



L7:

Plasma Protein

GNT Block



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Objectives:

- 💡 Identify types and various functions of plasma proteins.
- 💡 Discuss the role of plasma proteins in the diagnosis of diseases and conditions.
- 💡 Interpret the normal and abnormal electrophoretic patterns of plasma proteins.
- 💡 Identify the role positive and negative acute phase proteins in various diseases.

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Female Dr. info. you should know will for all proteins : 1- where they are synthesised 2- what is their role 3- what happens in deficiency. 4- is it a +ve or -ve acute phase protein.

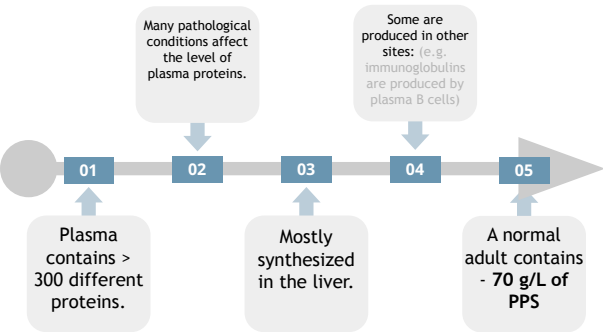


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Plasma Proteins (PPS)



Plasma Proteins Functions

Transport: Albumin, Prealbumin, Globulins
[1]

Maintain plasma on oncotic pressure:
Albumin

Defense: Immunoglobulin, Complements

Clotting & Fibrinolysis: Thrombin, Plasmin

[1]: HB → intracellular transporter (inside RBCs) Plasma proteins
→ extracellular transporter (in plasma)

Measurement of Plasma Proteins

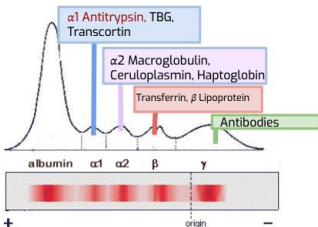
1- Quantitative measurement of a specific protein:

-Chemical or immunological reactions.

2- Semi Quantitative measurement by electrophoresis: (439: gives a general idea about the amount)

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

Normal Pattern of Plasma Protein Electrophoresis:



Dr Explanation :

The sample is put in an alkaline buffer gel and then you run a current through it. Remember, Currents move from -ve to +ve.

The Test separates the proteins in the blood based on their Electrical charge & Molecular weight:

- More negativity \rightarrow faster to arrive the cathode part
 - Less in molecular weight \rightarrow faster to arrive the cathode part

So, lighter proteins move further than heavier ones. Producing this ladder like appearance.

In the graph:

◆ Albumin: comes 1st (fastest) cause it has the smallest size.

◆ Gamma (γ): comes last (slowest) cause it's the largest.

Types of Plasma Proteins:

1 $\alpha 1$ - Globulins
 - $\alpha 1$ -Antitrypsin
 - α -Fetoprotein

2 $\alpha 2$ - Globulins
 -Ceruloplasmin
 -Haptoglobin

3 β -Globulins
 -CRP
 -Transferrin
 - $\beta 2$ -Microglobulin

4 γ - Globulins

5 Prealbumin

6 Albumin

Types of Plasma Proteins

Prealbumin (Transthyretin):

Information

- Migrates faster than albumin in electrophoresis. (thus the name PREalbumin)
- Separated by immunoelectrophoresis. Can't be seen in electrophoresis because it's smaller, faster than albumin and have very little amount except in:CSF, so it need specific measurement -immunoelectrophoresis -.
- Short half-life (2 days).

Function

- A transport protein for:
- 1.Thyroid Hormone. (439: why we call it transthyretin)
 - 2.Retinol (vitamin A).

Lowered levels in

- 1- Liver disease. (439: because they can't produce prealbumin)
- 2- Nephrotic Syndrome.
- 3- Acute phase inflammatory response. (439: negative acute phase protein)
- 4- malnutrition.

