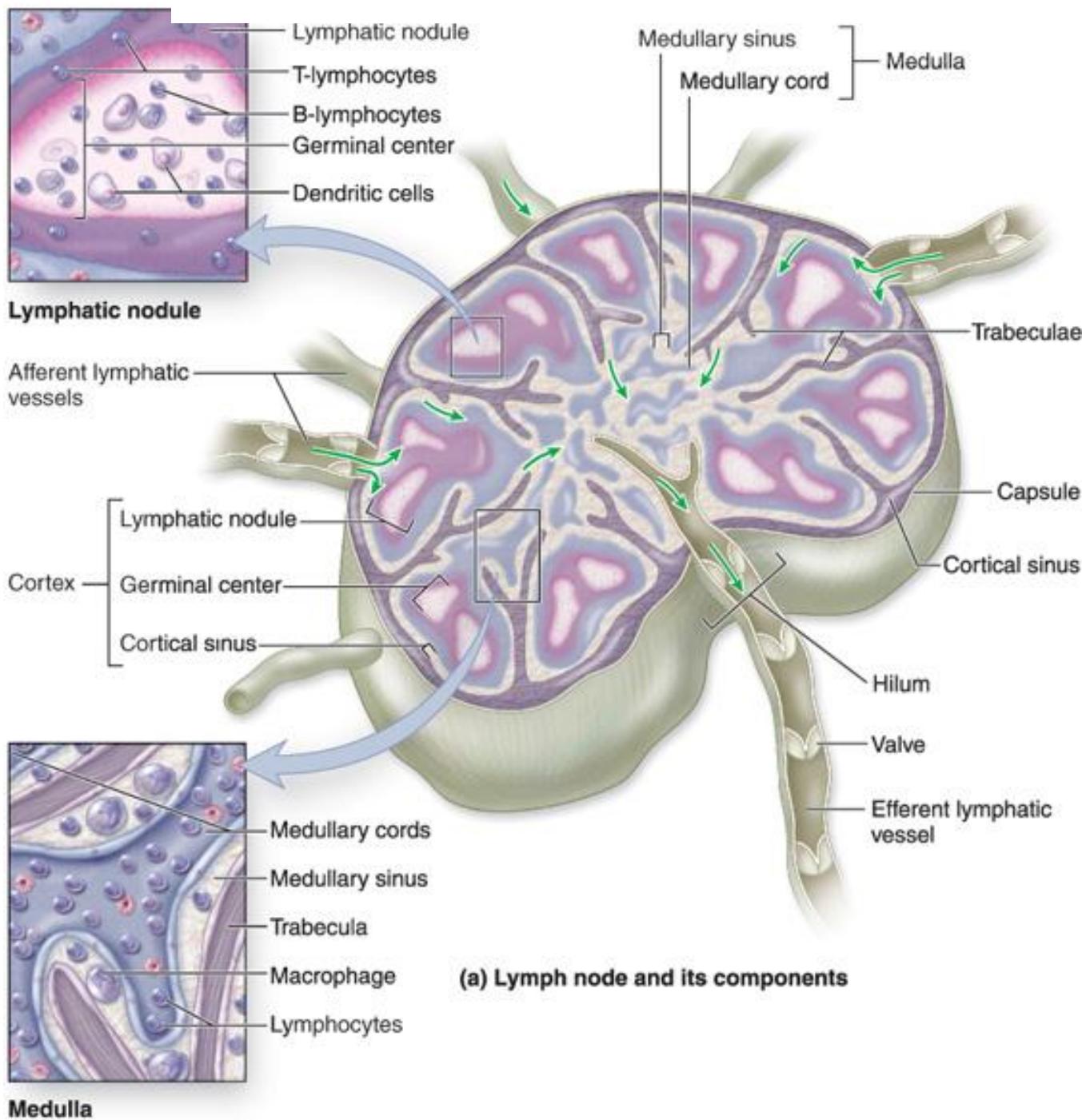
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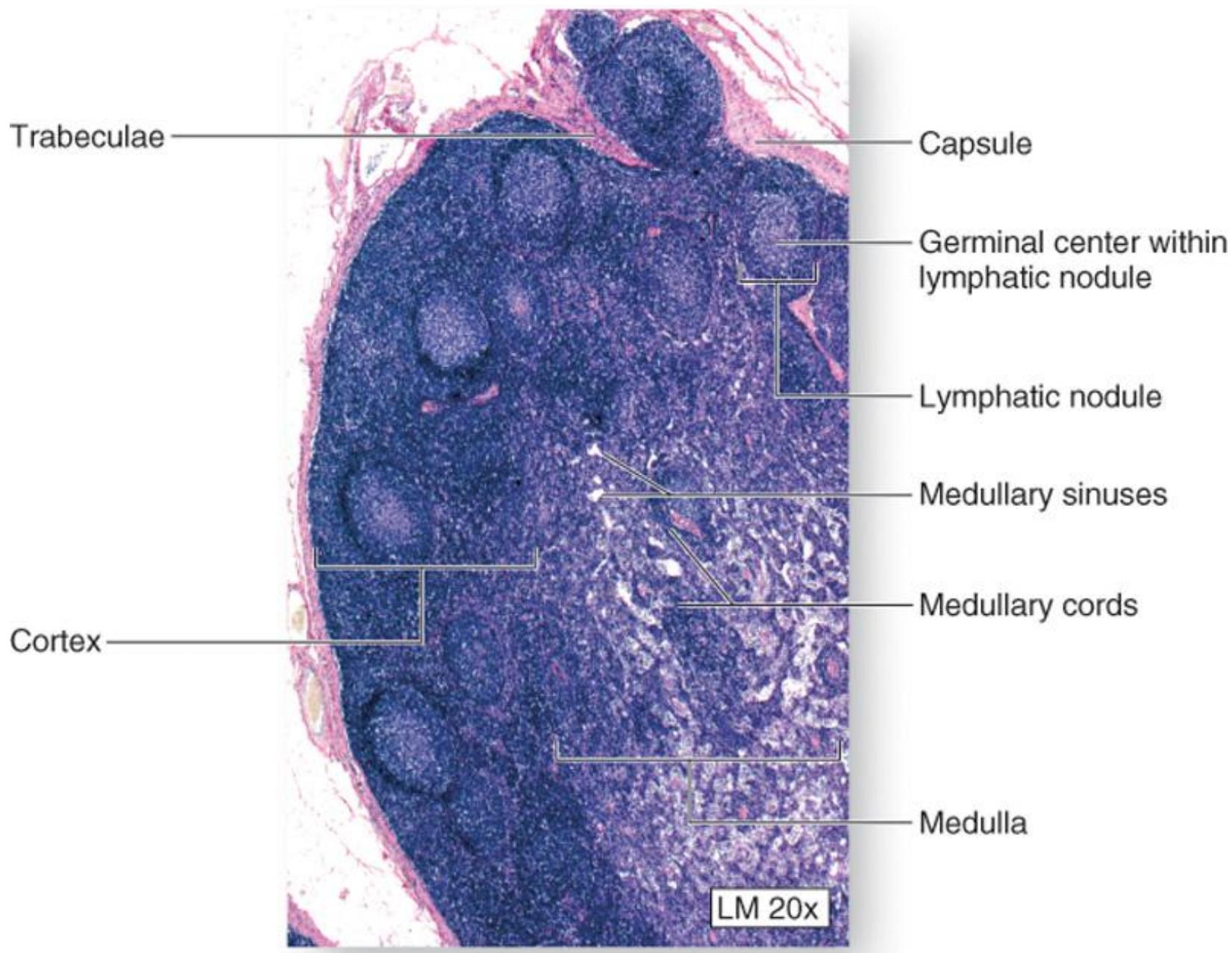


(c)

Lymph Nodes

- Small, round or oval structures located along the **pathways** of lymph vessels.
- Range in length from 1 to 25 millimeters, and typically are found in clusters that receive lymph from many body regions.
 - **axillary lymph nodes** receive lymph from the breast, axilla, and upper limb
 - **inguinal lymph nodes**, receive lymph from the lower limb and pelvis
 - **cervical lymph nodes** receive lymph from the head and neck
- Lymph nodes are also found individually throughout the body tissues.

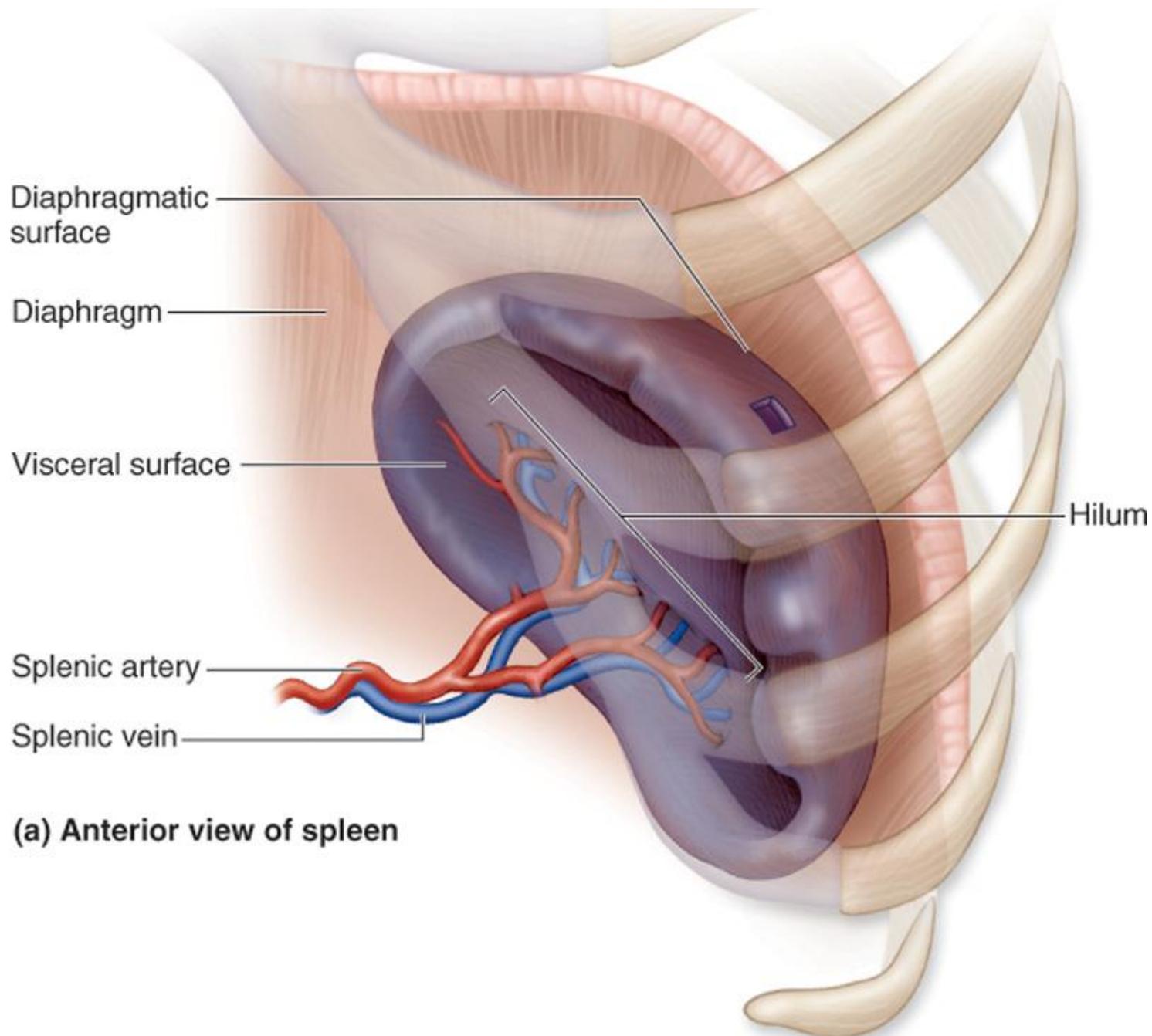


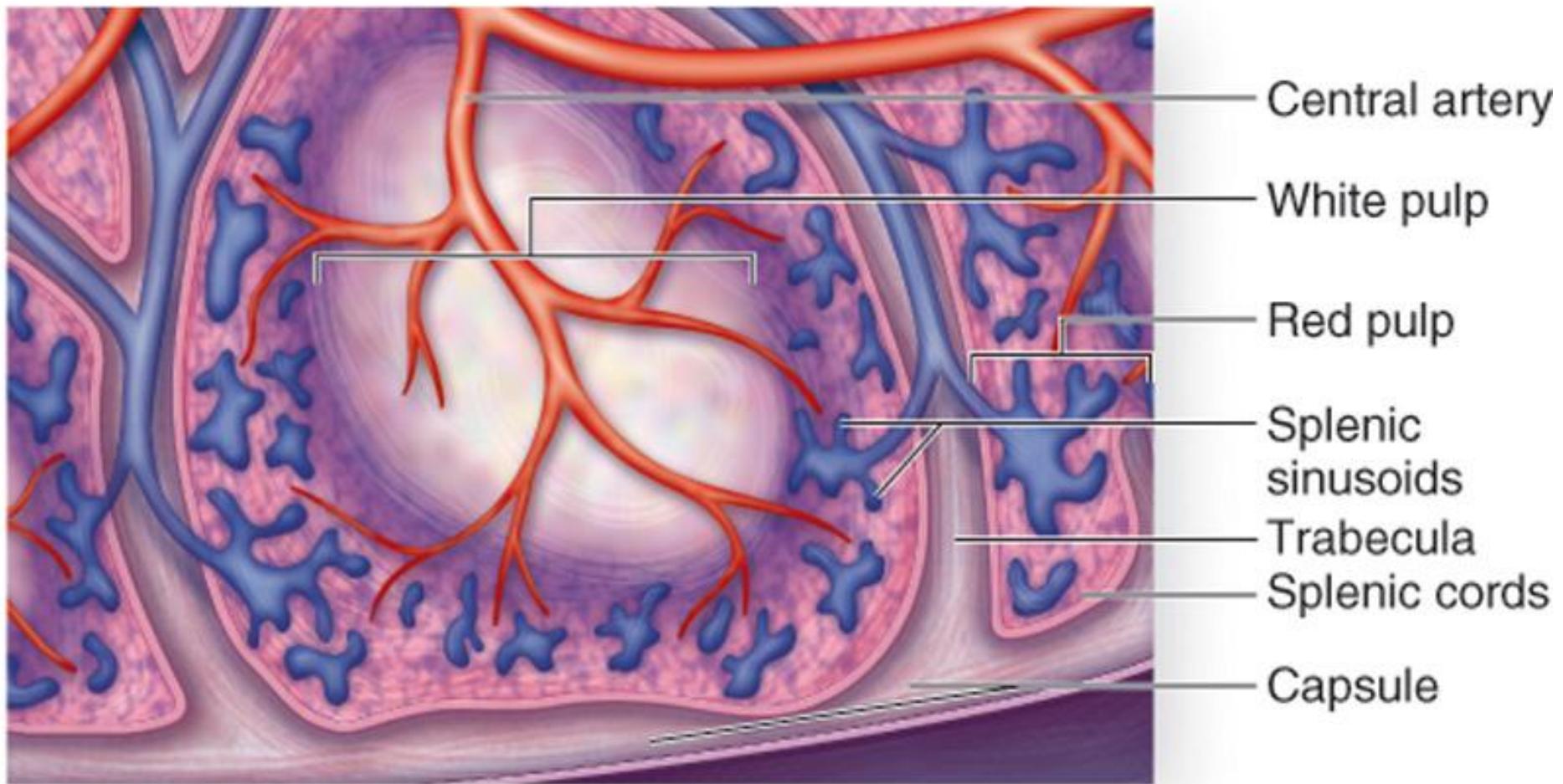


(b) Lymph node section

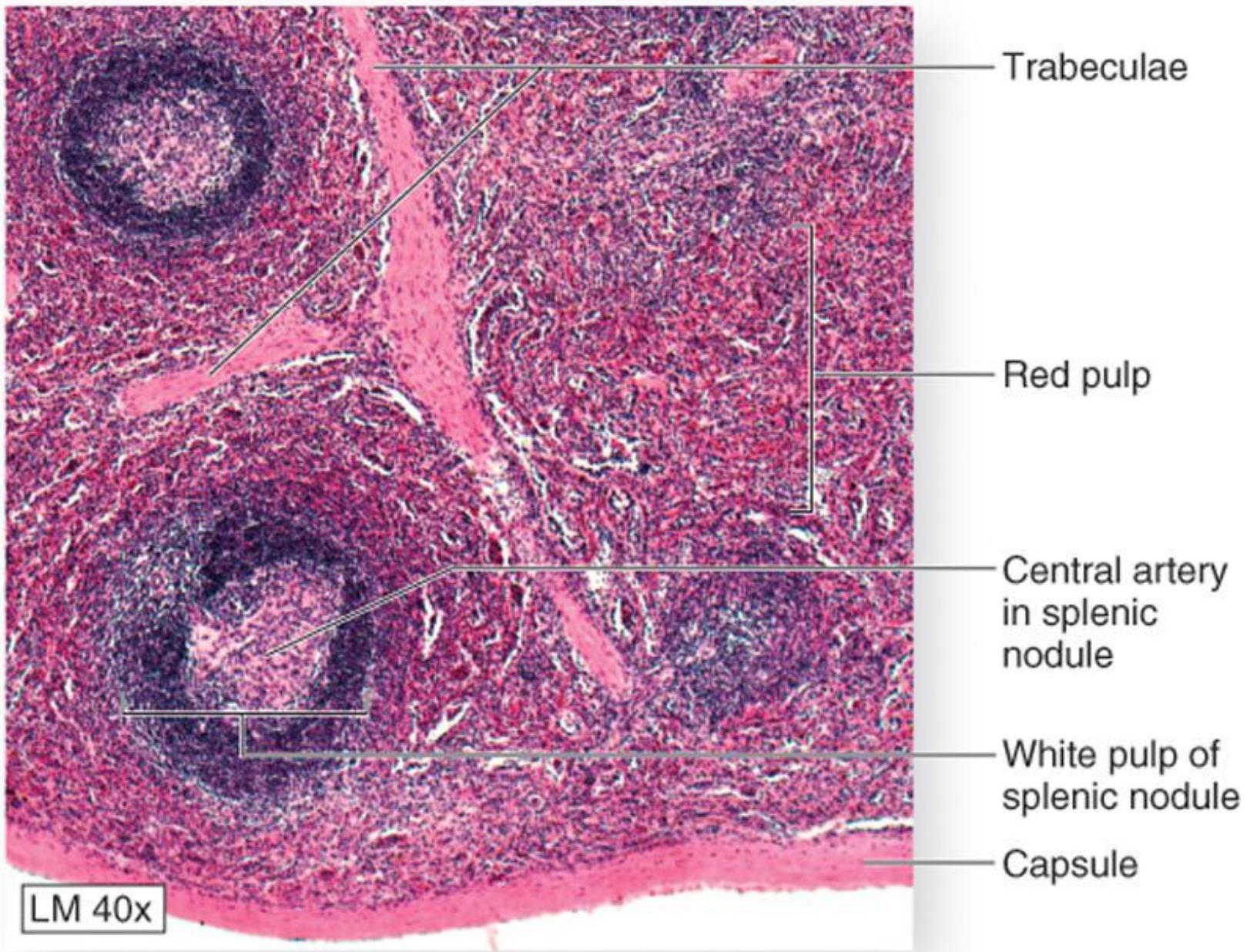
Spleen

- Largest lymphatic organ in the body.
- Located in the upper left quadrant of the abdomen, inferior to the diaphragm and posterior to ribs 9–11.
- Deep red organ lies lateral to the left kidney and posterolateral to the stomach.
- Can vary considerably in size and weight, but typically is about 12 centimeters long and 7 centimeters wide.

