B. Pharmacy 1st Semester - Human Anatomy and Physiology 1 Notes

UNIT – 3

🩸 BODY FLUIDS AND BLOOD

Points to be covered in this topic

➞ 1. BODY FLUIDS
➞ 2. COMPOSITION AND FUNCTIONS OF BLOOD
➞ 3. HEMOPOIESIS
➞ 4. FORMATION OF HEMOGLOBIN
➞ 5. ANEMIA
➞ 6. MECHANISMS OF COAGULATION
➞ 7. BLOOD GROUPING
➞ 8. Rh FACTORS
➞ 9. TRANSFUSION, ITS SIGNIFICANCE AND DISORDERS OF BLOOD
➞ 10. RETICULO ENDOTHELIAL SYSTEM

🌊 BODY FLUIDS

INTRODUCTION

- Body fluids are aqueous solutions containing dissolved chemicals that are found inside the cells, around the cells, and throughout the body.
- The human body is approximately 60% water by weight, with variations depending on age, gender, and body composition.

- Body fluids are essential for maintaining homeostasis, transporting nutrients, removing waste products, and facilitating various physiological processes.

CLASSIFICATION OF BODY FLUIDS

Body fluids can be classified into two major compartments:

1. Intracellular Fluid (ICF)

- The fluid found inside the cells of the body.
- Comprises approximately 40% of total body weight.
- Contains high concentrations of potassium, phosphates, and proteins.
- The composition is carefully regulated by the cell membrane and various transport mechanisms.

2. Extracellular Fluid (ECF)

- The fluid found outside the cells.
- Comprises approximately 20% of total body weight.
- Contains high concentrations of sodium and chloride.
- Further divided into:

a) Interstitial Fluid:

- The fluid that surrounds and bathes the body cells.
- Makes up about 15% of total body weight.
- Acts as a medium for exchange of substances between blood and cells.

b) Intravascular Fluid (Plasma):

- The liquid portion of blood.
- Makes up about 5% of total body weight.
- Contains proteins, electrolytes, nutrients, and waste products.

c) Transcellular Fluid:

- Specialized body fluids such as cerebrospinal fluid, synovial fluid, and digestive secretions.
- Makes up about 1-2% of total body weight.

COMPOSITION AND FUNCTIONS OF BLOOD

INTRODUCTION

- Blood is a specialized connective tissue that circulates throughout the body.
- It is a liquid tissue consisting of cells suspended in plasma.
- The average adult has approximately 5-6 liters of blood.
- Blood accounts for about 7-8% of total body weight.

COMPOSITION OF BLOOD

Blood consists of two main components:

1. Plasma (55% of blood volume)

- The liquid portion of blood.
- Composed of approximately 90% water and 10% solutes.

Components of Plasma:

- **Water (90%):** Acts as a solvent for various substances.
- **Plasma Proteins (7%):**
  - Albumin: Maintains osmotic pressure and transports substances
  - Globulins: Include antibodies and transport proteins
  - Fibrinogen: Essential for blood clotting
- **Electrolytes (1%):** Sodium, potassium, calcium, chloride, bicarbonate
- **Nutrients:** Glucose, amino acids, fatty acids, vitamins
- **Waste Products:** Urea, creatinine, bilirubin
- **Hormones and Enzymes:** Various regulatory substances

2. Formed Elements (45% of blood volume)

a) Red Blood Cells (Erythrocytes):

- Most numerous blood cells (4.5-5.5 million per µL).
- Biconcave disc shape without nucleus in mammals.
- Contain hemoglobin for oxygen transport.
- Lifespan of approximately 120 days.

b) White Blood Cells (Leukocytes):

- Fewer in number (4,000-10,000 per µL).
- Contain nucleus and are involved in immune defense.
- Types include neutrophils, lymphocytes, monocytes, eosinophils, and basophils.

c) Platelets (Thrombocytes):

- Small cell fragments (150,000-400,000 per µL).
- Essential for blood clotting and hemostasis.
- Lifespan of approximately 7-10 days.

FUNCTIONS OF BLOOD

1. Transportation Function

- **Oxygen Transport:** Red blood cells carry oxygen from lungs to tissues via hemoglobin.
- **Carbon Dioxide Transport:** Blood carries CO_2 from tissues to lungs for elimination.
- **Nutrient Transport:** Carries glucose, amino acids, fatty acids, and vitamins from digestive system to cells.
- **Waste Transport:** Transports metabolic waste products to excretory organs.
- **Hormone Transport:** Carries hormones from endocrine glands to target organs.

2. Regulatory Function

- **pH Regulation:** Buffer systems maintain blood pH between 7.35-7.45.
- **Temperature Regulation:** Blood distributes heat throughout the body.
- **Fluid Balance:** Helps maintain proper water distribution between body compartments.

3. Protective Function

- **Immune Defense:** White blood cells protect against pathogens and foreign substances.
- **Blood Clotting:** Prevents excessive blood loss through hemostasis.
- **Antibody Production:** Plasma contains antibodies for specific immunity.

🏭 HEMOPOIESIS

INTRODUCTION

- Hemopoiesis (or hematopoiesis) is the process of blood cell formation.
- It occurs primarily in the bone marrow in adults.
- All blood cells originate from pluripotent hematopoietic stem cells.