Albumin

Information

- 1- most abundant plasma protein (~40 g/L) in normal adult. (439: resembles 65% of plasma protein in our body and 35% rest of proteins)
- 2- Synthesized in the liver as **pre proalbumin** and secreted as albumin.
- 3- Half-life in the plasma: 20 Days. (439: longer than prealbumin)
- 4- Decreases rapidly in injury - due to loss of blood-, infection and surgery.

Function

- 1- 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.
- 2- 80 % of plasma oncotic pressure is maintained by albumin. (439: main function)
- 3- A non-specific carrier of: Hormones, Calcium, Free fatty acid, drugs, etc.
- 4- Tissue cell can take up albumin by **pinocytosis** -cellular drinking- where it is hydrolyzed to amino acids.
- 5-Useful in treatment of liver diseases, hemorrhage, shock and burns.

Types of Plasma Proteins

Albumin Abnormalities

Hypoalbuminemia

Hyperalbuminemia

Causes:

- 1- Decrease Albumin synthesis (liver cirrhosis, malnutrition)
- 2- Increased losses of albumin:
 - ⊙ Increased catabolism in infections or cancer.
 - ⊙ Excessive excretion by the kidneys (Nephrotic syndrome) (439: no filtration of albumin so albumin is excreted)
 - ⊙ Excessive loss in bowel (bleeding)
 - ⊙ Severe burns (plasma loss in the absence of skin barrier)

Effects:

- 1- Edema due to low oncotic pressure:
 - Albumin levels drops in liver disease causing low oncotic pressure . (439: albumin is the main plasma protein and it's the one mainly responsible of oncotic pressure so when albumin level decrease water will shift to tissue and cause edema.)
 - Fluid moves into the interstitial spaces causing edema.

2- Reduced transport of drugs and other substances in plasma.

3- Reduced protein-bound calcium

- Total plasma calcium level drops
- Ionized calcium level may remain normal. (439: because it's not bound to protein)

1- No clinical conditions are known that cause the liver to produce large amounts of albumin

2- **The only cause of hyperalbuminemia is dehydration.** (439: If there is dehydration → Intravascular fluid will decrease → Albumin amount will be high → Hyperalbuminemia.)

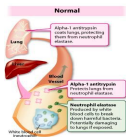
Due to loss of fluids , Albumin concentration% will increase (the increase not in production but in conc.in relation to low amount of fluid)

Types of plasma Proteins

α 1-Antitrypsin

Information

1. Synthesized by the liver and macrophages.
2. Over 30 types are known.
3. **The most common is M type** while **Z type is the one associated with disease**



Function

- 1- **An Acute-phase protein that inhibits proteases** (439: Protease enzymes that produced by organisms to destroy tissues (mainly with z type))
- 2- proteases are produced endogenously and from leukocytes and bacteria.
 - Digestive enzymes (trypsin, chymotrypsin)
 - Other proteases (elastase, thrombin)
- 3- Infection leads to protease release from bacteria and from leukocytes.

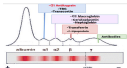
α 1-Antitrypsin Abnormalities

Genetic deficiency (mainly with type z)

- 1- Synthesis of the defective α 1-Antitrypsin occurs in the liver but it can not secret the Protein.
- 2- α 1-Antitrypsin accumulates in hepatocytes and is deficient in plasma.

Laboratory Diagnosis:

1. Lack of α 1-globulin band in protein electrophoresis
2. Quantitative measurement of α 1-Antitrypsin by:
 - Radial immunodiffusion
 - isoelectric focusing
 - nephelometry



Clinical Consequences of α 1-Antitrypsin Deficiency:

- Neonatal jaundice with evidence of cholestasis.
 - Childhood liver cirrhosis.
 - Pulmonary emphysema in young adults**
- elastase will become more active & cause destruction of lungs.



Pictures shows α 1-Antitrypsin / α 1-globulin is gone, which means the patient has no α 1-Antitrypsin.

