Plasma Proteins

Albumin, Globulin & Fibrinogen

By

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Learning Outcomes (LOs)

At the end of this lecture, the students should be able to:

1. Recognize different types of plasma proteins and their production.
2. Recognize function of different plasma proteins.
3. Recognize serum electrophoretic pattern in normal & abnormal state.
4. Define acute phase proteins and enumerate them.
5. Identify causes and effects of hypoproteinemia.

Case scenario (Clinical correlate)

A 50-year-old man presents to emergency room complaining of hematemesis and he has undergone endoscopic band ligation of grade II esophageal varices. He had a history of chronic hepatitis C that progressed to liver cirrhosis. Furthermore, he developed ascites and edema of both lower limbs.

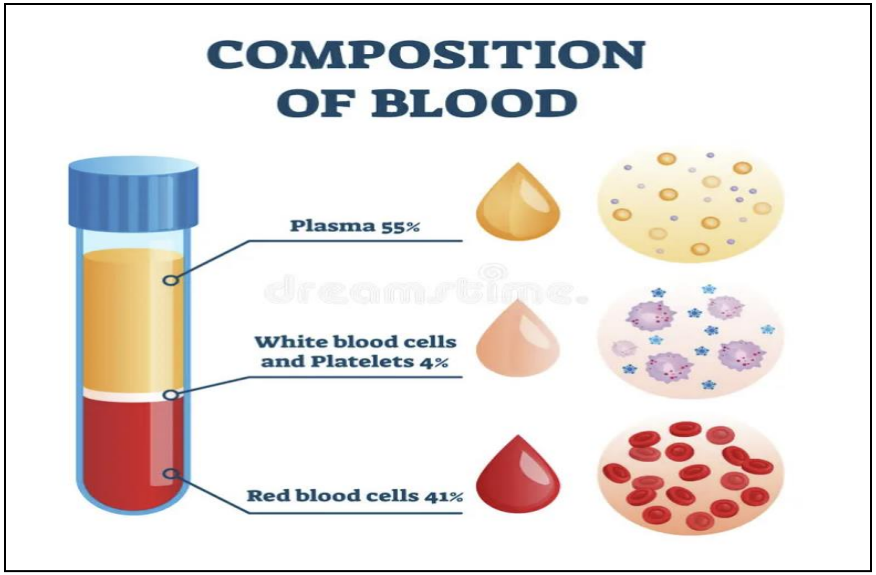
What is the possible cause of ascites and lower limb edema in this case?

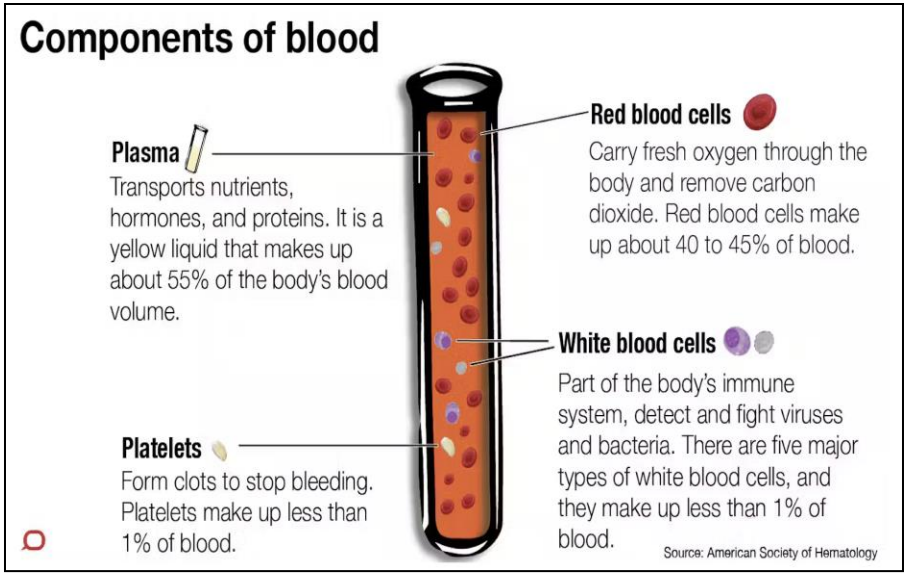
Composition of the blood

Plasma: 55%

Cellular elements: 45%

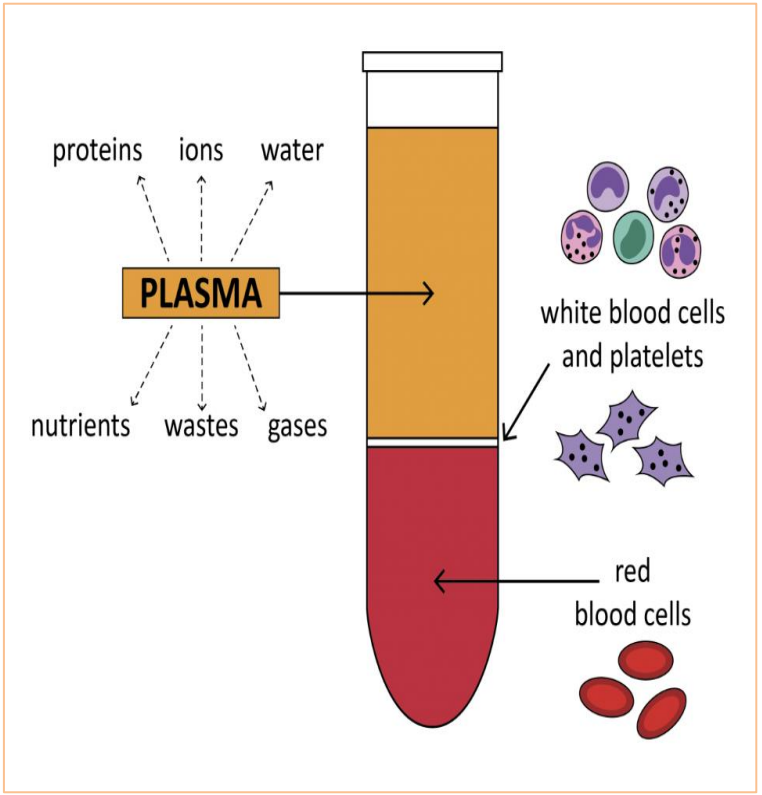
1. **RBCs**
2. **WBCs**
3. **Platelets**



