-Plasma Proteins-

Biochemistry Team

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Plasma Proteins

**What's the difference between Plasma and serum? Plasma – blood without cells. Serum – Blood without clotting factors.

**Electrophoresis is the separation of proteins based on their molecular weight, under electrical charge

(helpful Youtube video)

Objectives:

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

When damage happens they are the first to change

Functions of plasma proteins:

1) Transport (Albumin, prealbumin, globulins)
2) Maintain plasma oncotic pressure (Albumin)
3) Defense (Immunoglobulins and complement)
4) Clotting and fibrinolysis (Thrombin and plasmin)

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

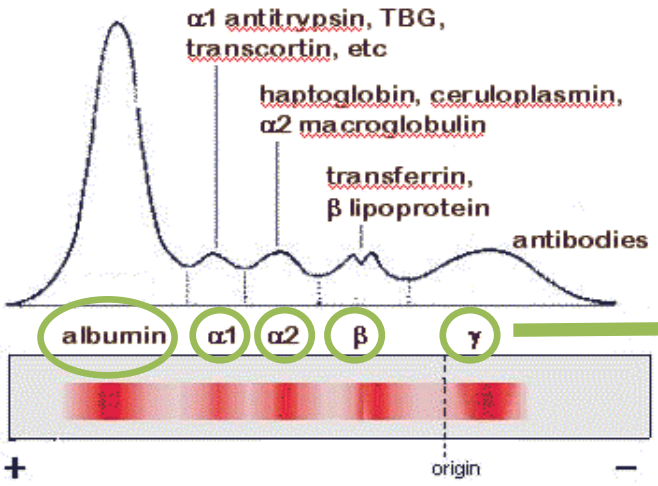
Measurement of Plasma Proteins:

A) Quantitative measurement of a specific protein:	B) Semiquantitative measurement by electrophoresis:
Chemical or immunological reactions	✓ Proteins are separated by their electrical charge in electrophoresis. ✓ Five separate bands of proteins are observed. ✓ These bands change in disease.

Measures the exact quantity of proteins

Measures the relative amount (how much of the protein is present in relation to other proteins

Normal Pattern of Plasma Protein Electrophoresis



These are the 5 bands

Types of plasma proteins

We don't count prealbumin as one of the 5 bands because we need immunoelectrophoresis to see it

1) Prealbumin
2) Albumin
3) α_1-Globulins:
a_1-Antitrypsin, α-fetoprotein
4) α_2-Globulins:
Ceruloplasmin, haptoglobin
5) β-Globulins:
CRP, transferrin, β2-microglobulin
6) γ- Globulins

1. Prealbumin

- 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)

2. Albumin

General information	▪ 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
Function	- 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 - 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)

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

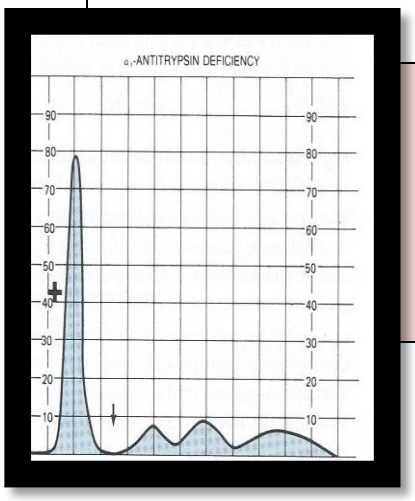
Hyperalbuminemia

- 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 (Protease inhibitor)

General information	- 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
Types	- 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.
Lab diagnosis	- Lack of α_1-globulin band in protein electrophoresis Quantitative measurement of α_1-Antitrypsin by: Radial immunodiffusion, isoelectric focusing or nephelometry

Because of hyper-active protease



α-Fetoprotein (AFP)

General Information	• 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
Clinical consequence	▪ 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

General information	• Synthesized by the liver. • Contains >90% of serum copper. • An oxidoreductase that inactivates ROS causing tissue damage in acute phase response. ROS= reactive oxygen species
Function	**Absorption of iron from the intestine**
Clinical consequence	Wilson's disease; ○ Due to low plasma levels of ceruloplasmin ○ Copper is accumulated in the liver and brain