Other plasma proteins

Plasma proteins	About	Pathology
a -Fetoprotein (AFP) a1-globulin	Synthesized in embryo & fetus by parenchymal cells of liver. AFP levels ↓ gradually during intrauterine 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 adult.	↑ maternal AFP levels: Neural tube defect (spina bifida), anencephaly ↓ maternal AFP levels: ↑ risk of Down's syndrome AFP is a tumor marker for: Hepatoma and testicular cancer.
Ceruloplasmin a2-globulin	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 a2-globulin	Synthesized by the liver & binds to free hemoglobin to form complexes that are metabolized in the reticuloendothelial system (RES) <i>(to spleen to be recycled)</i> . Limits iron loss by preventing Hb loss from kidneys.	Plasma level decreases during hemolysis .
B2-Microglobulin B-globulin	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.	↑ serum levels are found in: Overproduction in disease; severe inflammation (infections, SLE, and rheumatoid arthritis) May be a tumor marker for: Leukemia, lymphomas, multiple myeloma.
Transferrin B-globulin	A major iron-transport protein in plasma 30% saturated with iron & Iron deficiency results in increased hepatic synthesis. A negative acute phase protein.	Plasma ↓ level in: Malnutrition, liver disease, inflammation, malignancy
C-Reactive Protein(CRP) B-globulin	A Positive acute-phase protein synthesized by the liver & important for phagocytosis .	↑ plasma levels are found in many inflammatory conditions such as rheumatoid arthritis . A marker for ischemic heart disease . (not sensitive, & it is measured as high sensitivity CRP)

Hypergammaglobulinemia

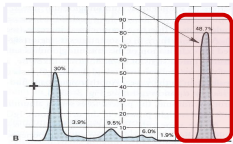
Monoclonal (Paraproteinemia)

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**. 3M:

Monoclonal - M band - Multiple myeloma
#Med438

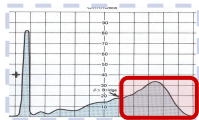


Polyclonal (B cells)

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 (Like Cirrhosis).



Acute phase reactive proteins

Positive

Plasma protein levels **increase** in: Infection, inflammation, malignancy, trauma, surgery Synthesized due to body's response to injury

Examples:

α1-Antitrypsin, haptoglobin, ceruloplasmin, fibrinogen, CRP

Mediators that cause these proteins to increase after injury are:

- Cytokines (IL-1, IL-6)
- tumor necrosis factors α & β
- interferons - platelet activating factor.

Mediators functions

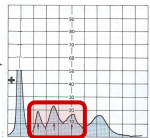
1. Bind to polysaccharides in bacterial walls.
2. Activate complement system.
3. Stimulate phagocytosis.

Negative

These are proteins which 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



Quiz

MCQs

Q1 :Which plasma protein maintains plasma oncotic pressure? ?

- A- Albumin
- B- Immunoglobulins
- C- Haptoglobin
- D- Ceruloplasmin

Q4 : **When the Ceruloplasmin is Decreased?**

- A- Wilson's disease
- B- Saleh's diseases
- C- HCC
- D- Liver disease

Q2 : **α 1-Antitrypsin proteins inhibit?**

- A- Prealbumin
- B- Macrophages
- C- Proteases
- D- Lipases

Q5 : When the hypergammaglobinemia indicates MM?

- A- Polyclonal band
- B- Monoclonal band
- C- Tetraclonal
- D- Normal increase

Q3 : Reduced protein-bound Calcium is due to?

- A- α 1-Antitrypsin Deficiency
- B- Increased Fibrinogen
- C- Hyperalbuminemia
- D- Hypoalbuminemia

Q6 : When the haptoglobin is decreased?

- A- Hemodynamically stable patients
- B- Hemoglobinopathies
- C- Thrombocytopenia
- D- Hemolysis

Answers:Q1:A | Q2:C | Q3:D | Q4:A | Q5:B | Q6:D

SAQ

Q: List and briefly describe the 2 methods of plasma proteins.

A: [Slide 5](#)

Q: What are the acute phase proteins and their types?

A: [Slide 10](#)

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Waad alqahtani

Special Thanks to Aleen Alkulyah for the Design!

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