Blood plasma

- 5 % of body weight:
  - 55 % of blood volume
  - 25 % of extracellular fluid volume
- composition:
  - 93 % = water
  - 6 % = organic compounds
  - 1% = inorganic compounds
    - Na+ = main extracellular cation, osmotic pressure
    - K+ = main intracellular ion, excitability
    - Ca2+ = both ionized and bound to the proteins of blood plasma
    - Cl- = volume of blood plasma, pH, osmotic pressure
    - HCO3- = buffering system, transport of carbon dioxide

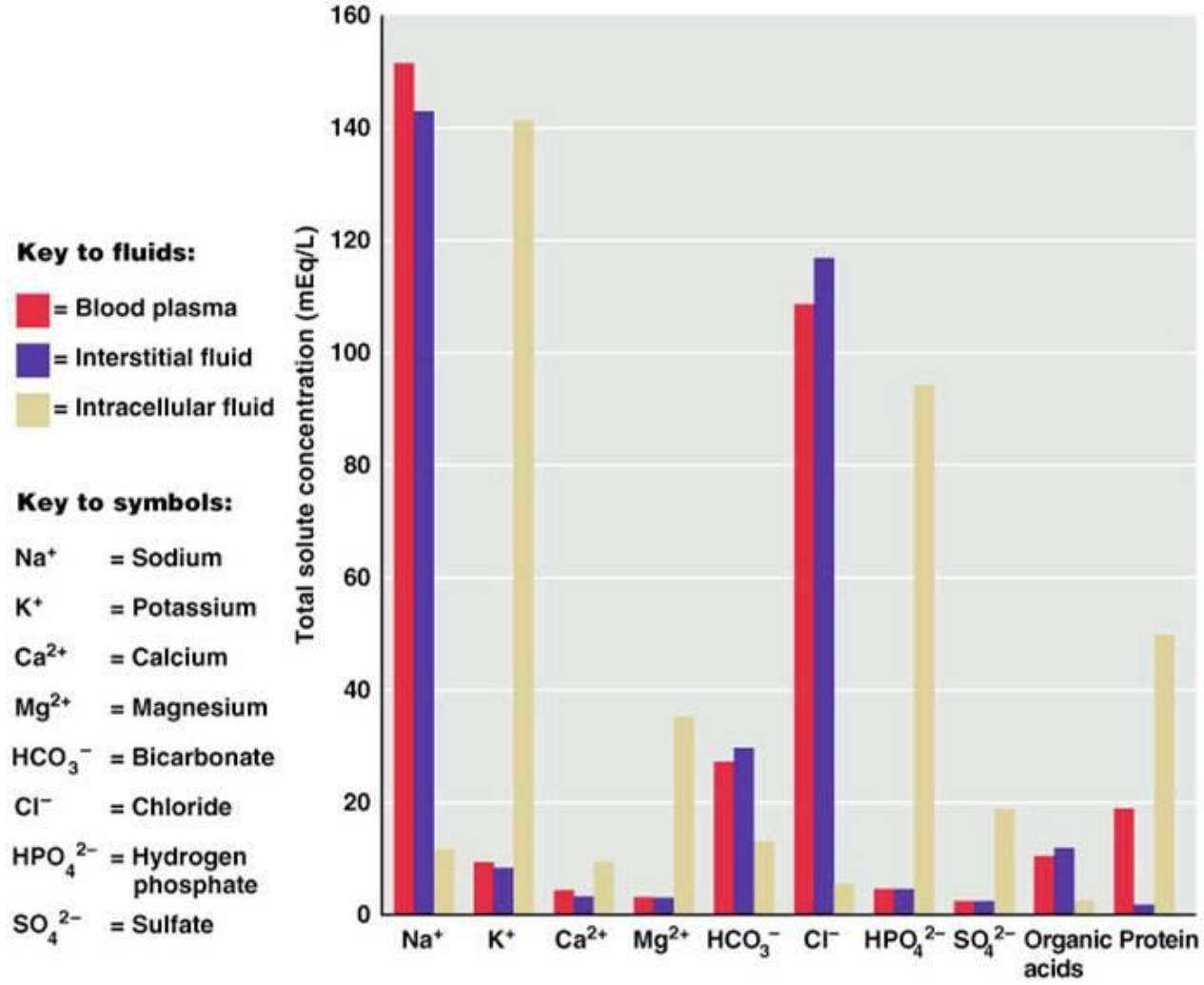
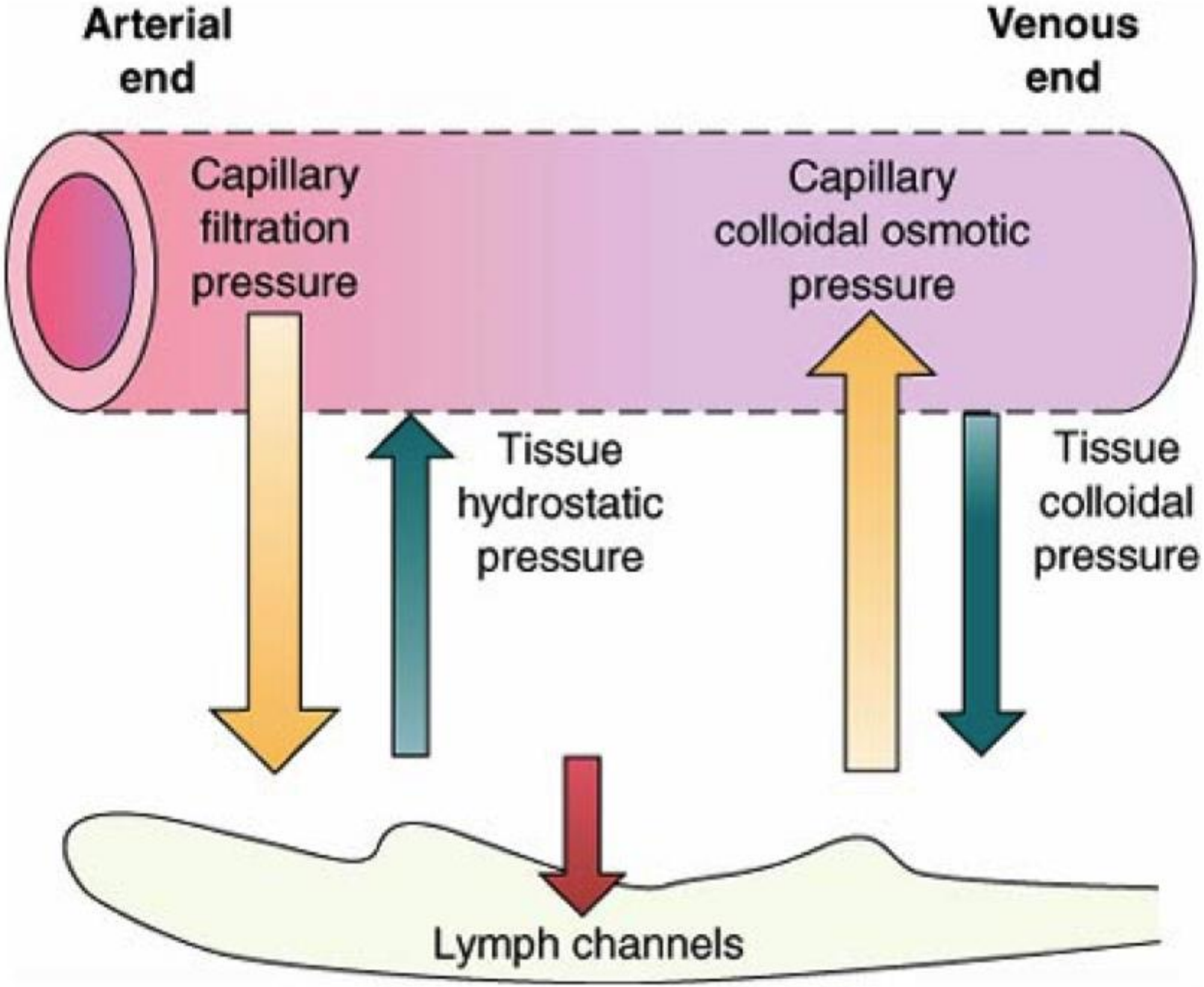