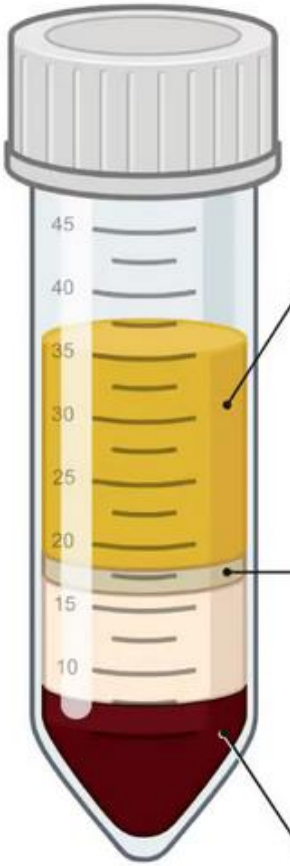


Composition of Plasma

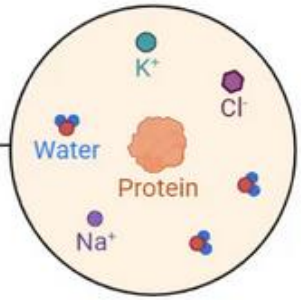
Water	Inorganic substances	Organic substances
90%	0.9%	9.1%
	• Cations such as Na^+ & K^+ • Anions such as Cl, CO_3, PO_4 & SO_4	• Plasma proteins (6-8 gm%) • Lipids • Others



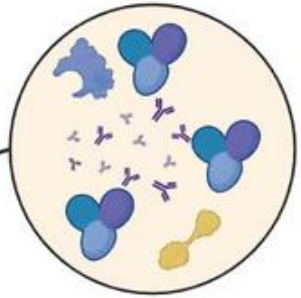
PLASMA PROTEINS



~55%

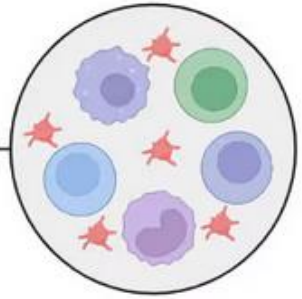


Plasma
- Water
- Proteins
- Electrolytes



Plasma Proteins
- Albumin
- Globulin
- Fibrinogen
- HTPP

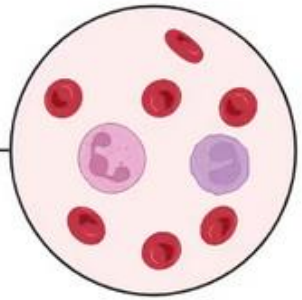
1 %



Platelets + Peripheral blood mononuclear cells (PBMCs)
- Lymphocytes
- Monocytes

Hormone-Transporting Plasma Proteins
- IGFBP3
- Thyroxine Binding Globulin
- Corticosteroid-binding Globulin
- SHBG