SITES OF HEMOPOIESIS

During Development:

- **Embryonic Period:** Yolk sac (first 2-3 weeks)
- **Fetal Period:** Liver and spleen (3-7 months)
- **Late Fetal/Postnatal:** Bone marrow becomes primary site

In Adults:

- **Red Bone Marrow:** Primary site in flat bones (sternum, ribs, vertebrae, pelvis, skull)

- **Yellow Marrow:** Contains fat cells and can revert to red marrow if needed

PROCESS OF HEMOPOIESIS

Stem Cell Hierarchy:

- **Pluripotent Stem Cells:** Can differentiate into all blood cell types
- **Multipotent Progenitor Cells:** Committed to specific cell lineages
- **Precursor Cells:** Undergo maturation to become mature blood cells

Major Cell Lineages:

- **Erythroid Lineage:** Produces red blood cells
- **Myeloid Lineage:** Produces neutrophils, eosinophils, basophils, monocytes, and platelets
- **Lymphoid Lineage:** Produces lymphocytes (T cells, B cells, NK cells)

REGULATION OF HEMOPOIESIS

- **Growth Factors:** Erythropoietin, colony-stimulating factors, interleukins
- **Hormones:** Thyroid hormones, androgens, growth hormone
- **Nutritional Factors:** Iron, vitamin B_{12}, folic acid, protein
- **Feedback Mechanisms:** Oxygen levels, blood cell counts

🔴 FORMATION OF HEMOGLOBIN

INTRODUCTION

- Hemoglobin is the iron-containing protein in red blood cells.
- It is responsible for oxygen transport from lungs to tissues.
- Normal hemoglobin levels: Men 14-16 g/dL, Women 12-14 g/dL.

STRUCTURE OF HEMOGLOBIN

- **Globin:** Four polypeptide chains (2 α-chains and 2 β-chains)
- **Heme:** Four iron-containing porphyrin rings
- Each hemoglobin molecule can carry four oxygen molecules

SYNTHESIS OF HEMOGLOBIN

Site of Synthesis:

- Begins in erythroblasts in the bone marrow
- Continues during reticulocyte stage
- Completed before mature RBC formation

Steps in Hemoglobin Synthesis:

1. Heme Synthesis:

- Occurs in mitochondria and cytoplasm of erythroblasts
- Requires iron, vitamin B_6, and various enzymes
- Key steps involve:
  - Formation of δ-aminolevulinic acid (ALA)
  - Condensation to form porphobilinogen
  - Formation of protoporphyrin IX
  - Insertion of iron to form heme

2. Globin Synthesis:

- Occurs on ribosomes in the cytoplasm
- α-globin chains synthesized continuously
- β-globin chains synthesized in balanced amounts
- Assembly of α and β chains with heme groups

Requirements for Hemoglobin Formation:

- **Iron:** Essential component of heme group
- **Vitamin B_{12}:** Required for DNA synthesis in erythroblasts
- **Folic Acid:** Necessary for DNA synthesis and cell division
- **Vitamin B_6:** Cofactor in heme synthesis
- **Protein:** Source of amino acids for globin chains
- **Copper:** Required for iron absorption and utilization

ANEMIA

DEFINITION

- Anemia is a condition characterized by a decrease in the number of red blood cells or hemoglobin concentration below normal levels.
- Results in reduced oxygen-carrying capacity of blood.
- Defined as hemoglobin levels below 12 g/dL in women and 13 g/dL in men.

CLASSIFICATION OF ANEMIA

A. Based on Cell Size (Morphological):

1. Microcytic Anemia (MCV < 80 fL):

- Small red blood cells
- Usually due to iron deficiency or thalassemia

2. Normocytic Anemia (MCV 80-100 fL):

- Normal-sized red blood cells
- Often due to chronic disease or blood loss

3. Macrocytic Anemia (MCV > 100 fL):

- Large red blood cells
- Usually due to vitamin B_{12} or folate deficiency

B. Based on Cause (Etiological):

1. Iron Deficiency Anemia:

- Most common type of anemia worldwide
- Caused by inadequate iron intake, absorption, or excessive loss
- Characterized by microcytic, hypochromic red blood cells
- Symptoms include fatigue, weakness, pale skin, brittle nails

2. Megaloblastic Anemia:

- Due to vitamin B_{12} or folic acid deficiency
- Results in large, immature red blood cells
- DNA synthesis is impaired while RNA synthesis continues

- Can cause neurological symptoms if due to B_{12} deficiency

3. Hemolytic Anemia:

- Results from increased destruction of red blood cells
- Can be inherited (sickle cell disease, thalassemia) or acquired
- Bone marrow increases production but cannot compensate
- May cause jaundice due to increased bilirubin

4. Aplastic Anemia:

- Bone marrow failure resulting in decreased production of all blood cells
- Can be congenital or acquired (drugs, radiation, infections)
- Requires bone marrow transplantation in severe cases

5. Chronic Disease Anemia:

- Associated with chronic infections, inflammatory conditions, or malignancies
- Results from impaired iron utilization and decreased erythropoietin response
- Usually normocytic and normochromic

SYMPTOMS OF ANEMIA

- **General:** Fatigue, weakness, shortness of breath
- **Cardiovascular:** Rapid heartbeat, chest pain, dizziness
- **Integumentary:** Pale skin, brittle nails, hair loss

- **Neurological:** Headaches, difficulty concentrating, restless legs

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MECHANISMS OF COAGULATION

INTRODUCTION

- Blood coagulation (clotting) is a complex process that prevents excessive bleeding when blood vessels are injured.
- It involves a cascade of enzymatic reactions leading to fibrin formation.
- The process must be carefully regulated to prevent inappropriate clotting.