TABLE 14–1 Reference Table of Plasma Constituents

Constituent	Amount/Concentration	Major Functions
Water	93% of plasma weight	Medium for carrying all other constituents
Electrolytes (inorganic)	Total < 1% of plasma weight	Keep H_2O in extracellular compartment; act as buffers; function in membrane excitability and blood clotting
Na^+	145 mM	
K^+	4 mM	
Ca^{2+}	2.5 mM	
Mg^{2+}	1.5 mM	
H^+	0.0004 mM	
Cl^-	103 mM	
HCO_3^-	24 mM	
Phosphate (mostly HPO_4^{2-})	1 mM	
SO_4^{2-}	0.5 mM	
Proteins	Total = 7% of plasma weight, 7.3 g/100 ml (2.5 mM)	Provide nonpenetrating solutes of plasma; act as buffers; bind and transport other plasma constituents (lipids, hormones, vitamins, metals, etc.); clotting factors; enzymes, enzyme precursors; antibodies (immune globulins); hormones
Albumins	4.2 g/100 ml	
Globulins	2.8 g/100 ml	
Fibrinogen	0.3 g/100 ml	Blood clotting
Gases		
CO_2	2 ml/100 ml (1 mM)	A waste product
O_2	0.2 ml/100 ml (0.1 mM)	Oxidative metabolism
N_2	0.9 ml/100 ml (0.5 mM)	No function
Nutrients		(See Chapters 2, 4, and 18)
Glucose and other carbohydrates	100 mg/100 ml (5.6 mM)	
Total amino acids	40 mg/100 ml (2 mM)	
Total lipids	500 mg/100 ml (7.5 mM)	
Cholesterol	150–250 mg/100 ml (4–7 mM)	
Individual vitamins	0.0001–2.5 mg/100 ml (0.00005–0.1 mM)	
Individual trace elements	0.001–0.3 mg/100 ml (0.0001–0.01 mM)	
Waste products		
Urea (from protein)	34 mg/100 ml (5.7 mM)	
Creatinine (from creatine)	1 mg/100 ml (0.09 mM)	
Uric acid (from nucleic acids)	5 mg/100 ml (0.3 mM)	
Bilirubin (from heme)	0.2–1.2 mg/100 ml (0.003–0.018 mM)	
Individual hormones	0.000001–0.05 mg/100 ml (10^{-9}–10^{-6} mM)	Messengers in control systems


Arterial end
Venous end
Capillary filtration pressure
Capillary colloidal osmotic pressure
Tissue hydrostatic pressure
Tissue colloidal pressure
Lymph channels

1. The Starling equation (Figure 3-18)

$$J_v = K_f[(P_c - P_i) - (\pi_c - \pi_i)]$$

where:

J_v = fluid movement (mL/min)
K_f = hydraulic conductance (mL/min • mm Hg)
P_c = capillary hydrostatic pressure (mm Hg)
P_i = interstitial hydrostatic pressure (mm Hg)
π_c = capillary oncotic pressure (mm Hg)
π_i = interstitial oncotic pressure (mm Hg)

a. J_v is fluid flow.

- When **J_v is positive**, there is net fluid movement out of the capillary **(filtration)**.
- When **J_v is negative**, there is net fluid movement into the capillary **(absorption)**.

b. K_f is the filtration coefficient.

- It is the hydraulic conductance (water permeability) of the capillary wall.

c. P_c is capillary hydrostatic pressure.

- An increase in P_c **favors filtration** out of the capillary.
- P_c is determined by arterial and venous pressures and resistances.
- An increase in either arterial or venous pressure produces an increase in P_c; increases in venous pressure have a greater effect on P_c.

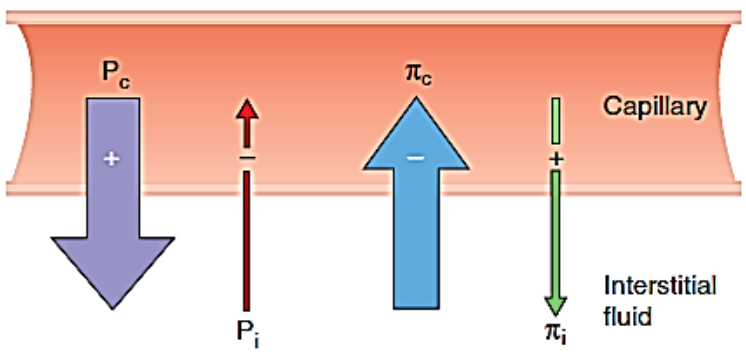


FIGURE 3-18 Starling forces across the capillary wall. + *sign* = favors filtration; – *sign* = opposes filtration; P_c = capillary hydrostatic pressure; P_i = interstitial hydrostatic pressure; π_c = capillary oncotic pressure; π_i = interstitial oncotic pressure.

- P_c is higher at the arteriolar end of the capillary than at the venous end (except in glomerular capillaries, where it is nearly constant).

d. P_i is interstitial fluid hydrostatic pressure.

- An increase in P_i **opposes filtration** out of the capillary.
- It is normally close to 0 mm Hg (or it is slightly negative).

e. π_c is capillary oncotic, or colloidosmotic, pressure.

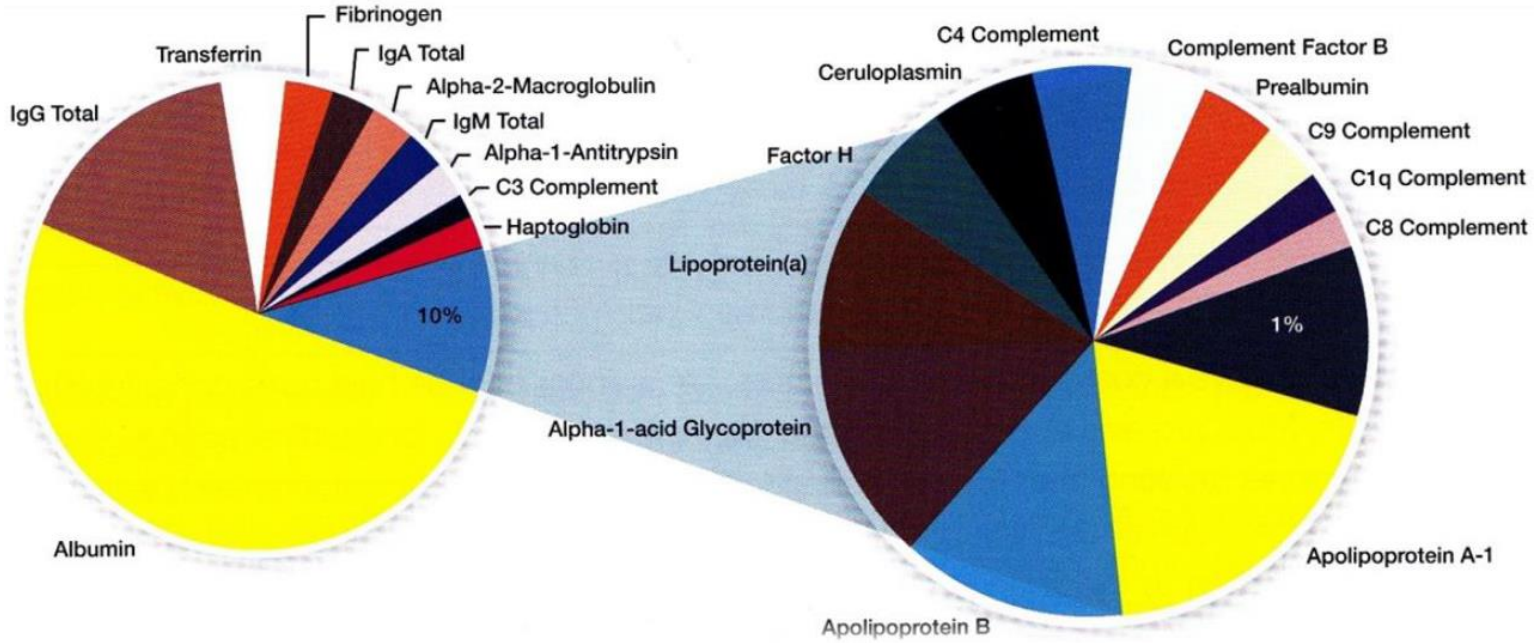
- An increase in π_c **opposes filtration** out of the capillary.
- π_c is increased by increases in the protein concentration in the blood (e.g., dehydration).
- π_c is decreased by decreases in the protein concentration in the blood (e.g., nephrotic syndrome, protein malnutrition, liver failure).
- Small solutes do not contribute to π_c.

