

Albumin;

Function;

- ** The main contributor to the osmotic pressure (75-80%)
- ** major transporter for almost everything in blood by binding to ABD (albumin binding domain)

Synthesis

- # Preproteins
- Synthesized from liver 12g/day (25% of total liver protein products is albumin)

CLINICAL DISORDERS

★ Albumin is used in liver function test (increase or decrease in albumin means that there is a problem in liver)

Notes :

- The major protein in blood plasma
- # MW = 69 kDa
- # half-life = 20 days.
- # One polypeptide chain,
- # 585 amino acids, 17 disulfide bonds.
- # Anionic at pH 7.4 with 20 negative charges
- # Ellipsoidal shape
- ** The normal albumin concentration is 3.5-5.5 g/dl

	Analbuminemia	Hypoalbuminemia:	Hyperalbuminemia
What?	(no albumin)	Decrease	Increase
Notes	very rare condition	less than 2 g/dl	
Cause	mutation that affects splicing # Autosomal recessive inheritance	<ul style="list-style-type: none"> • Malnutrition (generalised edema) • Nephrotic syndrome • Cirrhosis (mainly ascites) • Gastrointestinal loss 	caused by dehydration, and some liver cancer cases.
Symptoms	moderate Edema (other proteins increase, not specific) life threatening	EDEMA generalized (in the whole body) or localized (mostly in the abdomen (ASCITES))	
Treatment		This is treated by having a rough diet or by paracentesis	drink water (hydration).

★ drug-drug interaction

<p>Bilirubin toxicity</p> <p>** bilirubin: broken heme **</p> <p>Babies: high bilirubin (7-10) days \ jaundice</p> <p># Sun light as a treat #</p> <p>BBB : immature</p> <p>ASPIRIN + new baby = high accumulate bilirubin in brain "kernicterus" --> mental retardation</p>	<p>Phenytoin-dicoumarol interaction</p> <p># Phenytoin is an anti-epileptic drug .</p> <p># Dicoumarol is an anti-coagulant.</p> <p>(High affinity to albumin)</p> <p>(Bind to the same spot)</p>
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Prealbumin or Transthyretin (transport, thyroid gland t3, t4)

Function: carrying T3 and T4

Notes and compare

** small glycoprotein (rich in tryptophan, 0.5% carbohydrates)

** MW=62 kDa

** (faster than albumin) in gel electrophoresis

** short half-life (only 2 days)

** Blood level is a lot lower than albumin (0.25 g/L).

** more sensitive indicator for liver function

Globulins

α 1-globulins	α 2- globulins	β - globulins	γ -globulins
<ul style="list-style-type: none">■ α1-antitrypsin■ α1-fetoprotein■ α1- acid glycoprotein■ Retinol binding protein	<ul style="list-style-type: none">■ Ceruloplasmin■ Haptoglobin■ α2-macroglobulin	<ul style="list-style-type: none">■ CRP■ Transferrin■ Hemopexin■ β2- microglobulin	<ul style="list-style-type: none">■ IGG■ IGA■ IGM■ IGD■ IGE

α 1-fetoprotein

(Alpha 1 band)

Synthesis; fetal yolk sac \rightarrow liver parenchymal cells.

** not produced in adults (very low level)

Level of α 1-fetoprotein increases in: - -

- Fetus and pregnant women Normally
- Hepatoma & acute hepatitis (cancer in liver)

Functions of α 1-fetoprotein:

- Protecting fetus from immunotypic attacks
- Modulating the growth of fetus
- Transporting compounds e.g., steroids
- Low level in pregnancy: increased risk of Down's syndrome.

α 1 - antitrypsin / α 1 - antiprotease

(52 kDa), 90% of α 1

function: neutralize (work against) trypsin & trypsin like enzymes (elastase).

antagonist (neutralizer) for trypsin { serine protease (hydrolase) }

1- Elastase (\times Elastin) \rightarrow skin, blood vessels and lungs

Elastase is produced by macrophages (WBC) during inflammation to break down the elastin of microorganism, but it will also affect the elastin in the alveoli walls (lungs)

** Antitrypsin breaks down elastase then the lung tissue is regenerated. So, Antitrypsin prevents excessive damage of tissues.