COMPONENTS OF HEMOSTASIS

1. Vascular Response

- Immediate vasoconstriction reduces blood flow to injured area
- Mediated by smooth muscle contraction and local factors
- Helps limit blood loss and brings clotting factors into contact

2. Platelet Plug Formation (Primary Hemostasis)

- **Platelet Adhesion:** Platelets stick to exposed collagen at injury site
- **Platelet Activation:** Release of granule contents (ADP, thromboxane A_2)
- **Platelet Aggregation:** Formation of unstable platelet plug
- Process occurs within seconds of injury

3. Blood Coagulation (Secondary Hemostasis)

Formation of stable fibrin clot through coagulation cascade

COAGULATION CASCADE

Classical Pathway Division:

Intrinsic Pathway (Contact Activation):

- Activated by contact with negatively charged surfaces
- Involves factors XII, XI, IX, and VIII
- Longer process but amplifies coagulation response

Extrinsic Pathway (Tissue Factor):

- Activated by tissue factor released from damaged tissues
- Involves factor VII
- Rapid initiation of coagulation

Common Pathway:

- Both pathways converge to activate factor X
- Leads to thrombin formation and fibrin polymerization

Modern Understanding - Cell-Based Model:

1. Initiation Phase:

- Tissue factor (TF) exposed at injury site
- TF binds to factor VIIa forming TF-VIIa complex
- Activates factors IX and X on TF-bearing cells

2. Amplification Phase:

- Small amounts of thrombin generated
- Activates cofactors V, VIII, and XI on platelet surfaces
- Prepares for large-scale thrombin generation

3. Propagation Phase:

- Massive thrombin generation on activated platelet surfaces
- Factor Xa-Va complex (prothrombinase) converts prothrombin to thrombin
- Thrombin converts fibrinogen to fibrin

COAGULATION FACTORS

Factor	Name	Function
I	Fibrinogen	Converted to fibrin
II	Prothrombin	Converted to thrombin
III	Tissue Factor	Initiates extrinsic pathway
IV	Calcium	Cofactor for many reactions
V	Proaccelerin	Cofactor with Xa
VII	Proconvertin	Initiates extrinsic pathway
VIII	Antihemophilic Factor	Cofactor with IXa
IX	Christmas Factor	Activates factor X
X	Stuart Factor	Activates prothrombin
XI	Plasma Thromboplastin Antecedent	Activates factor IX
XII	Hageman Factor	Contact activation
XIII	Fibrin Stabilizing Factor	Cross-links fibrin

REGULATION OF COAGULATION

- **Natural Anticoagulants:** Antithrombin III, protein C, protein S
- **Fibrinolytic System:** Dissolves clots through plasmin action
- **Endothelial Factors:** Prostacyclin, nitric oxide prevent inappropriate clotting

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BLOOD GROUPING

INTRODUCTION

- Blood grouping is the classification of blood based on the presence or absence of specific antigens on red blood cell surfaces.
- These antigens are inherited genetic markers that determine blood compatibility.
- Knowledge of blood groups is essential for safe blood transfusions and organ transplantation.

ABO BLOOD GROUP SYSTEM

Discovery and Basis:

- Discovered by Karl Landsteiner in 1901
- Based on presence of A and B antigens on red blood cells
- Corresponding antibodies (anti-A, anti-B) present in plasma

Blood Types:

Type A:

- A antigens on red blood cells
- Anti-B antibodies in plasma
- Can receive blood from A and O donors
- Can donate to A and AB recipients

Type B:

- B antigens on red blood cells
- Anti-A antibodies in plasma
- Can receive blood from B and O donors
- Can donate to B and AB recipients

Type AB (Universal Recipient):

- Both A and B antigens on red blood cells
- No anti-A or anti-B antibodies in plasma
- Can receive blood from all ABO types
- Can only donate to AB recipients

Type O (Universal Donor):

- No A or B antigens on red blood cells
- Both anti-A and anti-B antibodies in plasma
- Can only receive blood from O donors
- Can donate to all ABO types

Genetics of ABO System:

- Controlled by three alleles: I^A, I^B, and i

- I^A codes for A antigen, I^B codes for B antigen, i codes for no antigen
- Inheritance pattern follows Mendelian genetics

OTHER BLOOD GROUP SYSTEMS

Rh Blood Group System:

- Second most important blood group system
- Based on presence of Rh(D) antigen
- Rh-positive: D antigen present
- Rh-negative: D antigen absent

MNS System:

- Based on M and N antigens
- Less clinically significant than ABO and Rh

Kell System:

- Can cause severe hemolytic disease
- Important in some transfusion reactions

🔬 Rh FACTORS

INTRODUCTION

- The Rh (Rhesus) blood group system is the second most important blood group system after ABO.
- Named after the Rhesus monkey in which it was first discovered.
- The most significant antigen in this system is the D antigen.

Rh ANTIGENS AND PHENOTYPES

Rh-Positive (Rh+):

- Presence of D antigen on red blood cells
- Approximately 85% of the population
- Genotypes: DD or Dd
- Do not naturally produce anti-D antibodies

Rh-Negative (Rh-):

- Absence of D antigen on red blood cells
- Approximately 15% of the population
- Genotype: dd
- Can develop anti-D antibodies upon exposure

CLINICAL SIGNIFICANCE

Rh Incompatibility:

- Occurs when Rh-negative person is exposed to Rh-positive blood
- Can happen through transfusion or pregnancy
- Results in production of anti-D antibodies

Hemolytic Disease of the Newborn (HDN):

- **First Pregnancy:** Rh-negative mother with Rh-positive fetus
  - Usually no problems as maternal and fetal blood don't mix significantly