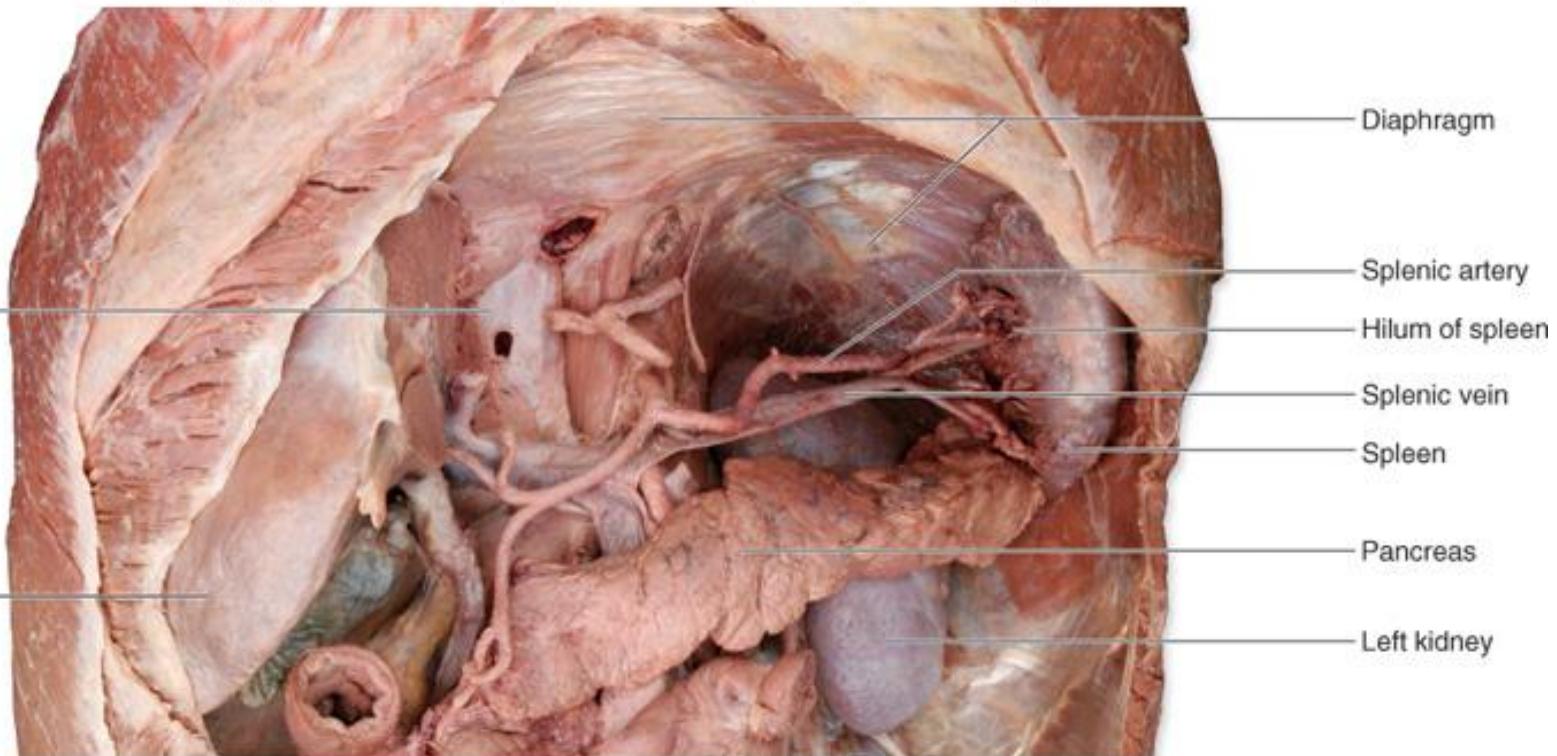




(b)



(c)



(d)

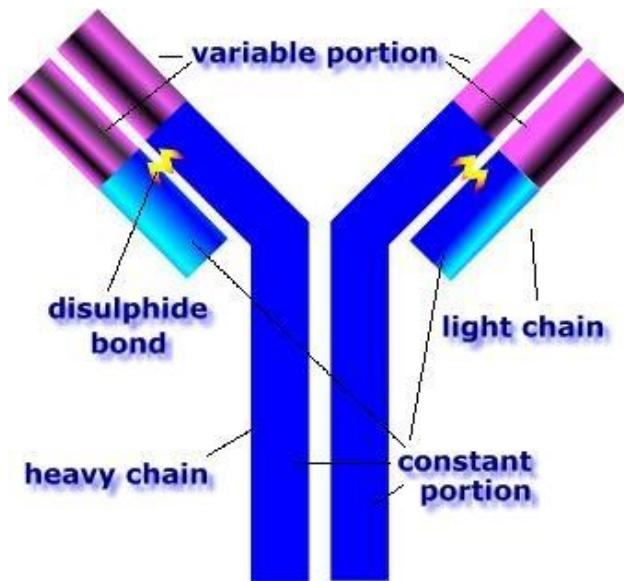
Functions of the Spleen

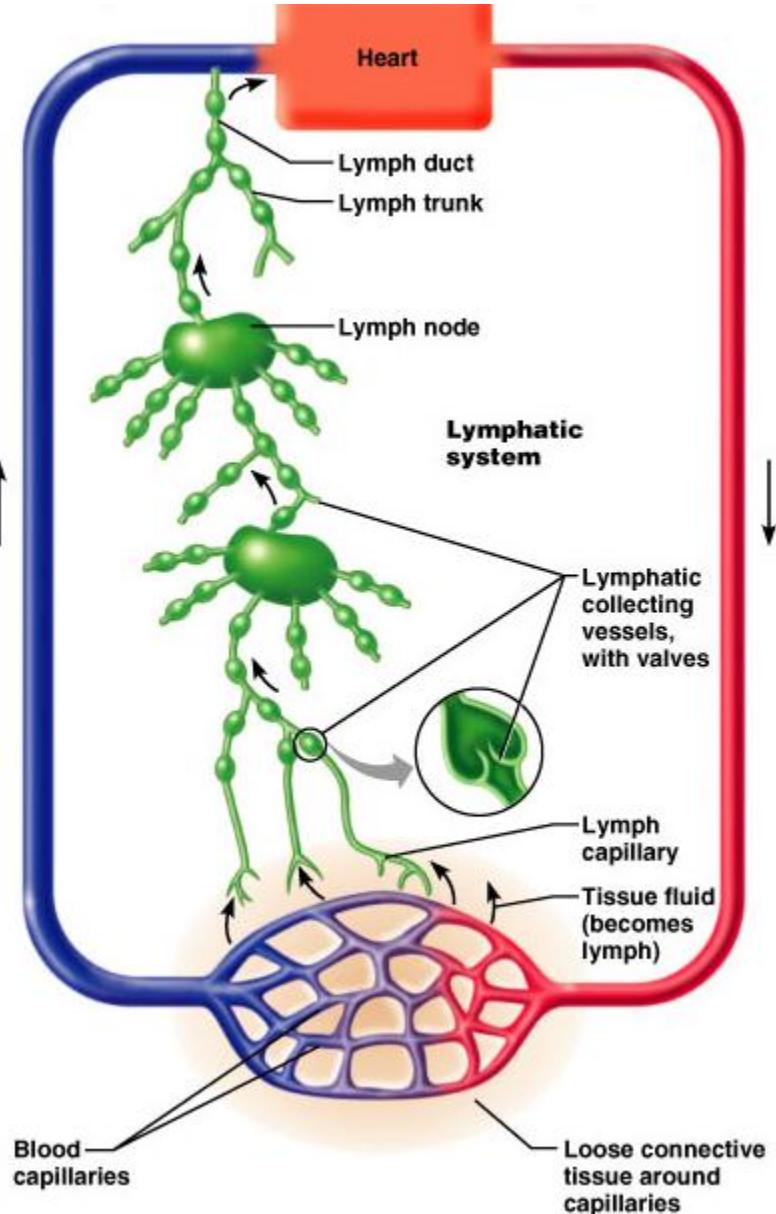
- Initiates an immune response when antigens are found in the blood (a white pulp function).
- Serves as a reservoir for erythrocytes and platelets (red pulp function).
- Phagocytizes old, defective erythrocytes and platelets (red pulp function).
- Phagocytizes bacteria and other foreign materials.

Aging and the Lymphatic System

- The thymus is **no longer able** to mature and differentiate T-lymphocytes.
- New T-lymphocytes can be produced only by replication (mitosis).
- Ability to provide immunity and fight disease **decreases**.
- Helper T-lymphocytes do not respond to antigens as well, and do not always reproduce rapidly.
- **Fewer B-lymphocytes and other kinds of T-lymphocytes.**
- The body's ability to acquire immunity and resist infection decreases, making elderly people **more susceptible** to illnesses and more likely to become **sicker**.
- **Faltering immune system** makes the elderly more prone to developing cancers.

Lymphatics and the Immune System

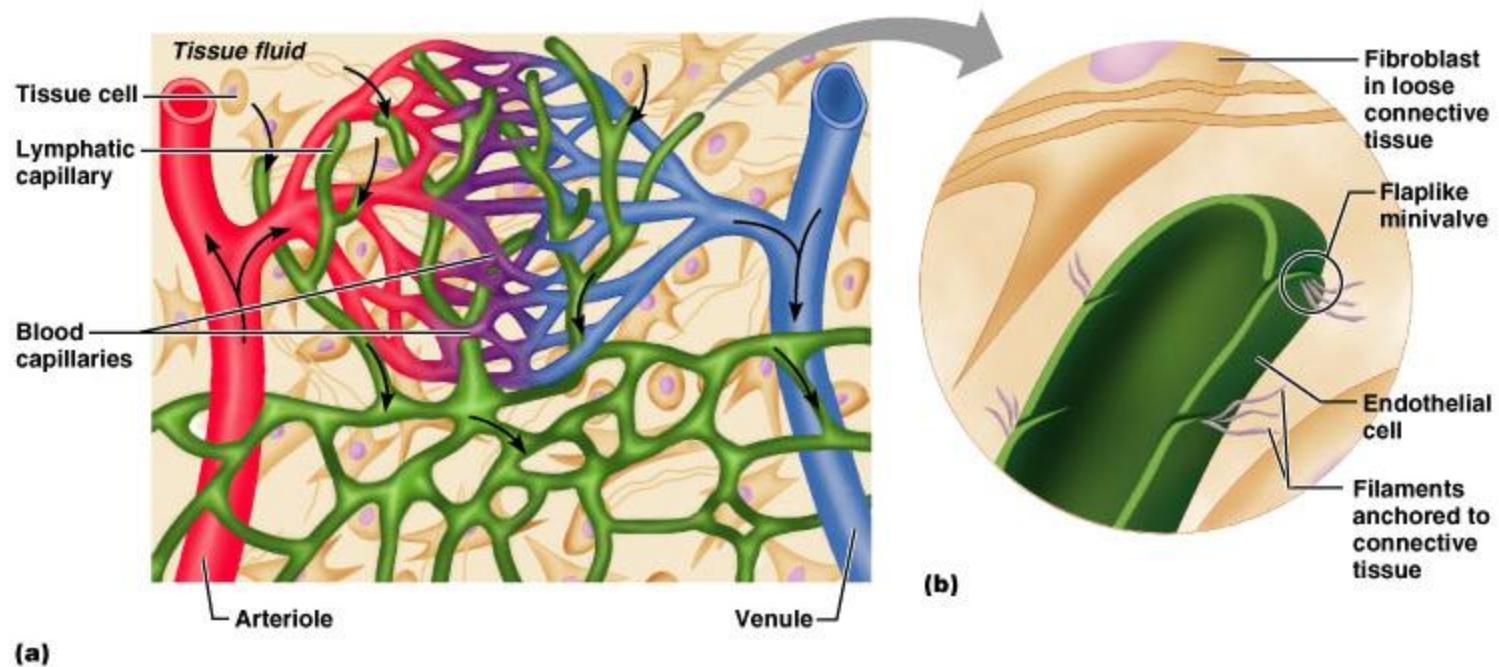
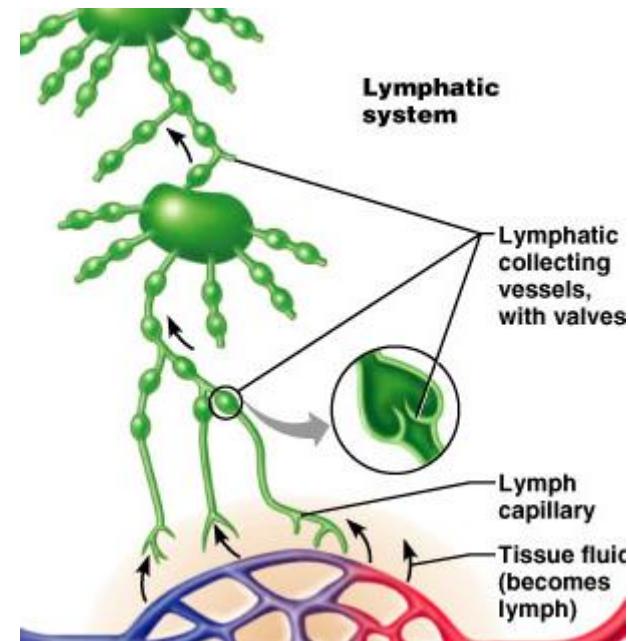


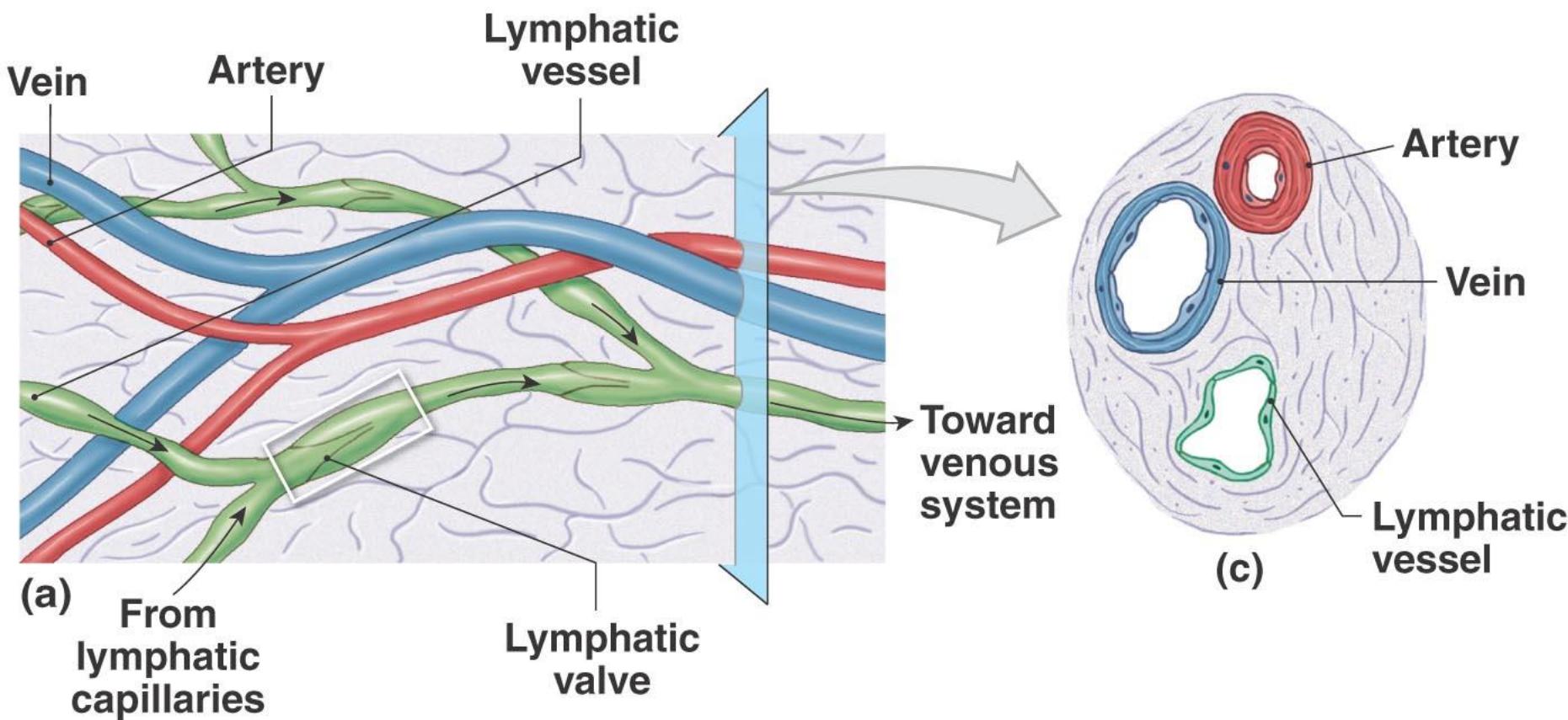


Lymphatic System

- One way system: to the heart
- Return of collected excess tissue fluid
- Return of leaked protein
- “Lymph” is this fluid
- Edema results if system blocked or surgically removed

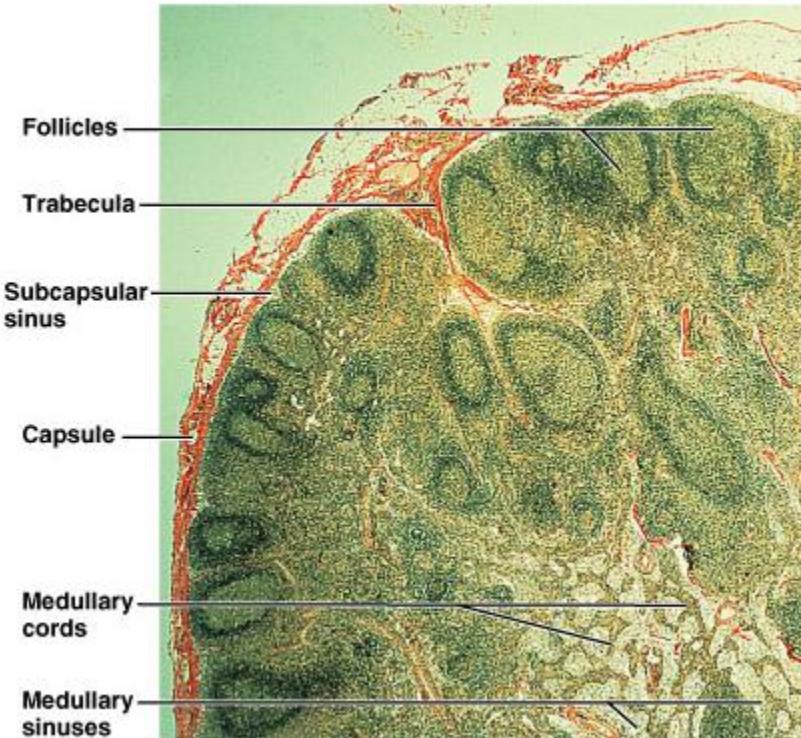
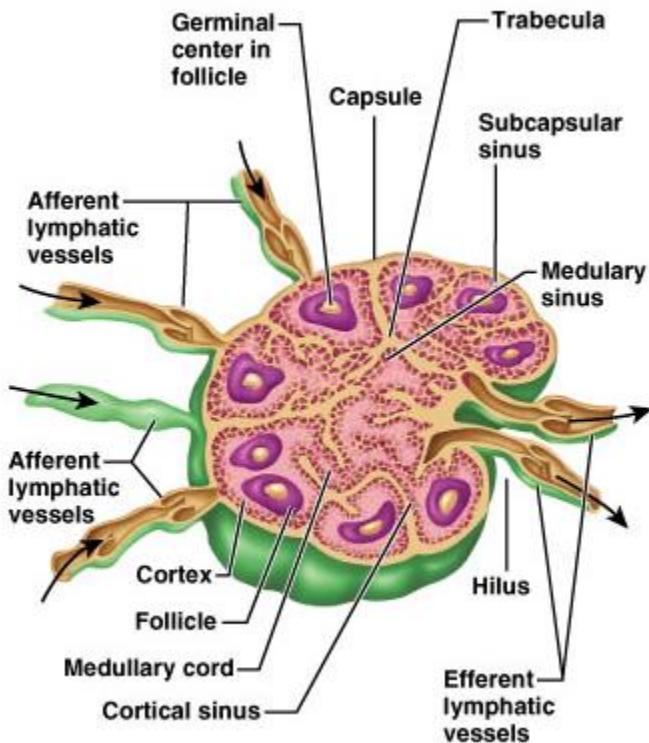
- Lymph capillaries
 - Have one way minivalves allowing excess fluid to enter but not leave
 - Picks up bacteria and viruses as well as proteins, electrolytes and fluid (lymph nodes destroy most pathogens)