A person will face a problem when;

1. A deficiency of Alpha-1 antitrypsin
2. Mutated alpha-1 antitrypsin

** Emphysema is characterized by having a barrel chest and difficulty in breathing

Active elastase + α_1 -AT \rightarrow Inactive elastase: α_1 -AT complex \rightarrow No proteolysis of lung \rightarrow No tissue damage

Active elastase + \downarrow or no α_1 -AT \rightarrow Active elastase \rightarrow Proteolysis of lung \rightarrow Tissue damage

2- Genetics and alpha1- antitrypsin

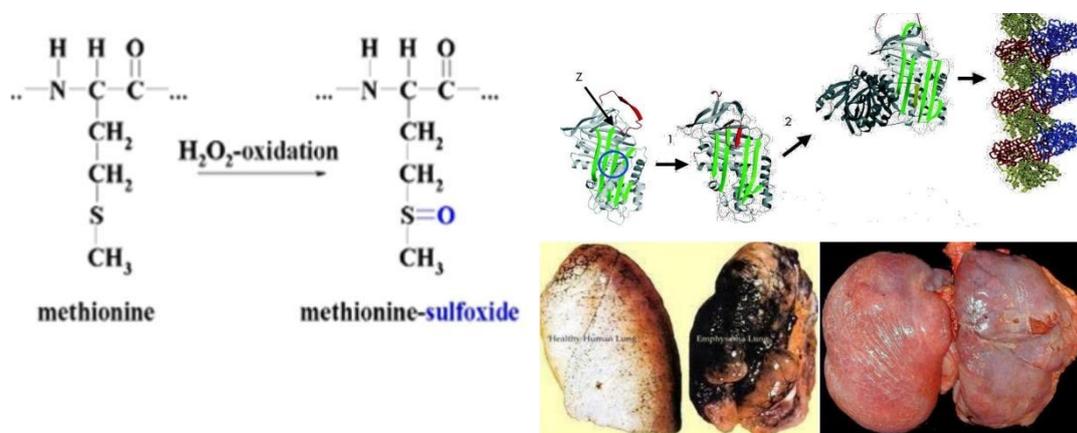
** plasma protein has at least 75 polymorphic forms.

alleles are: Pi^M Pi^S Pi^Z , Pi^F , phenotype MM is the most efficient and common one

If one M allele is present, antitrypsin will be effective. So, having 2 copies other than M will cause a problem.

ZZ phenotype can lead to emphysema

♥ Smoking can oxidize the 358th amino acid methionine to methionine sulfoxide in antitrypsin. This residue is on the surface and supposed to bind to the elastase, so smoking will decrease the ability to bind drastically



♥ Liver : The ZZ phenotype antitrypsin has an extra loop and beta sheet. The beta sheet of an antitrypsin protein has high affinity towards the loop of another, so they will polymerize and form alpha-1 antitrypsin aggregates in the liver which can't leave and results in the killing of liver cells, and then leads to fibrosis then to cirrhosis of the liver.

" 10% of people with ZZ antitrypsin have cirrhosis "

Ceruloplasmin (a 2 - band) • 6 atoms of copper

copper

A copper containing glycoprotein (MW=160 kDa)

• Copper is very important; many enzymes use it, such as:

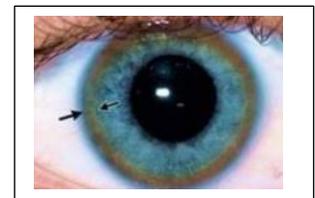
1. oxidative phosphorylation enzymes (complex IV) for ATP production
2. ferroxidase which oxidizes ferrous to ferric (transferrin) amine oxidase,
3. copper dependent superoxidase dismutase, cytochrome oxidase, tyrosinase.