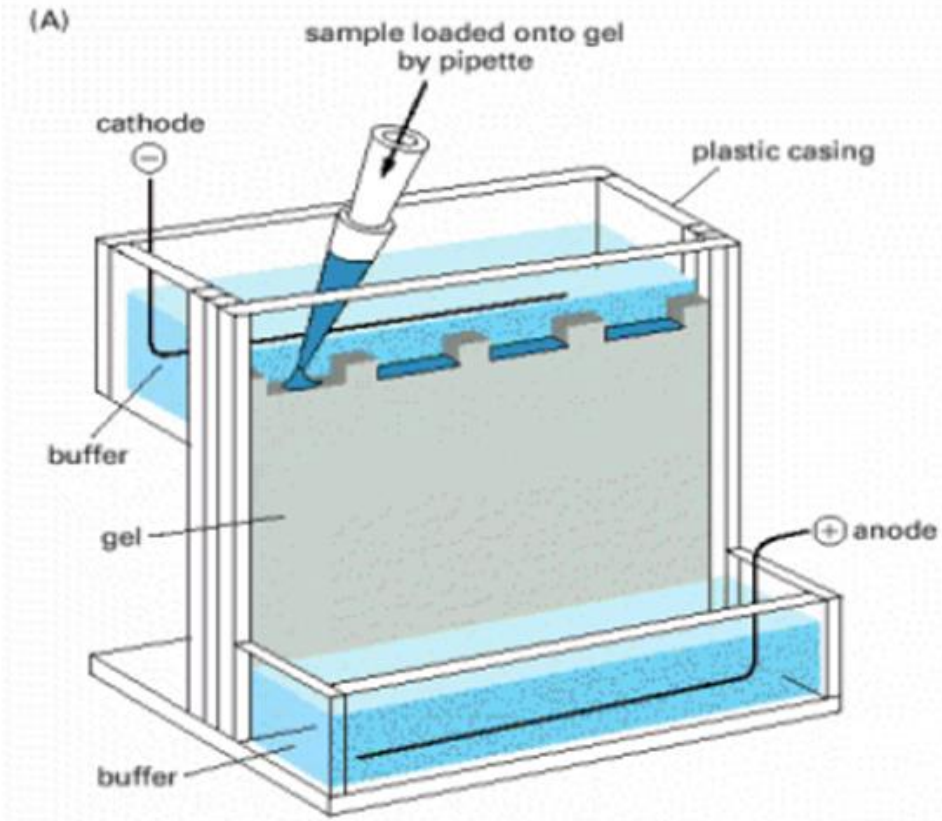
f. π_i is interstitial fluid oncotic pressure.

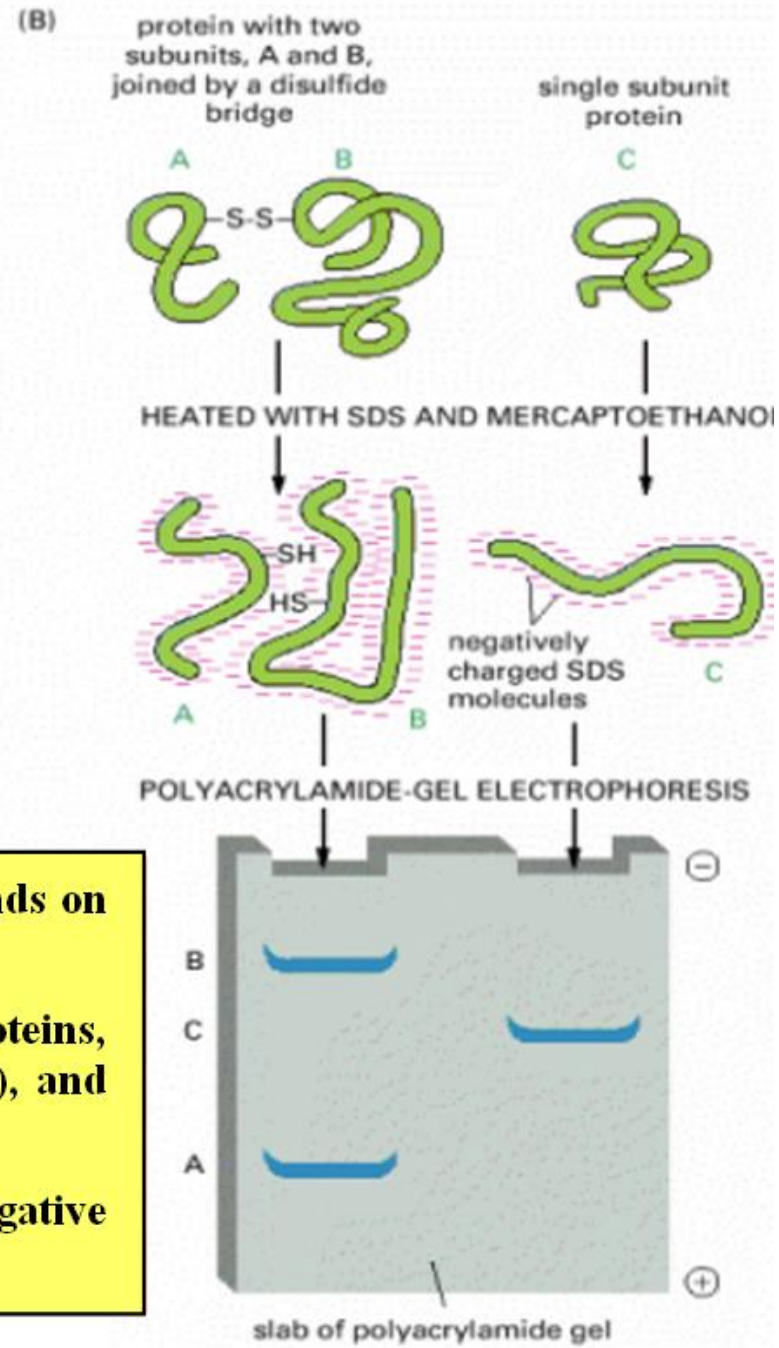
- An increase in π_i **favors filtration** out of the capillary.
- π_i is dependent on the protein concentration of the interstitial fluid, which is normally quite low because very little protein is filtered.

Plasma proteins

- concentration 65 – 80 g/l (<300 proteins)
    - 35 – 50 g/l = albumin
    - 20 – 35 g/l = serum globulins
- biosynthesis:
    - liver (most)
    - lymphocytes (immunoglobulins)
    - enterocytes (e.g. apoprotein B-48)
- degradation:
    hepatocytes, mononuclear phagocytic system (complexes of antigen-antibody, hemoglobin-haptoglobin)







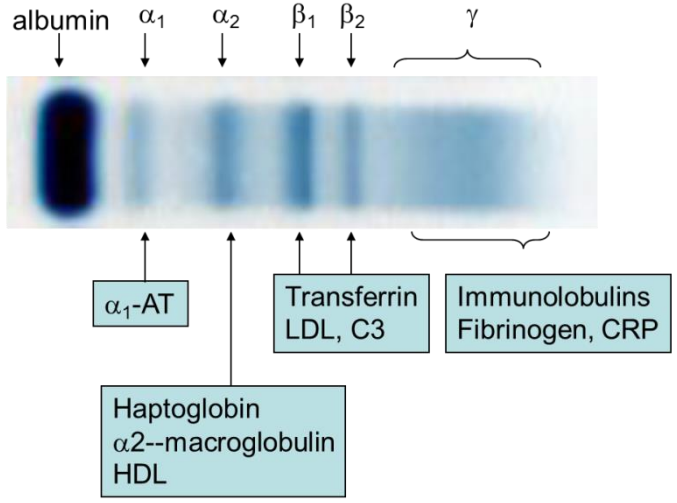
The speed of migration in an electrical field depends on the dimension, form and charge of the molecules.