- Lymph capillaries
 - Absent from bone, bone marrow, teeth, CNS
 - Enter lymphatic collecting vessels
- Lymphatic collecting vessels
 - Similar to blood vessels (3 layers), but thin & delicate
 - Superficial ones in skin travel with superficial *veins*
 - Deep ones of trunk and digestive viscera travel with deep *arteries*
 - Very low pressure
 - Distinctive appearance on *lymphangiography*
 - Drain into lymph nodes

- Lymph nodes: bean shaped organs along lymphatic collecting vessels
- Up to 1 inch in size
- Clusters of both deep and superficial LNs



Lymph Nodes

Superficial groups

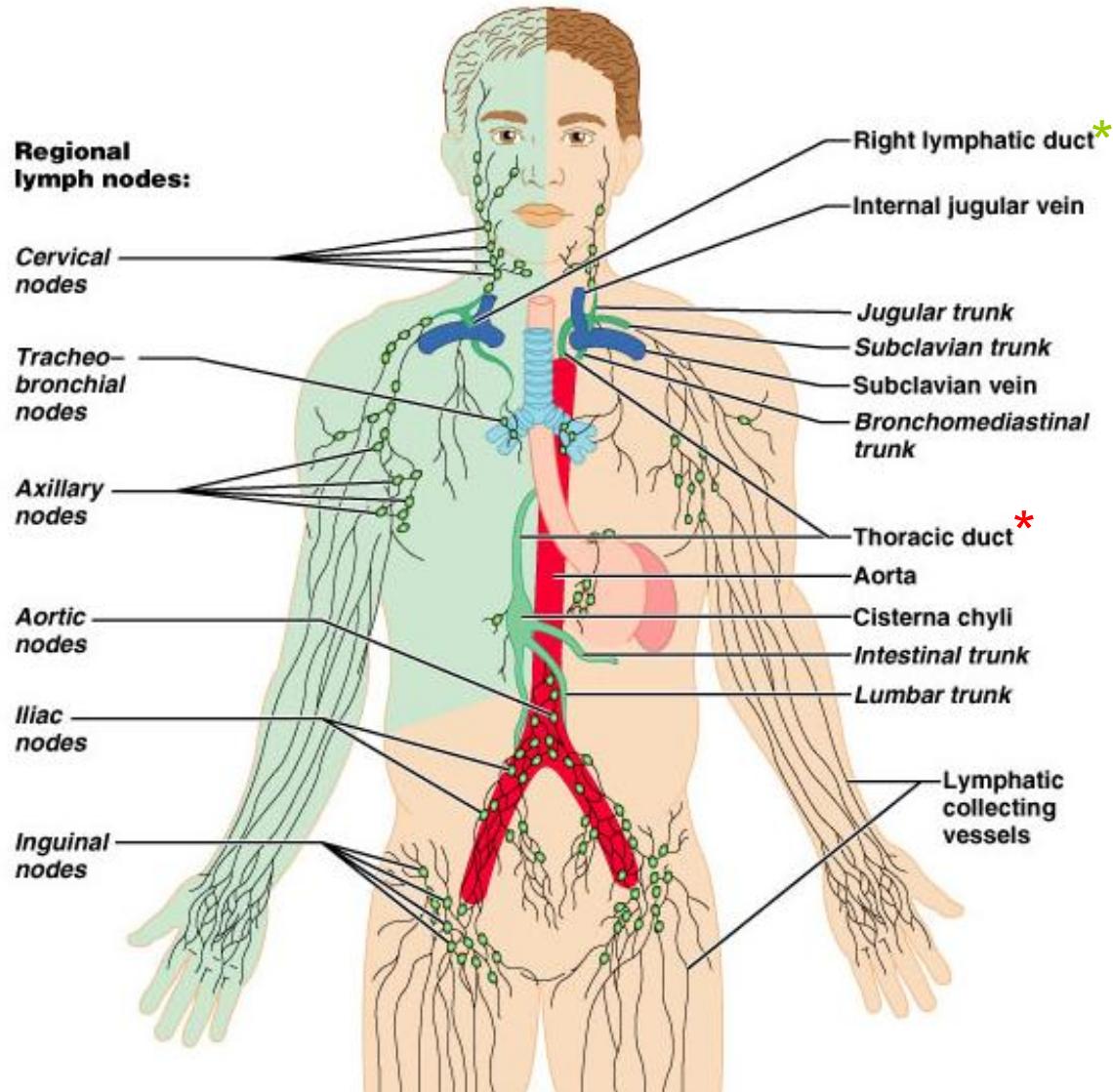
- Cervical
- Axillary
- Inguinal

Deep groups

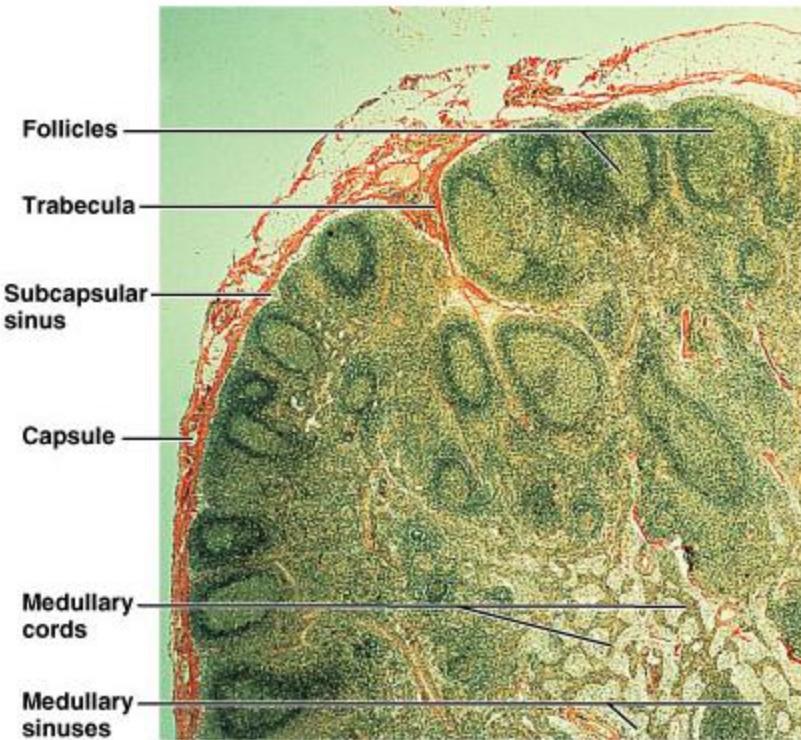
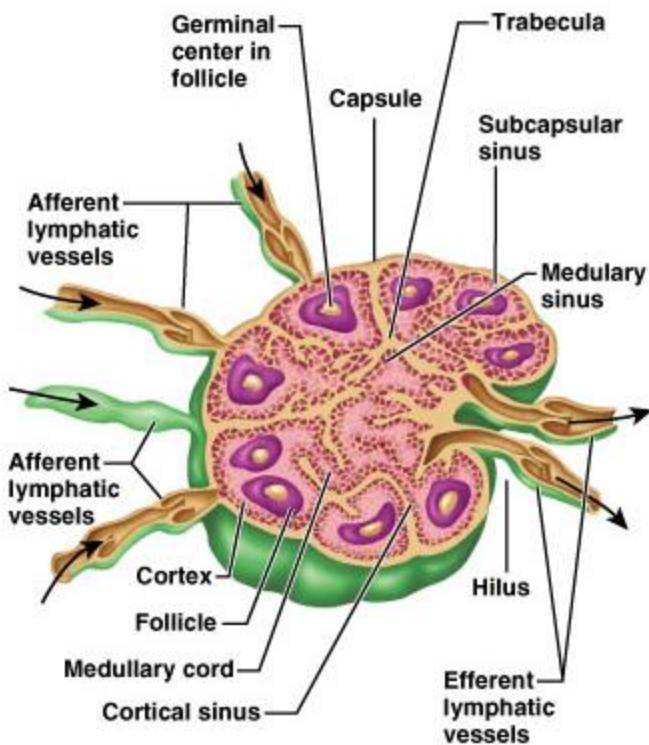
- Tracheobronchial
- Aortic
- Iliac

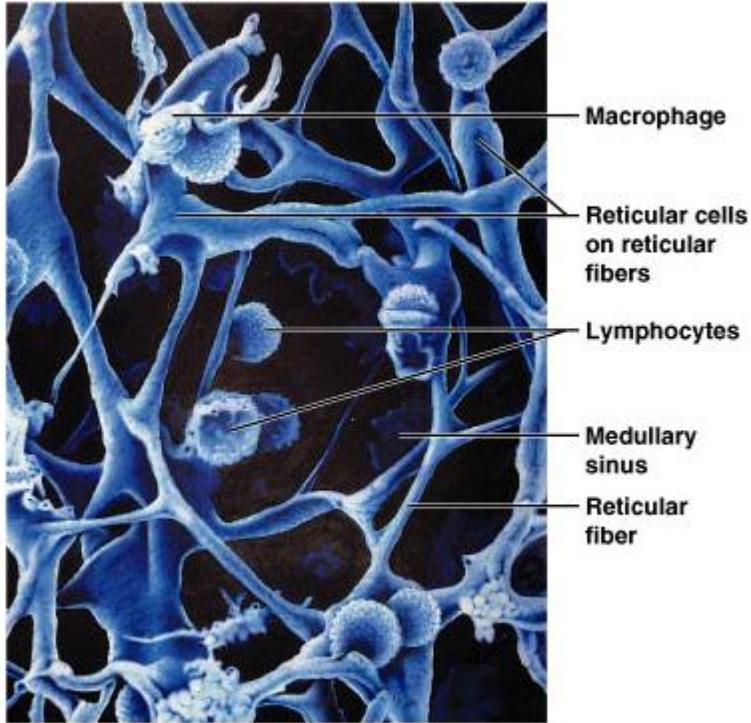
Drainage

- Superior R 1/4 of body: R lymphatic duct (green) *
- The rest: thoracic duct *



- Fibrous capsule sends in dividing trabeculae
- Afferent & efferent lymphatic vessels
- Lymph percolates through lymph sinuses
- Follicles: masses of lymphoid tissue divided into outer cortex & inner medulla (details in later slides)



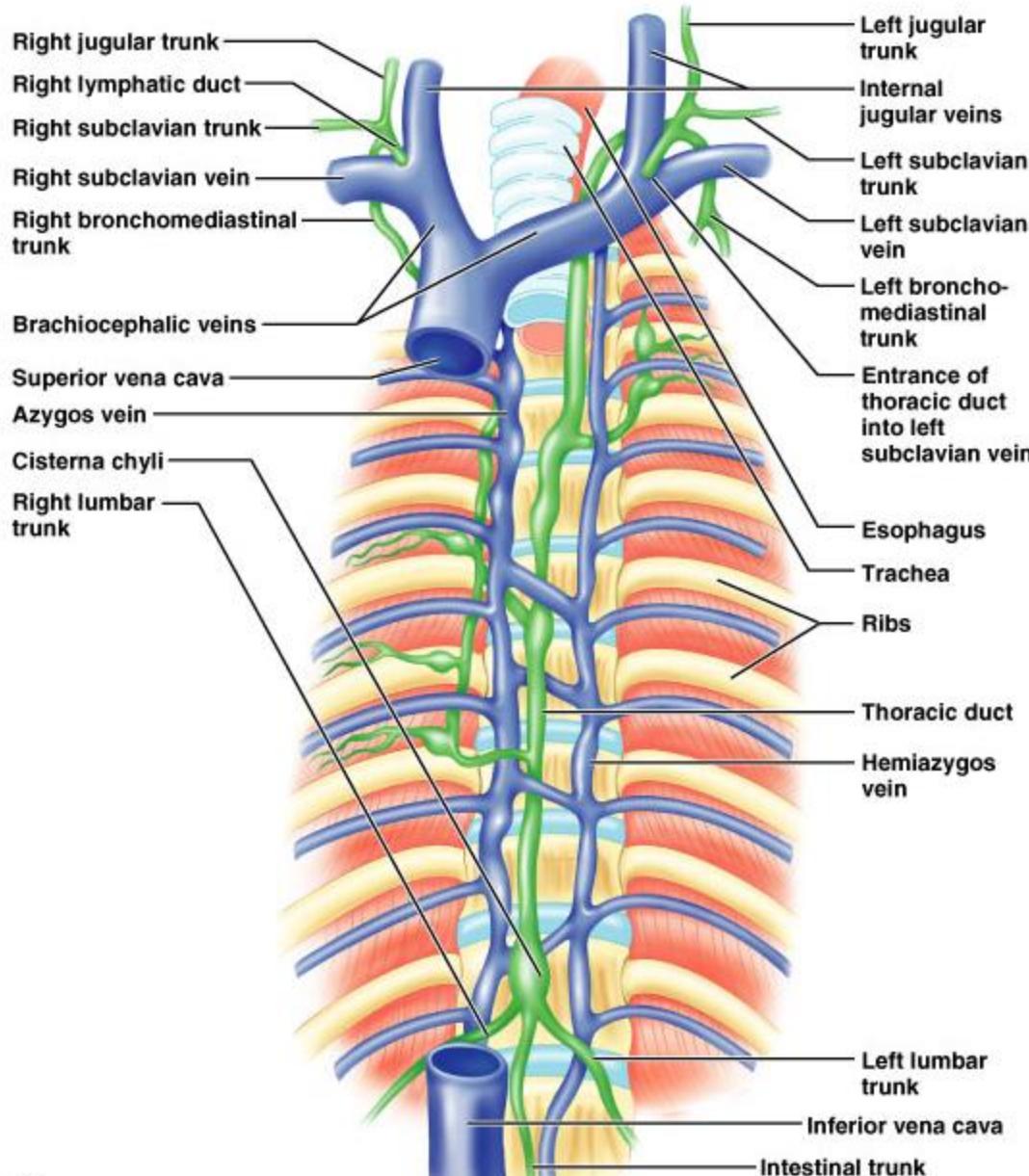


Macrophages
on reticular
fibers consume
pathogens and
foreign particles

Usually
pathogen free
lymph enters
lymph trunks

Lymphatic Trunks

(all are paired except the intestinal trunk)

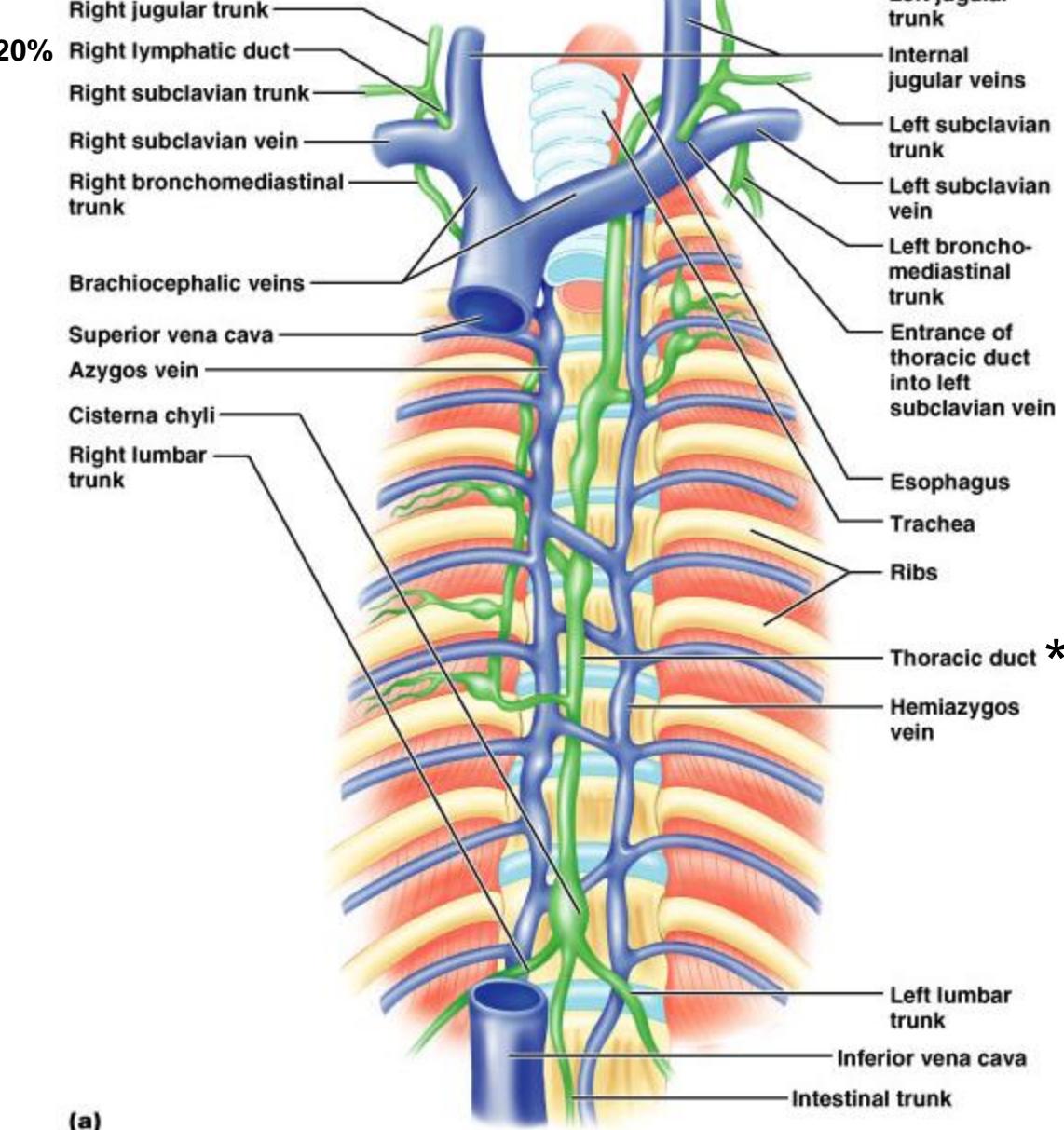


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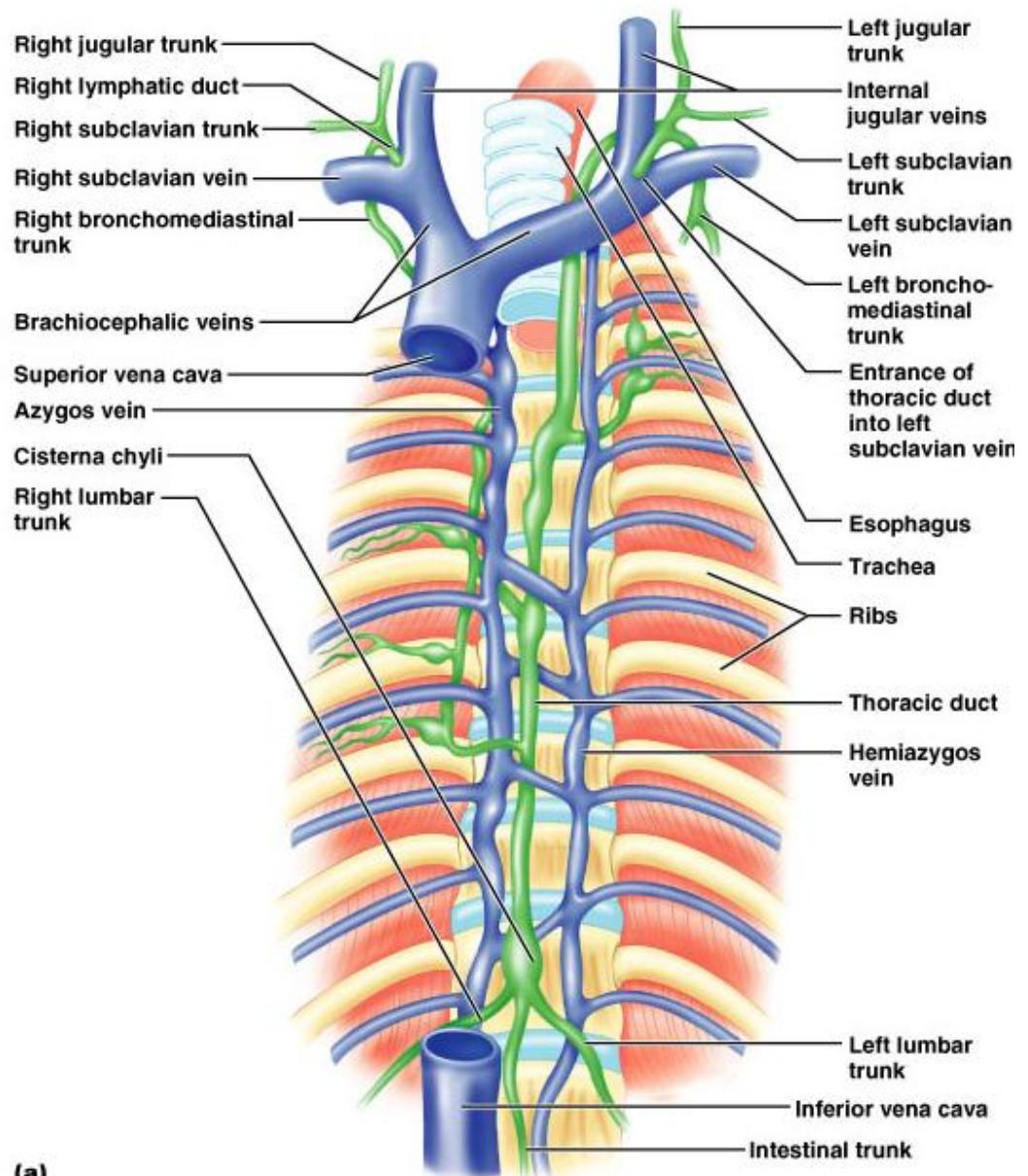
- Lumbar
- Intestinal
 - Receives fatty lymph (*chyle*) absorbed through *lacteals* in fingerlike villi of intestines
- Broncho-mediastinal
- Subclavian
- Jugular