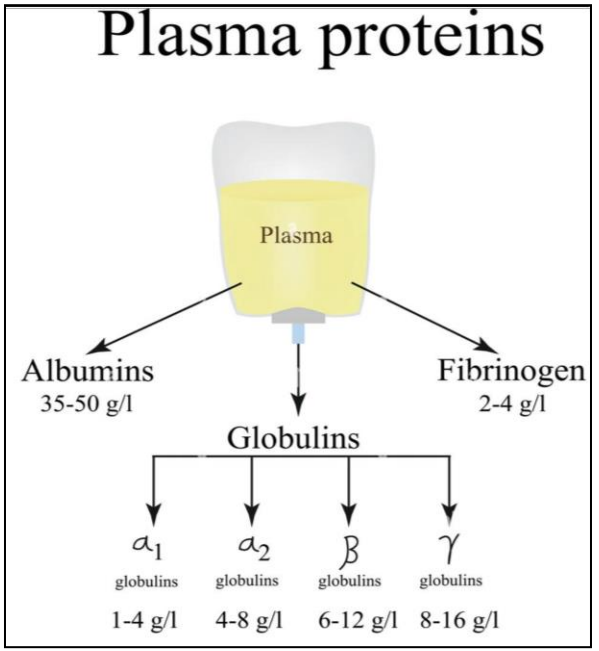
~45%



Red blood cells + Polymorphonuclear cells
- Eosinophil
- Neutrophil

Plasma proteins

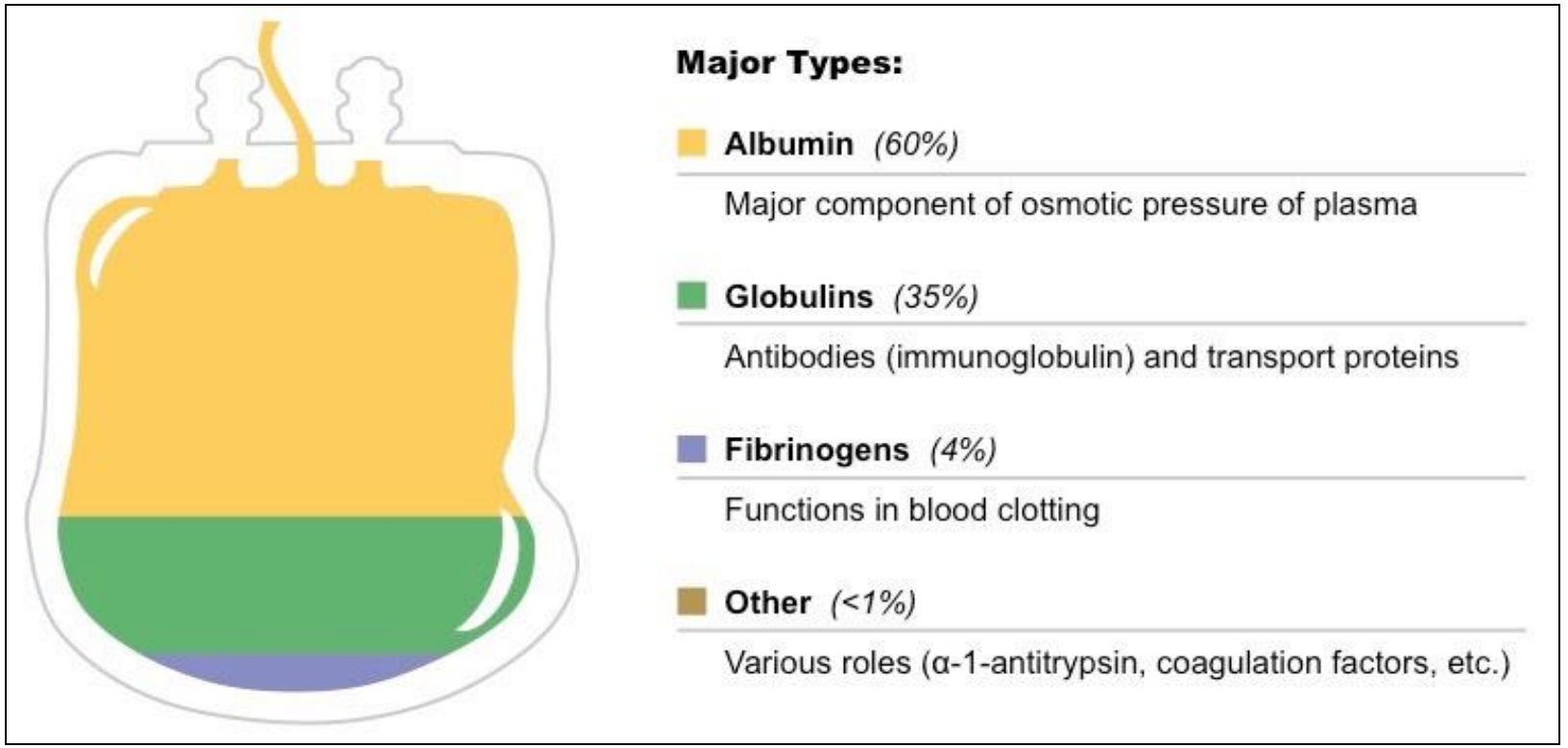
- **Normal level:** total proteins in plasma are about **6-8 g/dl**.
- Plasma proteins can be **classified into 3 main groups**:
  1. **Albumin**
  2. **Globulins (α1, α2, β and γ)**
  3. **Fibrinogen**



- **Site of synthesis**:
  1. Most plasma proteins are synthesized in **the liver**.
  2. γ globulins are synthesized by **plasma cells & B cells of lymphoid tissues**.

ALBUMIN

- It is the **major plasma protein** (represents **60%** of total plasma protein).
- Its normal level: **3.5 - 5.5 g/dl**.



ALBUMIN

Functions of albumin:

1. Responsible for 70 to 80% of **osmotic pressure of human plasma**.
2. Helps in **transport of several substances** e.g., unconjugated bilirubin, FFA, Ca^{++} and steroid hormones.
3. Albumin can also **bind and transport certain drugs to their target tissues** e.g., sulphonamides, aspirin, penicillin.
4. Preparations of human albumin have been **widely used in treatment of hemorrhagic shock and burns**.

α1-GLOBULINS

1. α1-acid glycoprotein (orosomucoid):

- It is a reliable **indicator of acute inflammation**.

2. α1-antitrypsin (α1-AT):

- It is the principal **protease inhibitor** (PI) of human plasma. It inhibits ***trypsin, elastase,* and other proteases** by forming complexes with them.
- It is **deficient in emphysema**.

α2-GLOBULINS

1. Haptoglobin:

- **Bind free Hb** and **minimizes its urinary loss**.
- After binding, Hp-Hb complex circulates in the blood, which cannot pass through glomerular filter and ultimately the complex is destroyed by RE cells.

β-GLOBULINS

1. **β- Lipoprotein (LDL)**
2. **Transferrin:** **transport of iron (Fe)** between intestine and site of synthesis of Hb and other Fe containing proteins.
3. **C-reactive Protein:**
   - It reacts and precipitates with group C-polysaccharide of pneumococci, in the presence of Ca, hence the name.
   - It can bind to T-lymphocytes and can activate complement.
   - Used as **a marker of tissue injury & inflammation**.