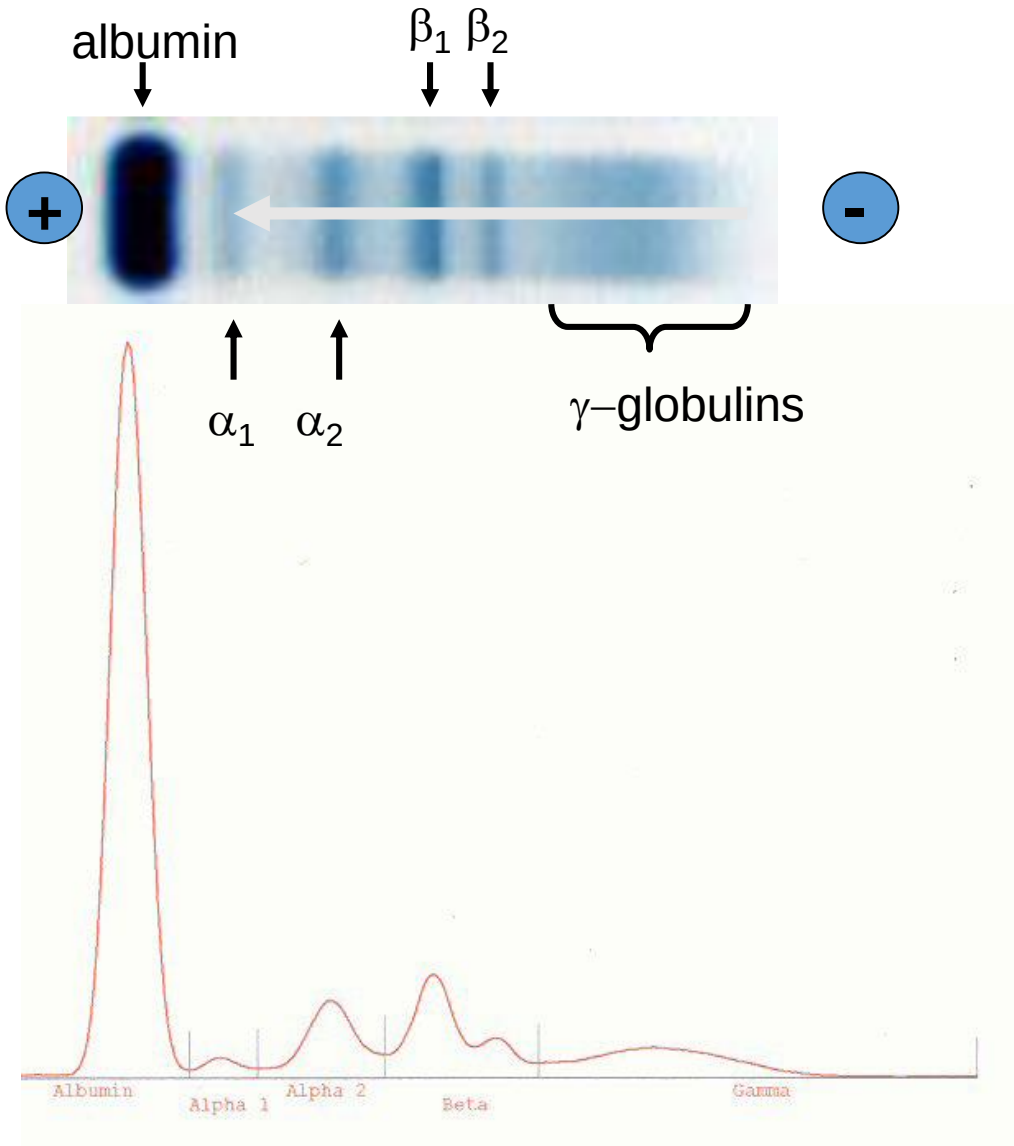
For deaggregation and denaturation of the proteins, SDS, β-mercaptoethanol or DTT (reducing agents), and heat is used.

SDS (strongly anionic detergent) provides negative charge to the proteins.

Types of plasma proteins

1. Albumin
2. Globulins
   - α-globulins : α_1 and α_2-globulins
   - β-globulins: β_1 and β_2-globulins
   - γ-globulins
3. Fibrinogen





Elfo fractions of plasma proteins

Fraction	*Rel. amount (%)*	*c (g/l)*
Albumins: albumin pre-albumin (transthyretin)	52 – 58	34 – 50
α_1-globulins: thyroxin-binding globulin, transcortin, α_1-acid glycoprotein, α_1-antitrypsin, α_1-lipoprotein (HDL), α_1-fetoprotein	2,4 – 4,4	2-4
α_2-globulins: haptoglobin, macroglobulin, ceruloplasmin	6,1 – 10,1	5 – 9
β-globulins: transferrin, hemopexin, lipoprotein (LDL), fibrinogen, C-reactive protein, C3 and C4 components of the complement system	8,5 – 14,5	6 – 11
γ-globulins: IgG, IgM, IgA, IgD, IgE	10 – 21	8 – 15

TABLE 32–6 Some of the proteins synthesized by the liver: Physiologic functions and properties.

Name	Principal Function	Binding Characteristics	Serum or Plasma Concentration
Albumin	Binding and carrier protein; osmotic regulator	Hormones, amino acids, steroids, vitamins, fatty acids	4500–5000 mg/dL
Orosomucoid	Uncertain; may have a role in inflammation		Trace; rises in inflammation
α_1-Antiprotease	Trypsin and general protease inhibitor	Proteases in serum and tissue secretions	1.3–1.4 mg/dL
α-Fetoprotein	Osmotic regulation; binding and carrier protein[a]	Hormones, amino acids	Found normally in fetal blood
α_2-Macroglobulin	Inhibitor of serum endoproteases	Proteases	150–420 mg/dL
Antithrombin-III	Protease inhibitor of intrinsic coagulation system	1:1 binding to proteases	17–30 mg/dL
Ceruloplasmin	Transport of copper	Six atoms copper/mol	15–60 mg/dL
C-reactive protein	Uncertain; has role in tissue inflammation	Complement C1q	< 1 mg/dL; rises in inflammation
Fibrinogen	Precursor to fibrin in hemostasis		200–450 mg/dL
Haptoglobin	Binding, transport of cell-free hemoglobin	Hemoglobin 1:1 binding	40–180 mg/dL
Hemopexin	Binds to porphyrins, particularly heme for heme recycling	1:1 with heme	50–100 mg/dL
Transferrin	Transport of iron	Two atoms iron/mol	3.0–6.5 mg/dL
Apolipoprotein B	Assembly of lipoprotein particles	Lipid carrier	
Angiotensinogen	Precursor to pressor peptide angiotensin II		
Proteins, coagulation factors II, VII, IX, X	Blood clotting		20 mg/dL
Antithrombin C, protein C	Inhibition of blood clotting		
Insulinlike growth factor I	Mediator of anabolic effects of growth hormone	IGF-I receptor	
Steroid hormone-binding globulin	Carrier protein for steroids in bloodstream	Steroid hormones	3.3 mg/dL
Thyroxine-binding globulin	Carrier protein for thyroid hormone in bloodstream	Thyroid hormones	1.5 mg/dL
Transthyretin (thyroid-binding prealbumin)	Carrier protein for thyroid hormone in bloodstream	Thyroid hormones	25 mg/dL

[a]The function of alpha-fetoprotein is uncertain, but because of its structural homology to albumin it is often assigned these functions.

Functions of plasma proteins

- Transport:
  - albumin – fatty acids, bilirubin, calcium, drugs
  - transferin – iron
  - ceruloplasmin – copper
  - transcortin – cortisol, corticosterone
  - lipoproteins – lipids
  - haptoglobin – free hemoglobin
  - thyroxin binding globulin – thyroxin
  - retinol binding protein – retinol
- Osmotic regulation:
  - Plasma proteins are colloidal and non-diffusable and exert a colloidal osmotic pressure, which helps to maintain a normal blood volume and a normal water content in the interstitial fluid and the tissues.
  - Albumin content is most important in regulation of colloidal osmotic or oncotic pressure.
  - Decrease in albumin level results in loss of water from blood and its entry into interstitial fluids causing edema.
- Catalytic function (= enzymes):
  - e.g lipases for removal of lipids from the blood

Functions of plasma proteins (cont.)

- Blood clotting:
  - Many factors are involved in clotting mechanism and prevent loss of excessive amount of blood; e.g. clotting factors IX, VIII, thrombin, fibrinogen etc.
  - An excess of deficiency leads to a disease; e.g. hemophilia, thrombus formation
- Anticoagulant activity (thrombolysis):
  - Plasmin breaks down thrombin and dissolves the clot
- Buffering capacity:
  - Proteins in plasma help to maintain acid-base balance

General properties of plasma proteins

- Most are synthesized in the liver
  - Exception: γ-globulins – synthesized in plasma cells
- Synthesized as *pre-proteins* on membrane-bound polyribosomes; then they are subjected to posttranslational modifications in ER and Golgi apparatus
- Almost all of them are glycoproteins
  - Exception: albumin
- They have characteristic half-life in the circulation (albumin – 20 days)
- Many of them exhibit polymorphism (immunoglobulins, transferrin…)

Acute phase reactants (APRs)

- Their levels change during acute inflammatory response
- Cause conditions where there is:
  - ✓ the destruction of cells
  - ✓ the reversible cell damage and subsequent repair
  - ✓ the metabolic activation of certain cells (immune cells)

- APRs concentration changes in:
  - infection
  - surgery
  - injury
  - cancer

Types of APRs:

Positive:

C-reactive protein:
~1000-fold increase!

