Plasma proteins

it's important

لانها تعتبر

bio markers

انواع البروتينات المختلفة بلي نستخدمها
لتشخيص الامراض المختلفة

لما نقرأ في اي مكان انه هنا negative acute phase protien معناها انه خلي ال AA لتحفظ منها عشان تصنع
ال (+) acute phase protien

- Plasma contains >300 different proteins, their levels are affected by many pathological conditions.
- Mostly synthesized in the liver

Phase protien

↳ (+) acute phase protien

- Plasma contains >300 different proteins, their levels are affected by many pathological conditions.
- Mostly synthesized in the liver
- Some are produced in other sites (immunoglobulins by plasma cell)
- A normal adult has 6-8g/dl of plasma proteins
- The proteins of the plasma are a complex mixture that includes not only simple proteins but also conjugated proteins such as glycoproteins and various types of lipoproteins.

Functions

- Transport (Albumin, prealbumin, globulins)
- Maintain plasma oncotic pressure (Albumin)
- Defense (Immunoglobulins and complement)
- Clotting and fibrinolysis (Thrombin and plasmin)
- Buffering pH
- Catalytic functions (enzymes as LPL)

positive acute phase protiens

under certien condition like inflammation infection, trumer injury, surgry, malignancy

↳ (+) acute phase protiens

negative acute phase protiens

تبيض سلايد (٣)

Bun measrement of plesmer protien

by immunological reaction → elysian

Ag Antibody reaction عبارة عن ←

Albumin كنوع بروتين معين بكيز

Antibody وبيتم اعرفه تركيزه باستخدم فجيب

→ Against the Antigene يلي هوه Albumin

وبعمل تفاعل بين الانتين و اكيد

→ Antibody اللي بيشتغل ع Antigene

وبعدين بجيب colored molecule بيشتغل ع الانتين

اللي بعمل → Conjugate that can be estimated on spectroretometer gas

← بقيس الـ Concentration التلاقح بيض.