γ-GLOBULINS

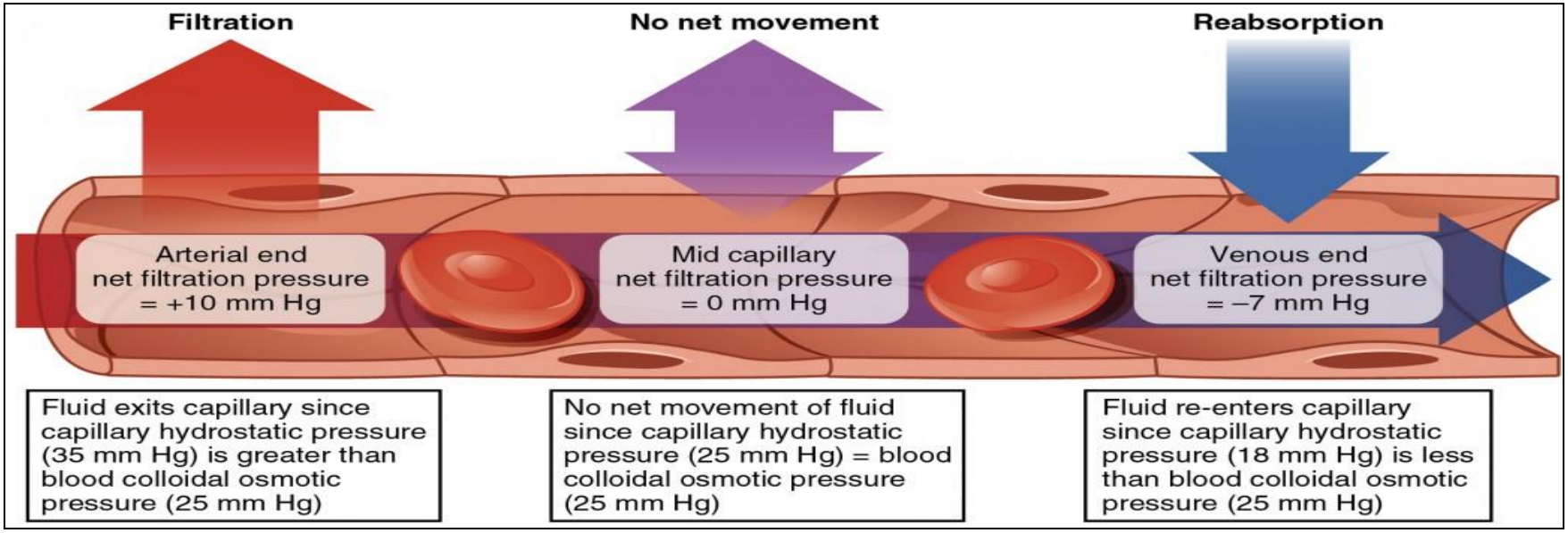
- These are **immunoglobulins** having antibody activity.

FIBRINOGEN

- also called **clotting factor I**, as it takes part in coagulation of blood.

Functions of different plasma proteins

1. They contribute amino acids for **tissue protein synthesis**.
2. **Regulation of blood volume and tissue fluid formation**: plasma proteins exert **colloid osmotic pressure (25 mmHg)** across the capillary wall which tend to pull water into the blood.



3. **Buffering action:** The serum proteins, like other proteins, are ***amphoteric***, they have free **acidic** (R-COOH) & **basic** (R-NH2) end **so can act as weak acid or base** and thus can combine with acids or bases.

4. **Binding and transport function:**

- **Albumin**: various ligands (thyroxin, steroids, bilirubin, Ca^{++} and FFA).
- **Haptoglobin**: extracorpuscular Hb (Hb released by dead RBCs)
- **Apolipoproteins** + lipids : Lipoproteins
- **Thyroid-binding globulin**: T3 & T4
- **Transferrin**: iron.
- **Ceruplasmin**: copper
- **Steroid hormone – binding globulin**: steroid hormones
- **Transcoblamin**: Vit B12

5. Role in **blood coagulation and fibrinolysis.**

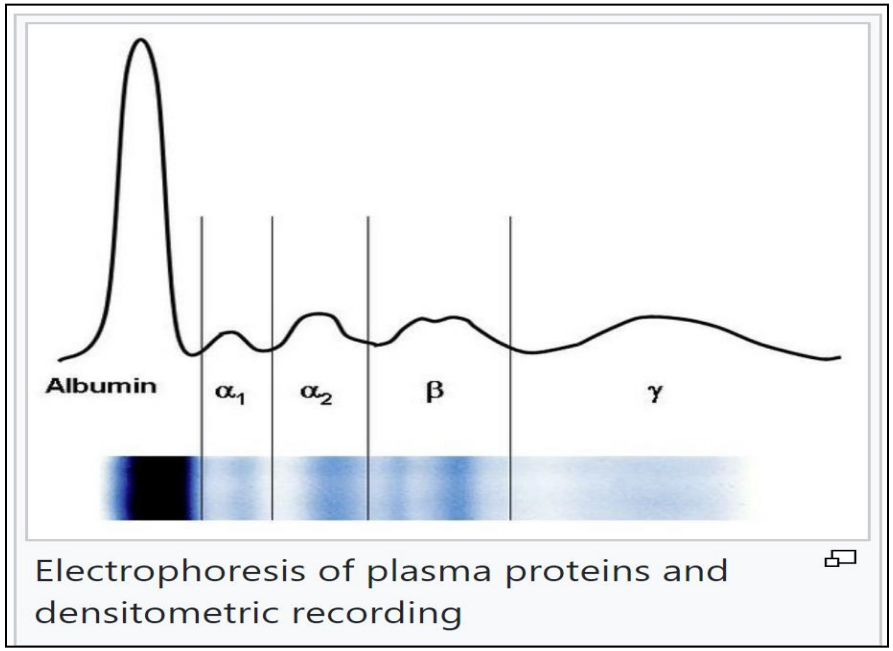
6. Immunological function (Body defense): γ-globulins protect the body against microbial infections.