α_1-antitrypsin

fibrinogen

haptoglobin (HP)

C3, C4

serum amyloid A (SAA)

Negative:

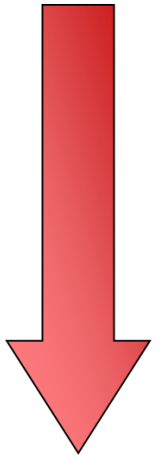
albumin

transferrin

antithrombin

transcortin

retinol binding protein



The importance of positive acute phase reactants

- Components of the immune response
  - C-reaktive protein, complement components (C3 a C4),TNF-α, Il-1, Il-6
- Protection against collateral tissue damage
  - scavergers of ROS and protein stabilizing transition metals and their complexes
    - haptoglobin
    - hemopexin
    - feritin
    - ceruloplasmin
  - *Inhibitors of proteases*
    - α_1-antitrypsin
    - α_1-antichymotrypsin
    - α_2-macroglobulin

- Transport of waste products produced during inflammation :
  - hemoglobin
  - hemopexin
  - serum amyloid A (SAA)
- Coagulation factors and proteins involved in tissue regeneration :
  - fibrinogen
  - prothrombin
  - factor VIII
  - von Willebrandt factor
  - plasminogen

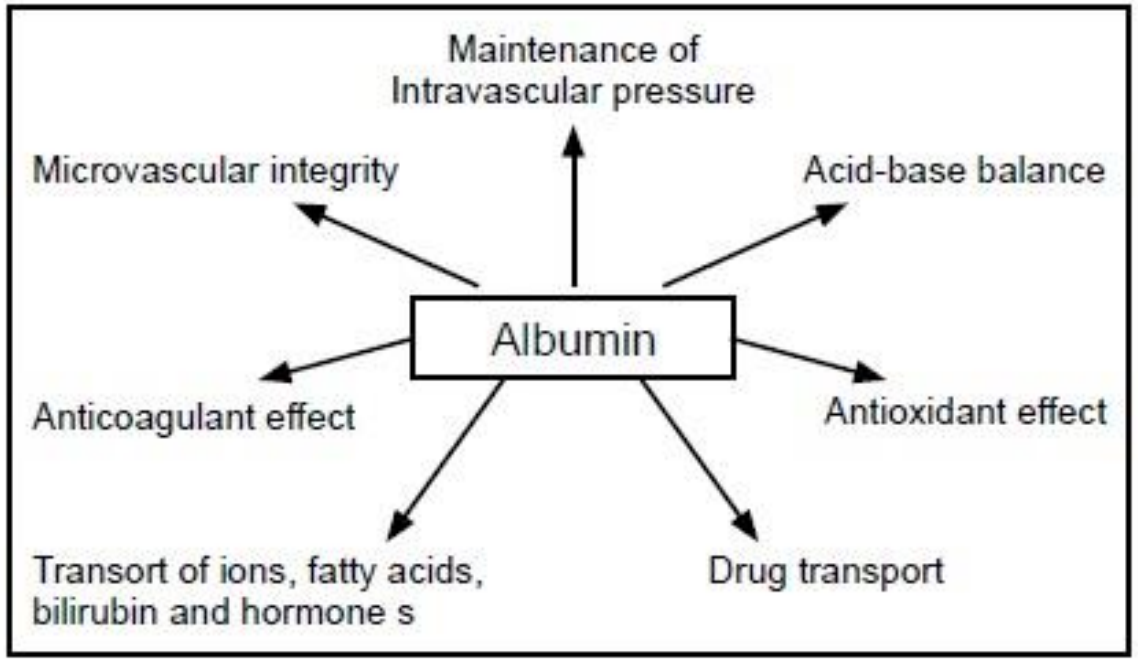
The importance of negative acute phase reactants

- The criterion for determining inflammation (decrease inflammation)
  - transcortin (corticosteroid-binding globulin (CBG) or serpin A6)

- The criterion for protein synthesis in the liver

Albumin

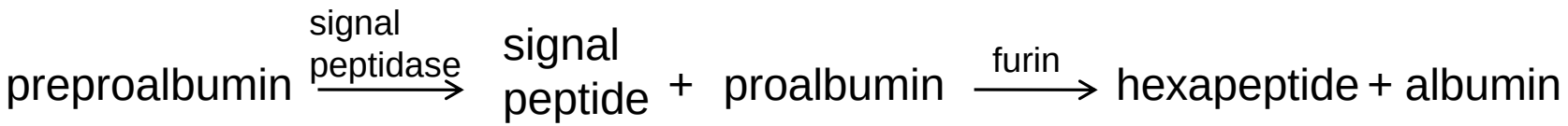
- Concentration in plasma: 45 g/l
- ~ 60% of the total plasma protein
- Functions:
  - maintenance of plasma oncotic pressure (values lower than 20 g leads to edema)
  - protein reserve, the source of amino acids
  - transport of:
    - steroid hormones
    - free fatty acids
    - bilirubin
    - drugs (sulfonamides, aspirin)
    - Ca^{2+}
    - Cu^{2+}



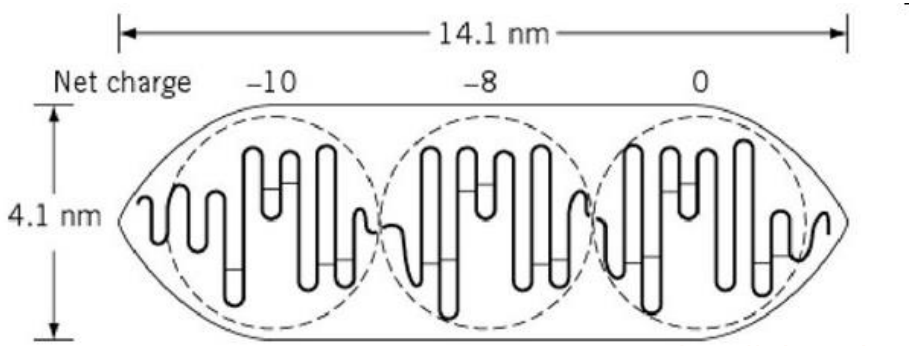
1. Figure 1 – Physiological effects of exogenous albumin.

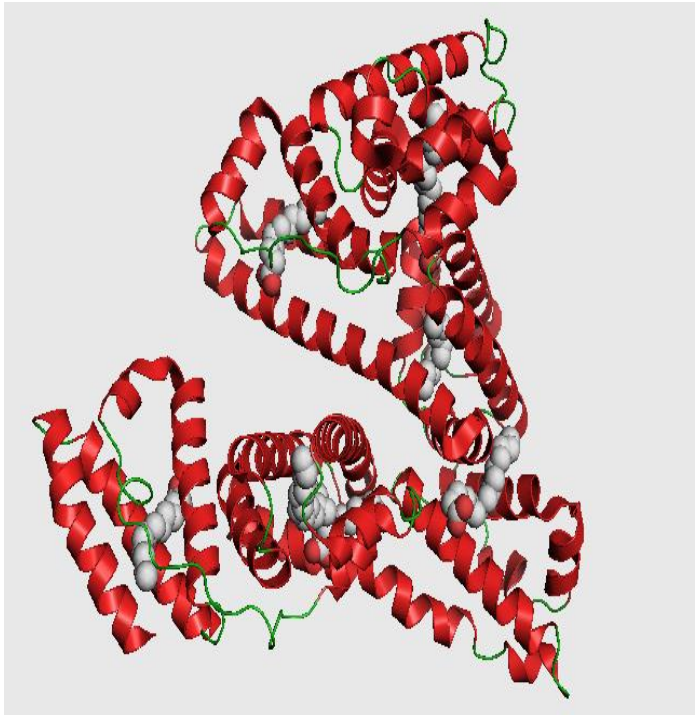
Albumin

- synthesized as a preproprotein



- Alb – chain of 585 AA, 17 disulfide bonds
- proteases – subdivide into 3 domains, which have different functions
- ellipsoidal shape – does not increase the viscosity of plasma X fibrinogen





http://what-when-how.com/molecular-biology/serum-albumin-molecular-biology/

Causes of Albumin Deficiency

- Liver diseases (cirrhosis) – decrease in the ratio of albumin to globulins
- Protein malnutrition
- Excessive excretion by kidneys (renal disease)
- Mutation causing analbuminemia (affects splicing)

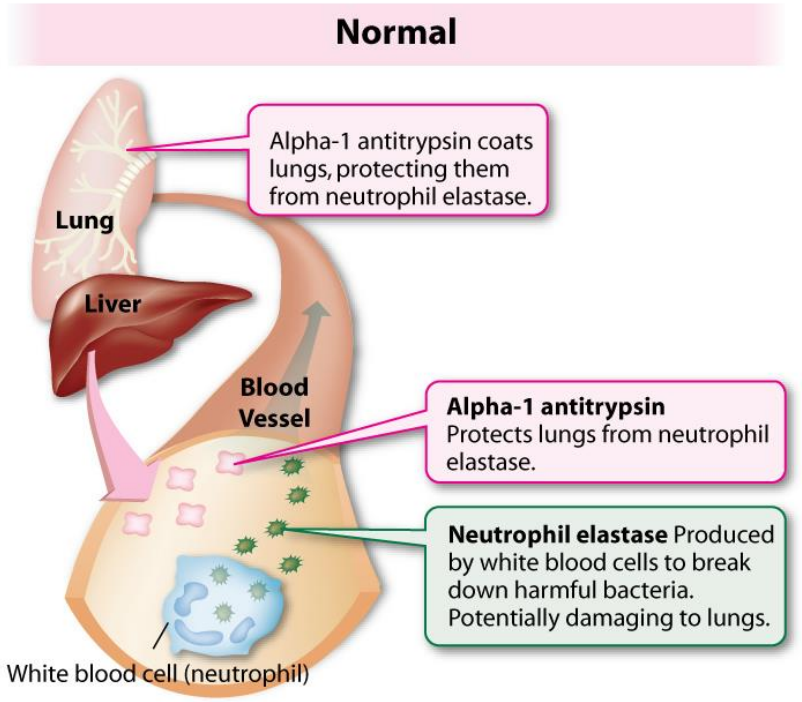
Table 1 | Localization of albumin-binding proteins and receptors.

