

Plasma Proteins

GIT Block

1 Lecture

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Overview:

- **Functions and characteristics of plasma proteins**
- **Measurement of plasma proteins and diagnosis of diseases**
- **Electrophoretic patterns of plasma proteins**
- **Acute phase proteins**

Plasma Proteins (pps)

- **Plasma contains >300 different proteins**
- **Many pathological conditions affect level of plasma proteins**
- **Mostly synthesized in the liver**
- **Some are produced in other sites**
- **A normal adult contains ~70 g/L of pps**

Functions of plasma proteins

- **Transport (Albumin, prealbumin, globulins)**
- **Maintain plasma oncotic pressure (Albumin)**
- **Defense (Immunoglobulins and complement)**
- **Clotting and fibrinolysis (Thrombin and plasmin)**

Measurement of Plasma Proteins

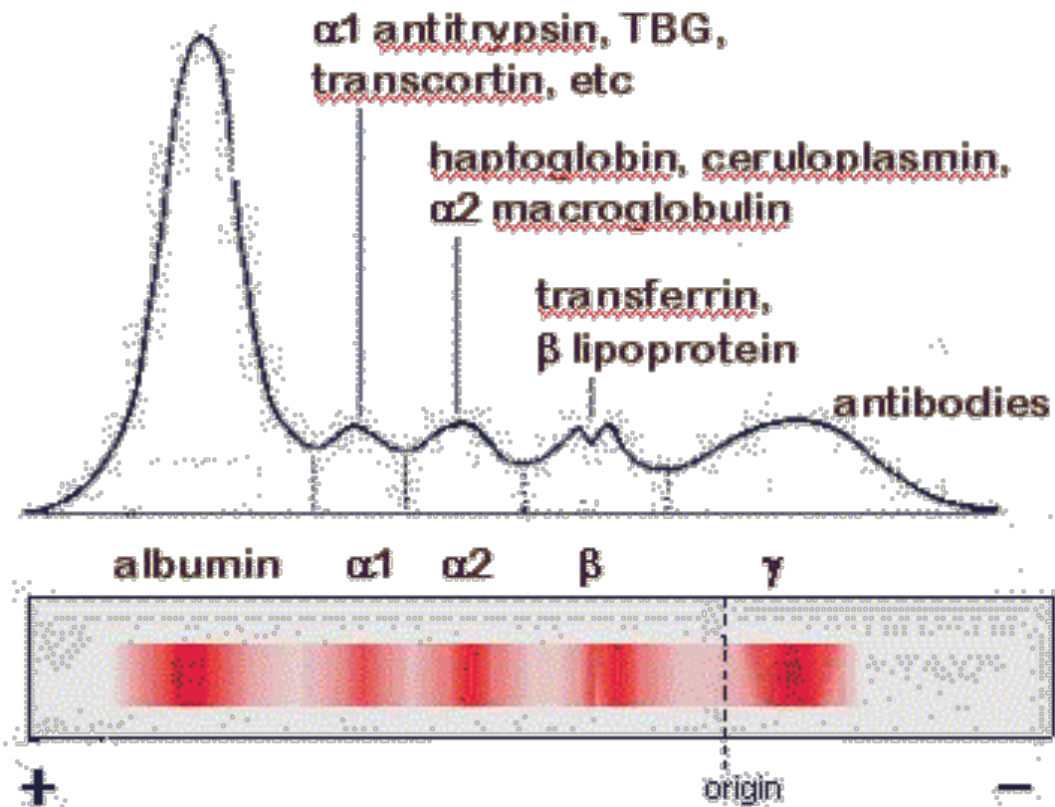
A) Quantitative measurement of a specific protein:

Chemical or immunological reactions

B) Semiquantitative measurement by electrophoresis:

- Proteins are separated by their electrical charge in electrophoresis
- **Five separate bands of proteins** are observed
- These bands change in disease

Normal Pattern of Plasma Protein Electrophoresis



Types of Plasma Proteins

- **Prealbumin**
- **Albumin**
- **α_1 -Globulins:**
 - **α_1 -Antitrypsin, α -fetoprotein**
- **α_2 -Globulins:**
 - **Ceruloplasmin, haptoglobin**
- **β -Globulins:**
 - **CRP, transferrin, β_2 -microglobulin**
- **γ - Globulins**

