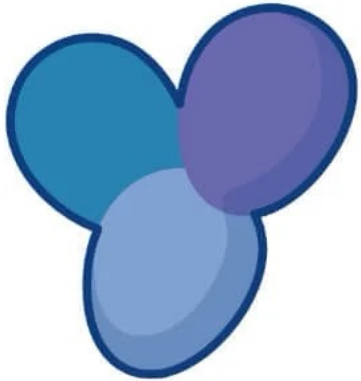
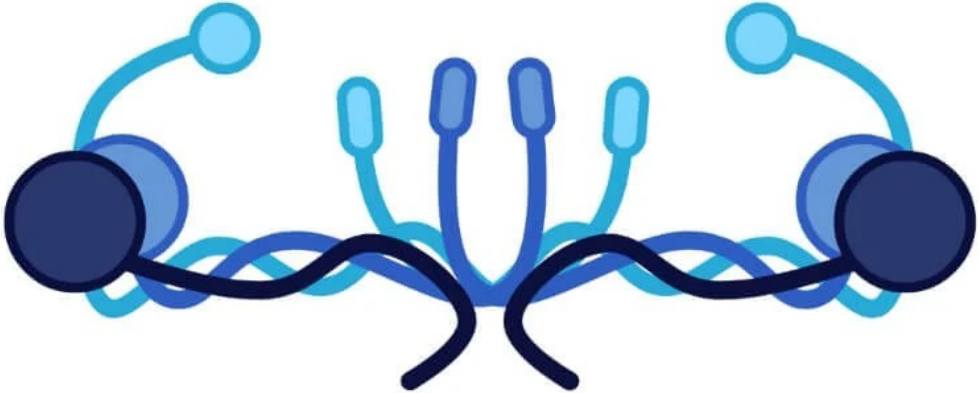
"يَا أَيُّهَا الَّذِينَ آمَنُوا اسْتَعِينُوا بِالصَّبْرِ وَالصَّلَاةِ إِنَّ اللَّهَ مَعَ الصَّابِرِينَ"

Mays Aljundi
Biochem

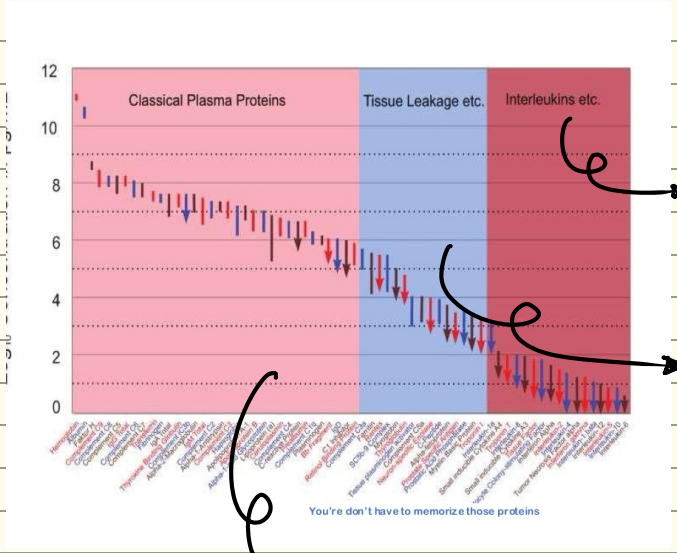
Plasma Protein





MEMORIZE

- Haprin is an anticoagulant
- Normal plasma range 6-8 g/dl

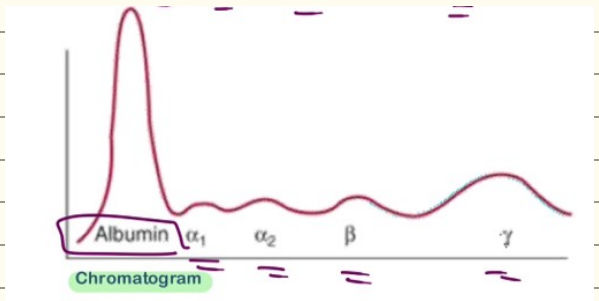


Inflammatory proteins that promote inflamation

low concentration proteins «when tissues are damaged or inflamed they become more permeable»

High concentration like albumin

- Normal values for:
  - Albumin: 46%
  - α_1 - globulin: 5%
  - α_2 - globulin: 9%
  - β - globulin: 12%
  - γ - globulin: 15%



