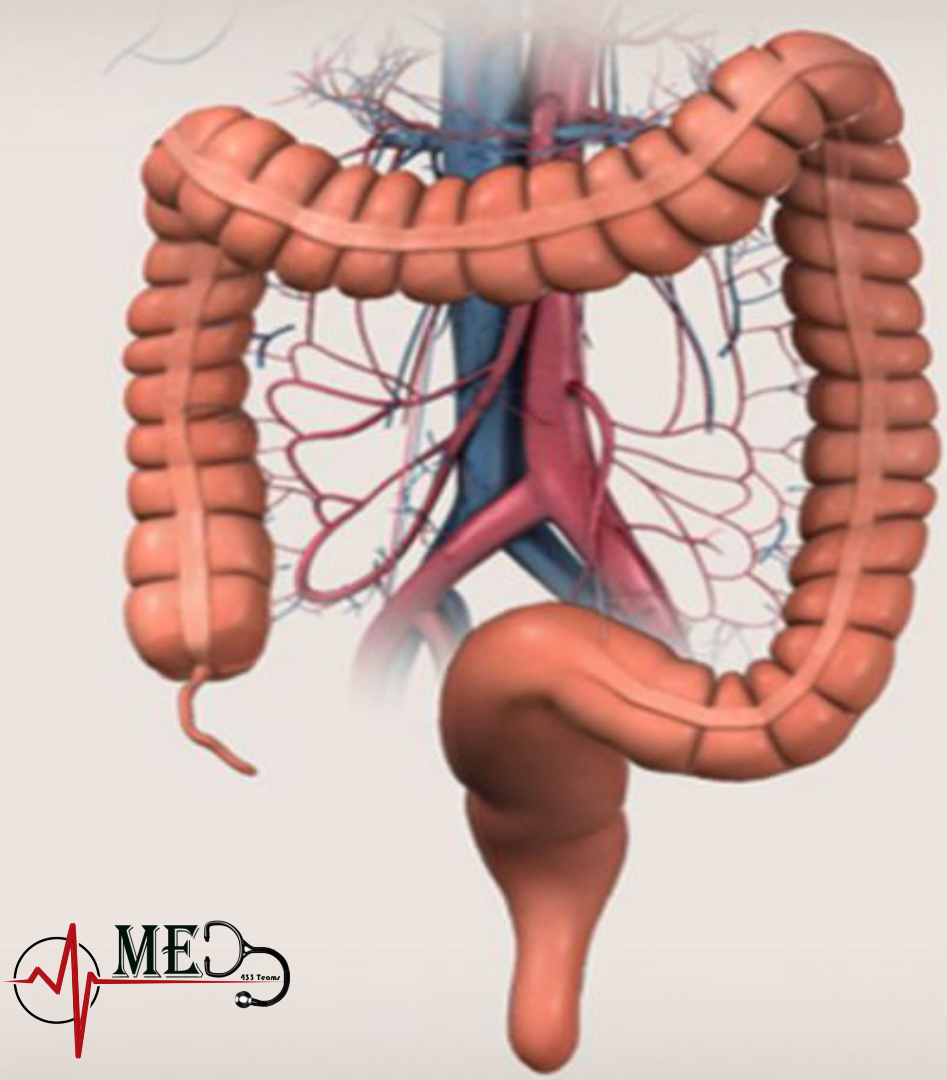

Plasma Proteins

OVERVIEW:

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

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Plasma Proteins (pps)

Measurement

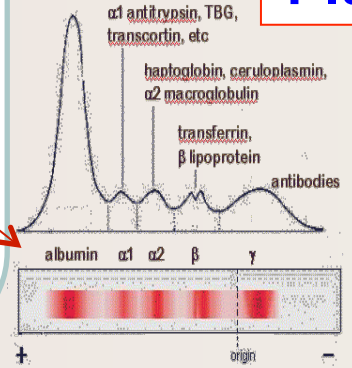
- Plasma contains >300 different proteins
- Many pathological conditions affect level of plasma proteins
- Mostly synthesized in the liver
- Some are produced in other sites
- A normal adult contains ~70 g/L of pps