Prealbumin (Transthyretin)

- **A transport protein for:**
 - **Thyroid hormones**
 - **Retinol (vitamin A)**
- **Migrates faster than albumin in electrophoresis**
- **Separated by immunoelectrophoresis**
- **Lower levels found in:**
 - **liver disease, nephrotic syndrome, acute phase inflammatory response, malnutrition**
- **Short half-life (2 days)**

Albumin

- **Most abundant plasma protein (~40 g/L) in normal adult**
- **Synthesized in the liver as preproalbumin and secreted as albumin**
- **Half-life in plasma: 20 days**
- **Decreases rapidly in injury, infection and surgery**

Functions

- Maintains oncotic pressure:
 - The osmotic pressure exerted by plasma proteins that pulls water into the circulatory system
 - Maintains fluid distribution in and outside cells and plasma volume
- 80% of plasma oncotic pressure is maintained by albumin

Functions

- **A non-specific carrier of**
 - hormones, calcium, free fatty acids, drugs, etc.
- **Tissue cells can take up albumin by pinocytosis where it is hydrolyzed to amino acids**
- **Useful in treatment of liver diseases, hemorrhage, shock and burns**

Hypoalbuminemia

- **Causes**

- Decreased albumin synthesis (liver cirrhosis, malnutrition)
- Increased losses of albumin
 - Increased catabolism in infections
 - Excessive excretion by the kidneys (nephrotic syndrome)
 - Excessive loss in bowel (bleeding)
 - Severe burns (plasma loss in the absence of skin barrier)

Hypoalbuminemia

Effects

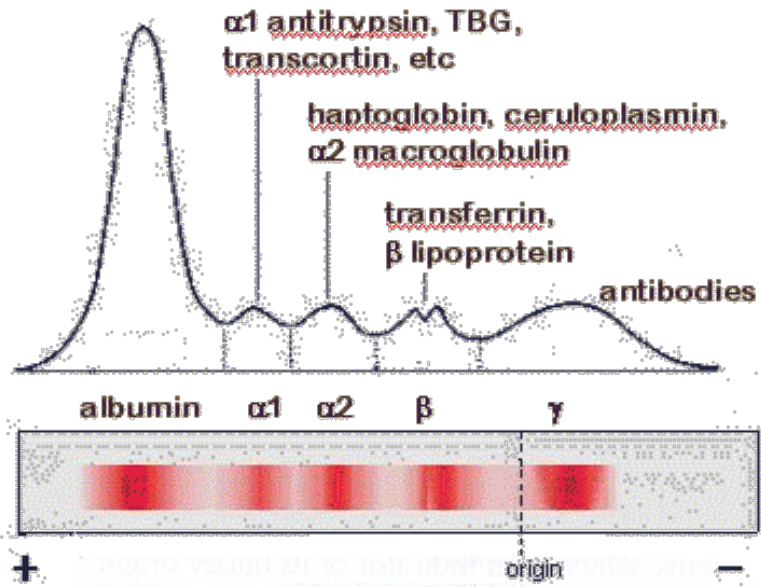
- Edema due to low oncotic pressure
 - Albumin level drops in liver disease causing low oncotic pressure
 - Fluid moves into the interstitial spaces causing edema
- Reduced transport of drugs and other substances in plasma
- Reduced protein-bound calcium
 - Total plasma calcium level drops
 - Ionized calcium level may remain normal