Lymph ducts (variable)

- Thoracic duct: everyone has
- 20% also have a right lymphatic duct



(a)



(a)



(b)

The Immune System

- Recognizes ***specific*** foreign molecules
 - Each exposure (to the same pathogen) increases the effectiveness of the response
- Lymphoid organs
 - Lymph nodes
 - Spleen
 - Thymus
 - Tonsils
 - Small intestine & appendix aggregated lymphoid nodules

Basic Immunology

- Depends on the ability of the immune system to distinguish between *self* and *non-self* molecules
- *Self* molecules are those components of an organism's body that can be distinguished from foreign substances by the immune system
 - *Autoimmunity* is an immune reaction against self molecules (causes various diseases)
- *Non-self* molecules are those recognized as foreign molecules
 - One class of non-self molecules are called **antigens** (short for *antibody generators*) and are defined as substances that bind to specific immune receptors and elicit an immune response

Lymphocytes

the primary cells of the lymphoid system

- Respond to:
 - Invading organisms
 - Abnormal body cells, such as virus-infected cells or cancer cells
 - Foreign proteins such as the toxins released by some bacteria
- Types of lymphocytes
 - T cells (**thymus-dependent**)
 - B cells (**bone marrow-derived**)
 - NK cells (**natural killer**)

T Cells

- 80% of circulating lymphocytes
- Some of the types:
 - Cytotoxic T cells: attack foreign cells or body cells infected by viruses (“cell-mediated immunity”)
 - Regulatory T cells: Helper T cells and suppressor T cells (control activation and activity of B cells)
 - Memory T cells: produced by the division of activated T cells following exposure to a particular antigen (remain on reserve, to be reactivated following later exposure to the same antigen)

B Cells

- 10-15% of circulating lymphocytes
- Can differentiate into plasmocytes (plasma cells) when stimulated by exposure to an antigen
- Plasma cells produce antibodies: soluble proteins which react with antigens, also known as immunoglobulins (Ig's)
- “Humoral immunity”, or antibody-mediated immunity
- Memory B cells: produced by the division of activated B cells following exposure to a particular antigen (remain on reserve, to be reactivated following later exposure to the same antigen)

NK Cells

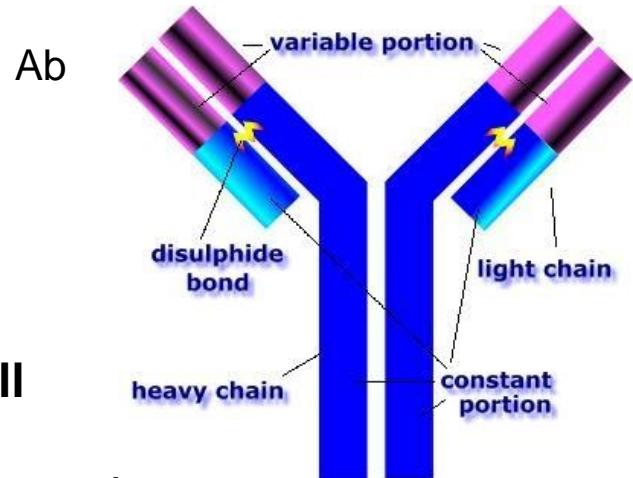
- 5-10% of circulating lymphocytes
- Attack foreign cells, normal cells infected with viruses, cancer cells that appear in normal tissues
- Known as “immunologic surveillance”

“Humoral” vs “Cell mediated”

- ***Cell-mediated immunity*** - direct attack by activated T cells (react with foreign antigens on the surface of other host cells)
- ***Antibody-mediated (humoral) immunity*** – attack by circulating antibodies, also called immunoglobins (Ig's), released by the plasma cells derived from activated B cells
 - “humor” – from old-fashioned word for stuff in the blood, like ‘good humors’ and ‘bad humors’

These two systems interact with each other

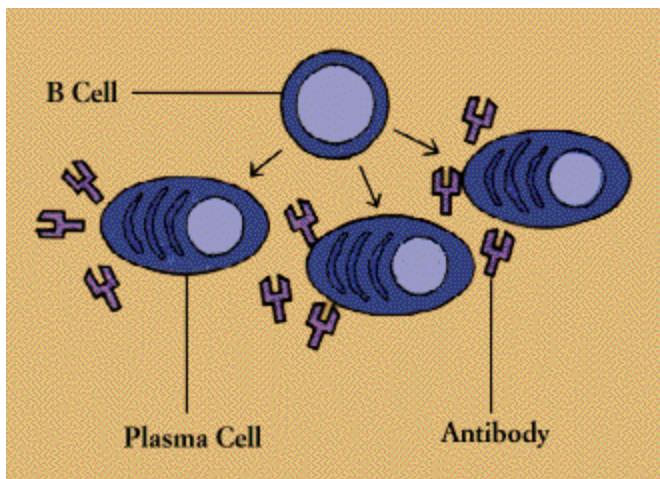
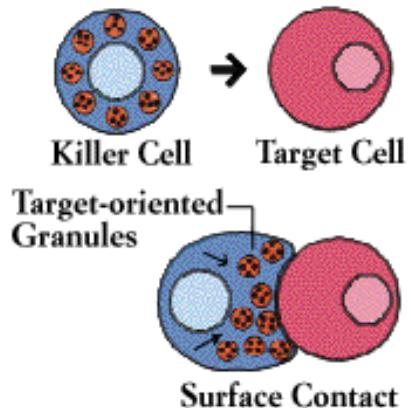
B Lymphocytes



- The receptor for antigens is an antibody on B cell surface
- B lymphocytes can respond to millions of foreign antigens
 - This capability exists *before* exposure to any antigens
 - Each lineage of B cell expresses a different antibody, so the complete set of B cell antigen receptors represent all the antibodies that the body can manufacture
- A B cell identifies pathogens when antibodies on its surface bind to a specific foreign antigen
- This antigen/antibody complex is taken up by the B cell and processed by proteolysis into peptides (small pieces)
- As the activated B cell then begins to divide (“clonal expansion”), its offspring secrete millions of copies of the antibody that recognizes this antigen
- These antibodies circulate in blood plasma and lymph, bind to pathogens expressing the antigen and mark them for destruction by complement activation or for uptake and destruction by phagocytes
- Antibodies can also neutralize challenges directly, by binding to bacterial toxins or by interfering with the receptors that viruses and bacteria use to infect cells

The needs...

- To be able to attack **cells** which have been infected
 - T cells target “alien” cells – they reject transplanted organs, destroy our own cells that have been infected, and kill some cancer cells: these are all treated as foreign because they have altered (antigenic) proteins on their surfaces
- To be able to take care of small extracellular antigens such as bacteria which multiply **outside** cells, the toxins they make, etc.
 - Antibodies made by plasma cells (differentiated B lymphocytes) bind to antigens on bacteria, marking them for destruction by macrophages



Helpful definitions (from Wikipedia)

The immune system

Cells in our bone marrow, thymus, and the lymphatic system of ducts and nodes, spleen, and blood that function to protect us.

Antigen

Anything causing an immune response, usually foreign material but may be our own tissues.

Pathogen

Any disease causing micro-organism.

Tolerance

Non-reactivity of the immune system, usually refers to "self" but may include foreign tissue in organ transplants.

Autoimmunity

A failure of tolerance, the immune system reacts to self.

Chemokines

Molecules released by pathogens and infected tissues to attract cells of the immune system.

Cytokines

Signaling molecules released by one cell to cause a response in another. Signaling is extremely important in our immune response.

Innate immunity

Protection that is always present. Includes phagocytic (cells that eat other cells) macrophages and dendritic cells.

Adaptive immunity

Protection that arises by an immune response, including humoral immunity producing antibodies and cellular immunity.

Development of lymphocytes

Originate in bone marrow from lymphoid stem cells

B cells stay in bone marrow, hence “**B**” cells

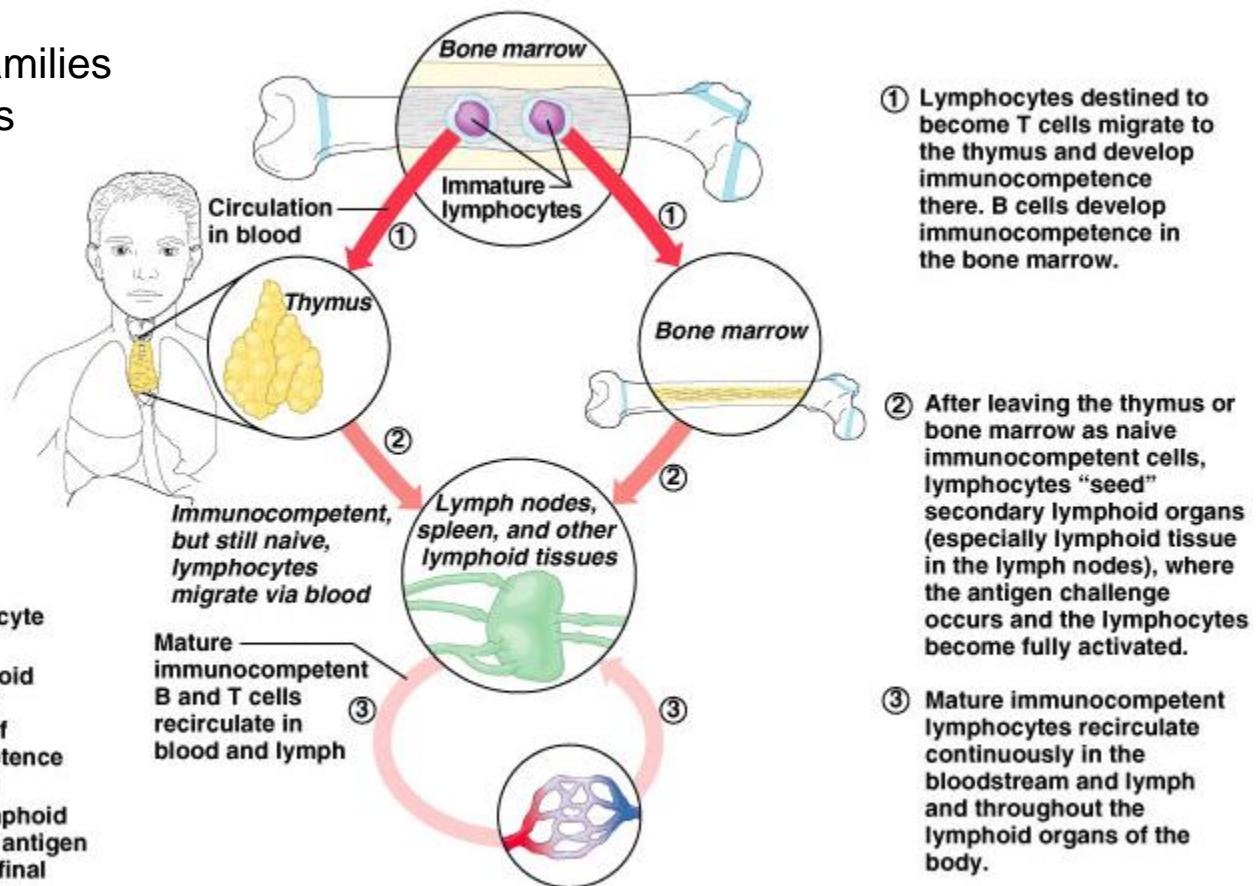
T cells mature in thymus, hence “**T**” cells

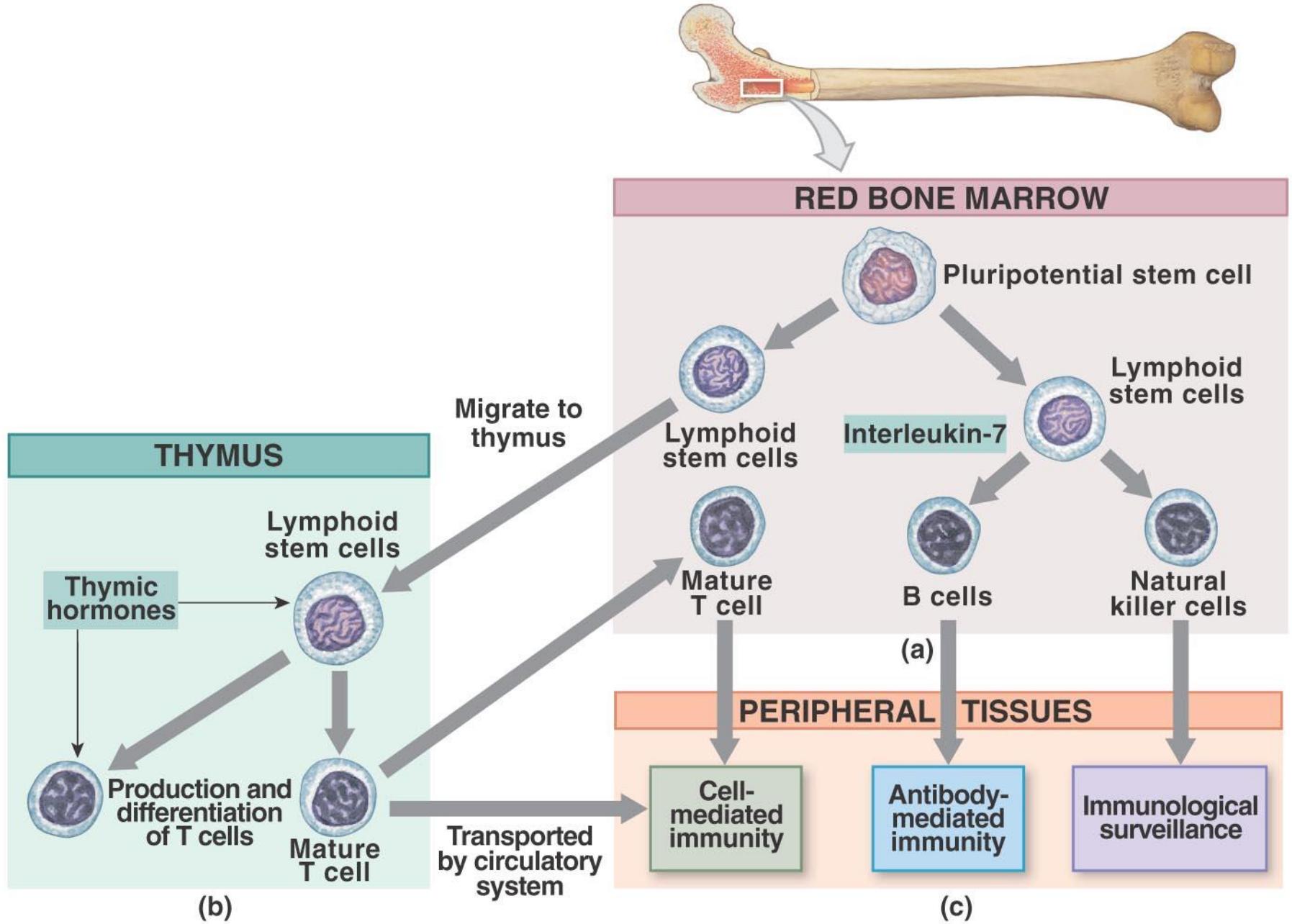
These divide rapidly into families

Each has surface receptors
able to recognize one
unique type of antigen=
immunocompetence

- Key:**
- [Grey square] = Site of lymphocyte origin
 - [Yellow square] = Primary lymphoid organs; site of development of immunocompetence as B or T cells
 - [Green square] = Secondary lymphoid organs; site of antigen challenge and final differentiation to mature B and T cells

(a)





Lymphocytes

- Naive immunocompetent lymphocytes “seed” secondary lymphoid organs (esp. lymph nodes)
- “Antigenic challenge” – full activation upon meeting and binding with specific antigen
 - The B cell’s antigen receptor is an antibody (see slide 20)
- Full activation
 - Gains ability to attack its antigen
 - Proliferates rapidly producing mature lymphocytes
 - Mature lymphocytes re-circulate seeking same pathogens

Immunologic Memory

- When B cells and T cells are activated and begin to replicate, some of their offspring will become long-lived memory cells
- Throughout the lifetime of an animal, these memory cells will remember each specific pathogen encountered and can mount a strong response if the pathogen is detected again
- This is "adaptive" because it occurs during the lifetime of an individual as an adaptation to infection with that pathogen and prepares the immune system for future challenges
 - For example immunity to chicken pox after you've had it
- Immunological memory can either be in the form of passive short-term memory or active long-term memory
 - Example of passive immunity: the antibodies in breast milk (wanes within a short time, weeks to months)

The immune system protects organisms with layered defenses of increasing specificity

- Most simply, **1. physical barriers** prevent pathogens such as bacteria and viruses from entering the body
- If a pathogen breaches these barriers, the **2. innate immune system** provides an immediate, but non-specific response
 - Innate immune systems are found in all plants and animals
- If pathogens successfully evade the innate response, vertebrates possess a third layer of protection, the **3. adaptive immune system**
 - Here, the immune system adapts its response during an infection to improve its recognition of the pathogen
 - This improved response is then retained after the pathogen has been eliminated, in the form of an immunological memory, and allows the adaptive immune system to mount faster and stronger attacks each time this pathogen is encountered

Components of the immune system

Innate immune system

- Response is non-specific
- Exposure leads to immediate maximal response
- Cell-mediated and humoral components
- No immunological memory
- Found in nearly all forms of life (plants & animals)

Adaptive immune system

- Pathogen and antigen specific response
- Lag time between exposure and maximal response
- Cell-mediated and humoral components
- Exposure leads to immunologic memory
- Found only in jawed vertebrates

Innate immunity

- The dominant system of host defense in most organisms
- Inflammation is one of the first responses
 - Redness, swelling, heat and pain
 - Chemical and cellular response
 - During the acute phase of inflammation, particularly as a result of bacterial infection, ***neutrophils*** migrate toward the site of inflammation in a process called chemotaxis, and are usually the first cells to arrive at the scene of infection

Innate immunity continued

- The innate leukocytes include the phagocytes (macrophages, neutrophils, and dendritic cells), mast cells, eosinophils, basophils, and natural killer cells
- These cells identify and eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms
- Innate cells are also important mediators in the activation of the adaptive immune system

Innate immunity continued

- **Macrophages** are versatile cells that reside within tissues and produce a wide array of chemicals including enzymes, complement proteins, and regulatory factors such as interleukin 1
 - Macrophages also act as scavengers, ridding the body of worn-out cells and other debris
 - Also as ***antigen-presenting cells*** that activate the adaptive immune system

