Blood Plasma

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Blood Plasma

- Fundamental role of blood → maintenance homeostasis.
- ↓ study of its constituents
- ↓ central importance.

- Vol : 2,5-3 liter.
- Plasma consists of : water,electrolytes,metabolites,nutrients,protein and hormones.
- Changes in plasma protein and immunoglobulin can be monitored by electrophoresis.
- Major compound : protein plasma.(complex mixture): 7-7,5 gr/dl.

- Protein plasma : fibrinogen,albumin,globulin.
- Can be separated by “salting out methods”→
- Use of solvents or electrolytes (or both) to remove different protein fractions in accordance with their solubility characteristics.
- **MAJOR FUNCTION OF BLOOD**

- Concentration of protein plasma:
  - Important in dfetermining the distribution of fluid between blood and plasma.
  - Hydrostatic pressure
  - Osmotic pressure
  - Starling force.
  - If plasma prot concentration ↓ due to severe malnutrition → fluid is not attracted back into intravascular compartment,accumulation in extravas tissue spaces ⟹ edema.

Characteristics of protein plasma

- Most synthesized in the liver,glycosylated except albumin.
- Each plasma prot has a characteristic half life in circulation.
  - Normal :half life alb and haptoglobulin: 20 & 5 days.
  - Crohn dis : plasma prot (including alb) lost into bowel through inflammed interstitial mucosa → protein losing gastroenteropathy → half life alb : 1 day.

- Levels of certain protein plasma ↑ during acute inflammatory states or secondary to certain types of tissue damage.
    - Acute phase protein
    - CRP (C Reactive Protein)
        - Play a role in body's response to inflammation.
        - Used as a marker of tissue injury,infection and inflammation.
        - Predictor of certain types of cardiovascular disease secondary to atherosclerosis.

– **Functions of plasma proteins .**

Albumin

- 60 % of total plasma protein.
- 40% of albumin is present in plasma
- 60 % in extracellular space.
- Liver produced about 12 gr alb/day.
- Synthesis ↓ → liver disease & protein malnutrition (kwashiorkor).
- Alb with low mol mass(69 kDa) and high concentration ➡ principal determinant of intravascular osmotic pressure.

- Binds with many ligands such as free fatty acid,calsium,certain steroid hormone,drugs (PNC,aspirin,sulfonamide) & bilirubin.
- Transport of copper in human .

Haptoglobulin (Hp)

- Plasma glycoprotein that binds extracorpuscular Hemoglobin in a tight noncovalent complex (Hb-Hp).
- 40-180 mg of Hb binding capacity perdeciliter.
- 10%of Hb is degraded each day ,released into circulation .
- 90 % → old,damaged red blood cells degraded by cells of histiocytic systems.

- Hp is an acute phase protein↗ in a variety of inflammatory states.
- Low level found in hemolytic anemia (Hb is constantly released fr red cells).

Transferrin (TF)

- Transporting iron around the body to sites where it is needed.
- ß1 globulin,with molecular mass : 76 kDa
- Synthesized in the liver.
- Abnormalities of the glycosylation occur in:
  - Congenital disease of glycosylation.
  - Chronic alkohol abuse.