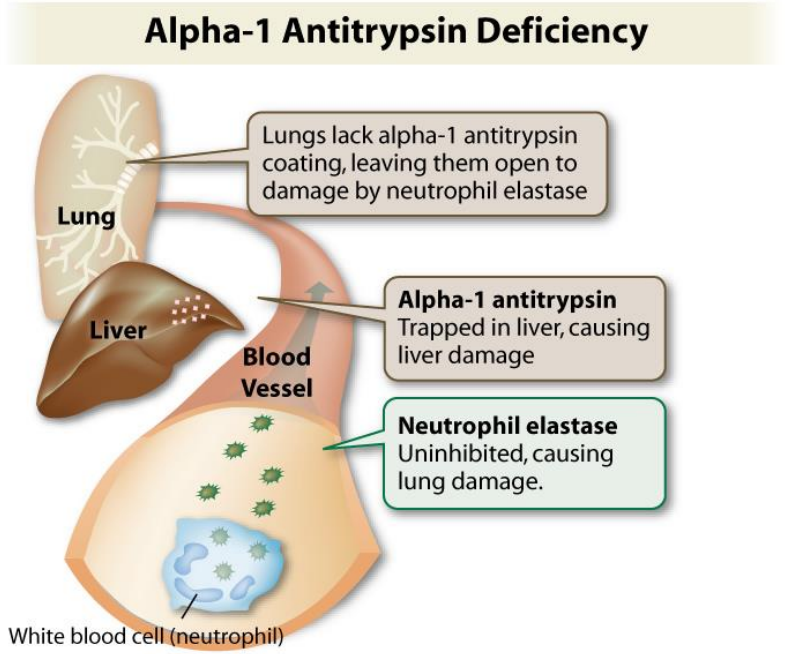
Protein/Receptor	Tissue	Substrate
Albondin/gp60	Continuous endothelium	Native albumin
gp18	Endothelium, macrophages, fibroblasts and MDA-MB-453 breast cancer cell surfaces	Modified-albumin
gp30	Endothelium, macrophages, fibroblasts and MDA-MB-453 breast cancer cell surfaces	Modified-albumin
SPARC	Endothelial cells, vascular smooth muscle cells, skeletal muscle, fibroblasts, testicular, ovarian, pancreatic and a range of tumor cells	Native albumin
hnRNPs	Human tumor cell lines: CEM T-cell leukemia cells, MCF-7 breast cancer cells and MV3 melanoma cells	Native albumin
Calreticulin	Human tumor cell lines: CEM T-cell leukemia cells, MCF-7 breast cancer cells and MV3 melanoma cells	Native albumin
FcRn	Endothelium, antigen-presenting cells, gut, kidneys, lungs and the blood-brain-barrier (central nervous system endothelium and choroid plexus)	Native albumin
Cubilin	Kidney proximal tubule cells, absorptive intestinal cells, placenta, and visceral yolk-sac cells	Native albumin and probably modified-albumin
Megalin	Kidney proximal tubule cells, absorptive intestinal cells, placenta, visceral yolk-sac cells, choroid plexus, thyrocytes, ciliary epithelium, lungs, parathyroid, endometrium, oviduct, inner ear, and epididymal epithelial cells	Native albumin and probably modified-albumin

Merlot AM, Kalinowski DS, Richardson DR: **Unraveling the mysteries of serum albumin-more than just a serum protein.** ***Frontiers in Physiology 2014, 5.***

α_1-antitrypsin

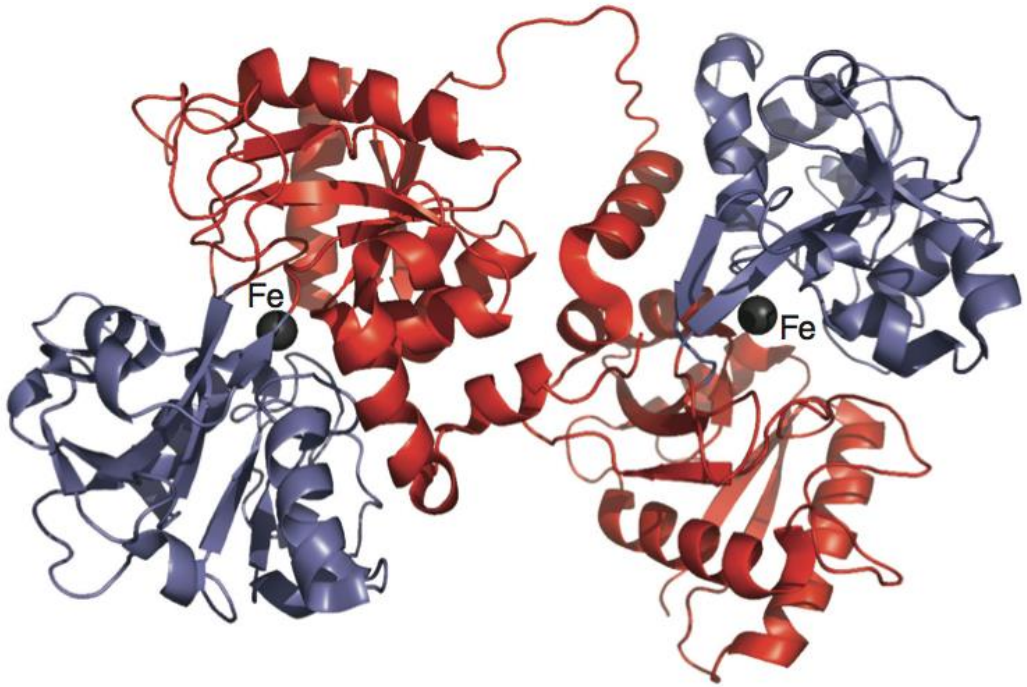
- Main globulin of α_1 fraction (90 %)
- is synthesized in the liver in hepatocytes and macrophages
- glycoprotein, highly polymorphous (≈75 forms)
- Function:
  - Main plasma inhibitor of serine proteases (trypsin, elastase...)
  - during the acute phase increases ⇒ inhibition of degradation of connective tissue by elastase
  - deficiency ⇒ proteolytic lung damage (emfyzem)