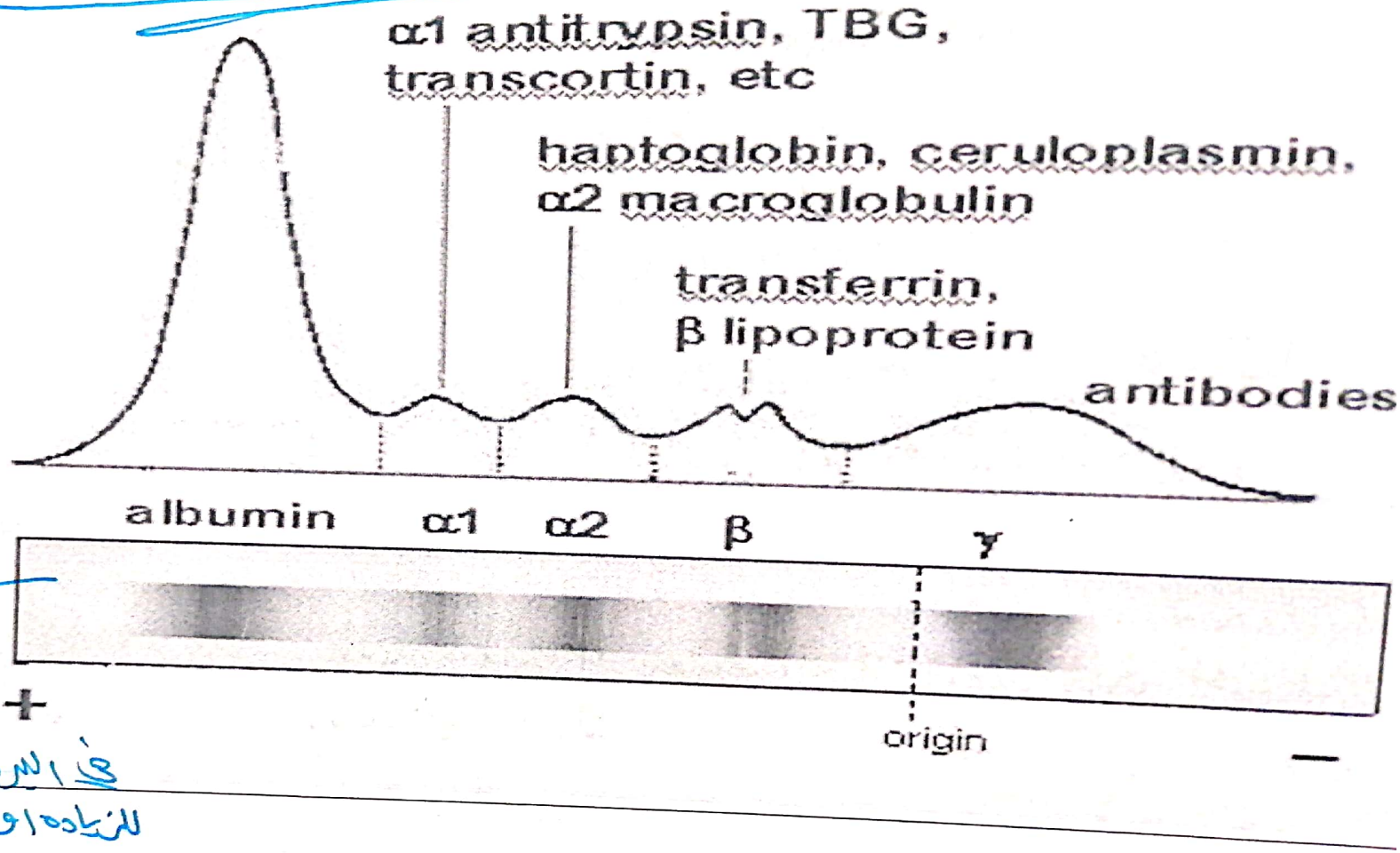
Not accurate ← هاي الطريقة

100%

لانه فيها تعير

→ non specific between Anti body and another types of protiens

observed, these bands change in disease).



كل فرقة هادا bands

نفرق لوفيه زيادة في البروتين بس سنشوف لوفيه فيه للزيادة او النقصان

Types of Plasma Proteins

- Prealbumin
- Albumin
- α1-Globulins: as α 1-Antitrypsin, α–fetoprotein
- α2-Globulins: as Ceruloplasmin, hapt...

origin

+

Types of Plasma Proteins

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- α2-Globulins: as Ceruloplasmin, haptoglobin
- β Globulins: as CRP, transferrin, β2-microglobulin
- γ Globulins (Antibodies)

Prealbumin (Transthyretin)

it is an albumin but it's still immature

- A transport protein for: thyroid hormones and retinol vit 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)

retinoic Acid the most active form ?! why? vit. having hormonal like action, transcription factor

(–) acute phase protien to help in synthesis of (+)

Albumin

- Most abundant plasma protein (3.5-5 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)
- A non-specific carrier of hormones, calcium, free fatty acids, drugs, etc.
- It is by pinocytosis in the cells where it is hydrolyzed to amino acids
- Nutritive function → can be endocytose inside the cell to be cleaved to AA
- Buffering function
- Useful in treatment of liver diseases, hemorrhage, shock and burns

Synthesis of albumin

-The liver produces albumin, it represents about 25% of total hepatic protein synthesis.

- Albumin is initially synthesized as a preproprotein
- Its signal peptide is removed as it passes into rough endoplasmic reticulum, and a hexapeptide at the resulting amino terminal is subsequently cleaved off farther along the secretory pathway.
- Mature human albumin consists of one polypeptide chain of 585 amino acids and contains 17 disulfide bonds
- It has an ellipsoidal shape, which means that it does not increase the viscosity of the plasma as much as an elongated molecule such as fibrinogen does.
- Has a relatively low molecular mass about 66 kDa

Clinical significance of albumin

Blood brain barrier

- Albumin- free fatty acid complex can not cross the blood brain barrier, hence fatty acids can not be utilized by the brain.
- Loosely bound bilirubin to albumin can be easily replaced by drugs like aspirin (2:1) molar ratio UCB to albumin (normal)
- In new born if such drugs are given, the released bilirubin gets deposited in brain causing Kernicterus.

Protein bound calcium

normal Ca. level 9-11 mg/dl → 50% ionized, 50% bind to albumin

- Calcium level is lowered in conditions of hypoalbuminemia
- Serum total calcium may be decreased
- Ionic calcium remains the same → the functioning portion fraction of calcium
- Tetany does not occur
- Calcium is lowered by 0.8 mg/dl for a fall of 1g/dl of albumin

hypercalcemia more dangerous than hypocalcemia and should given slowly because it can cause cardiac arrest

hypocalcemia (7.5-8 mg/dl) level of calcium

مثلاً ↓ 2g/dl Albumin → ↓ 1.5 mg/dl of calcium

Drug interactions

-Two drugs having same affinity for albumin when administered

Drug interactions

-Two drugs having same affinity for albumin when administered together, can compete for available binding sites with consequent displacement of other drug, resulting in clinically significant drug interactions. As phenytoin, dicoumarol interactions

So should not give together.