7. Enzymes: most enzymes are proteins in nature.

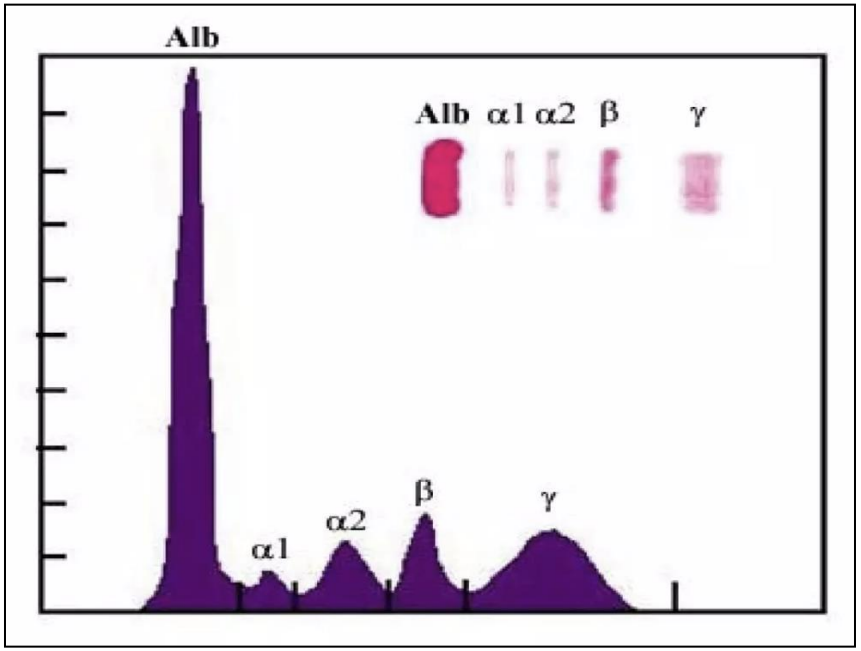
8. Carriage of CO_2: CO_2 combines with the **amino group** of plasma proteins and is carried as **carbamino compounds**.