Innate system continued

- **Dendritic cells** are phagocytes in tissues that are in contact with the external environment
 - Located mainly in the skin, nose, lungs, stomach, and intestines (are in no way connected to the nervous system)
 - Dendritic cells serve as a link between the innate and adaptive immune systems, as they **present antigens to T cells**, one of the key cell types of the adaptive immune system
- **Mast cells** reside in connective tissues and mucous membranes, and regulate the inflammatory response
 - They are most often associated with allergy and anaphylaxis (for example, they release histamine – this is why anti-histamines help allergic reactions)

Phagocytosis

- Phagocytosis is an important feature of cellular innate immunity performed by cells called 'phagocytes' that engulf, or eat, pathogens or particles
- Phagocytes generally patrol the body searching for pathogens, but can be called to specific locations by cytokines
- The pathogen is killed by the activity of digestive enzymes or following a respiratory burst that releases free radicals into the phagolysosome
- Phagocytosis probably represents the oldest form of host defense, as phagocytes have been identified in both vertebrate and invertebrate animals

Adaptive immunity

- The adaptive immune system evolved in early vertebrates and allows for a stronger immune response as well as immunological memory, where each pathogen is "remembered" by its signature antigen
- The adaptive immune response is antigen-specific and requires the recognition of specific "non-self" antigens during a process called antigen presentation
- Antigen specificity allows for the generation of responses that are tailored to specific pathogens or pathogen-infected cells
- The ability to mount these tailored responses is maintained in the body by "memory cells"
- Should a pathogen infect the body more than once, these specific memory cells are used to quickly eliminate it

Optional slide (in more detail next slide)

- MHC = Major HistoCompatibility
 - Self proteins
 - Class I: on most nucleated cells
 - Class II: only on a few cells (B lymphocytes & macrophages) which interact with Th cells
- CD8+ = proteins associated with Tc (cytotoxic or killer T cells)
- CD4+ = proteins associated with Th (helper T cells)
 - Reduced in AIDS

MHC = Major HistoCompatibility

Are “self” proteins, and have the most genetic (person to person) variability

Class I: on most nucleated cells

Class II: only on a few cells (B lymphocytes & macrophages) which interact with Th cells

CD8 is a protein on Tc's (cytotoxic or killer T cells) which recognizes class I MHCs

-The class I MHC binds the Ag inside the body's cell (any cell) which is being made because of its infection, and takes it to the surface of the cell

-The Tc cell recognizes Ag as foreign so treats this cell of the body as foreign and sends a chemical signal to cell for it to self-destruct (by apoptosis = programmed cell death)

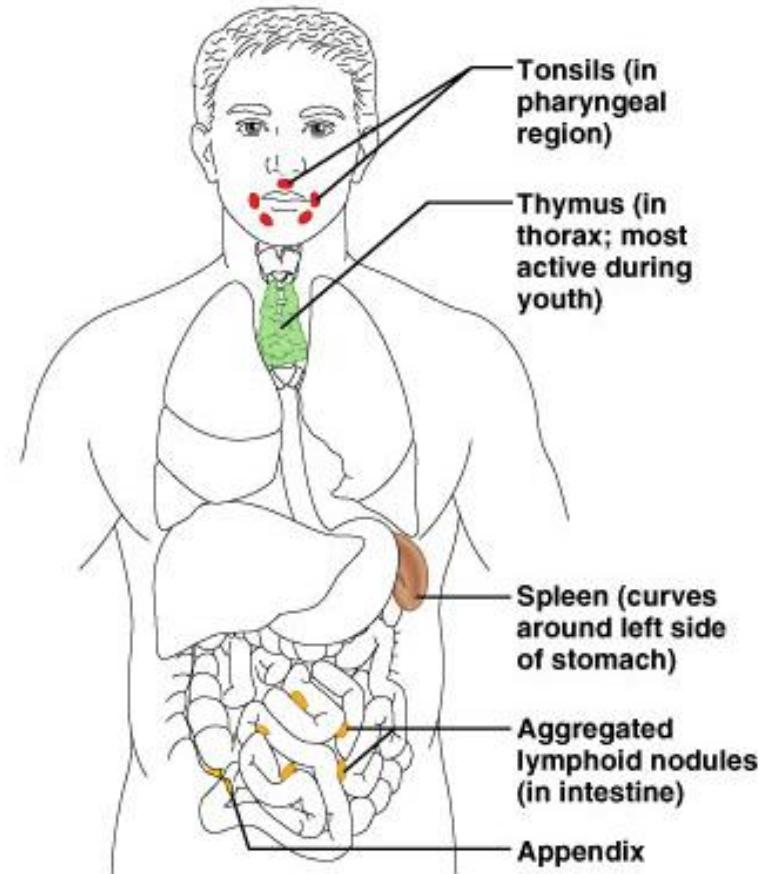
CD4 is a protein on Th (helper T cells) which recognizes class II MHCs

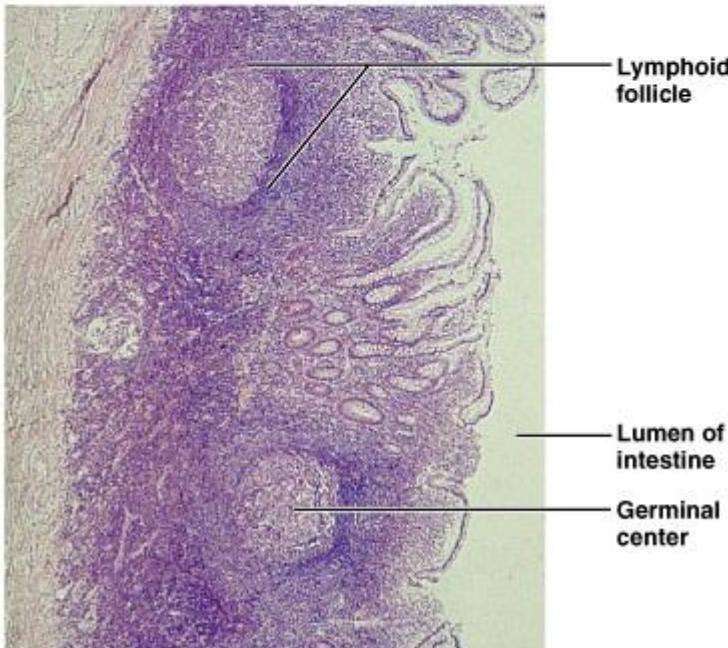
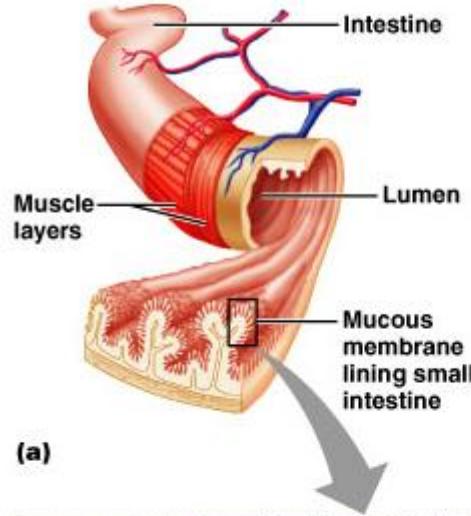
-Class II MHC cells are **only** B lymphocytes and macrophages: these take up extracellular antigens, e.g. bacteria which multiply outside cells, toxins produced by bacteria, etc.; MCH II binds these, takes them to surface, so the lymphocyte become an “antigen presenting cell”

-Helper (CD4) T cells secrete cytokines which stimulate the proliferation of activated B cells, cytotoxic T cells (CD8+) and macrophages and amplify their response

Lymphoid Organs

- Lymph nodes
- Spleen
- Thymus
- Tonsils
- Small intestine & appendix aggregated lymphoid nodules





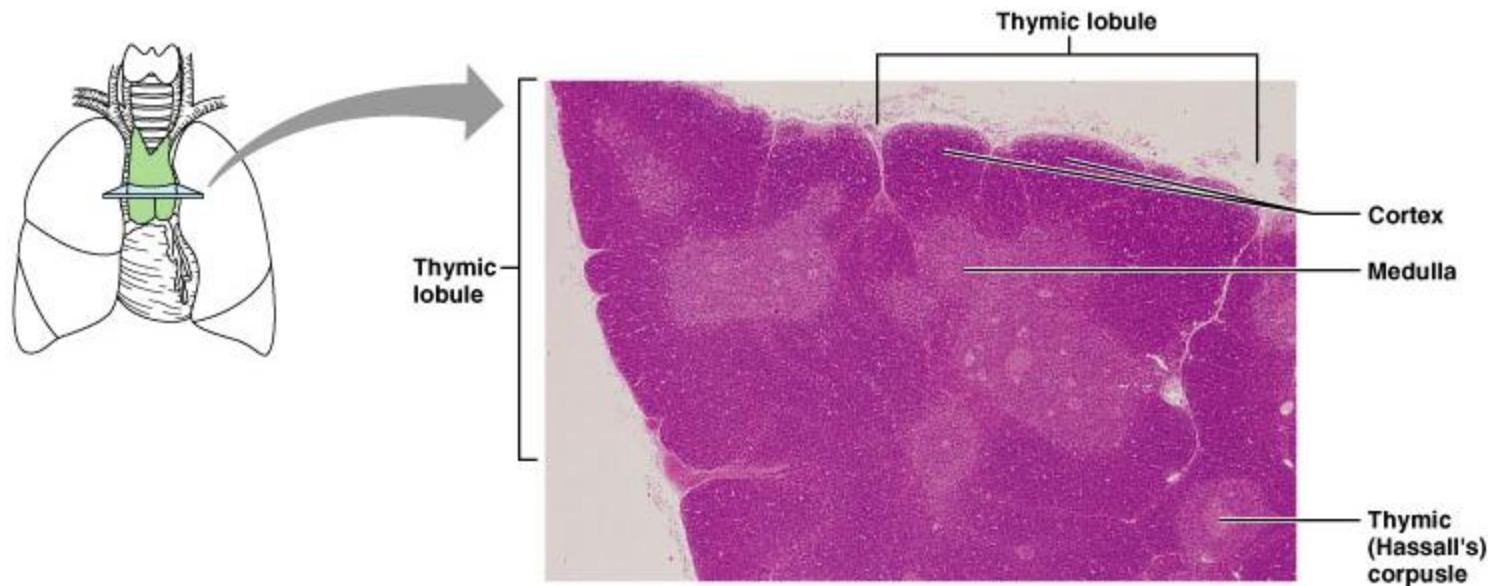
Lymphoid Tissue

Specialized connective tissue with vast quantities of **lymphocytes**

- Lymphocytes become activated
- Memory
- Macrophages & dendritic cells also
- Clusters of lymphoid nodules or follicles

Thymus

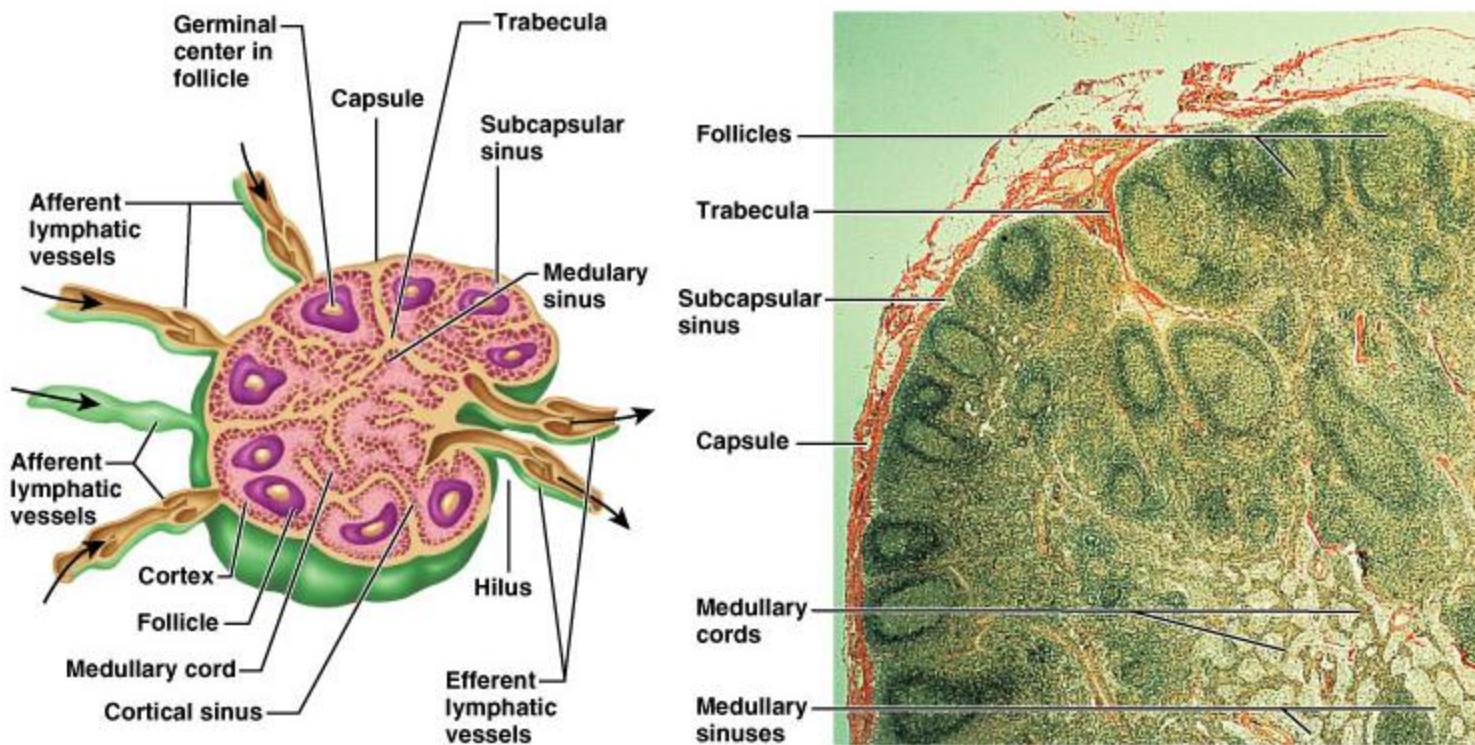
- Prominent in newborns, almost disappears by old age
- Function: T lymphocyte maturation (immunocompetence)
- Has no follicles because no B cells

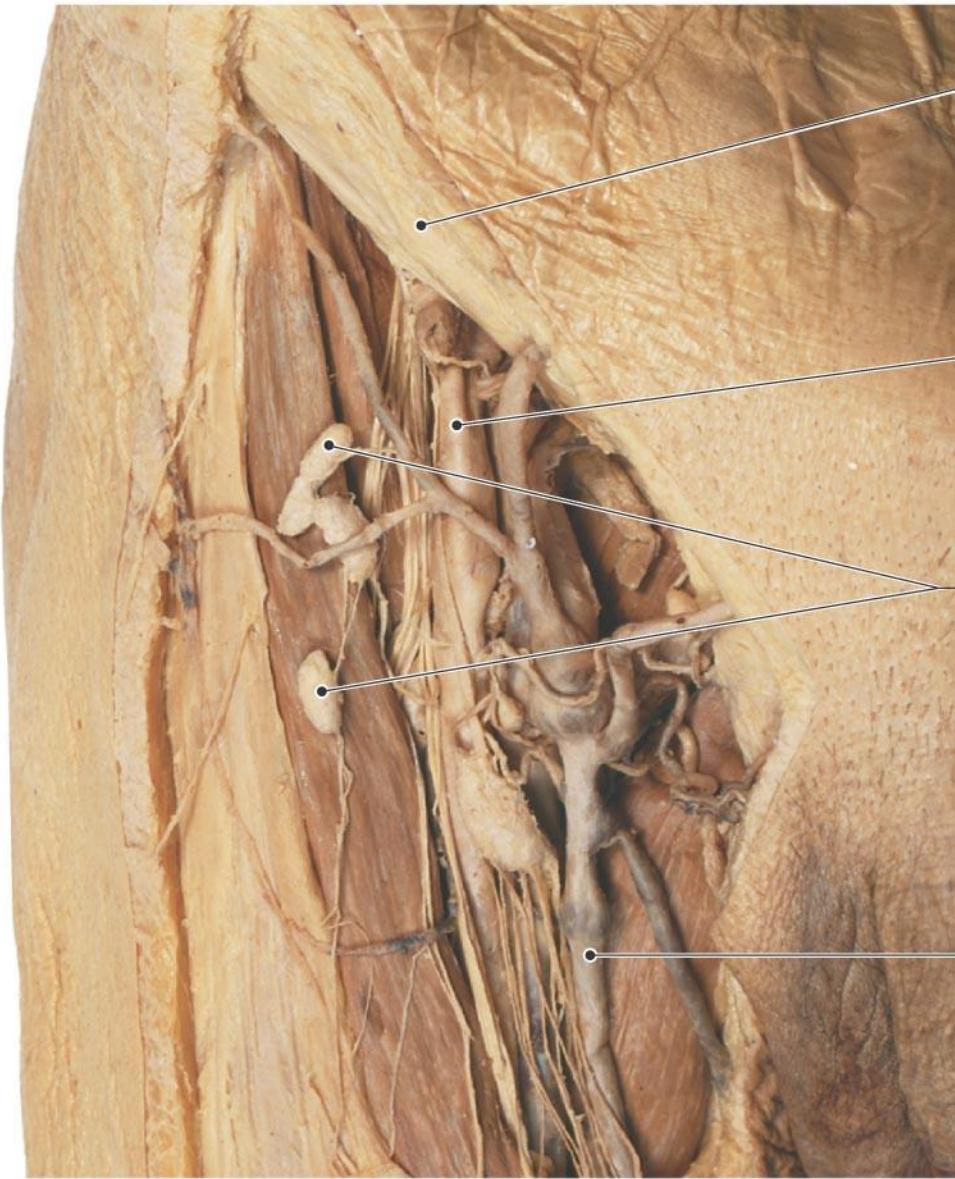


Lymph Nodes

- Lymphatic and immune systems intersect
- Masses of lymphoid tissue between lymph sinuses (see next slide)
- Some of antigens leak out of lymph into lymphoid tissue
- Antigens destroyed and B and T lymphocytes are activated: memory (aiding long-term immunity)

- Follicles: masses of lymphoid tissue divided into outer cortex & inner medulla
- All follicles and most B cells: outer cortex
- Deeper cortex: T cells, especially helper T cells
- Medullary cords: T & B lymphocytes and plasma cells