1-Quantitative measurement of a specific protein:

- Chemical or immunological reactions

2-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



Functions

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

Types of plasma proteins

Pre-albumin	Albumin	α_1-Globulins	α_2-Globulins	β-Globulins	γ-Globulins
		a_1-Antitrypsin, α-fetoprotein	Ceruloplasmin, Haptoglobin	CRP, Transferrin, β 2-microglobulin	

1) Prealbumin (Transthyretin)

- A *Transport Protein* for:
  - ✓ Thyroid hormones
  - ✓ Retinol (vitamin A)
- Migrates faster than Albumin in Electrophoresis
- Separated by **Immunoelectrophoresis**
- **Lower levels found in:**
  a) Liver disease
  b) Nephrotic Syndrome
  c) Acute Phase Inflammatory Response
  d) Malnutrition
- Short half-life **(2 days)**

2) Albumin

- **Most abundant plasma protein** (~40 g/L) in normal adult
- It is synthesized in the Liver as **PreProAlbumin** & secreted as **Albumin**
- **Decreases** rapidly in Injury, Infection and Surgery
- Half-life in Plasma is 20 days

Functions

- **Maintains 80% of plasma** *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**
- **A non-specific carrier** of: Hormones, Ca , FFA, Drugs, etc.
- Tissue cells can take up Albumin by **Pinocytosis** where it is hydrolyzed to AA.
- **Useful in treatment of:**
  1) Liver Diseases
  2) Hemorrhage
  3) Shock
  4) Burns

Electrophoresis: The separation of ionic solutes based on differences in their rates of migration in an applied electric field.

Albumin

HYPOalbuminemia

❑ Causes:

- **Decreased albumin synthesis**
  - *I. Liver cirrhosis*
  - *II. Malnutrition*
- **Increased losses of Albumin**
  - *I. Increased catabolism in Infections*
  - *II. Excessive excretion by the Kidneys (Nephrotic syndrome)*
  - *III. Excessive loss in bowel (bleeding)*
  - *IV. Severe burns (plasma loss in the absence of skin barrier)*

❑ Effects:

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

HYPERalbuminia

No clinical conditions are known that cause the Liver to produce large amounts of Albumin

The only cause is:
Dehydration

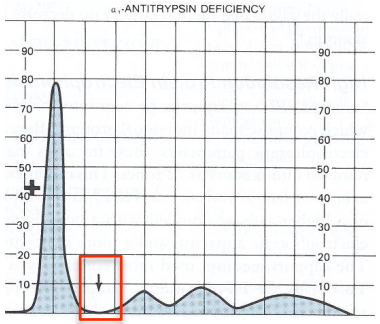
- Synthesized by: the Liver and Macrophages
- An **Acute-Phase protein** that inhibits proteases
- Proteases are produced endogenously and from leukocytes and bacteria:
  - ✓ Digestive enzymes (Trypsin, Chymotrypsin)
  - ✓ Other Proteases (Elastase, Thrombin)
- Infection leads to protease release from bacteria and from leukocytes

3) α_1-Antitrypsin

Lab Diagnosis

- Lack of α_1-globulin band in protein electrophoresis
- Quantitative measurement of α_1-Antitrypsin by:

Radial immunodiffusion, isoelectric focusing Or Nephelometry



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 can't secrete protein
  - ✓ **α_1-Antitrypsin accumulates in hepatocytes** and is deficient in plasma