Oedema

Hypoalbuminemia

Causes

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

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

decrease volume of blood does not mean increase synthesis of albumin.

Ratio volume of ~~blood~~ plasma to concentration of protein in plasma

α1-antitrypsin

- Called α1- antiprotease
- Synthesized by the liver and macrophages
- An acute-phase protein that inhibits proteases (trypsin, elastase, and other proteases) by forming complexes with them.
- Infection leads to protease release from bacteria and leukocytes.
- Normally α1-antitrypsin protects the lung tissues from the released active elastase from macrophages.
- In its deficiency, the active elastase destroys the lung tissue by proteolysis.

emphysema loss of elasticity of lung

Types of α_1-Antitrypsin

- Over 30 types are known (the most common is M type).
- Genetic deficiency of α1-antitrypsin (synthesis of the defective α1-antitrypsin occurs in the liver but it cannot secrete the protein) → its accumulation in hepatocytes and its deficiency in plasma

Clinical consequences of α1-antitrypsin deficiency

- Neonatal jaundice
- Childhood liver cirrhosis
- Pulmonary emphysema in young adults

Laboratory Diagnosis

- Lack of α1-globulin band in protein electrophoresis
- Quantitative measurement of α1-antitrypsin by: radial immunodif and isoelectric focusing.

α-Fetoprotein (AFP)

- Synthesized in the developing embryo and fetus by the parench cells of the liver.
- AFP levels decrease gradually during intra-uterine life and reac levels at birth (normal level is 1 μg/100 ml).
- Function is unknown but it may protect fetus from immunologic by the mother.
- No known physiological function in adults

- No known physiological function in adults

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

Ceruloplasmin → Ferroxidase enzyme

↳ but it's not specific, so we can not depend on AFP alone to diagnose any cancer

- Synthesized by the liver (glycoprotein with enzymatic activity).
- Carries about 90% of serum copper, albumin carries 10%.
- An oxidoreductase that inactivates ROS causing tissue damage in acute phase response
- Important for iron absorption from the intestine → Fe^{+2} to Fe^{+3} to bind transferrin.
- Wilson's disease:
  - Due to low plasma levels of ceruloplasmin
  - Copper is accumulated in the liver and brain
- The amount of ceruloplasmin in plasma is also decreased in liver diseases, malnutrition and nephrotic syndrome. (-) acute phase protein

MRI / CT scan

Haptoglobin

- Synthesized by the liver (glycoprotein).
- Binds to free hemoglobin to form complexes that are metabolized in the RES, when bound to hemoglobin, it is cleared from the plasma about 80 times faster than normally.
- Limits iron losses by preventing Hb loss from kidneys
- Plasma level decreases during hemolysis and increases in inflammation.

(+) acute phase protien

Hb ارتباط هابتوجلوبين
to prevent its dergrow effect in renal tubule.

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

β2– 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
  - Impaired kidney function
- May be a tumor marker for:
  - Leukemia, lymphomas, multiple myeloma

C-reactive protein (CRP)

- An acute-phase protein synthesized by the liver (so named because it reacts with the polysaccharide of the capsule of pneumococci, important for phagocytosis
- High plasma levels are found in many inflammatory conditions such as rheumatoid arthritis
- A marker for ischemic heart disease

α2– Macroglobulin

- Major component of α2 proteins
- Comprises 8–10% of the total plasma protein in humans.
- Tetrameric protein with molecular weight of 725 kDa.
- Synthesized by hepatocytes and macrophages
- Inactivates all proteases and thus is an important in vivo anticoagulant.
- Carrier of many growth factors
- Normal serum level-130-300 mg/dl
- Concentration is markedly increased in nephrotic syndrome, since other proteins are lost through urine in this condition.

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 All type IgM, IgG, IgA ...
- γ-globulin band appears large in electrophoresis very thick
- 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

Abnormal proteins

1- Bence Jone's proteins

- Abnormal proteins (monoclonal light chains).
- Present in the urine of a patient suffering from multiple myeloma (50% of patients)
- Molecular weight 45 kDa
- Identified by heat coagulation test
- Best detected by zone electrophoresis and immunoelectrophoresis

2- Cryoglobulins

- These proteins coagulate when serum is cooled to very low temperature
- Commonly monoclonal IgG or IgM or both
- Increased in rheumatoid arthritis, multiple myeloma, lymphocytic leukemia, lymphosarcoma and systemic lupus erythematosus