Hyperalbuminemia

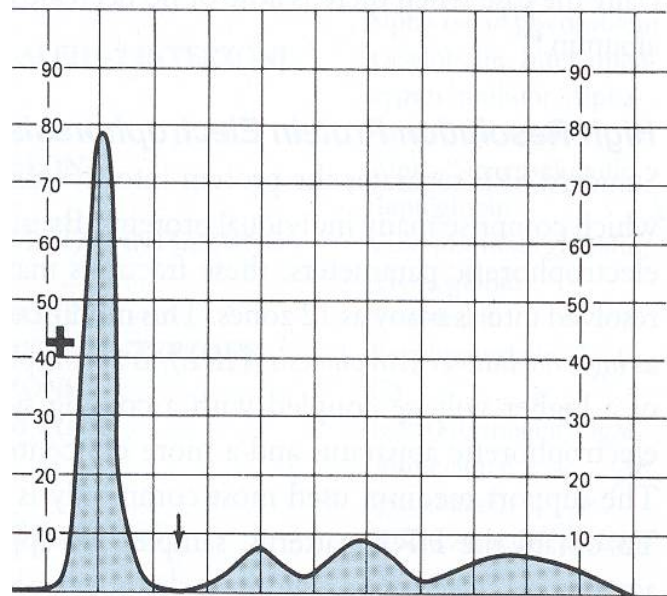
- No clinical conditions are known that cause the liver to produce large amounts of albumin
- The only cause of hyperalbuminemia is dehydration

α_1 -Antitrypsin

- **Synthesized by the liver and macrophages**
- **An acute-phase protein that inhibits proteases**
- **Proteases are produced endogenously and from leukocytes and bacteria**
 - Digestive enzymes (trypsin, chymotrypsin)
 - Other proteases (elastase, thrombin)
- **Infection leads to protease release from bacteria and from leukocytes**



α_1 -ANTITRYPSIN DEFICIENCY



Types of α_1 -Antitrypsin

- Over 30 types are known
- The most common is M type
- Genetic deficiency of α_1 -Antitrypsin
 - Synthesis of the defective α_1 -Antitrypsin occurs in the liver but it cannot secrete the protein
 - α_1 -Antitrypsin accumulates in hepatocytes and is deficient in plasma

Clinical Consequences of α_1 -Antitrypsin Deficiency

- Neonatal jaundice with evidence of cholestasis
- **Childhood liver cirrhosis**
- Pulmonary emphysema in young adults

Laboratory Diagnosis

- Lack of α_1 -globulin band in protein electrophoresis
- Quantitative measurement of α_1 -Antitrypsin by:
 - **Radial immunodiffusion, isoelectric focusing or nephelometry**

α -Fetoprotein (AFP)

- Synthesized in the developing embryo and fetus by the parenchymal cells of the liver
- AFP levels decrease gradually during intra-uterine life and reach adult levels at birth
- Function is unknown but it may protect fetus from immunologic attack by the mother
- No known physiological function in adults

α -Fetoprotein (AFP)

- **Elevated maternal AFP levels are associated with:**
 - **Neural tube defect, anencephaly**
- **Decreased maternal AFP levels are associated with:**
 - **Increased risk of Down's syndrome**
- **AFP is a tumor marker for:**
Hepatoma and testicular cancer

Ceruloplasmin

- **Synthesized by the liver**
- **Contains >90% of serum copper**
- **An oxidoreductase that inactivates ROS causing tissue damage in acute phase response**
- **Important for iron absorption from the intestine**
- **Wilson's disease:**
 - **Due to low plasma levels of ceruloplasmin**
 - **Copper is accumulated in the liver and brain**

Haptoglobin

- **Synthesized by the liver**
- **Binds to free hemoglobin to form complexes that are metabolized in the RES**
- **Limits iron losses by preventing Hb loss from kidneys**
- **Plasma level decreases during hemolysis**

Transferrin

- **A major iron-transport protein in plasma**
 - **30% saturated with iron**
- **Plasma level drops in:**
 - **Malnutrition, liver disease, inflammation, malignancy**
- **Iron deficiency results in increased hepatic synthesis**
- **A negative acute phase protein**

β_2 -Microglobulin

- **A component of human leukocyte antigen (HLA)**
- **Present on the surface of lymphocytes and most nucleated cells**
- **Filtered by the renal glomeruli due to its small size but most (>99%) is reabsorbed**
- **Elevated serum levels are found in**
 - **Overproduction in disease**
- **May be a tumor marker for:**
 - **Leukemia, lymphomas, multiple myeloma**

C-Reactive Protein (CRP)