- Some sensitization may occur during delivery

- **Subsequent Pregnancies:** If mother is now sensitized
  - Anti-D antibodies cross placenta and attack fetal RBCs
  - Can cause severe anemia, jaundice, and fetal death

Prevention of Rh Sensitization:

- **RhoGAM (Anti-D Immunoglobulin):**
  - Given to Rh-negative mothers at 28 weeks of pregnancy
  - Given within 72 hours after delivery of Rh-positive baby
  - Prevents maternal sensitization to Rh antigen
  - Also given after miscarriage, abortion, or invasive procedures

GENETICS OF Rh SYSTEM

- More complex than initially thought
- Involves multiple genes and antigens
- D antigen is most immunogenic
- Inheritance follows Mendelian patterns

🩸 TRANSFUSION, ITS SIGNIFICANCE AND DISORDERS OF BLOOD

BLOOD TRANSFUSION

Definition and Purpose:

- Blood transfusion is the transfer of blood or blood components from a donor to a recipient.
- Used to replace blood loss, treat anemia, or provide specific blood components.
- Can be life-saving in cases of severe blood loss or certain medical conditions.

Types of Blood Transfusion:

1. Whole Blood Transfusion:

- Contains all blood components
- Rarely used except in massive blood loss
- Volume: 450-500 mL per unit

2. Component Transfusion:

- **Red Blood Cell Concentrate:** For anemia or blood loss
- **Fresh Frozen Plasma:** For clotting factor deficiencies
- **Platelet Concentrate:** For thrombocytopenia or platelet dysfunction
- **Cryoprecipitate:** For fibrinogen deficiency or hemophilia

Compatibility Testing:

1. ABO Compatibility:

- Donor and recipient must be ABO compatible
- Cross-matching prevents hemolytic reactions

2. Rh Compatibility:

- Especially important for Rh-negative recipients
- Rh-positive blood should not be given to Rh-negative recipients

3. Cross-Matching:

- Direct testing of donor cells with recipient serum
- Detects unexpected antibodies
- Major cross-match: Donor cells + recipient serum
- Minor cross-match: Recipient cells + donor serum

SIGNIFICANCE OF BLOOD TRANSFUSION

Medical Benefits:

- **Life-Saving:** Essential in trauma, surgery, and severe anemia
- **Treatment of Blood Disorders:** Thalassemia, sickle cell disease, hemophilia
- **Support During Cancer Treatment:** Chemotherapy-induced cytopenias
- **Surgical Procedures:** Major operations requiring blood replacement

Social and Ethical Aspects:

- Voluntary blood donation saves lives
- Blood banking systems ensure adequate supply
- Ethical considerations in allocation and access

BLOOD TRANSFUSION REACTIONS

Immediate Reactions:

1. Acute Hemolytic Reaction:

- Most serious type of reaction
- Due to ABO incompatibility
- Symptoms: Fever, chills, back pain, hemoglobinuria
- Can lead to kidney failure and death

2. Febrile Non-Hemolytic Reaction:

- Most common type of reaction
- Due to antibodies against white blood cells
- Symptoms: Fever, chills, headache
- Usually mild and self-limiting

3. Allergic Reactions:

- Due to plasma proteins in transfused blood
- Range from mild urticaria to severe anaphylaxis
- Treated with antihistamines or epinephrine

4. Transfusion-Related Acute Lung Injury (TRALI):

- Acute respiratory distress within 6 hours
- Due to antibodies against neutrophils
- Can be life-threatening

Delayed Reactions:

1. Delayed Hemolytic Reaction:

- Occurs days to weeks after transfusion
- Due to anamnestic antibody response
- Usually milder than acute reactions

2. Iron Overload:

- Results from multiple transfusions
- Can damage liver, heart, and other organs
- Requires iron chelation therapy

3. Graft-vs-Host Disease:

- Rare but serious complication
- Transfused lymphocytes attack recipient tissues
- Prevented by irradiation of blood products

INFECTIOUS DISEASES AND BLOOD SAFETY

Screening Tests:

- **Viral Infections:** HIV, Hepatitis B and C, HTLV
- **Bacterial Contamination:** Especially in platelet products
- **Parasitic Infections:** Malaria, Chagas disease (in endemic areas)

Safety Measures:

- Donor screening and questionnaires
- Laboratory testing of donated blood
- Nucleic acid testing for viral infections

- Bacterial culture of platelet products
- Pathogen reduction technologies

RETICULO ENDOTHELIAL SYSTEM

INTRODUCTION

- The reticuloendothelial system (RES), now known as the mononuclear phagocyte system (MPS), is a network of cells distributed throughout the body.
- These cells are involved in phagocytosis, immune responses, and tissue maintenance.
- The system includes various types of macrophages and dendritic cells.

COMPONENTS OF THE SYSTEM

Fixed Macrophages:

- **Liver:** Kupffer cells - filter blood and remove old RBCs
- **Spleen:** Splenic macrophages - remove aged blood cells and pathogens
- **Lymph Nodes:** Resident macrophages - filter lymph and process antigens
- **Lungs:** Alveolar macrophages - remove particles and pathogens from airways
- **Bone Marrow:** Macrophages support hematopoiesis and remove cellular debris
- **Brain:** Microglial cells - immune surveillance and synaptic pruning

- **Connective Tissue:** Histiocytes - tissue maintenance and wound healing

Mobile Macrophages:

- **Blood Monocytes:** Circulate and migrate to tissues when needed
- **Inflammatory Macrophages:** Recruited to sites of inflammation or infection

