Plasma proteins

Synthesized in liver, except Abs (Bcell) | 70g\L of PPs | Transpotr (prealbumin), oncotic p (albumin) defense (Ig & complement), clotting & fibrinolysis (thrombin & plasmin)

Measurement of PPs	1- Quantitative for specific protein: chemical or immunological reaction (ELISA)	2- Semiquantitative by electrophoresis: 5 bands are in the plasma (albumin is the smallest → the fastest)
Types of plasma proteins:	1- Prealbumin 2- Albumin 3- α_1-Globulins: a. α_1-Antitrypsin. b. α-fetoprotein.	4- α_2-Globulins: a. Ceruloplasmin. b. Haptoglobin. 5- β-Globulins: a. CRP, transferrin, β_2-microglobulins. 6- γ-Globulins

Albumin

- Most abundant plasma protein (40g\L). - $T_{1\2}$ = 20 ds.
- Synthesized in liver as preproalbumin, secreted as albumin.
- Function:
 - Maintain oncotic pressure → maintain fluid distribution in & out cells & plasma volume. → colloid particles (proteins) cause water to come into circulatory syst. → that's why in nephrotic synd there is edema, bc no proteins cause water to come in → water goes to interstitial tissue to make an edema.
- non-specific carrier of hormons, Ca^{2+}, free FA, drugs.
 - Tissue cells take it by pinocytosis → hydrolyzed to AA.
 - Useful in treatment of liver ds, hemorrhage, shock, burns
- Low in: injury, infection, surgery. (Why in infection or inflam.?)

Bc liver is trying to produce defense proteins other than albumin in this case!

- Hypoalbuminemia →
  - ↓ albumin synthesis (liver cirrhosis, malnutrition)
  - ↑ loss of albumin → (↑ catabolism in infection), (excessive excretion (neph. Synd.) , excessive loss in bowel (bleeding) , sever burns (plasma loss in absence of skin barrier)
  - one of the manifestation: ↓ protein-bound Ca^{2+} → total plasma Ca^{2+} level drop, ionized Ca^{2+} level may remain normal.
- Hyperalbuminemia → seen in dehydration.

Prealbumin (Transthyretin)

-Transport protein for:
Thyroid hormone, Retinol (vit.A)
- Migrate faster than albumin in electroPh (but can't be seen) → seperated by immunoelectrophoresis.
- has short $t_{1\2}$ → use to assist how person is eating + in pts w\ malabsorption → أقدر أعرف إذا المريض استجاب للعلاج أو لا.
- Low in: liver Ds, nephrotic syn, acute phase inflammatory response, malnutrition.
- Negative Acute phase protein

α_1-Antitrypsin.

- the most common type is M type.
- synthesized in liver & macroph.
- Acute phase protein that inhibit proteases enzymes. → proteases are produced endogenously & from leukocytosis & bacteria.
- Digestive enzymes (trypsin, chymotrypsin), other proteases (elastase, thrombin)
- Genetic deficiency of **α_1**-Antitrypsin:
 - synthesis of the defective **α_1**-Antitrypsin → in liver, but can't be secreted.
- **α_1**-Antitrypsin accumulate in hepatocyte & ↓ in plasma.
- if ↓→ Neonatal: jaundice+cholestasis | Adult: emphysema (COPD)
  - Dx → lack of α_1-Globulins by electrophoresis.
    → Quantitative measure: radial immunodiffusion, isoelectric focusing or nephelometry.

α-fetoprotein	Ceruloplasmin	Haptoglobin
- May protect the fetus from mother's immunoglobulins. - If ↓ in pregnant → Down synd. - If ↑ in pregnant → neural tube defect, anencephalopathy. - for adult, it is a tumor marker for Hepatoma, testicular cancer.	- Contain 90% of serum copper in hepatocyte. (bound to it) - Oxidoreductase → inactivate ROS in acute phase response. - **imp for iron absorption in GIT.** How? Transferrin carry ferric (3+) form of iron, and what we digest is ferrous form, ceruloplasmin help to reductase Fe^{2+}. - Low: Wilsons's disease: → due to low levels of ceruloP. → copper accumulate in liver & brain	- binds to free Hb to form complexed that are metabolized in RER. Why? **To prevent iron loss from Hb loss from kidney.** - ↓ during: Hemolysis. - Acute phase protein
Transferrin	**β_2-microglobulins**	**C-reactive protein (CRP)**
- Major iron transport protein in plasma in ferric form → 30% saturated w\ iron. - Low in: malnutrition, liver ds, inflammation, malignancy. ↓ Iron → cause ↑ hepatic synthesis of transferrin. → for example in celiac ds → increased transferrin is because there is low iron delivered by the body absorbed from intestine, hence the liver think the problem is that there is low transferrin to carry iron, that's why we see increased TF level. - Negative acute phase protein	- Component of HLA. - Present on the surface of lymphocyte & most nucleated cells (MHC I) - Filtered by the renal glomeruli (small size) → 99% is absorbed. - ↑ due to: overproduction in disease (increased in autoimmune ds) - A tumor marker for: **Leukemia, lymphoma**, multiple myeloma. → it indicates the tumor loud (how big is it)	- Acute phase protein, synthesized by liver. - imp. for phagocytosis. - ↑ due to: always increase in inflammatory conditions e.g. Rheumatoid arthritis. - Marker → for ischemic heart ds.

Hypergammaglobulinemia

- may result from stimulation of Bcells (polyclonal) or monoclonal proliferation (paraproteinemia)
- Polyclonal:
  - Stimulation of many clones of Bcells.
  - γ-Globulins in electrophoresis: Large longitudinal & horizontal.
  - Clinical condition: acute & chronic infections, autoimmune disease.
- Monoclonal:
  - proliferation of single Bcell → single type of Ig.
  - Appears in electroPh. → dense band (paraprotein or M band. (large longitudinally)
  - Paraproteins are characteristic of malignant B-cell proliferation.
  - Clinical condition → **multiple myeloma**.

Positive Acute phase protein	Negative Acute phase protein
- Mediators cause their proteins to increase after injury. → Cytokines (IL-1, IL-6) TNF α & β, Interferons, PAF. - Function: bind to polysaccharides in bacterial walls, Activate complement system, Stimulate phagocytosis. - Examples: α1-Antitrypsin, haptoglobin, ceruloplasmin, fibrinogen, CRP.	- Proteins ↓ in response to inflammation, mediated by inflammatory response via cytokines & hormones. Synthesis ↓ to save AA for positive acute phase proteins. - Examples: Albumin, prealbumin, transferrin.

★ Done by Atheer Alnashwan