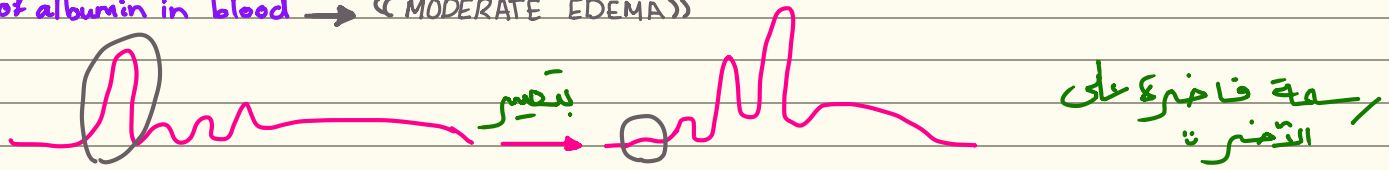
- Globulin has 3 bands:
  - α band:
    - α_1 region consists of «α_1 antitrypsin»
    - α_2 region consists of «Haptoglobin, α_2 macroglobulin, ceruloplasmin»
  - β band: «Transferrin, LDL, Complement System proteins»
  - γ band: « Immunoglobulins »

- Most plasma proteins are glycoproteins «Albumin is an exception»
- Albumin half life is 20 days while haptoglobin 5 days
- Crohn's disease «protein-losing gastroenteropathy» albumin half life may be reduced to 1 day

① Albumin :

- Major protein in human plasma
- 69 KDa , elipsoidal shape , negatively charged , monomeric
- Main contributor to the osmotic pressure (75% – 80%)
- Liver : 12g/day
- Synthesized as preproprotein

- Can bind with various ligands one example is «Hormones Bilirubin »
  This product is produced during the normal breakdown of RBC
- Analbuminemia : genatic disorder characterized by the absence or extremely low levels of albumin in blood → « MODERATE EDEMA »



- Hypoalbuminemia : Albumin is less than 2g/dl → EDEMA
- Hyperalbuminemia : Dehydration «relative increase»

- Clinical disorders :
  - Bilirubin toxicity : When Children take lots of aspirin which inhibits bilirubin to bind to albumin
  - phenytoin - dicoumarol interaction : Both bind to albumin at same place , so if taken together they will compete on who binds to albumin.

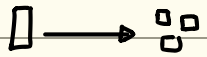
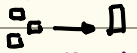
② prealbumin (transthyretin) :

- comes before albumin ~~in~~ Chromatogram
- 62 KDa glycoprotein
- Main function : Carrier of thyroid hormones T_3 + T_4

- Acute phase proteins are plasma proteins whose levels increase (Acute inflammation, cancer etc)
  - Interleukin-1 stimulates the releasing of acute phase proteins

Protein	Function
C-reactive protein β	Stimulates the complement pathway
α1-antitrypsin α_1	neutralizes certain proteases released during acute inflammation
Fibrinogen	Coagulation factor
Transferrin β	Iron binding (preventing microbe uptake of iron)
Haptoglobin α_2	Hemoglobin binding (iron protection)
Ceruloplasmin α_2	Iron oxidation (iron binding by ferritin)

① C-reactive protein (CRP):
- Binds to a polysaccharide called fraction in the cell wall of the bacteria (pneumococci)
- undetectable in healthy individuals, detectable in many inflammatory diseases

② α_1-antitrypsin (AKA):
- 52 KDa
- Neutralizes trypsin & elastase → (proteinase) 
- Antiproteinase 
- MM most common allele ↔ 4 alleles: M, F, S, Z
- Emphysema is found in ppl with ZZ, SZ
  - Not realy active in stopping the trypsin
  - cirrhoses can be caused by ZZ (liver damage)

③ Haptoglobin (HP): α_2
- 90 KDa
- Tetramer (2α, 2β)
- 2 genes designated Hp 1 & Hp 23 producing phenotypes:
  - Hp 1-1: $\alpha_1, \alpha_1 + 2\beta$
  - Hp 2-1: $\alpha_1, \alpha_2 + 2\beta$
  - Hp 2-2: $\alpha_2, \alpha_2 + 2\beta$
- It binds to hemoglobin to maintain it
- Decreased level in hemolytic anemia
- Hp+ Hb complex has short half life (90 min)