Iron metabolism

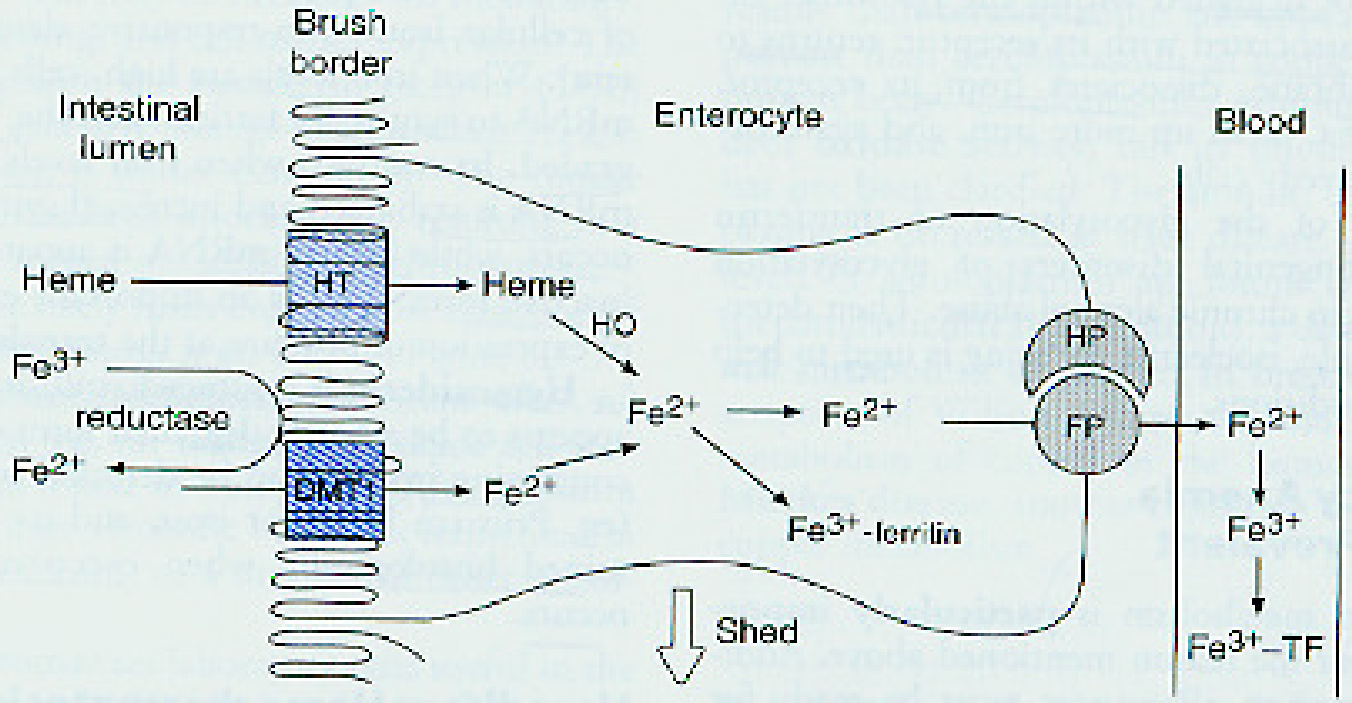

Figure 50–4. Absorption of iron. Fe^{3+} is converted to Fe^{2+} by ferric reductase, and Fe^{2+} is transported into the enterocyte by the apical membrane iron transporter DMT1. Heme is transported into the enterocyte by a separate heme transporter (HT), and heme oxidase (HO) releases Fe^{2+} from the heme. Some of the intracellular Fe^{2+} is converted to Fe^{3+} and bound by ferritin. The remainder binds to the basolateral Fe^{2+} transporter (FP) and is transported into the bloodstream, aided by hephaestin (HP). In plasma, Fe^{3+} is bound to the iron transport protein transferrin (TF). (Reproduced, with permission, from Ganong WF: *Review of Medical Physiology*, 21st ed. McGraw-Hill, 2003.)

- Concentration of TF : 300 mg/dl → this can bind 300µ/dl ⟶ this represent : total iron binding capacity of plasma.
- Iron def anemia due to :
    - Inadequate intake
    - Inadequate utilization
    - Excessive iron loss.

Ferritin

- Stores iron that can be used as cond required.
- Hemosiderin :
  - Partly degraded form of ferritin but still containing iron.
  - Can be detected by Pressian blue for iron.
  - Presence when excessive storage of iron occurs.
- Hemochromatosis.
  - Autosomal resesif disorder.
  - Excessive storage of ir4on in tissues → tissue damage
  - Herediter : mutation HFE
  - Secondary : repeated transfusion.

- Ceruloplasmin
  - A2 globulin ,160 kDa
  - Carrries 90 % of copper in plasma (bind very tightly)
  - 10 % carries by albumin (less tightly)
  - Copper
    - Essential trace element.
    - 100 mg,located mostly in bone,liver,kidney anad muscle.
    - Daily intake 2-4 mg,50% being absorbed in stomach,upper small intestine and excreted in feces.

- Involved in : dismutation, hydroxylation, oxygenation.
- Excess copper ⟹ oxidize protein,lipid,bind to nucleic acids, ↗ free radicals.

– Menkes Disease

- Disorder of copper metabolism.
- X-linked,male,fatal in infancy.
- Involves : nervous system,connective tissue and vasculature.
- Mutation: P-type ATPase .(copper is not mobilized fr intestine ⟹ accumulate .
- Absence of hepatic involvement.

- Wilson Disease
  - Genetic disorder
  - Non functional ATPase → copper toxicosis → hemolytic anemia,cirrh hepatis,neurologic syndrome.
  - Kasyer-Fleischer ring.
  - Diag : liver biopsy
  - Copper value?
- Aceruloplasminemia
  - ?

  severe neurologic signs and DM.

- Metallothioneins
  - Group of small protein (about 6,5 kDa)
  - High contein of sistein
  - SH group of systein ⟶ involves in binding metal.
  - Store metals in a nontoxic form,and involved in overall metabolism in the body.

- α1-antitrypsin
  - Major compound (> 90%) of α1 fraction human plasma.
  - Synthesized by hepatocytes and macrophages.
  - Principal serine protease inhibitorof human plasma ⟶ inhibits trypsin,elastase and certain other protease by forming complexes with them.

- Associates with emphysema
  - Smoking ⟹ oxidized methionine → methionine sulfoxide → inactivate α1 antitrypsin → ↗ proteolytic destruction of lung tissue → empysema.
- Liver disease → cirrhosis hepatis.

THANK YOU