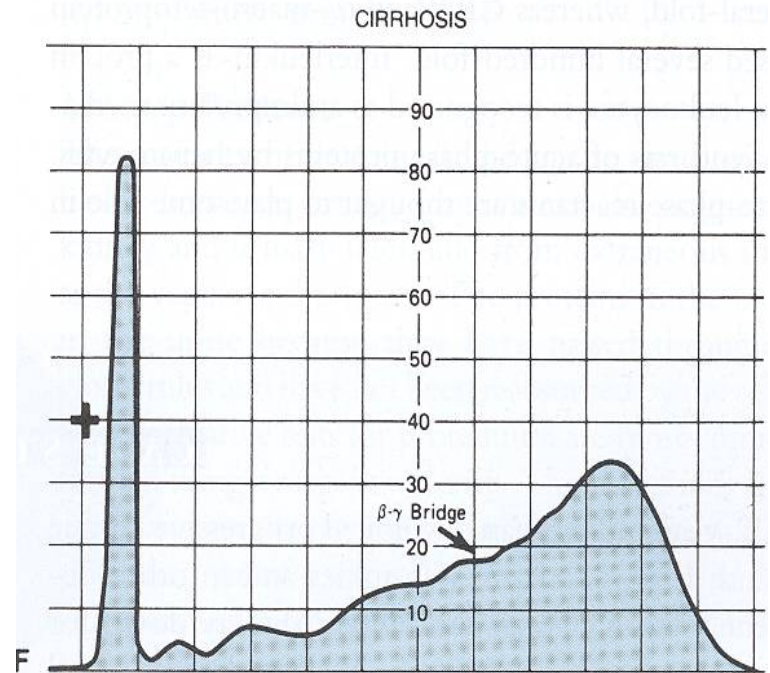
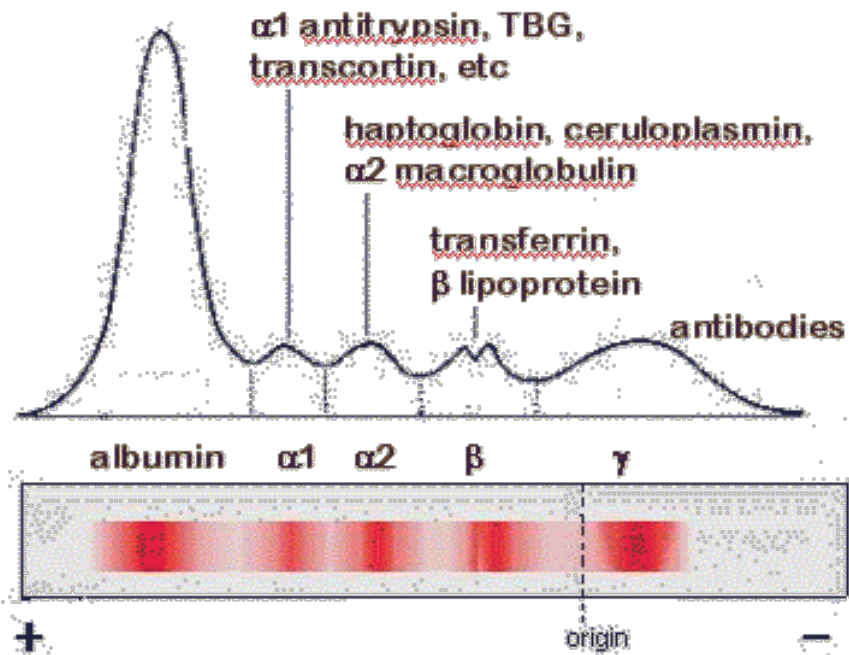
- **An acute-phase protein synthesized by the liver**
- **Important for phagocytosis**
- **High plasma levels are found in many inflammatory conditions such as rheumatoid arthritis**
- **A marker for ischemic heart disease**

Hypergammaglobulinemia

- **May result from stimulation of**
 - **B cells (Polyclonal hypergammaglobulinemia)**
 - **Monoclonal proliferation (Paraproteinemia)**