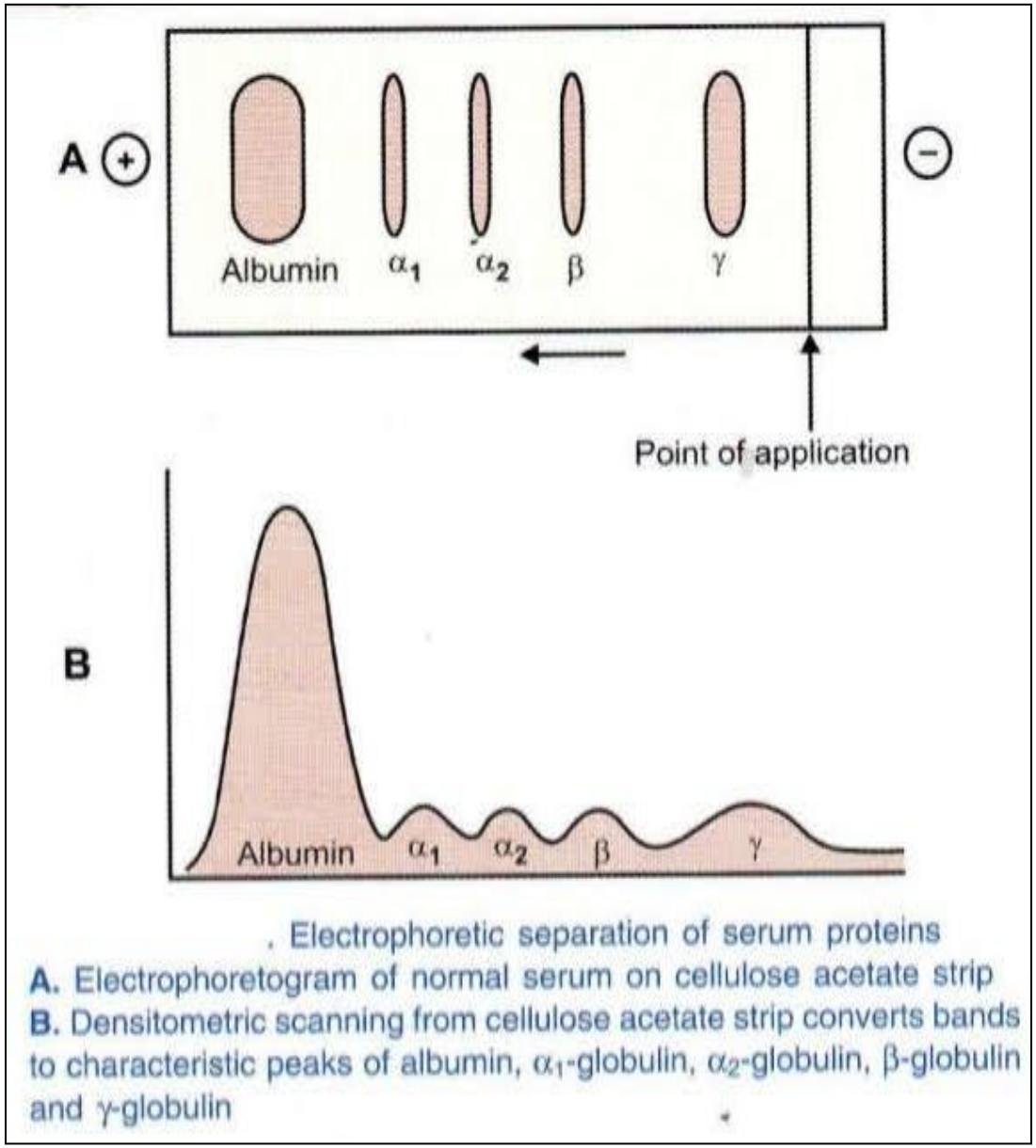
Serum Protein Electrophoresis

- The **most common method** for analyzing plasma proteins is **Electrophoresis**.
- By **cellulose acetate** electrophoresis, the plasma proteins can be separated into several fractions including albumin, α1, α2, β and γ globulins.

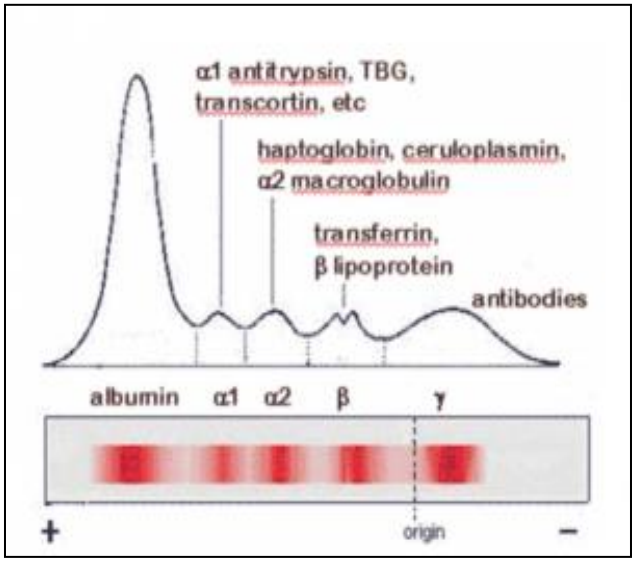


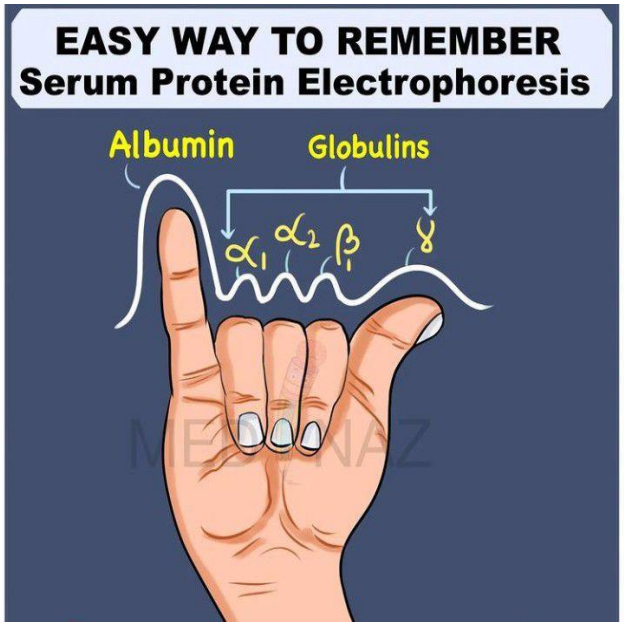
Electrophoresis of plasma proteins and densitometric recording





. Electrophoretic separation of serum proteins
A. Electrophoretogram of normal serum on cellulose acetate strip
B. Densitometric scanning from cellulose acetate strip converts bands to characteristic peaks of albumin, α_1-globulin, α_2-globulin, β-globulin and γ-globulin