Inguinal ligament

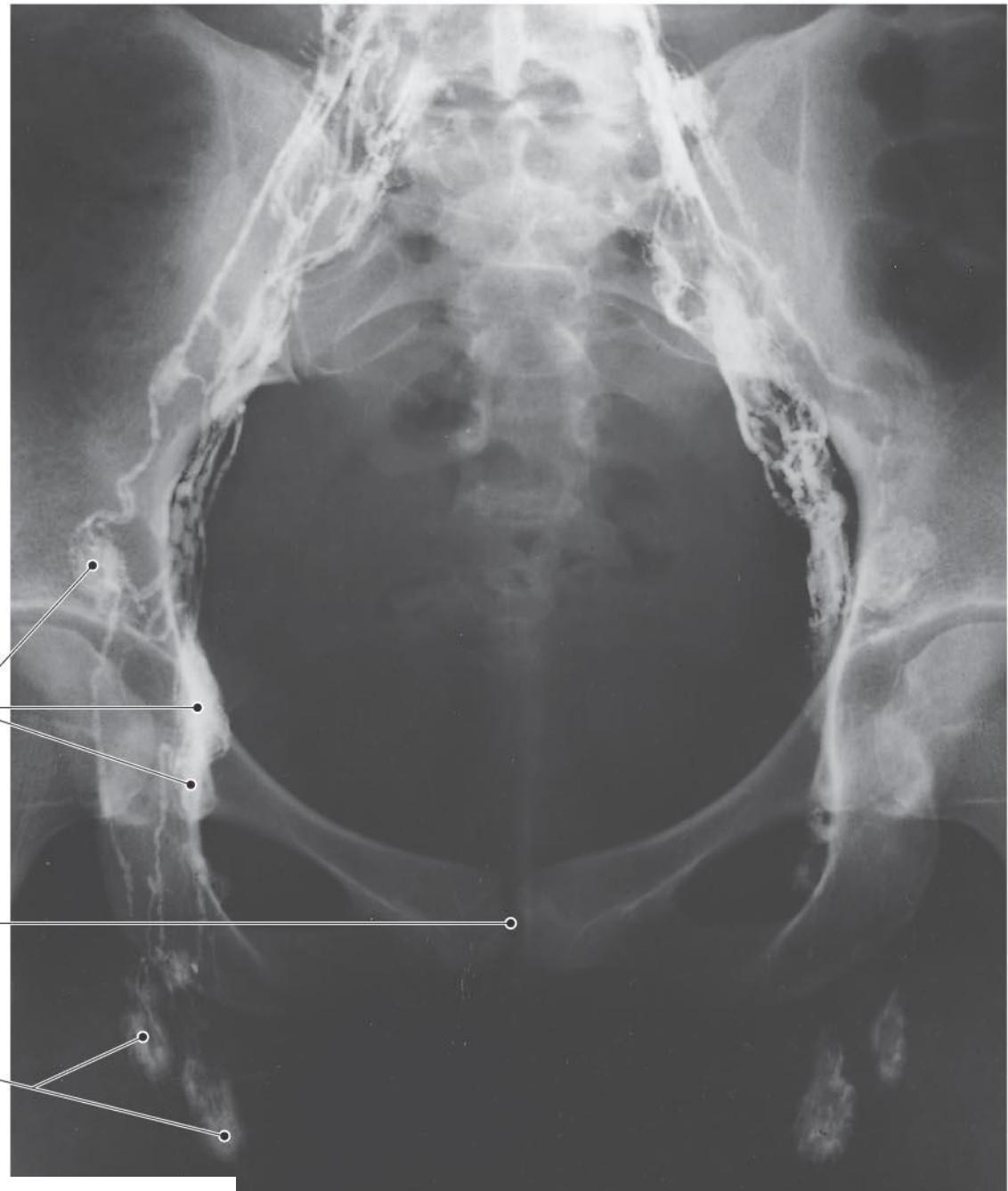
Femoral artery

Deep inguinal lymph nodes

Great saphenous vein

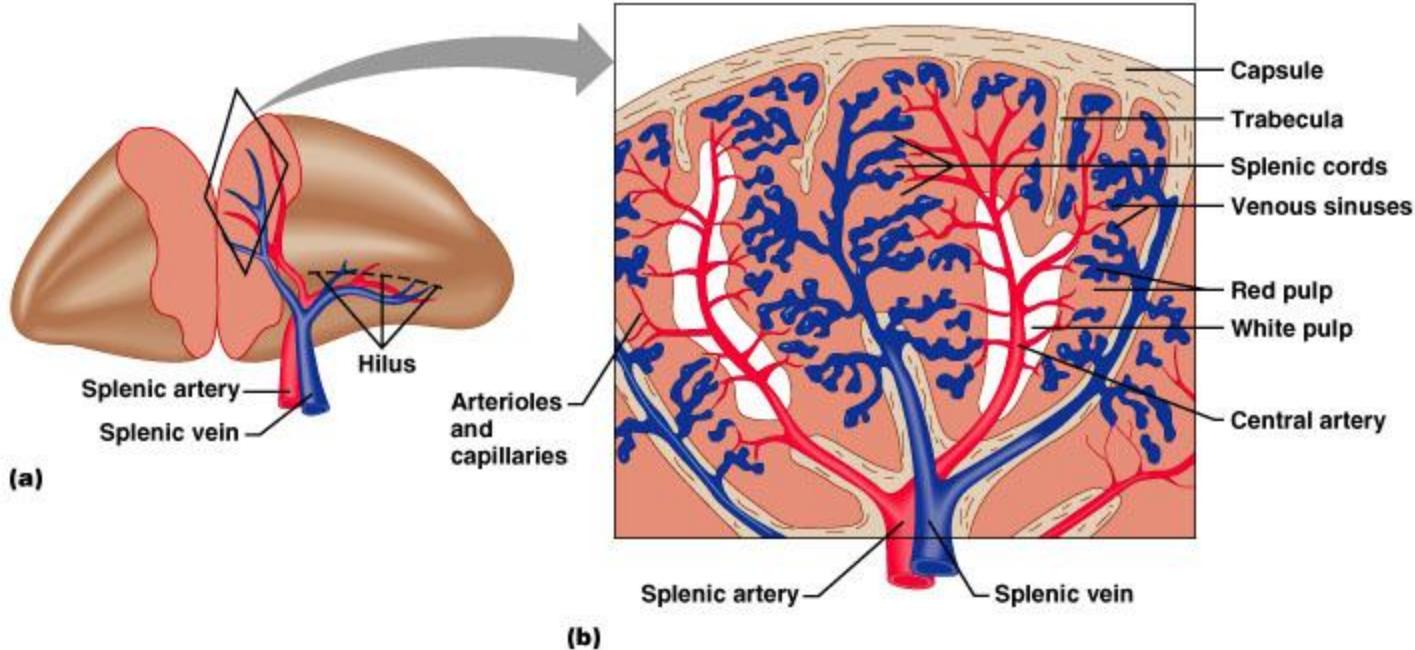
(a) Dissection of the upper right inguinal region in a male

lymphangiogram

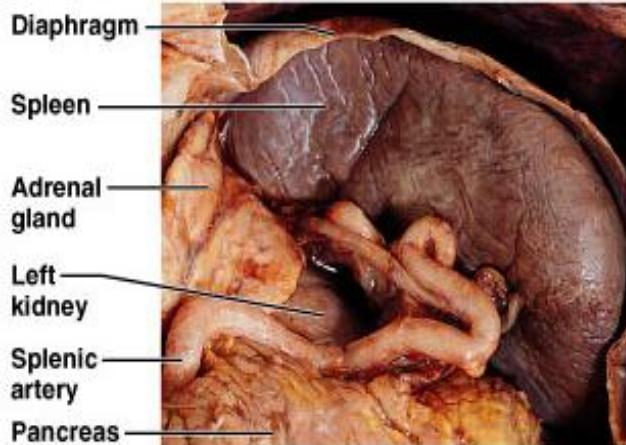


Spleen

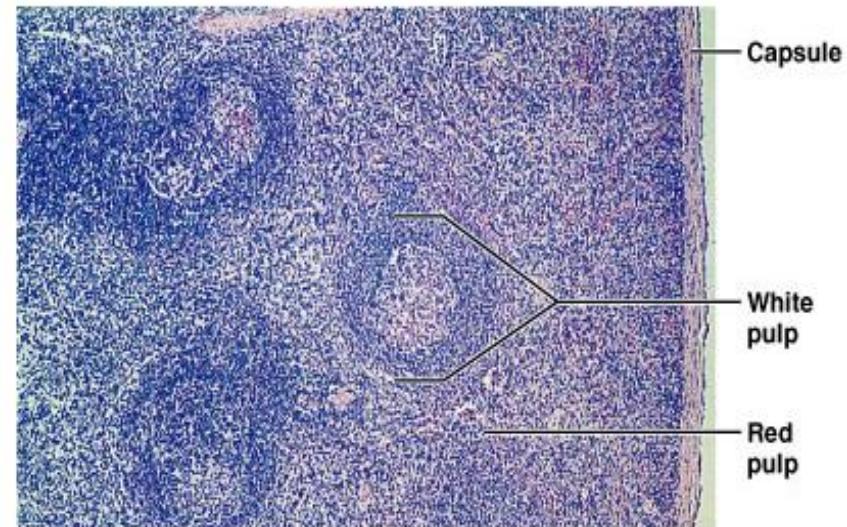
- Largest lymphoid tissue; is in LUQ posterior to stomach
- Functions
 - Removal of blood-borne antigens: “white pulp”
 - Removal & destruction of aged or defective blood cells: “red pulp”
 - Stores platelets
 - In fetus: site of hematopoiesis
- Susceptible to injury; splenectomy increases risk of bacterial infection



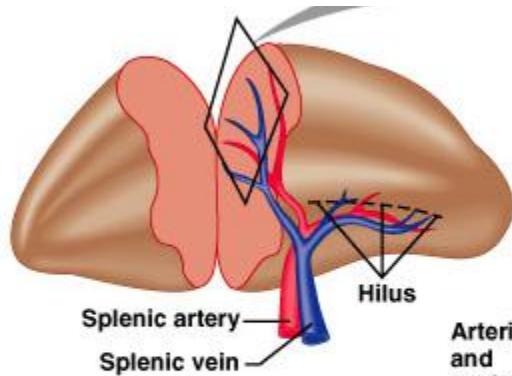
Spleen



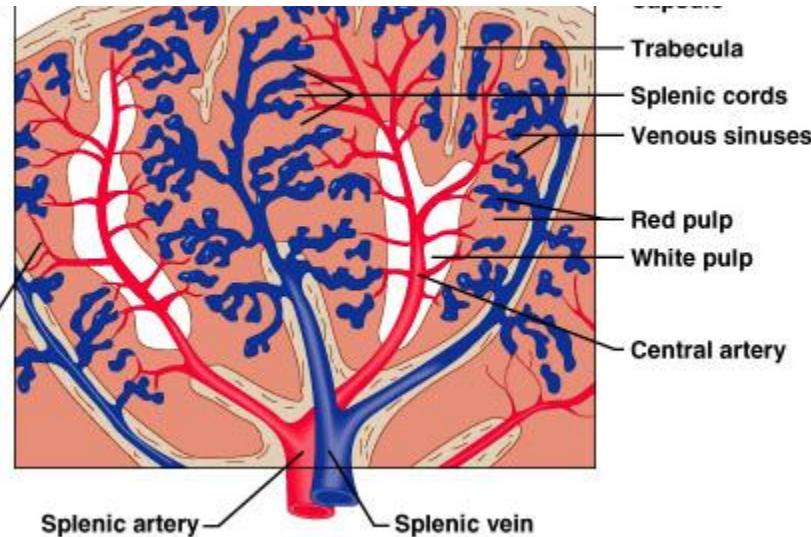
(c)



(d)



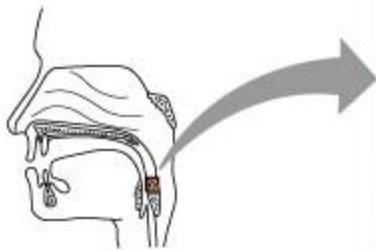
(a)



(b)

Tonsils

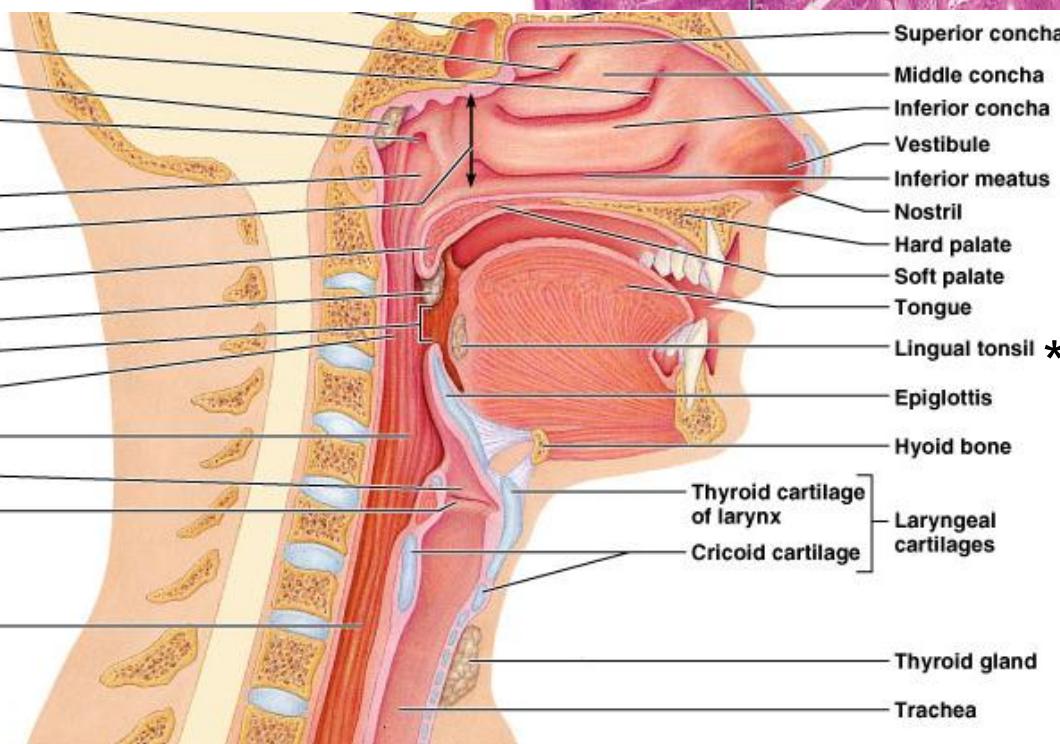
Simplest lymphoid tissue:
swellings of mucosa, form a circle



Crypts get infected in childhood

Crypt

Germinal centers in lymphoid follicles

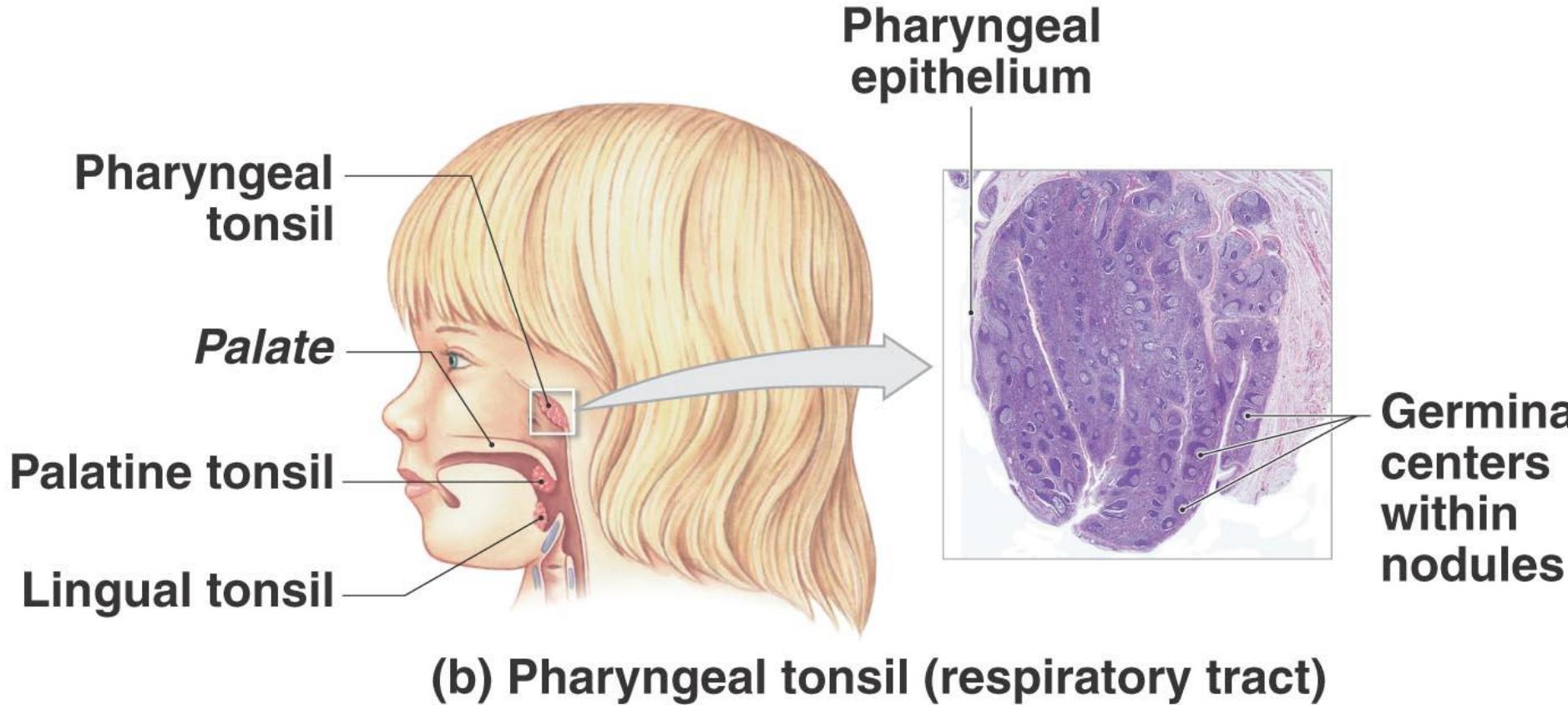


Palatine (usual tonsillitis)

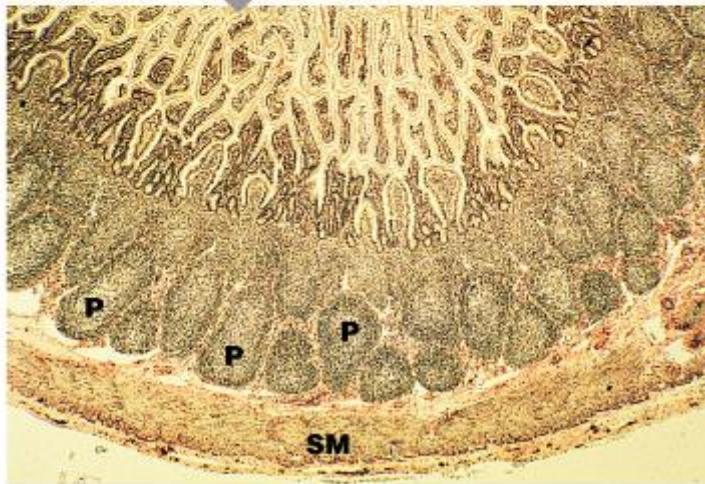
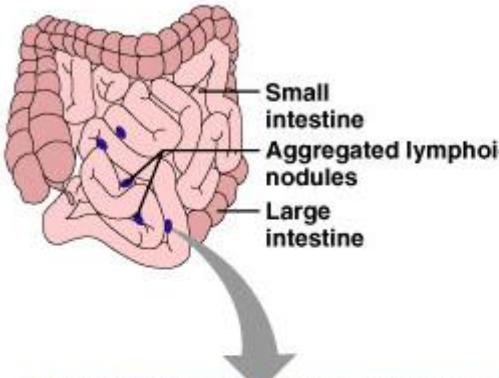
Lingual (tongue)

Pharyngeal (“adenoids”)

Tubal



Parts of the intestine are so densely packed with MALT (mucosa-associated lymphoid tissue) that they are considered lymphoid organs



- Aggregated lymphoid nodules (“Peyer’s Patches”)
 - About 40 follicles, 1 cm wide
 - Distal small intestine (ileum)
- Appendix

LYMPHATIC SYSTEM

REVIEW

- Lymph: fluid that is pushed out of capillary beds into tissue spaces—similar to interstitial fluid
- Absorbed by lymphatic capillaries through one-way minivalves → allow fluid to enter but not leave
- Valves are different from those found in veins

LYMPHATIC VESSELS

- Lymphatic vessels also pick up cell debris, bacteria and viruses—enter lymph nodes for “cleaning”
- Fluid moved toward heart through larger and larger lymphatic vessels
- Vessels contain valves to prevent backflow