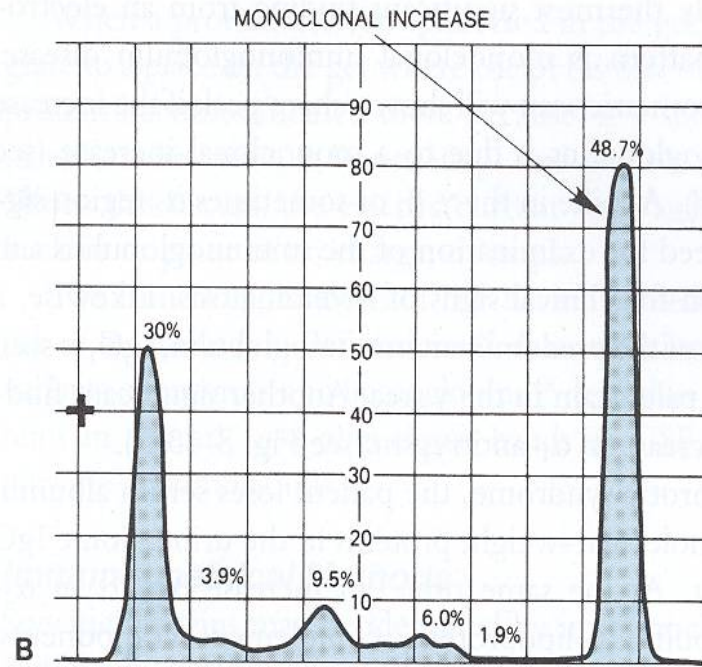
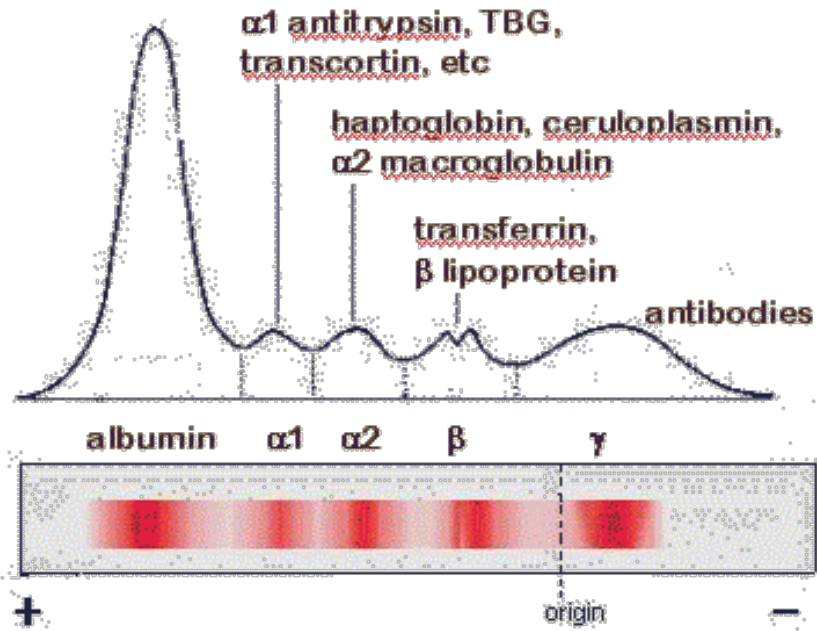
Polyclonal hypergammaglobulinemia:

- **Stimulation of many clones of B cells produce a wide range of antibodies**
- **γ -globulin band appears large in electrophoresis**
- **Clinical conditions: acute and chronic infections, autoimmune diseases, chronic liver diseases**



Monoclonal Hypergammaglobulinemia

- **Proliferation of a single B-cell clone produces a single type of Ig**
- **Appears as a separate dense band (paraprotein or M band) in electrophoresis**
- **Paraproteins are characteristic of malignant B-cell proliferation**
- **Clinical condition: multiple myeloma**