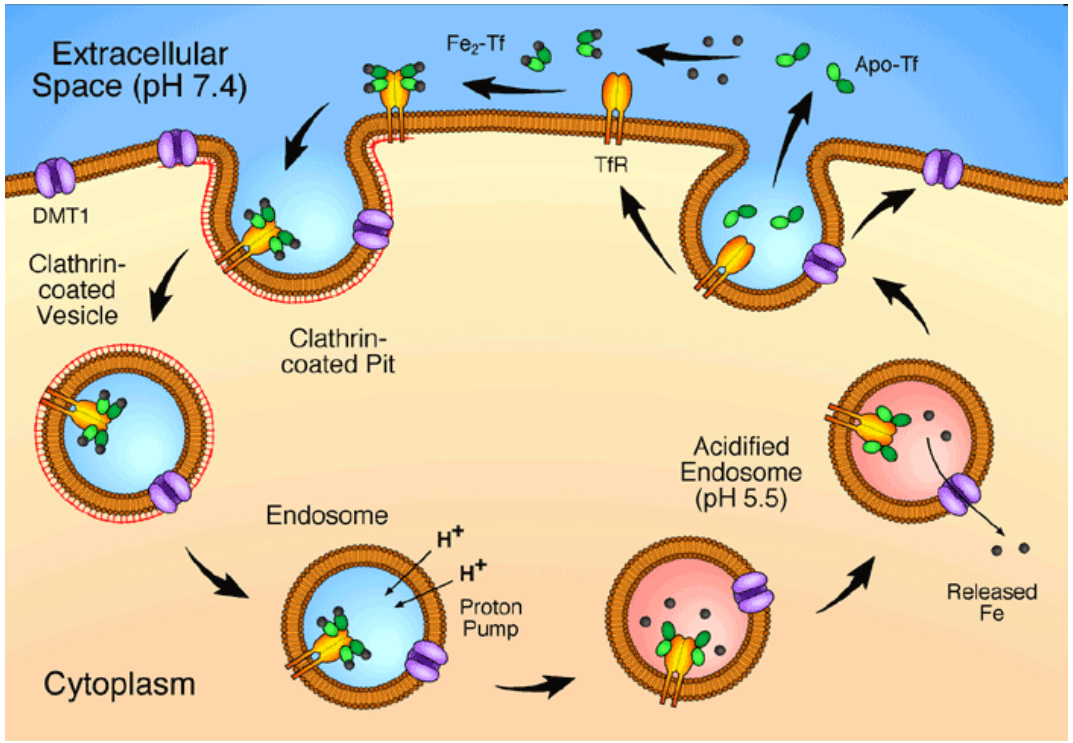
Transferrin

- Transferrin is a β-globulin
- It binds free iron in serum
- Normally it is about one third saturated with iron
- Transferrin levels are decreased in:
  - *liver disease (e.g. cirrhosis)*
  - *Chronic infections*
  - *Nephrosis*
  - *Congenital atransferrinaemia*
- Increased serum transferrin levels occur during increased transferrin synthesis caused as a result of iron deficiency anemia



Receptor-mediated transferrin endocytosis

- Ferro-transferrin binds to the receptors on the cell surface → the complex is internalized into an endosome
- In endosomes, iron dissociates from transferrin (enabled by low pH & $Fe^{3+} \rightarrow Fe^{2+}$ reduction) and enters cytoplasm
- Iron is delivered to intracellular sites or bound to ferritin ($Fe^{2+} \rightarrow Fe^{3+}$ oxidation and Fe^{3+} storage)
- Apotransferrin, associated with the receptor, returns to the membrane, dissociates from the receptor and re-enters plasma.



Transferrin

- Free Fe^{2+} ions are toxic for organism – catalyses Fenton reaction (formation of highly toxic $^{\cdot}OH$ radical)

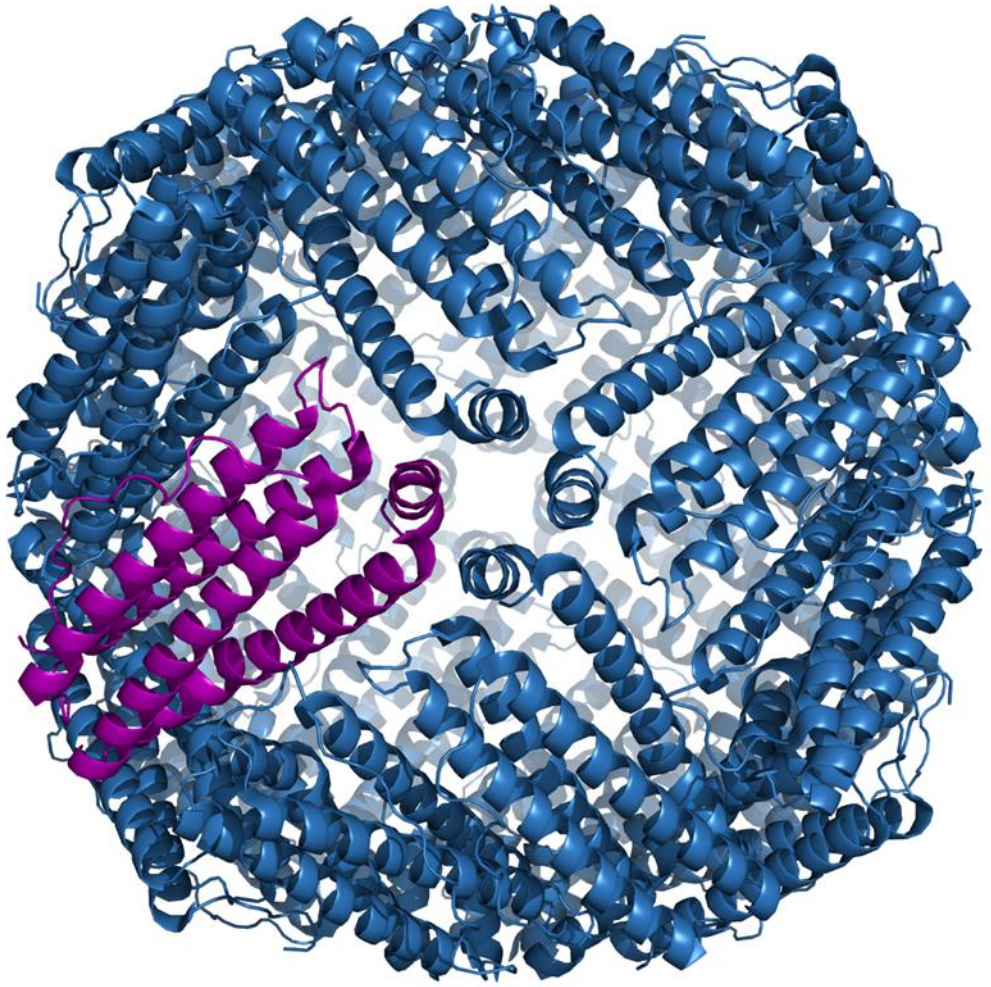
  $H_2O_2 + Fe^{2+} \rightarrow OH^- + {}^{\cdot}OH + Fe^{3+}$

- Transferrin with other plasma proteins that bind iron or heme, acts as an antioxidant (prevents ROS)
- Causes of decline in transferrin :
  - burns, infections, malignant processes and liver and kidney diseases
- Cause of relative transferrin excess:

  Iron-deficiency anemia

Ferritin

- Intracellular protein; only small portion in plasma
- 24 subunits surround 3000 - 4500 ions of Fe^{3+}
- Function: stores iron that can be called upon for use when needed
- Primary hemochromatosis – genetic disorder characterized by increased absorption of iron from the intestine $\Rightarrow$ accumulated iron damages organs such as the liver, skin, heart, and pancreas. Concentration of ferritin is elevated.