LYMPHATIC VESSELS

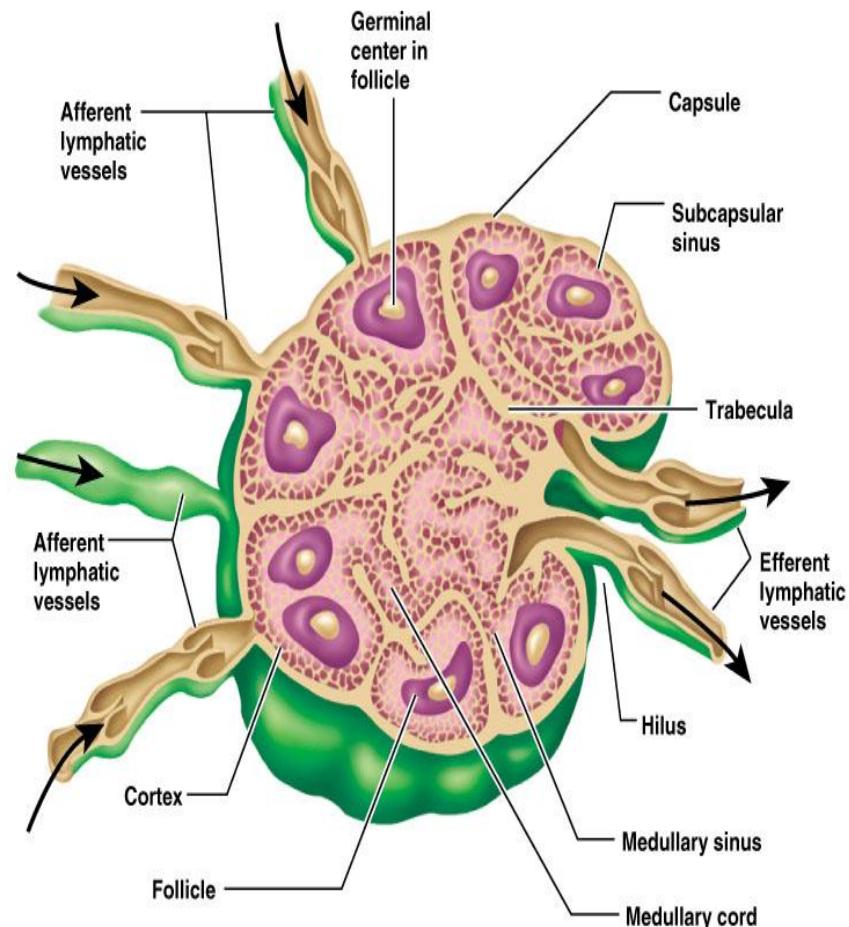
- Lymph is not pumped; - moved by milking action of skeletal muscles & thoracic pressure changes
- Right lymphatic duct - drains lymph from right arm and right side of head and thorax
- Thoracic duct—receives lymph from rest of body
- Re-enters venous system through subclavian veins

LYMPH NODES

- Act as filters along lymphatic vessels removing foreign material
- Contain macrophages and lymphocytes
- Outer cortex—collections of lymphocytes in follicles—(germinal centers)—enlarge when B lymphocytes are producing plasma cells which release antibodies
- Sinuses—dilated channels; collect lymph
- Trabeculae—compartmentalize the node
- Medulla—contains phagocytes

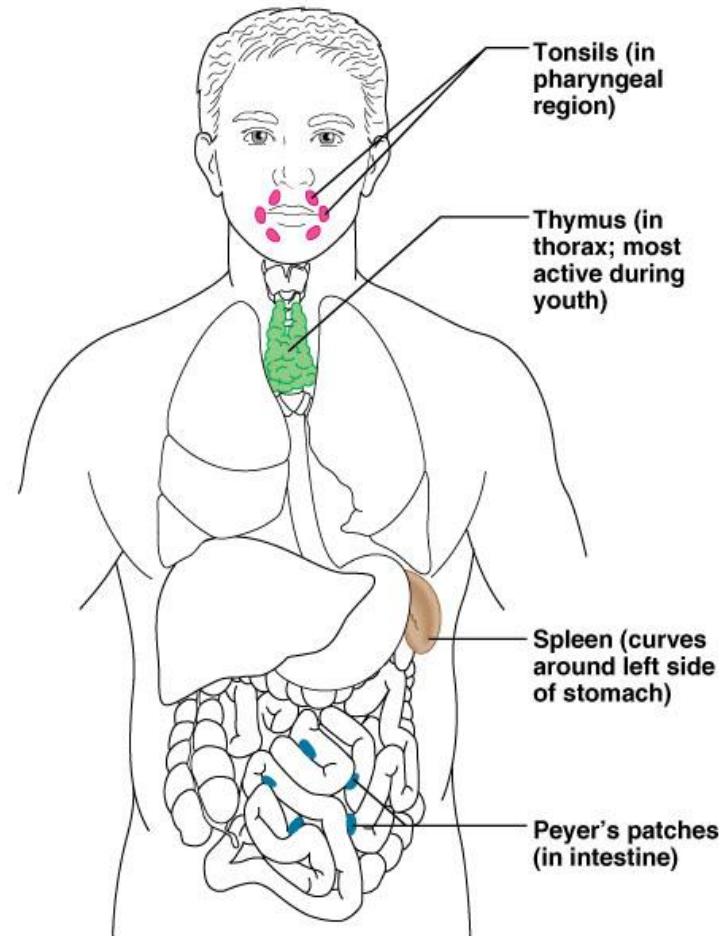
LYMPH NODES

- Outer cortex—collections of lymphocytes in follicles—germinal centers
- Enlarge when B lymphocytes are producing plasma cells which release antibodies
- Sinuses—collection area
- Trabeculae—compartmentalize the node
- Medulla—contains phagocytotes



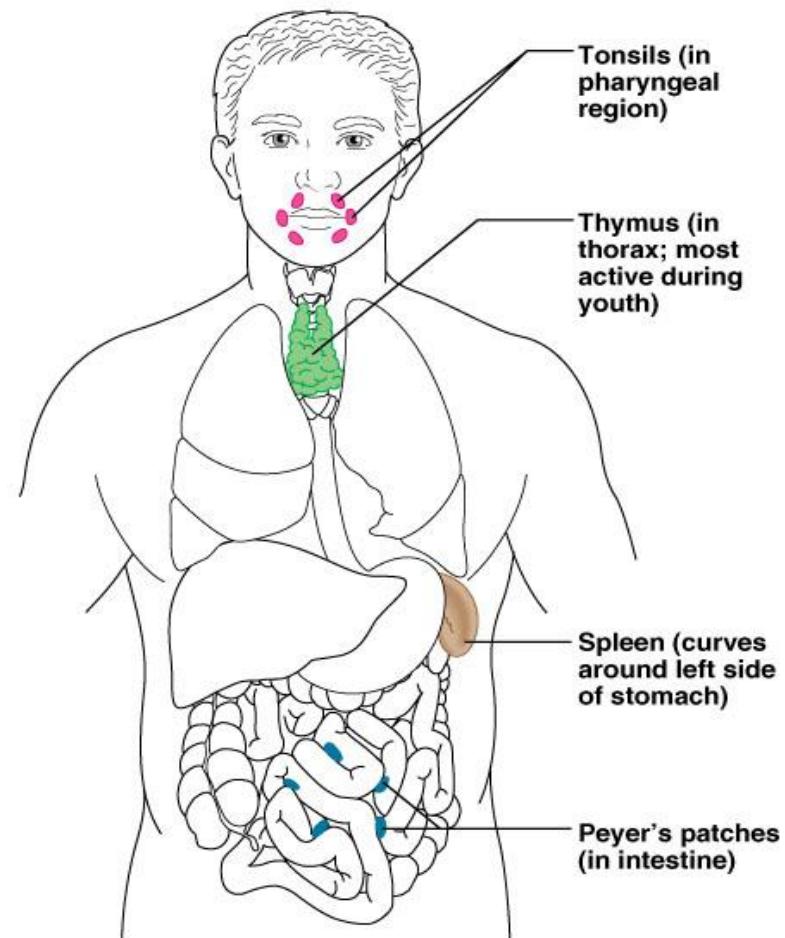
OTHER LYMPHOID ORGANS

- **Spleen:** filters and cleanses blood of bacteria, viruses and debris—destroys worn out blood cells returning breakdown products to liver
- **Thymus:** low in the throat; produces thymosin that functions at peak levels in youth programming of T cells



OTHER LYMPHOID ORGANS

- **Tonsils:** pharynx; removes bacteria and other pathogens
- **Peyer's Patches:** small intestine; contain macrophages that collect and destroy bacteria
- **MALT:** mucosa-associated lymphatic tissue—Peyer's Patches and tonsils—protect upper respiratory and digestive tracts



**NON-SPECIFIC BODY
DEFENSES**

**MECHANICAL
BARRIERS,
CELLS, &
CHEMICALS**

FIRST LINE OF DEFENSE

- Surface Membrane Barriers:
- Skin
- Physical barrier—covers internal tissues
- Acidic pH—skin is acidic; prevents bacterial growth
- Sebum—bacteria killing enzymes
- Keratin—protects against acids, alkalis, bacterial enzymes
- Hair—prevents attachment of microbes to skin

FIRST LINE OF DEFENSE

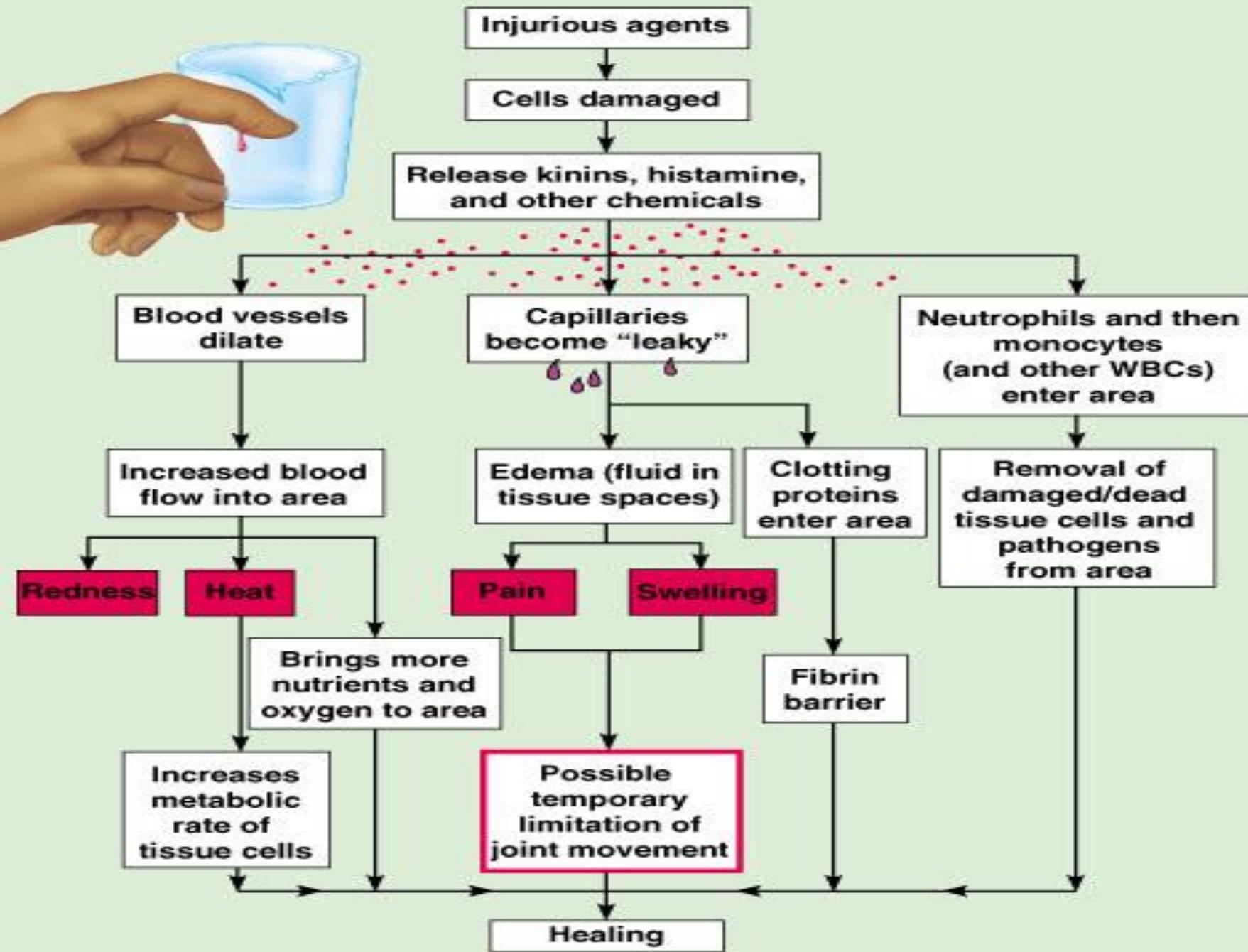
- Surface Membrane Barriers:
- Mucous Membranes:
- Mucus
- Gastric juice—HCl and protein-digesting enzymes
- Lysozyme—saliva and lacrimal fluid (tears)
- Acidic vaginal secretions—acid mantle
- Cilia

SECOND LINE OF DEFENSE

- **Non-specific Cellular Defense:**
- **Phagocytes**—engulf and destroy pathogens
- **Natural Killer Cells**—promote lysis by secretion of perforin → breaks down cell membrane

NON-SPECIFIC CELLULAR DEFENSE

- **Inflammatory Response**—redness, heat, swelling (edema), pain – the 4 “cardinal signs”
- Begins with “chemical alarm”—release of histamine and kinins from mast cells
- Blood vessels become dilated
- Capillaries become “leaky”
- Pain receptors activated
- **Chemotaxis**—phagocytes and WBCs attracted to the area



NON-SPECIFIC CELLULAR DEFENSE

- Antimicrobial Chemicals:
- Complement—proteins that attach to membrane
- Causes lysis, intensifies inflammation, enhances phagocytosis by opsonization
- Opsonization: coating of pathogen with complement (and antibodies) making them easier to attack

NON-SPECIFIC CELLULAR DEFENSE

- Antimicrobial Chemicals:
- Interferons—protect uninfected cells; released by cells infected by viruses
- Urine—normally acidic; inhibits bacterial growth

NON-SPECIFIC CELLULAR DEFENSE

- Fever: body “thermostat” regulated by hypothalamus; does the following:
 - increases metabolic rate
 - stimulates liver/spleen to gather Fe & Zn
 - denatures proteins – (inhibits bacteria)
 - speeds the repair process
- Can be reset by pyrogens (fever promoting compounds) released by WBCs

THIRD LINE OF DEFENSE

- The Immune System: specific defense system!!!
- Acts more slowly than non-specific defenses
- acts to recognize foreign molecules → antigens
- antigens: excite immune system; provoke immune response;
 - foreign proteins
 - microorganisms
 - large carbohydrates
 - nucleic acids

CELLS OF THE IMMUNE SYSTEM

- Lymphocytes:
- produced in bone marrow from hemocytoblasts—are immature
- 2 types: B cells and T cells
- Which type the immature lymphocyte becomes depends on where it becomes immunocompetent → capable of responding to antigen by binding to it

CELLS OF THE IMMUNE SYSTEM

- T cells arise from lymphocytes that migrate to the thymus → directed by thymosin
- B cells become immunocompetent in bone marrow—how is ???
- Which types of antigens our body can respond to is **genetically determined**

CELLS OF THE IMMUNE SYSTEM

- After becoming immunocompetent both T cells and B cells migrate to lymph nodes, spleen, and loose connective tissues where they will encounter antigens
- Lymphocytes circulate continuously throughout the body—especially T cells

MACROPHAGES

- Arise from monocytes
- Major role is to engulf foreign particles and “present” fragments of these antigens on their cell surfaces where they can be recognized by immunocompetent T cells
- Secrete proteins—monokines—which aid T cells in the immune response

MACROPHAGES

- Activated T cells secrete lymphokines which causes macrophages to become “killer macrophages”—vigorous response results
- Macrophages remain fixed in lymphoid organs → DO NOT circulate like lymphocytes

- INTERACTIONS BETWEEN LYMPHOCYTES AND MACROPHAGES UNDERLIE VIRTUALLY ALL PHASES OF THE IMMUNE RESPONSE

TYPES OF IMMUNITY

- **Humoral immunity**
 - Antibody-mediated immunity
 - Cells produce chemicals for defense
- **Cellular immunity**
 - Cell-mediated immunity
 - Cells target virus infected cells

Humoral (Antibody-Mediated) Immune Response:

- Immunocompetent (but immature) B cells are “activated” when antigens bind to their cell surfaces
- clonal selection: lymphocyte multiplies producing identical copies of itself—clone
- This is the primary immune response
- Most B cell clone cells become plasma cells producing antibodies capable of binding to a specific antigen

Humoral (Antibody-Mediated) Immune Response:

- **Memory cells**: B cell clone members that do not become plasma cells—capable of responding to the same antigen at a later time
- **Secondary response**: much faster and longer lasting than primary response

Primary Response
(initial encounter
with antigen)

B lymphoblasts

Proliferation to
form a clone

Plasma
cells

Secreted
antibody
molecules

Secondary Response
(can be years later)

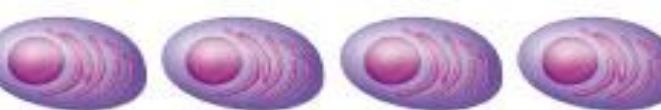
Antigen

Antigen binding
to a receptor on a
specific B lymphocyte
(B lymphocytes with
non-complementary
receptors remain
inactive)

Memory
B cell

Subsequent challenge
by same antigen

Clone of cells
identical to
ancestral cells



Plasma
cells

Secreted
antibody
molecules

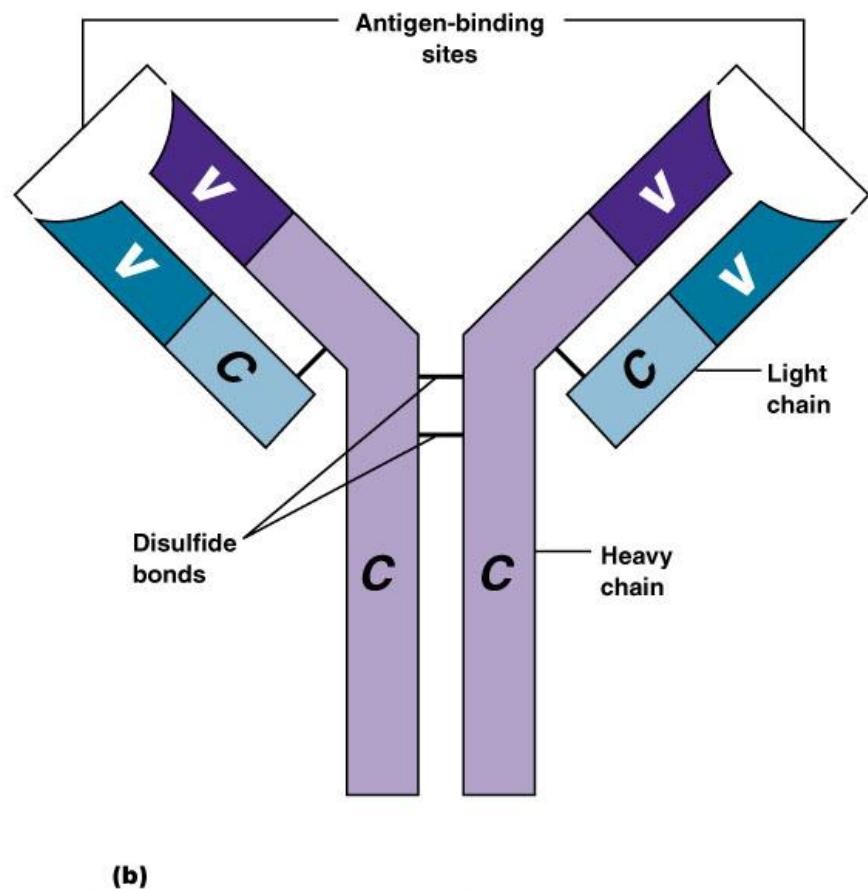
Memory
B cells

Antibodies (Immunoglobulins) (Igs)

- Soluble proteins secreted by B cells (plasma cells)
- Carried in blood plasma
- Capable of binding specifically to an antigen