Positive Acute Phase Proteins

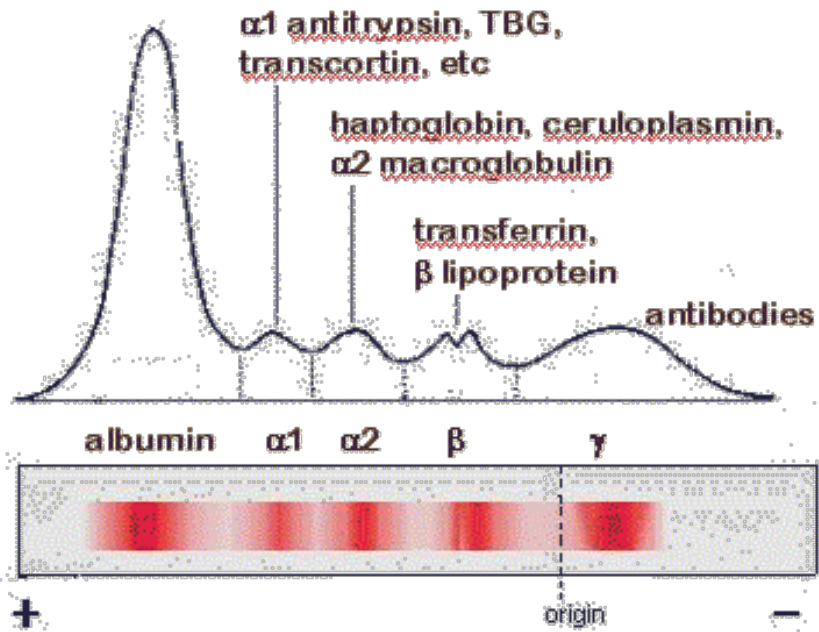
- Plasma protein levels **increase** in:
 - Infection, inflammation , malignancy, trauma, surgery
- These proteins are called acute phase reactants
- Synthesized due to body's response to injury
- Examples: α_1 -Antitypsin, haptoglobin, ceruloplasmin, fibrinogen, c-reactive protein

Positive Acute Phase Proteins

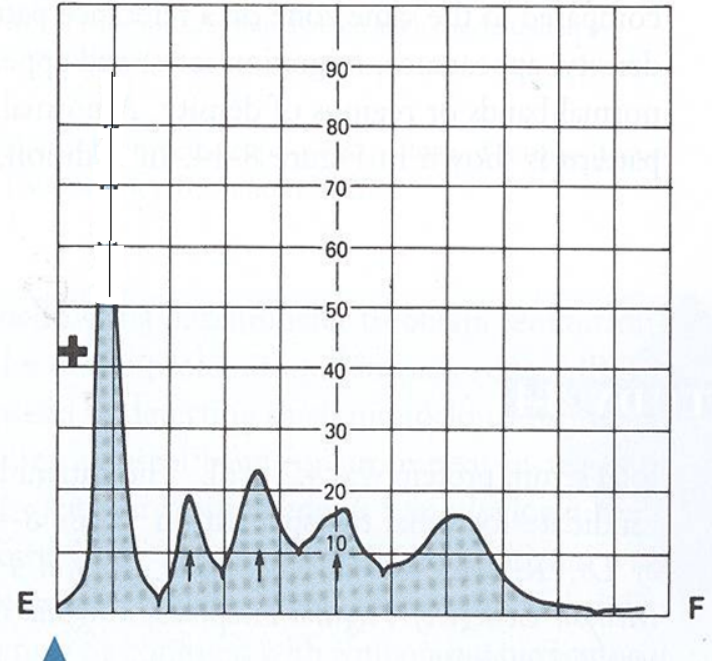
- **Mediators cause these proteins to increase after injury**
- **Mediators: Cytokines (IL-1, IL-6), tumor necrosis factors α and β , interferons, platelet activating factor**

Functions:

- 1. Bind to polysaccharides in bacterial walls**
- 2. Activate complement system**
- 3. Stimulate phagocytosis**



INFLAMMATION



Negative Acute Phase Proteins

- **These proteins decrease in inflammation**
 - **Albumin, prealbumin, transferrin**
- **Mediated by inflammatory response via cytokines and hormones**
- **Synthesis of these proteins decrease to save amino acids for positive acute phase proteins**

References

- Lecture Notes in Clinical Biochemistry 7th edition, pages 92-98
- Clinical Biochemistry An Illustrated Colour Text pages 48-51