④ Ceruloplasmin α_2
- Binds to copper
- 160 K Da, contains 6 atoms of copper
- Metallothionein: regulates tissue level of Cu
- Ferroxidase: Oxidizes ferrous to ferric
  - Albumin is more IMP in binding + transporting copper

Pathological conditions related to ceruloplasmin

- Ceruloplasmin deficiency can arise from genetic causes or lack of dietary copper.
  - Low amount
- Hypoceruloplasmenia
  - Ceruloplasmin levels are ~50% of normal
  - No clinical abnormalities
- Aceruloplasminemia
  - No ferroxidase activity of ceruloplasmin
  - If left untreated, accumulation of iron in tissues and organ failure
- Wilson's disease — Depending on transporting of copper not ceruloplasmin
  - Defective transporter (copper-binding P-type ATPase or ATP7B protein) leading to excess liver copper, increased apoceruloplasmin, and copper toxicosis.

albumin

⑤ Transferrin : β

- It transfers Iron
- Synthesized in liver (glycoprotein)

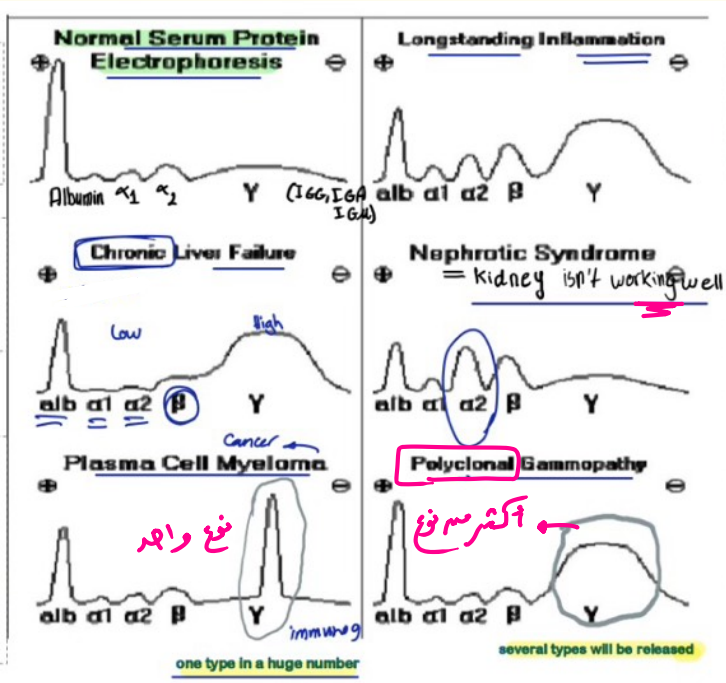
⑥ α_2 - macroglobulin : α_2

- Larg plasma protein
- Responsible for the transport of 10% of Zinc and CytoKines in blood
- Inactivates divers type of proteases

All of them are peaks, except gamma band, because of large quantities and different sizes.

Can't synthesize albumin + alpha one + alpha 2 -> All will be of low level compared with gamma, which relatively looks high.

Maturation of B cells and they make and release one antibody, they become plasma cells. These plasma cells could be cancerous, when it becomes cancerous it will release one type of antibody ->> increase in number of cells and increase in antibody number. This peak look sharp because only one antibody level will increase in blood.