Haptoglobin

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

Transferrin

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

β_2–Microglobulin

General information	✓ 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.
Clinical consequence	- Elevated serum levels are found in ▪ Overproduction in disease ▪ Impaired kidney function - May be a tumor marker for: ▪ Leukemia, lymphomas, multiple myeloma

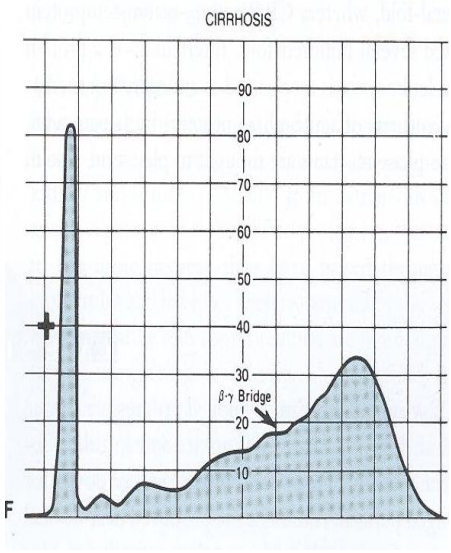
C-Reactive Protein (CRP)

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

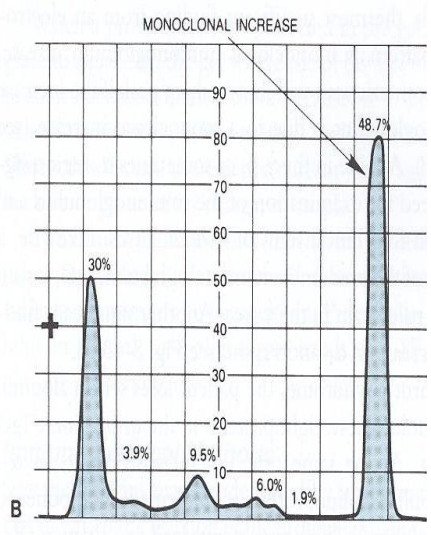
Hypergammaglobulinemia

Types	- **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.	

Polyclonal hypergammaglobulinemia

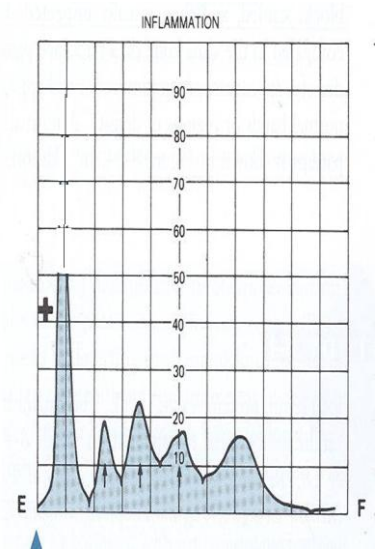


Monoclonal Hypergammaglobulinemia



Acute phase proteins

Positive:



- 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.
- 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

Negative:

- 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

Questions:

1-Which of the following is not a feature of Hypoalbuminemia ?

A. Reduced transport of drugs
B. Edema due to low oncotic pressure
C. The only cause for it is dehydration
D. Decreased albumin synthesis

Answer: C

2-Increased risk of Down's syndrome is associated with which of the following?

A. Elevated maternal AFP
B. Decreased maternal AFP
C. Polyclonal hypergammaglobulinemia
D. Monoclonal Hypergammaglobulinemia:

Answer: B

3- Which one of the following is Positive Acute Phase Proteins?

A. Albumin, α1-Antitypsin and fibrinogen
B. haptoglobin, ceruloplasmin and transferrin
C. Antitypsin , transferrin and haptoglobin
D. haptoglobin, ceruloplasmin and fibrinogen

Answer: D

4-Which one of the following conditions results in decreased level of Albumin?

A. nephritic syndrome
B. nephrotic syndrome
C. dehydration
D. none of the above

Answer: B

5-Deficiency in which of following proteins results in emphysema?

A- Albumin
B- α-fetoprotein
C- α1-Antitypsin
D- fibrinogen

Answer: C