FUNCTIONS OF THE RES

1. Phagocytosis:

- **Cellular Debris Removal:** Eliminate dead and dying cells
- **Pathogen Elimination:** Engulf bacteria, viruses, and other microorganisms
- **Foreign Material Clearance:** Remove carbon particles, dust, and other foreign substances

2. Blood Cell Destruction:

- **Aged RBC Removal:** Spleen and liver macrophages remove old red blood cells
- **Hemoglobin Breakdown:** Convert hemoglobin to bilirubin for excretion
- **Iron Recycling:** Salvage iron from destroyed red blood cells for reuse

3. Immune Functions:

- **Antigen Presentation:** Process and present antigens to lymphocytes

- **Cytokine Production:** Release inflammatory mediators and immune regulators
- **Complement Activation:** Participate in complement cascade

4. Metabolic Functions:

- **Lipid Metabolism:** Store and metabolize lipids
- **Iron Storage:** Maintain body iron stores as ferritin and hemosiderin
- **Hormone Metabolism:** Process various hormones

ORGANS OF THE RES

Spleen:

- **Structure:** Red pulp (blood filtration) and white pulp (immune function)
- **Functions:** Blood filtration, immune surveillance, blood cell storage
- **Clinical Significance:** Splenomegaly in various diseases

Liver:

- **Kupffer Cells:** Largest population of fixed macrophages
- **Functions:** Detoxification, blood filtration, bile production
- **Role in RES:** Remove bacteria and toxins from portal circulation

Bone Marrow:

- **Stromal Macrophages:** Support hematopoiesis
- **Iron Storage:** Central iron recycling facility
- **Cell Production:** Generate new macrophages and other blood cells

🔗 LYMPHATIC SYSTEM

Points to be covered in this topic

➞ 1. LYMPHATIC ORGANS AND TISSUES
➞ 2. LYMPHATIC VESSELS
➞ 3. LYMPH CIRCULATION
➞ 4. FUNCTIONS OF LYMPHATIC SYSTEM

🏛️ LYMPHATIC ORGANS AND TISSUES

INTRODUCTION

- The lymphatic system is a network of tissues, vessels, and organs that help maintain body fluid balance and defend against infections.
- It consists of primary and secondary lymphoid organs that work together to produce and mature immune cells.
- The system is closely integrated with the cardiovascular and immune systems.

PRIMARY LYMPHOID ORGANS

1. Bone Marrow 🦴

Structure:

- Soft tissue inside hollow bones
- Contains hematopoietic stem cells and stromal cells
- Two types: red marrow (active) and yellow marrow (inactive)

Functions:

- **B Cell Development:** Site of B lymphocyte maturation
- **Hematopoiesis:** Production of all blood cell types
- **Stem Cell Niche:** Maintains pluripotent stem cell populations
- **Immune Memory:** Houses long-lived plasma cells

Location:

- Flat bones: sternum, ribs, vertebrae, pelvis, skull
- Ends of long bones in adults
- Throughout skeleton in children

2. Thymus 🫁

Structure:

- Located in the mediastinum, anterior to the heart
- Consists of two lobes divided into cortex and medulla
- Contains epithelial cells, dendritic cells, and thymocytes

Functions:

- **T Cell Maturation:** Site where T lymphocytes develop and mature
- **Self-Tolerance:** Eliminates T cells that react to self-antigens
- **Hormone Production:** Secretes thymosin and other thymic hormones
- **Immune Education:** Teaches T cells to recognize self vs. non-self

Age-Related Changes:

- Largest during childhood and adolescence
- Gradually involutes (shrinks) with age
- Replaced by adipose tissue in adults
- Maintains some function throughout life

SECONDARY LYMPHOID ORGANS

1. Lymph Nodes 🔗

Structure:

- Small, bean-shaped organs along lymphatic vessels
- Surrounded by fibrous capsule with trabeculae
- Contains cortex (B cell areas) and medulla (T cell areas)
- Specialized areas: germinal centers for B cell activation

Distribution:

- **Cervical:** Neck region - drain head and neck
- **Axillary:** Armpit region - drain arms and chest wall
- **Inguinal:** Groin region - drain legs and lower abdomen
- **Mesenteric:** Abdominal cavity - drain intestines
- **Mediastinal:** Chest cavity - drain lungs and heart

Functions:

- **Filtration:** Remove pathogens and foreign particles from lymph
- **Immune Activation:** Site of antigen presentation and lymphocyte activation

- **Antibody Production:** B cells differentiate into plasma cells
- **Immune Memory:** Generate memory B and T cells

2. Spleen

Structure:

- **Red Pulp:** Network of sinusoids for blood filtration
  - Contains macrophages and red blood cells
  - Removes old and damaged red blood cells
- **White Pulp:** Lymphoid tissue around arterioles
  - Contains T cells, B cells, and antigen-presenting cells
  - Sites of immune activation

Functions:

- **Blood Filtration:** Removes old RBCs, platelets, and pathogens
- **Immune Surveillance:** Monitors blood for foreign antigens
- **Blood Storage:** Stores platelets and some red blood cells
- **Hematopoiesis:** Can resume blood cell production if needed

Clinical Significance:

- Splenomegaly: Enlargement due to various diseases
- Hypersplenism: Overactive destruction of blood cells
- Asplenia: Increased susceptibility to encapsulated bacteria

3. Mucosa-Associated Lymphoid Tissue (MALT)

Components:

- **GALT (Gut-Associated):** Peyer's patches, appendix, isolated lymphoid follicles
- **BALT (Bronchus-Associated):** Lymphoid tissue in respiratory tract
- **NALT (Nasal-Associated):** Adenoids and tonsillar tissue
- **Skin-Associated:** Lymphoid tissue in skin and mucous membranes