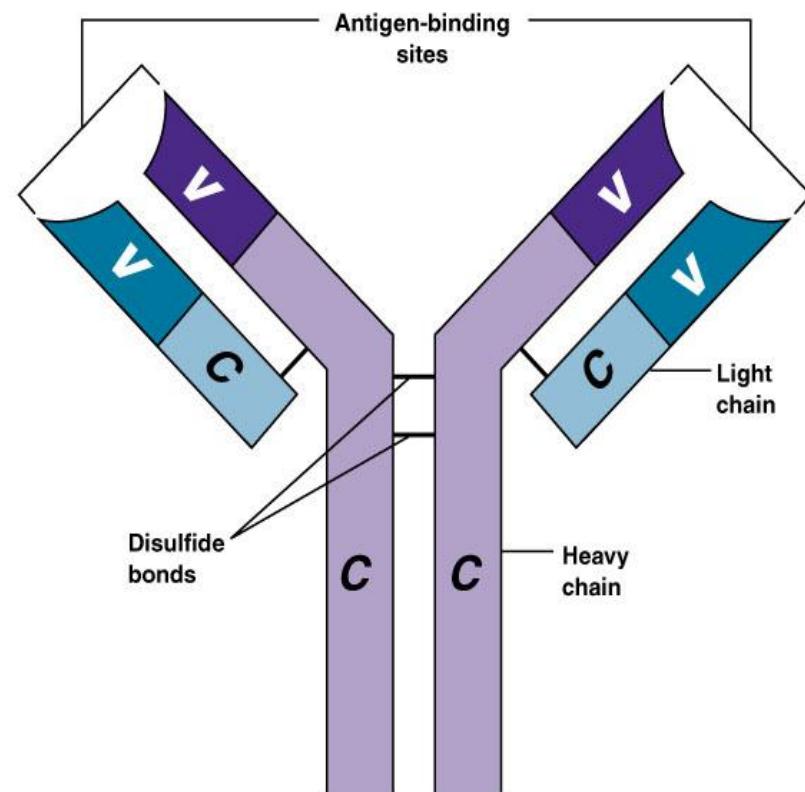
ANTIBODY STRUCTURE

- Y or T shaped: 4 polypeptide chains linked by disulfide bonds
- 2 chains identical—heavy chains
- 2 shorter chains—light chains—also identical to one another



ANTIBODY STRUCTURE

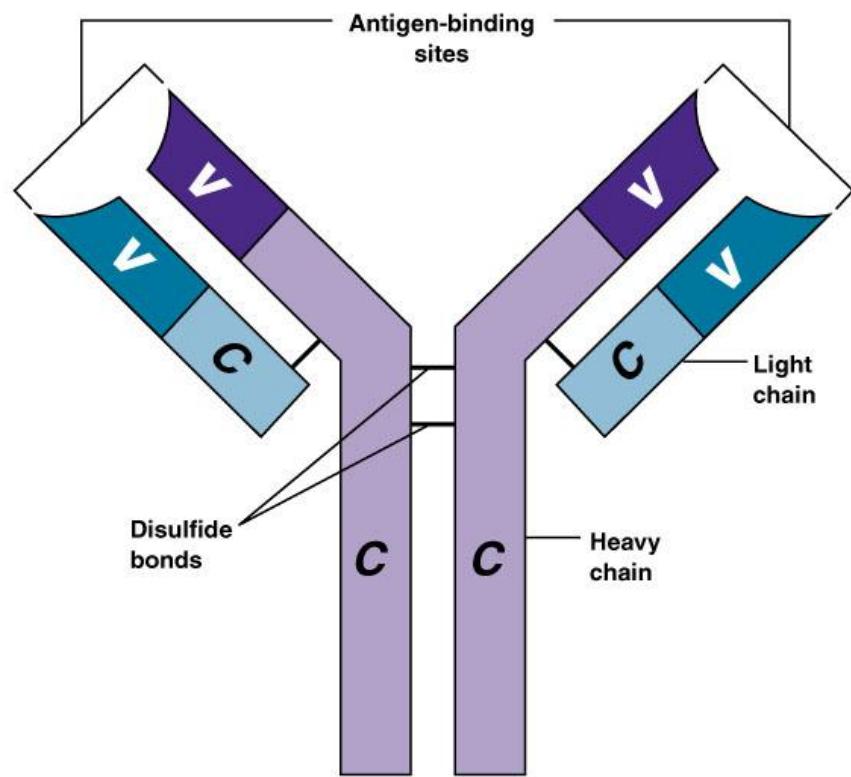
- **Constant region:**
- **Nearly the same on all antibodies**
- **Determines the class of the antibody**
- **Determines how the antibody carries out its immune role**
- **Forms the “stem” of the antibody**



(b)

ANTIBODY STRUCTURE

- Variable region:
- **Regions on both heavy and light chains which form antigen-binding site**
- **Each antibody has two antigen-binding sites**



(b)

ANTIBODY CLASSES

- **MADGE:**
- Ig M
- Ig A
- Ig D
- Ig G
- Ig E
- All have same basic Y-shaped structure—
monomer

ANTIBODY CLASSES

- **Ig M:**
- **Consists of 5 linked monomers**
- **First Ig class released class released to plasma by plasma cells during primary response**
- **Potent agglutinating agent**
- **Fixes complement**

ANTIBODY CLASSES

- **Ig A:**
- Occurs in both monomer and dimer forms
- Bathes and protects mucosal cells from attachment by pathogens

- **Ig D:**
- Cell surface receptor of immunocompetent B cells

ANTIBODY CLASSES

- **IgG:**
- **Main antibody of primary and secondary responses**
- **Crosses placenta and provides passive immunity to fetus**
- **Fixes complement**

ANTIBODY CLASSES

- **IgE:**
- “**Troublemaker**” antibody involved in allergies
- Binds to mast cells and basophils
- Triggers release of histamine and other chemical that mediate inflammation

ANTIBODY FUNCTION

- **4 major ways to inactivate antigens:**
- 1. **Complement Fixation:** (also during non-specific responses)
- Binds to antibodies attached to cellular targets → results in lysis of foreign cell and enhancement of inflammatory response

ANTIBODY FUNCTION

- 2. Neutralization:
- Occurs when antibodies bind to specific sites on bacterial endotoxins or on viruses to block harmful effects
- 3. Agglutination:
- Cross-linking of antigen-antibody complexes causing clumping of foreign cells
- Type of reaction involved with mismatched blood is transfused

ANTIBODY FUNCTION

- 4. Precipitation:
- Cross-linking of antigen-antibody complexes that become so large they settle out of solution

NATURALLY ACQUIRED IMMUNITY

- **Active Immunity:**
- Acquired by infection or contact with a pathogen
- Immunological memory is established

NATURALLY ACQUIRED IMMUNITY

- **Passive Immunity:**
- Antibodies (IgG) pass from mother to fetus via placenta
- Antibodies can also be passed to fetus through breast milk
- **NO immunological memory is**
established

ARTIFICIALLY ACQUIRED IMMUNITY

- **Active Immunity:**
- **Provided by vaccines—most contain dead or attenuated (extremely weakened) pathogens**
- **Boosters sometimes available to intensify later immune response**
- **Prevent most of the signs and symptoms of the disease they are given for**
- **Provide immunological memory**

ARTIFICIALLY ACQUIRED IMMUNITY

- **Passive Immunity:**
- Provided by injection of **immune serum** (gamma globulin)
- Sera are used for hepatitis, poisonous snakebites, botulism, rabies, and tetanus
- These diseases/toxins would kill the individual before active immunity could occur
- **NO immunological memory established**

Acquired immunity

Naturally acquired

**Active
Infection;
contact
with
pathogen**

Passive
Antibodies pass from mother to fetus via placenta; or to infant in her milk

Artificially acquired

Active
Vaccine; dead or attenuated pathogens

Passive
Injection of immune serum (gamma globulin)

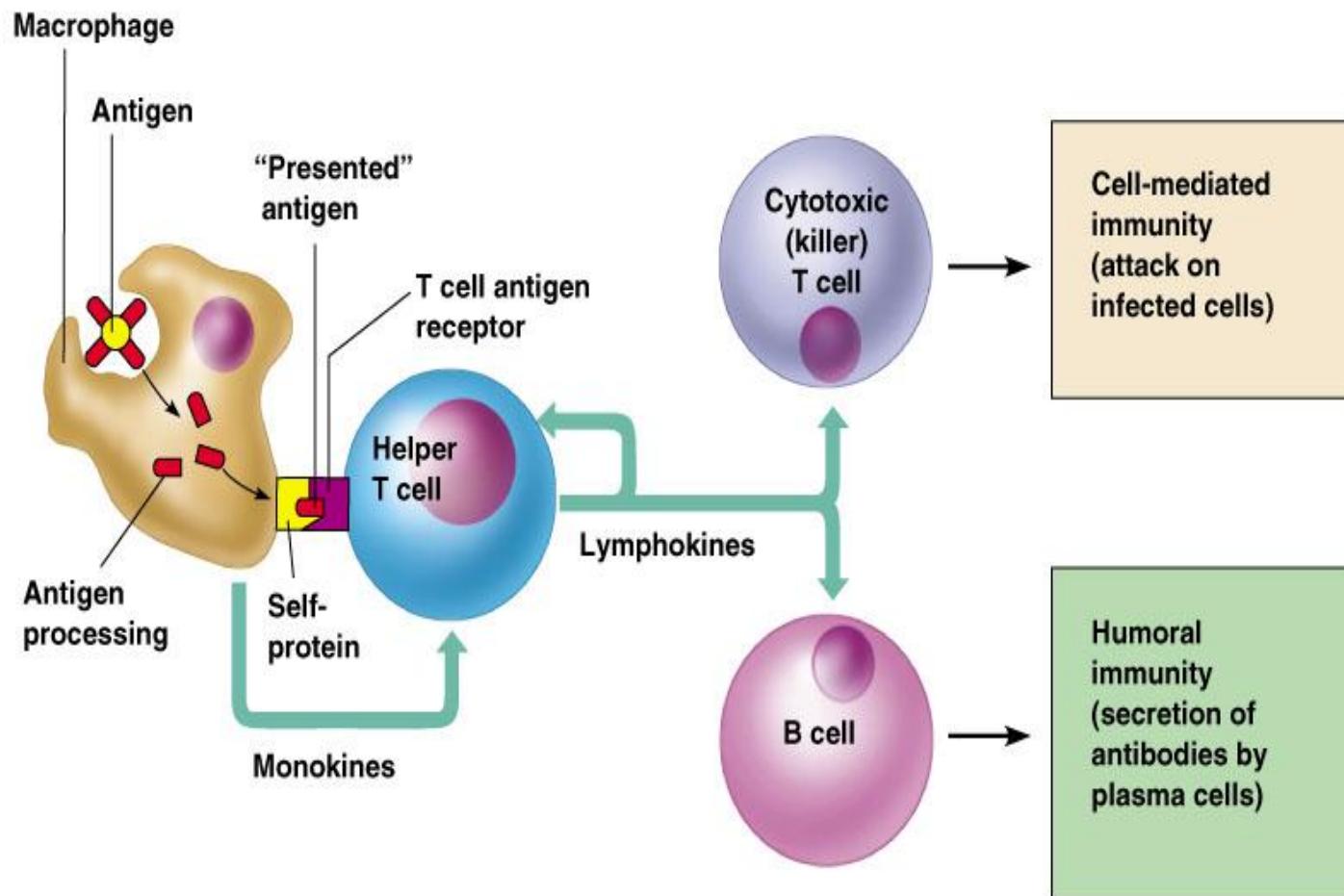
CELL MEDIATED IMMUNE RESPONSE

- Immunocompetent T cells are activated to form a clone by binding with a “recognized” antigen
- T cells cannot bind with “free” antigens like B cells can

CELL MEDIATED IMMUNE RESPONSE

- **Antigens must be presented by macrophages to an immunocompetent T cell (antigen presentation)**
- **T cells must recognize non-self and self (double recognition)**
- **After antigen binding, clones form as with B cells, but different classes of cells are produced**

CELL MEDIATED IMMUNE RESPONSE



ANTIGEN RECOGNITION

- “Double recognition” must occur:
- Antigens must be “presented” by macrophages
- Macrophages engulf antigens and break them down
- Fragments of the antigen appear on the outer surface of the macrophage
- T cells can then bind with the antigen fragments presented

CLASSES OF T CELL CLONES

- **Cytotoxic (Killer) T Cells**
- **Helper T Cells**
- **Suppressor T Cells**
- **Delayed Hypersensitivity T Cells**
- **Memory Cells**

CYTOTOXIC (KILLER) T CELLS

- Specialize in killing virus-infected, cancer, or foreign graft cells
- Act by binding and inserting toxic chemical (perforin) which causes target cell to rupture

HELPER T CELLS

- Act as “managers” of the immune system
- Circulate throughout the body recruiting other cells to fight invaders
- Interact directly with B cells to increase clone production
- Release chemicals (lymphokines) to:
 - 1) stimulate killer T cells and B grow and divide
 - 2) attract protective WBCs (neutrophils) into affected area
 - 3) enhance ability of macrophages

SUPPRESSOR T CELLS

- Release chemicals to wind down activity of both T and B cells**

DELAYED HYPERSENSITIVITY T CELLS

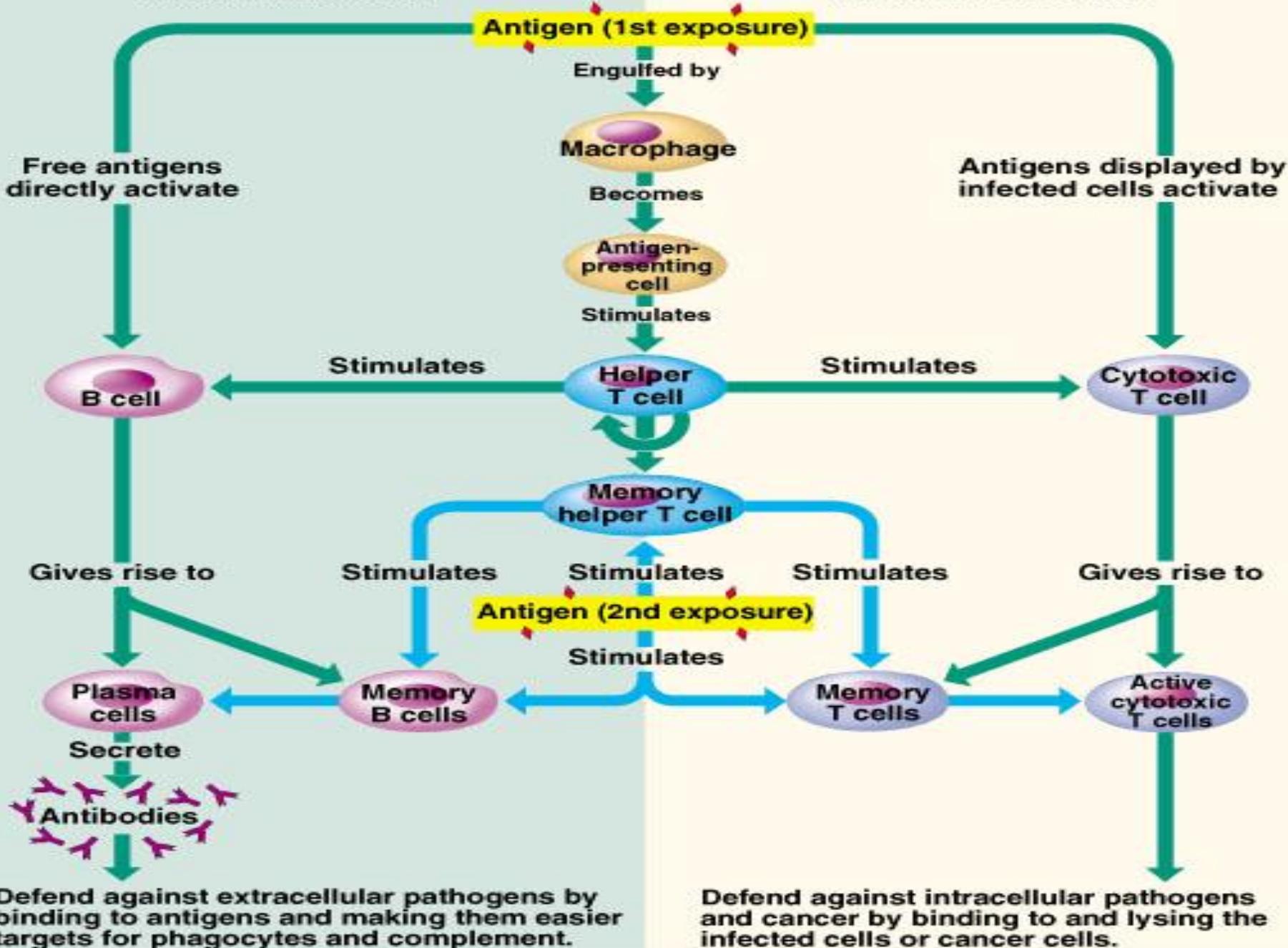
- Effector cells that play major role in allergic and chronic infections**

MEMORY CELLS

- Respond to subsequent infections or meetings with the same antigen**

HUMORAL (ANTIBODY-MEDIATED) IMMUNE RESPONSE

CELL-MEDIATED IMMUNE RESPONSE



TRANSPLANTS

- **Autografts:**
- Same person
- **Isograft:**
- Identical twin
- **Allograft:**
- Unrelated person; 75% match needed
- **Xenograft:**
- Different animal species

IMMUNOSUPPRESSIVE THERAPY

- **Corticosteroids, radiation, cytotoxic drugs, immunosuppressor drugs**
- **Major problem** → bacterial or viral infection while the immune system is suppressed

ALLERGIES

- Many small molecules (called haptens or incomplete antigens) are not antigenic, but link up with our own proteins
- The immune system may recognize and respond to a protein-hapten combination
- The immune response is harmful rather than protective because it attacks our own cells

ALLERGIES

- **Immediate hypersensitivity (acute hypersensitivity)**
- **Anaphylactic shock**
- **Delayed hypersensitivities**
- **Mantoux and tine tests**

ACUTE HYPERSENSITIVITY

- Runny nose, watery eyes, itchy reddened skin (hives)**
- Ig E antibodies bind to mast cells**
- Histamine release**
- Antihistamines used to treat**

ANAPHYLACTIC SHOCK

- **Systemic acute response**
- **Allergen directly enters blood and rapidly circulates**
- **Bee sting; spider bite; penicillin or other drug which acts as a hapten (small molecule; incomplete antigen)**
- **Epinephrine used to treat**

DELAYED HYPERSENSITIVITIES

- Mediated by cytotoxic T cells
- Contact dermatitis—poison ivy, heavy metals, cosmetics, deodorants
- Corticosteroids used to treat

MANTOUX AND TINE TESTS

- Used to detect TB
- Depend on delayed hypersensitivity reactions

IMMUNODEFICIENCIES

- **SCID: severe combined immunodeficiency**
- **Marked deficit of both B and T cells**
- **Lack of sufficient T cells affects both arms of the immune response**
- **Have almost no protection against pathogens of any type**
- **“bubble children”**

IMMUNODEFICIENCIES

- **AIDS: acquired immune deficiency syndrome**
- HIV specifically targets helper T cells resulting in depression of cell-mediated immunity
- Drug therapies have improved outlook
- *Pneumocystis pneumonia* and *Kaposi's sarcoma* are characteristic

AUTOIMMUNE DISEASES

- **Multiple sclerosis**
- **Myasthenia gravis**
- **Graves' disease**
- **Juvenile (Type I) diabetes mellitus**
- **Systemic lupus erythematosus (SLE)**
- **Glomerulonephritis**
- **Rheumatoid arthritis**

Disorders of Immunity: Immunodeficiencies

- Production or function of immune cells or complement is abnormal**
- May be congenital or acquired**
- Includes AIDS – Acquired Immune Deficiency Syndrome**

Disorders of Immunity: Autoimmune Diseases

- The immune system does not distinguish between self and non-self**
- The body produces antibodies and sensitized T lymphocytes that attack its own tissues**

AUTOIMMUNE DISEASES

- Examples of autoimmune diseases
 - Multiple sclerosis: white matter of brain and spinal cord are destroyed
 - Myasthenia gravis: impairs communication between nerves and skeletal muscles
 - Juvenile diabetes: destroys pancreatic beta cells that produce insulin
 - Rheumatoid arthritis: destroys joints

AUTOIMMUNE DISEASES

- Examples of autoimmune diseases (continued)
 - Systemic lupus erythematosus (SLE): affects kidney, heart, lung and skin
 - Glomerulonephritis: impairment of renal function

Self Tolerance Breakdown

- Inefficient lymphocyte programming
- Appearance of self-proteins in the circulation that have not been exposed to the immune system
 - Eggs
 - Sperm
 - Eye lens

Self Tolerance Breakdown

- **Cross-reaction of antibodies produced against foreign antigens with self-antigens**
 - Rheumatic fever

Developmental Aspects of the Lymphatic System and Body Defenses

- **Except for thymus and spleen, the lymphoid organs are poorly developed before birth**
- **A newborn has no functioning lymphocytes at birth; only passive immunity from the mother**
- **If lymphatics are removed or lost, severe edema results, but vessels grow back in time**