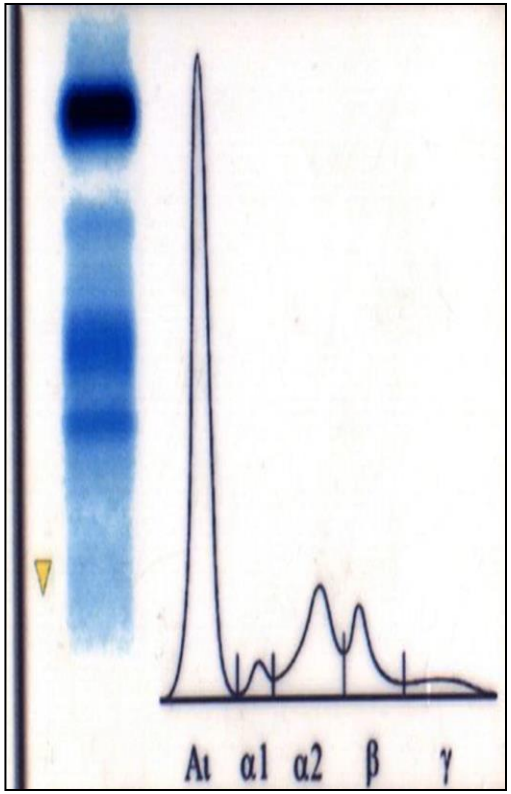




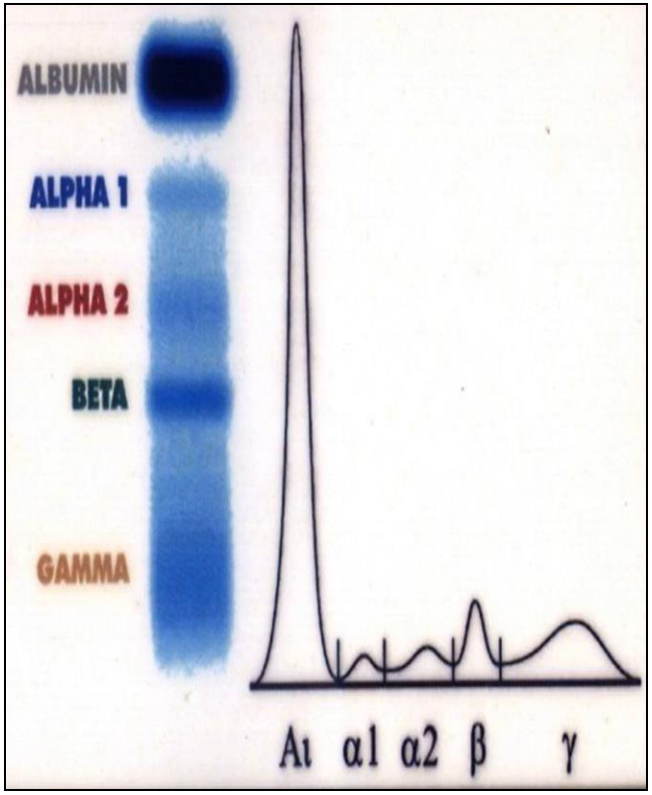
ELECTROPHORETIC PATTERNS OF SERUM PROTEINS

THE PATTERN OF SERUM PROTEINS ELECTROPHORESIS MAY BE USED IN THE DIAGNOSIS OF DISEASE

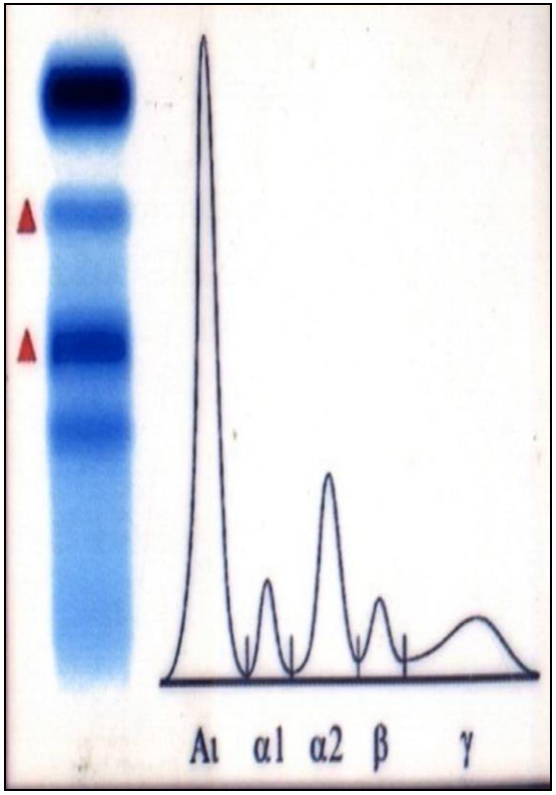
Serum protein Electrophoresis & Disease patterns