FUNCTION:

1. Regulates copper level in blood (A protein called **metallothionein** regulates the tissue level of Cu) as it contains 90% of serum Cu (it stores Cu)
2. The other 10% is bound to Albumin for transport (albumin has a lower affinity for Cu)

Pathological conditions:

1. Decreased levels in liver disease (it is produced in the liver) (Ex. Wilson's, autosomal recessive genetic disease)
2. Ceruloplasmin concentration is decreased, less affinity for binding to the copper, this results in increment of Cu in plasma thus it enters tissues, the person's skin and eyes will become bronzy



Haptoglobin (HP) a-2 band

acute phase reactant protein

• (MW=90kDa), a tetramer (2 α , 2 β)

• 3 phenotypes (polymorphs):

Hp 1-1 \rightarrow $\alpha_1, \alpha_1 + 2\beta$

Hp 2-1 \rightarrow $\alpha_1, \alpha_2 + 2\beta$

Hp 2-2 \rightarrow $\alpha_2, \alpha_2 + 2\beta$

2 beta subunits are fixed

In cases of hemolytic anemia

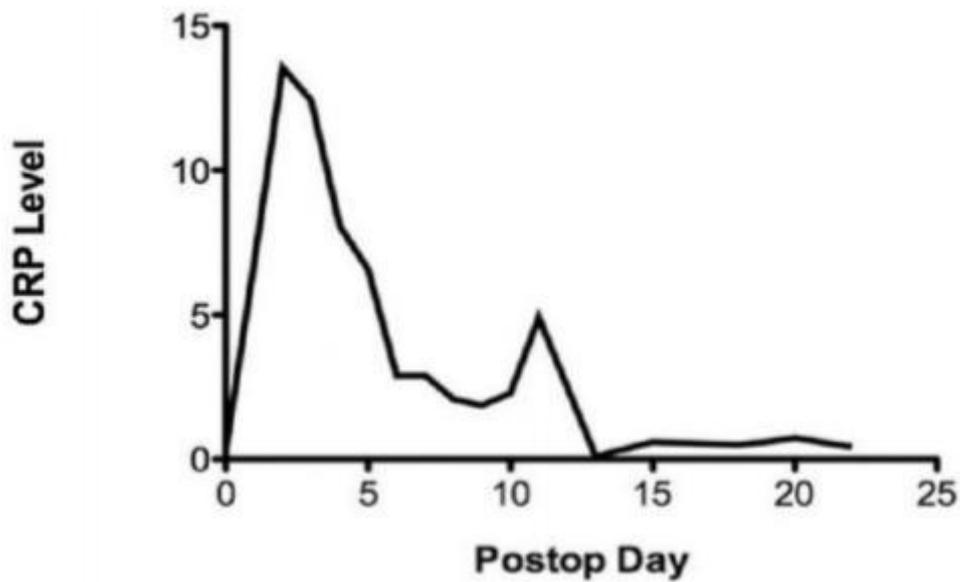
(damaged RBC \rightarrow more hemoglobin in plasma) the

level of HP decreases as it binds to the hemoglobin and gets broken in the liver.

Some hemoglobin molecules leave RBCs to plasma, the function of HP is to bind to free hemoglobin (65 kDa) to prevent them from getting filtrated in their kidneys and leaving with urine, because even though our body can produce heme and globin, it can't produce iron (trace metal). Half-life of free HP is 5 days, when it is bound to hemoglobin the half-life of the complex becomes 90 mins (MW=150 kDa), so the complex is transported and broken in the liver quickly, and iron is extracted from the complex

C Reactive Protein (CRP)

- **Synthesis** : first discovered, binds with the **C fraction of the polysaccharide** that is present in the **cell wall** of a type of bacteria called **pneumococci**.
 - **function** : helps in the defense against bacteria and foreign object in the body.
 - **acute phase protein**. It is undetectable in healthy individuals.
- ** Its level reaches a peak after 48 hours of the incident. Which is used as a monitoring marker ****



Past papers / Lecture 2

1-Select the one of the following statements that is NOT CORRECT:

- A. Albumin is synthesized as a preproprotein.
- B. Albumin is stabilized by multiple intrachain disulfide bonds.
- C. Albumin is a glycoprotein.
- D. Albumin facilitates the movement of fatty acids through the circulation.
- E. Albumin is the major determinant of plasma osmotic pressure.