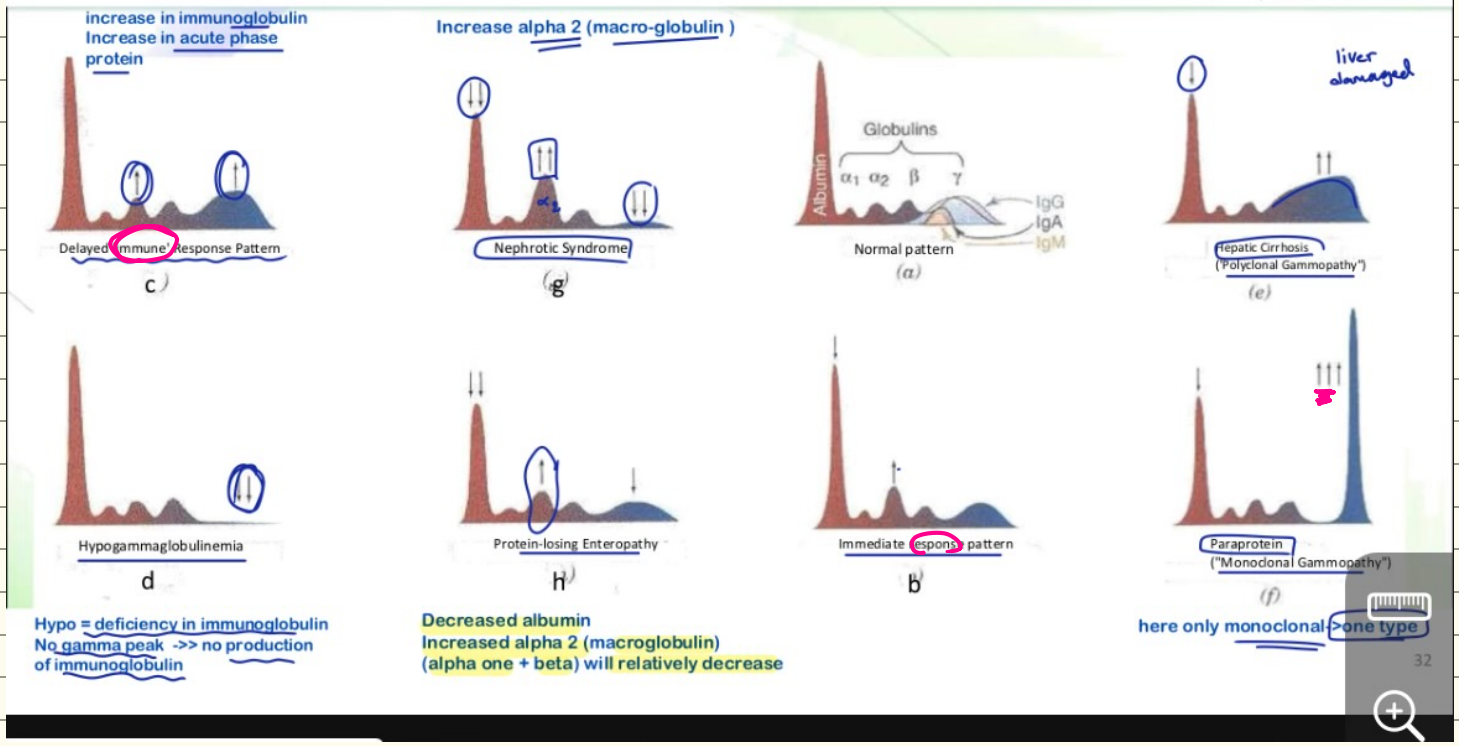


Acute phase proteins level + immunoglobulin (different types) will be high -> inflammation all the time.

Kidney will make filtration so proteins is lost in urine since renal tissue is damaged -» loosing albumin.
Alpha 2 represents a macro-globulin (large proteins that can't be lost, only small ones get lost).

Different types of B cells will be damaged, so it will synthesize different types of immunoglobulins (IGA, IGG, IGM) so the peak looks wide and big. Here different types of immunoglobulins are being released, that's why it looks wide.

☺ وأخيرا!!! يعطيكم العافية



SUMMARY

emzyme	Function	Condition
Prealbumin	➢ Transport :- 1) Thyroid hormones. 2) Retinol.	➢ Lower level in :- 1) liver disease. 2) Nephrotic syndrome. 3) Malnutrition. 4) Acute phase inflammatory response.
Albumin	1) Maintain oncotic pressure. 2) Non specific carrier. 3) Useful in treatment of liver disease & shock & hemorrhage.	➢ Hypoalbuminemia :- ❖ Decrease albumin synthesis. ❖ Loss of albumin:- • Excessive loss in bowel • Nephrotic syndrome. • Burns.
a_1 -antitrypsin		➢ Genetic deficiency of a_1–antitrypsin:- ❖ Neonatal jaundice. ❖ Childhood liver cirrhosis. ❖ Pulmonary emphysema.
α_2 a-fetoprotein	Unknown function .	[redacted]
Ceruloplasmin	Important in iron absorption from intestine .	Wilson's disease.
Haptoglbin	Bind to free hemoglobin to form complexes to limit iron loss and to prevent Hb loss in kidney .	Decrease during hemolysis.
B_2 -Microglobulin		➢ Elevated level found in → overproduction in disease. ➢ Tumor marker → leukemia & lymphomas & multiple myeloma.
C-Reactive protein	Important in phagocytosis.	➢ Elevated in:- ❖ Inflammation (rheumatoid arthritis). ❖ Marker for ischemic heart disease.