Structure:

- Collections of lymphoid cells without distinct capsules
- Located beneath epithelial surfaces
- Contains specialized antigen-sampling cells (M cells)

Functions:

- **First Line Defense:** Protects mucosal surfaces from pathogens
- **Local Immunity:** Produces secretory IgA antibodies
- **Antigen Sampling:** M cells transport antigens from lumen
- **Tolerance Induction:** Prevents immune reactions to harmless antigens

LYMPHOID TISSUES

Tonsils 👄

Types:

- **Palatine Tonsils:** Located on sides of throat
- **Pharyngeal Tonsil (Adenoids):** Located in nasopharynx
- **Lingual Tonsils:** Located at base of tongue

Functions:

- Guard against inhaled and ingested pathogens
- Initiate immune responses in upper respiratory tract
- Produce antibodies against common pathogens

Appendix 🦠

Structure:

- Small, finger-like projection from cecum
- Contains abundant lymphoid tissue
- Part of GALT system

Functions:

- Immune surveillance of intestinal contents
- Reservoir for beneficial gut bacteria
- May help establish normal gut microbiome

🚰 LYMPHATIC VESSELS

INTRODUCTION

- Lymphatic vessels form a one-way drainage system that returns excess tissue fluid to the bloodstream.
- They begin as lymphatic capillaries and gradually merge into larger vessels.

- The system parallels the venous system but has important structural and functional differences.

STRUCTURE OF LYMPHATIC VESSELS

1. Lymphatic Capillaries 🌐

Structure:

- Smallest vessels in the lymphatic system
- Single layer of endothelial cells with overlapping edges
- No basement membrane, allowing easy fluid entry
- Blind-ended tubes that begin in tissue spaces
- Anchored to surrounding tissues by anchoring filaments

Specialized Types:

- **Lacteals:** Lymphatic capillaries in intestinal villi
  - Absorb dietary fats and fat-soluble vitamins
  - Transport chylomicrons from intestine
- **Initial Lymphatics:** First collecting vessels from capillaries
  - Have primitive valves to prevent backflow

Distribution:

- Present in most tissues except:
  - Central nervous system (has glymphatic system)
  - Bone marrow
  - Cartilage

- Cornea and lens of eye
- Placenta

2. Collecting Lymphatic Vessels 🔁

Structure:

- Larger than capillaries with distinct layers
  - **Intima:** Endothelial lining with one-way valves
  - **Media:** Smooth muscle layer for propulsion
  - **Adventitia:** Connective tissue outer layer
- Valves similar to those in veins prevent backflow
- Segments between valves called lymphangions

Functions:

- Transport lymph from capillaries to lymph nodes
- Undergo rhythmic contractions (lymphatic pump)
- Respond to various stimuli (stretch, inflammatory mediators)

3. Lymphatic Trunks 🌳

Major Trunks:

- **Jugular Trunks:** Drain head and neck
- **Subclavian Trunks:** Drain upper limbs
- **Bronchomediastinal Trunks:** Drain thoracic organs
- **Intestinal Trunk:** Drains digestive organs
- **Lumbar Trunks:** Drain lower limbs and pelvis

Characteristics:

- Formed by convergence of collecting vessels
- Have well-developed muscle layers
- May pass through multiple lymph node groups

4. Lymphatic Ducts

Right Lymphatic Duct:

- **Formation:** Junction of right jugular, subclavian, and bronchomediastinal trunks
- **Drainage Area:** Right side of head, neck, thorax, and right upper limb
- **Termination:** Right subclavian vein at junction with internal jugular vein
- **Length:** Approximately 1-2 cm

Thoracic Duct:

- **Formation:** Begins at cisterna chyli (L1-L2 level)
- **Course:** Ascends through posterior mediastinum
- **Drainage Area:** Rest of body (about 75% of lymph)
- **Termination:** Left subclavian vein at junction with internal jugular vein
- **Length:** Approximately 38-45 cm (largest lymphatic vessel)

LYMPHATIC VESSEL FUNCTION

Fluid Transport:

- Return excess interstitial fluid to circulation
- Maintain fluid balance between blood and tissues
- Transport amounts to 2-4 liters per day

Protein Recovery:

- Return leaked plasma proteins to circulation
- Prevent accumulation of proteins in tissues
- Maintain oncotic pressure gradients

Fat Absorption:

- Lacteals absorb dietary lipids from intestine
- Transport fat-soluble vitamins (A, D, E, K)
- Deliver nutrients to systemic circulation

🔄 LYMPH CIRCULATION

INTRODUCTION

- Lymph circulation is the movement of lymph through the lymphatic system.
- Unlike blood circulation, lymphatic circulation is unidirectional (toward the heart).
- The system lacks a central pump like the heart, relying on various mechanisms for flow.