2-Select the one of the following statements that is NOT CORRECT:

- A. Wilson disease caused by increased the concentration of the Ceruloplasmin in blood
- B. Wilson disease is characterized by copper toxicosis (abnormally high levels of copper).
- C. Wilson's disease is an autosomal recessive genetic disease.
- D. Wilson caused bronzy skin and eyes tissue

3- The functions of plasma albumin are:

- (A) Osmosis
- (B) Transport
- (C) Immunity
- (D) both (A) and (B)

4-In one molecule of albumin the number of amino acids is:

- (A) 510
- (B) 585
- (C) 610
- (D) 650

5-Ceruloplasmin is:

- (A) α_1 -globulin
- (C) β -globulin
- (B) α_2 -globulin
- (D) None of these

6-In the total proteins, the percentage of albumin is about:

- A) 20-40
- (C) 50-60
- (B) 30-45
- (D) 80-90

7-Molecular weight of human albumin is about:

- (A) 156,000
- (C) 69,000
- (B) 90,000
- (D) 54,000

8-Albumin is involved in the transport of all of the following except:

- A) Free fatty acids
- B) Aspirin
- C) Steroids
- D) Some cations
- E) Hemoglobin

9-A deficiency in which of the following proteins causes Wilson disease:

- A) Ceruloplasmin
- B) Albumin
- C) C reactive protein
- D) Haptoglobin
- E) Alpha 1 antitrypsin

10-Choose the correctly matched pair of words:

- A) Liver disease - Increased albumin concentration
- B) Bacterial infection - Decreased C reactive protein concentration
- C) Increased alpha 1 antitrypsin concentration - trypsin inactivation
- D) Smoking - oxidation of methionine in elastase
- E) C+D

11-Choose the mismatched pair among the following:

- A) Hemolytic anemia - Elevated Haptoglobin levels
- B) Acute inflammation - Elevated C-reactive protein levels
- C) PiZZ genotype - Decreased activity of Alpha 1 antitrypsin
- D) Down syndrome - Low alpha 1 fetoprotein levels
- E) None of the above

12-True about Prealbumin:

- A) Migrates at a lower speed than albumin in gel electrophoresis
- B) Converted to albumin after cleavage of hexapeptide
- C) Is a sensitive marker of protein malnutrition due to its long half-life
- D) A+B
- E) None of the above

13-A 50 g sample of plasma was obtained. How many grams of plasma proteins (approximately) would there be in this sample:

- A) 10 grams
- B) 3.5 grams
- C) 45 grams
- D) 35 grams
- E) 1 gram

14-Which of the following statements regarding blood composition is FALSE:

- A) Blood of a patient with anemia is expected to contain more than 55% plasma.
- B) Fibrinogen is present in plasma while absent in serum
- C) The blood cells that makes up the most of hematocrit are: Red Blood Cells
- D) The most abundant plasma protein is synthesized in the liver
- E) None of the above is false

15-Which of the following proteins would you least expect to be initially tagged with an N-terminal signal peptide:

- A) Fibrinogen
- B) Hemoglobin
- C) Albumin
- D) Alpha globulins
- E) Gamma globulins

16-Which of the following represents a TRUE statement:

- A) Albumin is glycosylated
- B) The main copper-binding plasma protein is albumin
- C) Transferrin oxidizes Fe^{2+} to Fe^{3+}
- D) Elastase activity is elevated in smokers
- E) Alpha 1 antitrypsin is the main contributor to blood oncotic pressure

18-Which plasma protein binds iron?

- A) Fibrinogen
- B) Albumin
- C) Transferrin
- D) Gamma-globulins
- E) Haptoglobin

19-What is the most abundant plasma protein in normal individuals?

- A) alpha1-antitrypsin
- B) haptoglobin
- C) albumin
- D) gamma globulin
- E) fibronogen



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