QUESTIONS

https://quizlet.com/88335132/plasma-proteins-study-questions-flash-cards/?i=5m79vu&x=1jqY

MCQs

1)Prealbumin found in lower level in:

A. Liver disease.
B. Nephrotic syndrome.
C. Malnutrition.
D. All.

2)80 % of plasma oncotic pressure is maintained by albumin.

A. True.
B. False.

3)Hypoalbuminemia could be carried by:-

A. Decrease in synthesis in liver.
B. Loss of albumin.
C. Sever burns.
D. All of them.

4)Clinical consequences of alpha (a)-antitrypsin deficiency :-

A. Jaundice.
B. Pulmonary emphysema.
C. Liver cirrhosis.
D. All above.
E. A & B.

5) Ceruloplasmin important in :-

A. Iron absorption from intestine.
B. Transplant.
C. Non of them.
D. Both of them.

6)Which protein is important in prevent Hb loss from kidney :

A. Haptoglobin.
B. Ceruloplasmin.
C. Transferrin.
D. Non of them.

7)High plasma level found in rheumatoid arthritis.

A. Haptoglobin.
B. C-reactive protein.
C. B_2 –Microglobin.
D. Ceruloplasmin.

8)Monoclonal proliferation marker for multiple sclerosis.

A. True.
B. False.

9)Which one is true regarding transferrin :-

A. Negative acute phase protein.
B. Major iron transport .
C. Limit iron loss by prevent Hb loss from kidney.
D. Positive acute phase protein.
E. A & B

- what are the Functions of plasma proteins?
  1. Transport.
  2. Maintain plasma oncotic pressure.
  3. Defense .
  4. Clotting & fibrinolysis.
- What are the Types of plasma proteins?
  1. Prealbumin.
  2. Albumin.
  3. a_1 –Globulins (a_1 antitrypsin, a-fetoprotein)
  4. a_2 Globulins (ceruloplasmin, haptoglobin)
  5. B-Globulins. (CRP, transferrin, B_2 –microglobulin).
  6. Y-globulins
- What are the Functions of albumin?
  1. Maintain oncotic pressure.
  2. Non specific carrier.
  3. Useful in liver disease & hemorrhage & shock and burns
  4. Tissue cells take up and hydrolyzed it to amino acid.
- What are the Effects of hypoalbuminemia?
  1. Edema b/c of decrease oncotic pressure.
  2. Decrease transport of drugs .
  3. Decrease protein bound calcium (ionized ca is intact).

What are the deferences between polyclonal hypergammaglobulinemia & monoclonal?

Polyclonal	Monoclonal
• Many clones of B cells → wide range of antibodies. • Y-globulin band appear large in electrophoresis. • Clinical condition : acute &chronic infection. autoimmune disease. Chronic liver disease.	• Single B cell → single type of Ig. • Appear as a separated dense band. • Clinical condition: Multiple myeloma.

The normal reference range for total plasma proteins is.....

a) 2.5-4.5 gm/dl

b) 4.5-6.0 gm/dl

c) 6.0-8.3 gm/dl

4) >8.3gm/dl

6) Which of the following plasma protein is not involved in iron homeostasis?

a) Haptoglobin ✓

b) Transferrin ✓

c) Ferritin ✓

d) Ceruloplasmin copper

Which of the following protein is present in the gamma-globulin fraction?

a) Ceruloplasmin

b) Haptoglobin

c) Immunoglobulin

d) Transthyretin

3) C-reactive protein, a plasma protein that is elevated during inflammation and infections.

C-reactive protein falls into the category of which of the following proteins?

a) Transport proteins

b) Clotting proteins

c) Plasma Enzymes

d) Acute-phase proteins

4) Albumin (69kDa) is the major plasma protein constituting 60% of total plasma protein content.

Which of the following is not the function of albumin?

a) Maintenance of osmotic pressure ✓

b) Binding and transport of fatty acids and bilirubin ✓

c) Transport of iron

d) Transport of drugs such as sulphonamides

غالبا موجودة

5) Which of the following protein has a half-life of approximately 48 hours and is also measured as a biomarker for acute hepatic failure or malnutrition?

a) Albumin

b) Transthyretin (prealbumin)

3) Ceruloplasmin

d) Haptoglobin