COMPOSITION OF LYMPH

Normal Lymph Composition:

- **Water:** 95% of lymph volume
- **Proteins:** Lower concentration than plasma (2-5 g/dL)
  - Albumin, globulins, fibrinogen
  - Concentration varies by location
- **Lipids:** Higher after meals, especially from intestine
- **Electrolytes:** Similar to interstitial fluid
- **Cells:** Mainly lymphocytes (2,000-20,000/μL)
- **Other:** Enzymes, hormones, waste products

Variations in Composition:

- **Thoracic Duct Lymph:** Mixed lymph from entire body
- **Intestinal Lymph:** High in lipids after meals (chyle)
- **Liver Lymph:** High in protein content
- **Peripheral Lymph:** Lower protein, mainly tissue fluid

MECHANISMS OF LYMPH FLOW

1. Intrinsic Mechanisms (Lymphatic Pump) 💪

Spontaneous Contractions:

- Smooth muscle in collecting vessels contracts rhythmically
- Frequency: 1-10 contractions per minute
- Each lymphangion acts as individual pump unit
- Coordinated contractions propel lymph forward

Valve Function:

- One-way valves prevent backflow
- Open during forward flow, close during reverse pressure
- Ensure unidirectional movement toward venous system

2. Extrinsic Mechanisms 🏃

Skeletal Muscle Pump:

- Muscle contractions compress lymphatic vessels
- Alternating compression and relaxation propels lymph
- Most effective during physical activity
- Important for lymph flow from extremities

Respiratory Pump:

- Breathing creates pressure changes in thoracic cavity
- Inspiration: Decreased thoracic pressure draws lymph upward
- Expiration: Increased pressure helps empty thoracic duct
- Deep breathing enhances lymphatic drainage

Arterial Pulsations:

- Pulsating arteries adjacent to lymphatics aid flow
- Particularly important in areas with close arterial-lymphatic proximity
- Provides rhythmic external compression

Gravitational Forces:

- Assist flow from upper body regions
- Oppose flow from lower extremities
- Overcome by muscle pump and vessel contractions

FACTORS AFFECTING LYMPH FLOW

Factors that Increase Flow:

- **Physical Activity:** Enhances muscle and respiratory pumps
- **Massage:** External compression aids drainage
- **Heat:** Vasodilation and increased tissue metabolism
- **Increased Capillary Pressure:** More fluid filtration
- **Inflammation:** Increased vascular permeability

Factors that Decrease Flow:

- **Immobility:** Reduced muscle pump activity
- **Cold:** Vasoconstriction and reduced muscle activity
- **Dehydration:** Decreased fluid available for lymph formation
- **Lymphatic Obstruction:** Tumors, fibrosis, or infections
- **Heart Failure:** Increased venous pressure impedes drainage

LYMPH FLOW RATES

Normal Flow Rates:

- **Total Daily Flow:** 2-4 liters per day
- **Thoracic Duct:** 1-3 mL/minute at rest
- **Right Lymphatic Duct:** 0.1-0.5 mL/minute

- **Increases:** Up to 10-fold during exercise or inflammation

Regional Variations:

- **Intestinal:** Highest flow rate, especially postprandial
- **Hepatic:** High protein content, significant volume
- **Peripheral:** Lower flow rates but important for tissue drainage

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🛡️ FUNCTIONS OF LYMPHATIC SYSTEM

INTRODUCTION

- The lymphatic system performs multiple vital functions essential for health and survival.
- These functions integrate fluid balance, immune defense, and nutrient absorption.
- Dysfunction of the lymphatic system can lead to serious health consequences.

1. FLUID HOMEOSTASIS 💧

Interstitial Fluid Balance:

- **Fluid Return:** Returns 2-4 liters of excess interstitial fluid daily to circulation
- **Starling Forces:** Balances hydrostatic and oncotic pressures
- **Edema Prevention:** Prevents tissue swelling under normal conditions
- **Volume Regulation:** Helps maintain blood volume and pressure

Mechanism of Fluid Balance:

- Capillary filtration creates interstitial fluid
- Most fluid reabsorbed at venous end of capillaries
- Excess fluid (10-20%) collected by lymphatic capillaries
- Returned to venous circulation via thoracic and right lymphatic ducts

Clinical Significance:

- **Lymphedema:** Swelling due to lymphatic obstruction or dysfunction
- **Primary:** Congenital malformations of lymphatic system
- **Secondary:** Acquired due to surgery, radiation, infection, or trauma

2. IMMUNE FUNCTION

Immune Surveillance:

- **Antigen Collection:** Lymphatics transport antigens from tissues to lymph nodes
- **Pathogen Filtering:** Lymph nodes filter and trap bacteria, viruses, and toxins
- **Immune Cell Transport:** Carries lymphocytes between immune organs
- **Memory Formation:** Sites for generating immunological memory

Components of Immune Function:

Cellular Immunity:

- T lymphocytes mature in thymus

- Circulate through lymphatic system
- Recognize and eliminate infected or abnormal cells
- Coordinate immune responses

Humoral Immunity:

- B lymphocytes mature in bone marrow
- Activated in secondary lymphoid organs
- Differentiate into plasma cells producing antibodies
- Memory B cells provide long-term protection

Innate Immunity:

- Macrophages in lymph nodes phagocytose pathogens
- Dendritic cells process and present antigens
- Natural killer cells eliminate infected cells
- Complement activation and inflammatory responses

Immune Responses in Lymphoid Organs:

Organ	Primary Function	Key Cells	Immune Response
Lymph Nodes	Antigen filtration	B cells, T cells, Macrophages	Adaptive immunity
Spleen	Blood filtration	B cells, T cells, Macrophages	Systemic immunity
MALT	Mucosal protection	B cells, T cells, Plasma cells	Local immunity
Thymus	T cell education	Thymocytes, Epithelial cells	Self-tolerance

3. LIPID ABSORPTION AND TRANSPORT

Intestinal Fat Absorption:

- **Lacteals:** Specialized lymphatic capillaries in intestinal villi
- **Chylomicron Transport:** Carry dietary fats and fat-soluble vitamins
- **Bypasses Portal Circulation:** Directly enters systemic circulation
- **Postprandial Changes:** Lymph becomes milky (chyle) after fat-rich meals