❑ **Clinical Consequences of α_1-Antitrypsin Deficiency:**

1. Neonatal Jaundice with evidence of Cholestasis
2. Childhood Liver Cirrhosis
3. Pulmonary Emphysema in young adults

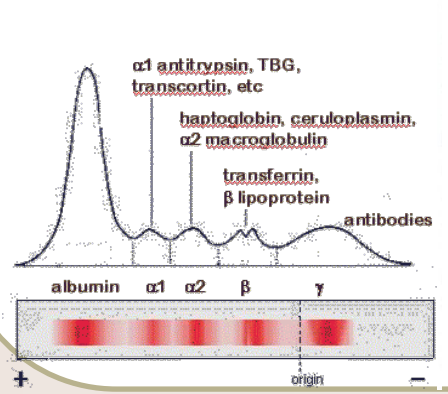
	4) α-Fetoprotein (AFP)	5) Ceruloplasmin	6) Haptoglobin
Synthesized in	○ The developing **Embryo** and **Fetus** by the parenchymal cells of the **Liver**	○ the **Liver**	○ the **Liver**
Function	○ Function is **unknown** but it may **protect fetus from immunologic attack by the mother** ○ No known physiological function in adults ○ AFP levels ↓ gradually during intra-uterine life and reach adult levels at birth ○ **AFP is a tumor marker for: Hepatoma and Testicular Cancer**	○ **Contains >90% of serum copper** ○ An oxidoreductase that **inactivates ROS** causing tissue damage in Acute Phase Response ○ Important for iron absorption from the intestine	○ Binds to free hemoglobin to form complexes that are metabolized in the rES ○ Limits Iron losses by preventing Hb loss from Kidneys.
Imbalances	○ ↑ Maternal AFP levels are associated with: ✓ Neural tube defect ✓ Anencephaly ○ ↓ Maternal AFP levels are associated with: ✓ ↑ Risk of Down's Syndrome.	○ **Wilson's disease**: ✓ Due to low plasma levels of Ceruloplasmin ✓ Copper is accumulated in the Liver and Brain.	○ ↓ Plasma level during Hemolysis

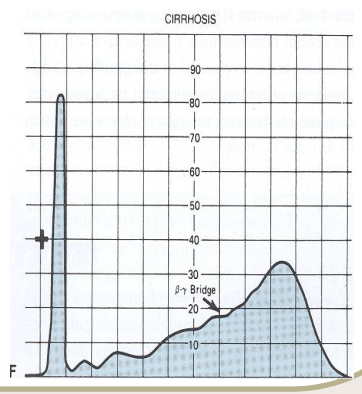
	7) Transferrin	8) β2–Microglobulin	9) C-Reactive Protein (CRP)
Features	○ A **major iron-transport protein** in plasma (30% saturated with iron) ○ A **negative acute phase protein**	○ Component of HLA ○ Present on the surface of lymphocytes and most nucleated cells ○ Filtered by the **Renal Glomeruli** due to its small size but most (>99%) is reabsorbed. ○ May be a tumor marker for: ✓ Leukemia ✓ Lymphomas ✓ multiple myeloma	○ An **acute-phase protein** synthesized by the Liver ○ Important for **phagocytosis** ○ **A marker for:** ✓ Ischemic Heart Disease (IHD)
Imbalances	○ Plasma level drops in: ✓ Malnutrition ✓ Liver disease ✓ Inflammation ✓ Malignancy ○ Iron deficiency in increased Hepatic synthesis.	○ Elevated serum levels are found in **Overproduction in disease**	○ High plasma levels are found in many inflammatory conditions such as **Rheumatoid Arthritis.**

HLA: human leukocyte antigen

Hypergammaglobulinemia

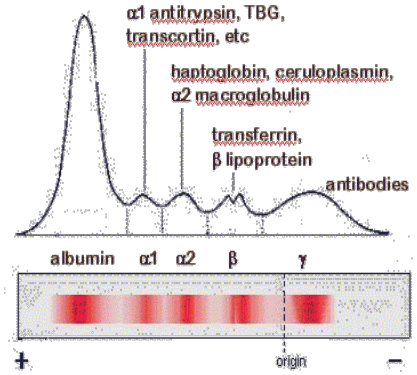
- May result from stimulation of:
  - ✓ B cells (Polyclonal Hypergammaglobulinemia)
  - ✓ Monoclonal proliferation (Paraproteinemia)
- Polyclonal Hypergammaglobulinemia:
  - ✓ Stimulation of many clones of **B cells** produce a wide range of antibodies
  - ✓ **γ-globulin** band appears large in Electrophoresis.
  - ✓ **Clinical conditions:** Acute & Chronic Infections, autoimmune diseases, Chronic Liver Disease