Hypogammaglobulinemia

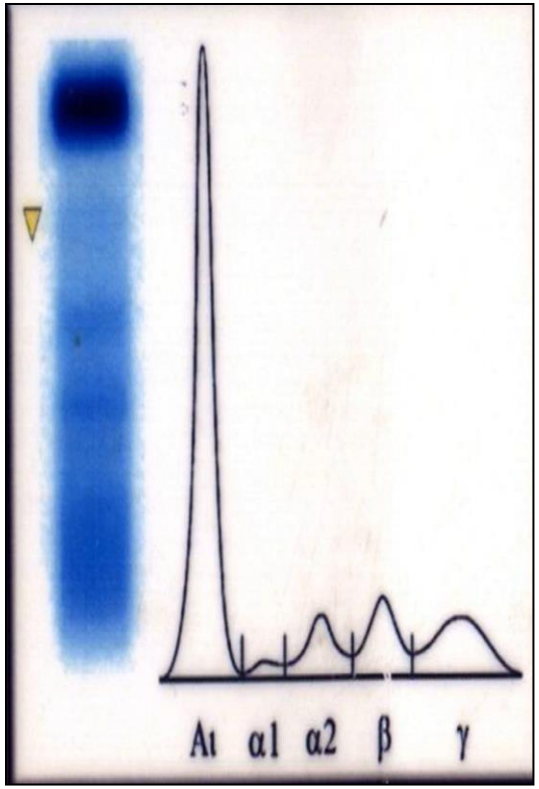


Normal profile

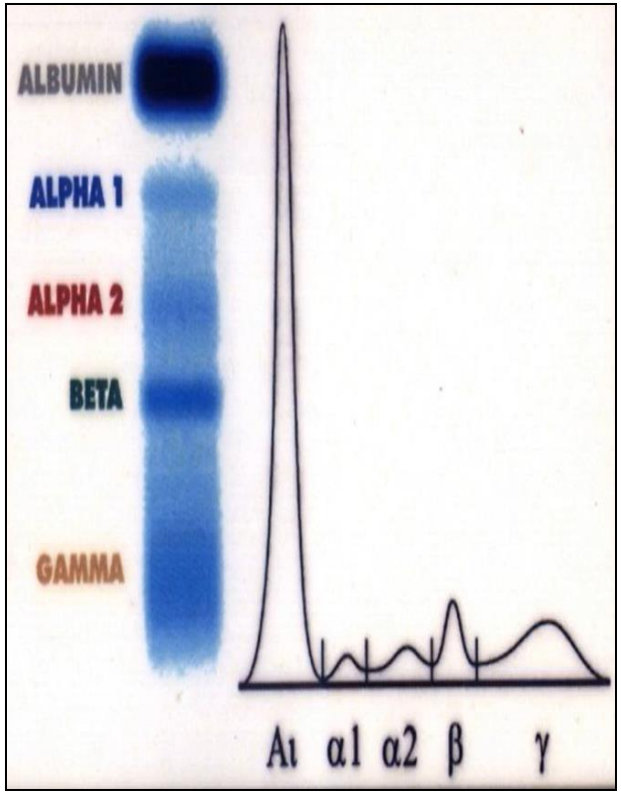


Acute inflammatory response

Serum protein Electrophoresis & Disease patterns



α1-antitrypsin deficiency



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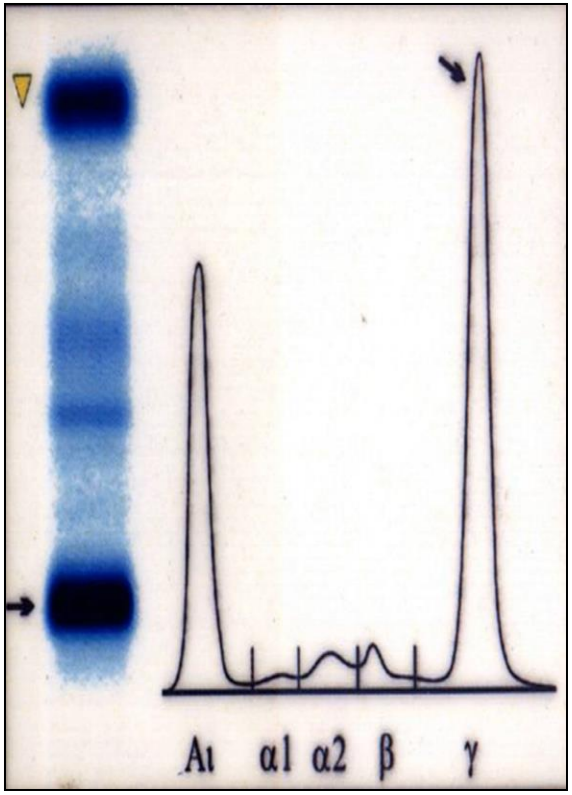

Multiple myeloma

Acute Phase Proteins (or Reactants)

Definition: are certain proteins which their levels are increased in plasma during **acute inflammatory states** or secondary to **certain types of tissue damage**.

They include:

1. **C-reactive protein (CRP)**
2. **Haptoglobin (Hp)**
3. **α1-antitrypsin**
4. **α1-acid glycoprotein**
5. **Fibrinogen**

Hypoproteinemia

Causes:

I. **Hemodilution**: overload from IV infusion.

II. **Hypoalbuminemia:**

a. ***Albumin Loss from the body***

1. **Renal:** Loss of albumin in urine in **nephrotic syndrome**.
2. **GI Tract:** Protein losing enteropathy.
3. **Skin:** Severe burns.

b. Decreased synthesis of albumin **in** **severe liver diseases** such as **chronic hepatitis and liver cirrhosis**.

c. Miscellaneous: Pregnancy and chronic illness.

III. Hypogammaglobulinemia:

(a) Protein loss: Same as above

(b) Decreased synthesis:

1. **Primary:** Genetic deficiency
2. **Secondary:** Certain toxins and drugs: uremia, cytotoxic therapy, corticosteroid therapy, AIDS.

(c) Miscellaneous: Pregnancy.

Effects:

1. **Most important sign is L.L edema, swelling of face and of other parts of the body.**
2. **Loss of muscle mass = muscle wasting**
3. **Infections**
4. **Fatigue**
5. **Dry brittle hair**
6. **Lack of growth in children.**

Summary

- **Plasma proteins:** types, production & functions.
- **Serum electrophoretic pattern** in normal & abnormal state.
- **Acute phase proteins:** types & clinical importance.
- **Hypoproteinemia:** causes & effects.

Question Time

Question 1

- **Normal range of serum albumin:**

A) 1.0-2.5 g/dl.

B) 2.0-3.0 g/dl.

C) 3.5-5.5 g/dl.

D) 6-8 g/dl.

E) 7-7.5 g/dl.

Question 2

- **Which of the following proteins is present in γ globulin fraction:**

A) Ceruloplasmin

B) Haptoglobin

C) Immunoglobulin

D) C-reactive protein

E) Transferrin

Question 3

A 70-year-old male presents with 3 month of peripheral edema. He doesn't smoke, drink or use drugs. No weight loss, no fever or joint pain. On examination: BP 160/110, ascites and edema were found. The doctor suspects nephrotic syndrome and asks for serum protein electrophoresis. What is the suspected finding?

A. ↓↓α1 globulins.

B. ↓↓α2 globulins.

C. ↓↓β globulins.

D. ↓↓Albumin.

E. ↓↓α1 antitrypsin.

References

- **Chatterjea's Textbook of Medical Biochemistry, 8th edition.**
- **Harper's illustrated Biochemistry 30th edition.**


Thank You