Fat-Soluble Vitamin Transport:

- **Vitamin A:** Essential for vision and immune function
- **Vitamin D:** Important for calcium metabolism and bone health
- **Vitamin E:** Antioxidant protecting cell membranes
- **Vitamin K:** Required for blood clotting

Clinical Implications:

- **Malabsorption:** Lymphatic disorders can cause fat-soluble vitamin deficiencies
- **Chylous Ascites:** Lymphatic fluid accumulation in abdomen
- **Protein-Losing Enteropathy:** Loss of proteins through damaged lymphatics

4. PROTEIN HOMEOSTASIS 🧬

Protein Recovery:

- **Plasma Protein Retrieval:** Returns leaked albumin and globulins to circulation
- **Maintains Oncotic Pressure:** Prevents excessive fluid accumulation in tissues
- **Enzyme Transport:** Carries tissue enzymes back to circulation
- **Hormone Clearance:** Removes excess hormones from tissues

Protein Concentration Gradients:

- Higher protein concentration in lymph than interstitial fluid
- Varies by organ: liver lymph > intestinal lymph > peripheral lymph
- Important for maintaining vascular-interstitial fluid balance

5. WASTE REMOVAL AND DETOXIFICATION 🧹

Cellular Debris Clearance:

- **Dead Cell Removal:** Macrophages in lymph nodes eliminate cellular debris
- **Foreign Particle Filtration:** Removes dust, carbon particles, and other materials
- **Toxin Processing:** Helps eliminate bacterial toxins and metabolic waste
- **Cancer Cell Surveillance:** May trap and eliminate circulating cancer cells

Inflammatory Response:

- **Mediator Transport:** Carries inflammatory substances from sites of injury
- **Resolution of Inflammation:** Helps clear inflammatory debris
- **Tissue Repair:** Supports healing by removing damaged tissue components

6. MAINTENANCE OF TISSUE ENVIRONMENT 🌱

Tissue Pressure Regulation:

- **Hydrostatic Pressure:** Helps maintain optimal tissue pressure
- **Nutrient Distribution:** Ensures proper nutrient delivery to cells
- **Waste Clearance:** Removes metabolic products from tissue spaces
- **pH Balance:** Helps maintain tissue pH within normal ranges

Specialized Functions by Region:

Central Nervous System:

- **Glymphatic System:** Brain's lymphatic-like drainage system
- **Cerebrospinal Fluid Clearance:** Removes waste products from brain
- **Amyloid Clearance:** May help prevent neurodegenerative diseases

Skin and Subcutaneous Tissues:

- **Thermal Regulation:** Assists in temperature control
- **Wound Healing:** Supports tissue repair processes
- **Infection Control:** First line of defense against pathogens

CLINICAL SIGNIFICANCE OF LYMPHATIC DYSFUNCTION

Primary Lymphatic Disorders:

- **Congenital Lymphedema:** Malformed lymphatic vessels
- **Lymphangiomatosis:** Abnormal proliferation of lymphatic vessels
- **Primary Immunodeficiencies:** Defects in lymphoid organ development

Secondary Lymphatic Disorders:

- **Post-Surgical Lymphedema:** After lymph node removal
- **Radiation-Induced Damage:** From cancer treatment
- **Infectious Lymphangitis:** Bacterial infection of lymphatic vessels
- **Malignant Obstruction:** Tumors blocking lymphatic drainage

Assessment and Treatment:

- **Lymphoscintigraphy:** Nuclear imaging of lymphatic function

- **Compression Therapy:** External pressure to reduce swelling
- **Manual Lymphatic Drainage:** Specialized massage technique
- **Surgical Options:** Lymphaticovenous anastomosis, lymph node transfer

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📊 SUMMARY TABLE: COMPARISON OF BLOOD AND LYMPHATIC SYSTEMS

Feature	Blood System	Lymphatic System
Circulation	Closed loop (heart → tissues → heart)	Open, one-way (tissues → heart)
Central Pump	Heart	None (multiple mechanisms)
Fluid	Blood (plasma + cells)	Lymph (tissue fluid + cells)
Vessels	Arteries, veins, capillaries	Capillaries, vessels, trunks, ducts
Primary Function	Transport O_2, nutrients, waste	Fluid balance, immunity, fat absorption
Flow Rate	5L/minute (cardiac output)	2-4L/day (total lymph flow)
Protein Content	7-8 g/dL	2-5 g/dL (varies by location)
Pressure	High (systolic/diastolic)	Low (near venous pressure)

🎯 KEY LEARNING OBJECTIVES ACHIEVED

Upon completion of this unit, students should understand:

✅ **Body Fluids:** Composition, distribution, and functions of body fluid compartments

✅ **Blood:** Complete understanding of blood composition, functions, and formation processes

✅ **Hemopoiesis:** Process of blood cell formation and its regulation

✅ **Hemoglobin:** Structure, synthesis, and clinical significance

✅ **Anemia:** Types, causes, and pathophysiology of various anemias

✅ **Blood Coagulation:** Detailed mechanisms of blood clotting and its regulation

✅ **Blood Groups:** ABO and Rh systems, genetics, and clinical applications

✅ **Blood Transfusion:** Principles, compatibility, reactions, and safety measures

✅ **RES:** Structure and functions of the reticuloendothelial system

✅ **Lymphatic System:** Complete anatomy and physiology of lymphatic organs, vessels, and functions

This comprehensive coverage provides the foundation for understanding cardiovascular physiology, immunology, and hematology in advanced pharmaceutical sciences. 🎓