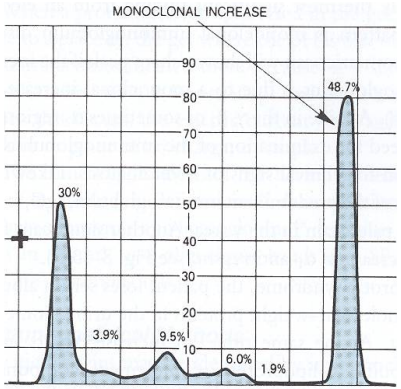




Monoclonal Hypergammaglobulinemia

- 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



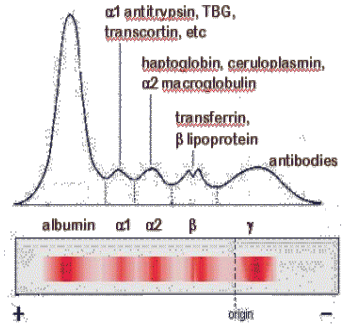


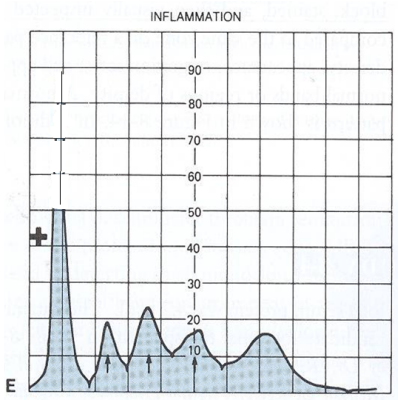
Negative Acute Phase Proteins

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

Positive Acute Phase Proteins

- Examples: **α1-Antitypsin**, **Haptoglobin**, **Ceruloplasmin**, **Fibrinogen**, **C-Reactive Protein**
- 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
- Mediators cause these proteins to increase after injury
- Mediators: **Cytokines (IL-1, IL-6), Tumor Necrosis Factors α & β , Interferons, Platelet Activating Factor**





- **Functions:**

1) Bind to Polysaccharides in bacterial walls
2) Activate Complement System
3) Stimulate Phagocytosis

1) Which of the following is the function of Haptoglobin?
   A. Preventing loss of iron
   B. Inhibits proteases
   C. Maintains oncotic pressure
   D. Antibodies
2) A patient has Hepatoma, which one of the following will increase?
   A. β2-microglobulin
   B. α-fetoprotein
   C. Gamma globulin
   D. Ceruloplasmin
3) A pregnant women has an increase level of α -Fetoprotein, that mean the fetus may have?
   A. Williams syndrome
   B. Down's syndrome
   C. Spina bifida
   D. Fetal alcohol syndrome
4) A patient has rheumatoid arthritis which one of the following will increase?
   A. Prealbumin
   B. Albumin
   C. C-Reactive protein
   D. Ceruloplasmin
5) A patient has Nephrotic Syndrome, which one of the following will decease?
   A. Prealbumin
   B. Ceruloplasmin
   C. β 2-microglobulin
   D. C-Reactive protein
6) Which one of the following is a Major iron-transport protein?
   A. Transferrin
   B. Haptoglobin
   C. Ceruloplasmin
   D. Gamma globulin
7) Aα_1-Antitrypsin Deficiency may cause?
   A. Restrictive lung disease
   B. Emphysema
   C. Recurrent infections
   D. Ischemic heart disease

Answers: 1) A 2) B 3) C 4) C 5) A 6) A 7) B

Thank You!

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