FERRITIN

- Iron storage protein
- 24 subunits of H and L

H-rich ferritin

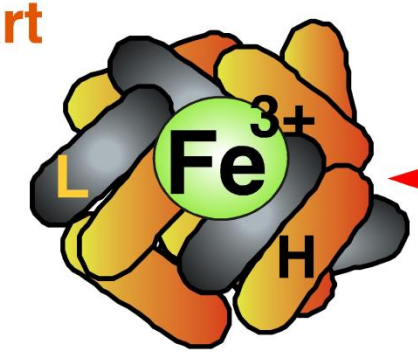
rapid iron-uptake and release

heart

L-rich ferritin

long term iron-storage

liver, spleen



Reactive Metabolites

O_2 — Oxygen

e

redox cycling

$O_2^{\cdot}$ — Superoxide

H_2O_2 — Hydrogen Peroxide

$OH^{\cdot}$ — Hydroxyl Radical

Fe^{3+}

TOXICITY

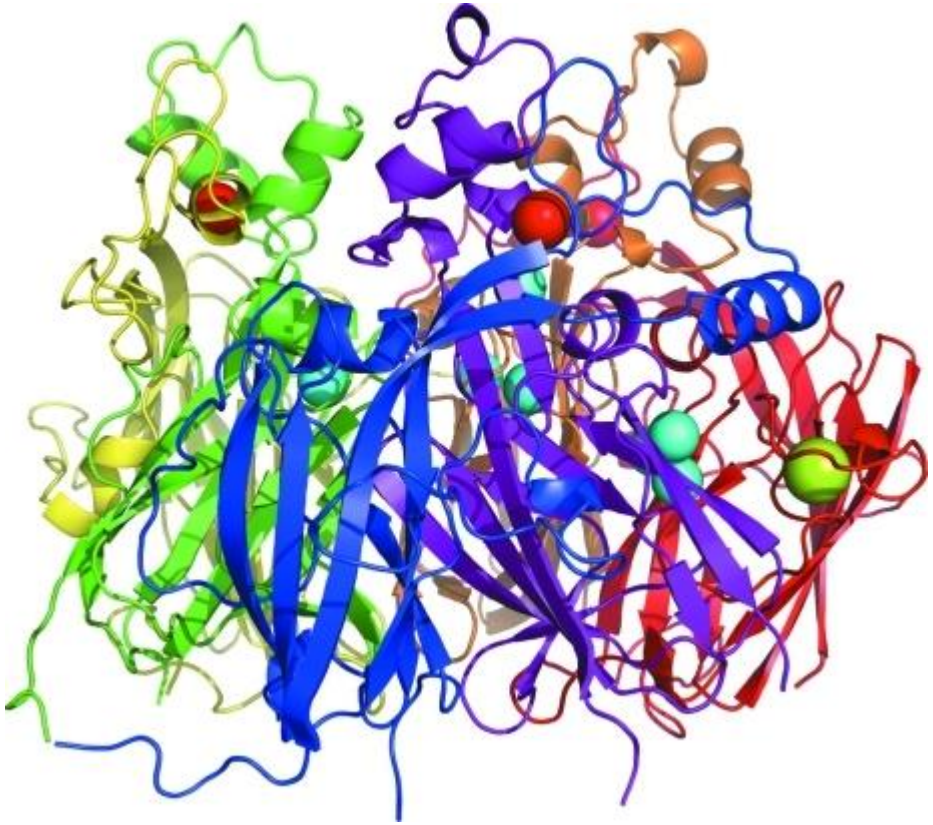
Ceruloplasmin

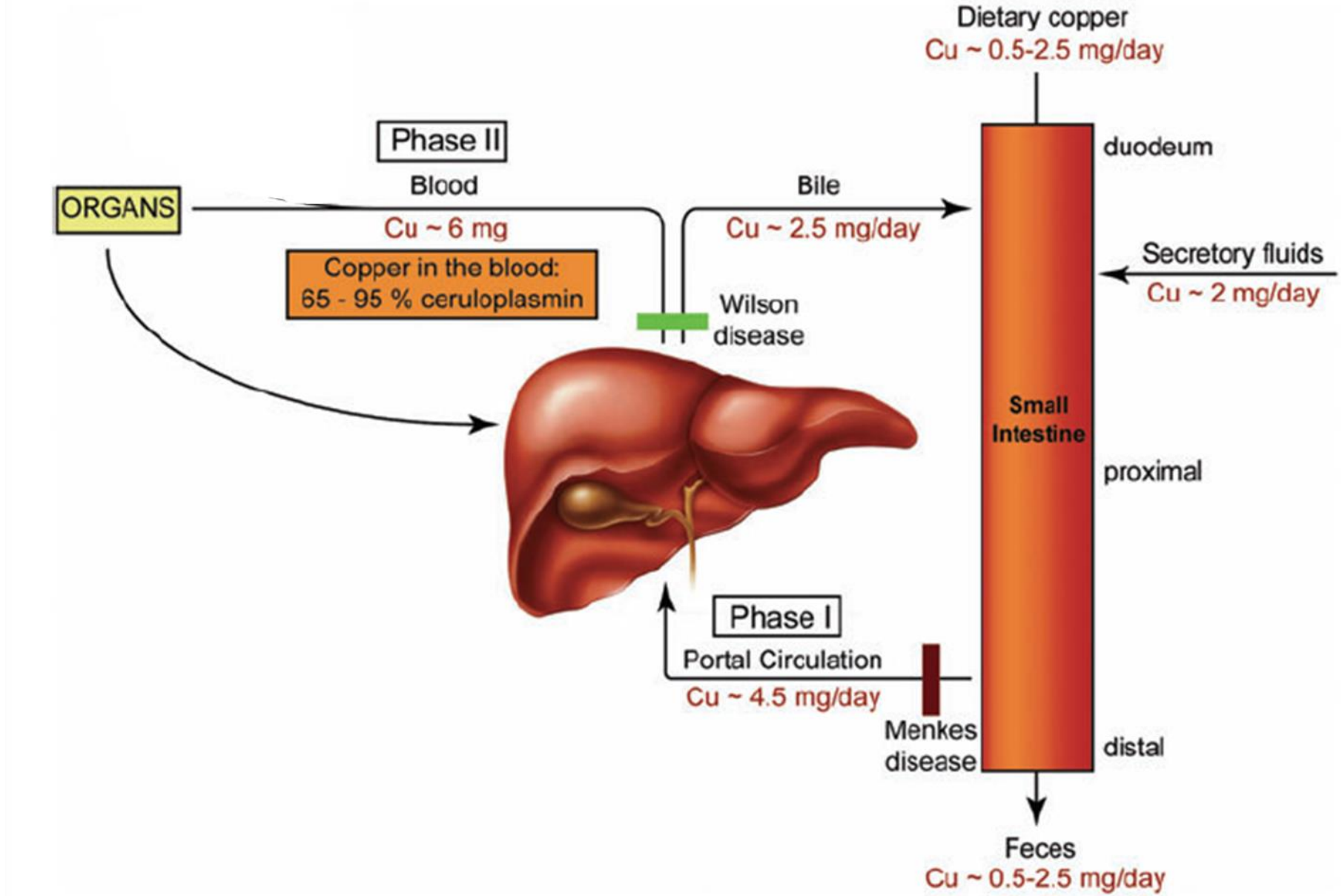
- Conc. in plasma: 300 mg/l

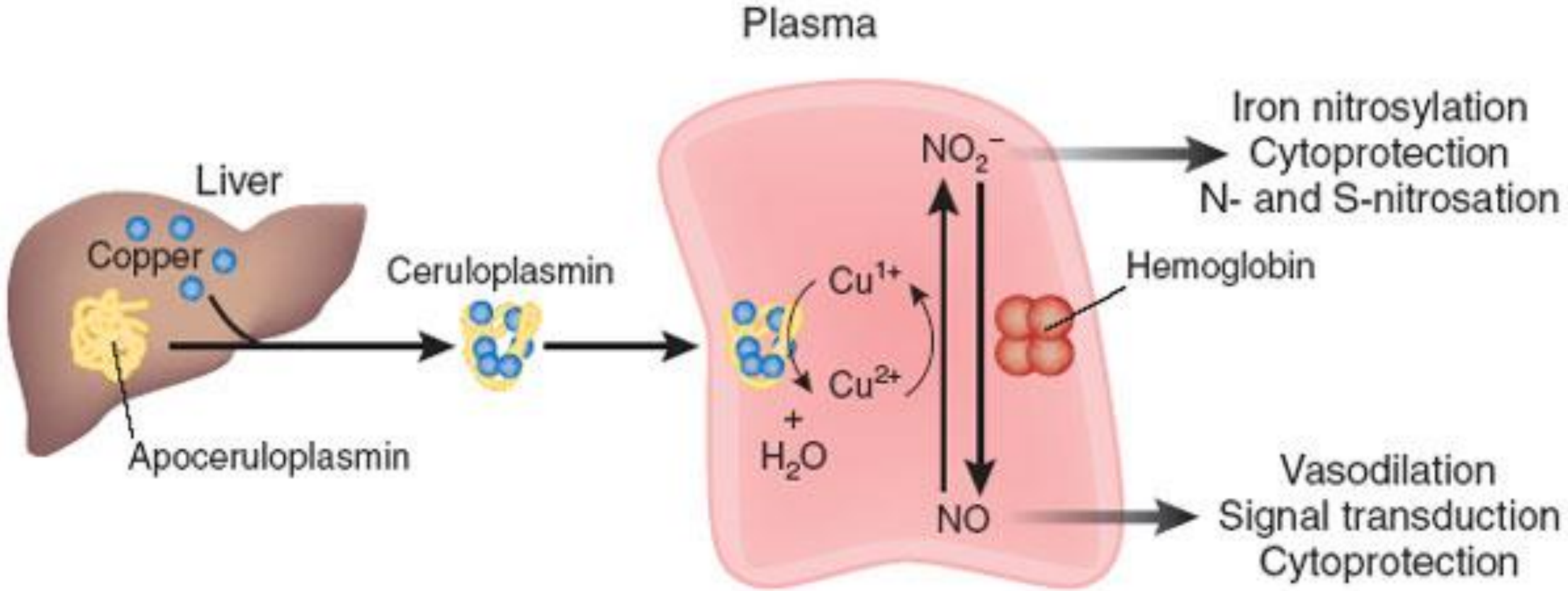
- Functions:
  - carries 90% of copper in plasma (copper – cofactor for a variety of enzymes)

    1 molecule binds 6 atoms of copper

    binds copper more tightly than albumin that carries other 10% of plasma copper ⇒ albumin may be more important in copper transport (donates copper to tissues more readily)




Dietary copper
Cu ~ 0.5-2.5 mg/day
Phase II
Blood
Cu ~ 6 mg
ORGANS
Copper in the blood:
65 - 95 % ceruloplasmin
Bile
Cu ~ 2.5 mg/day
Wilson
disease
duodeum
Secretory fluids
Cu ~ 2 mg/day
Small
Intestine
proximal
Phase I
Portal Circulation
Cu ~ 4.5 mg/day
Menkes
disease
distal
Feces
Cu ~ 0.5-2.5 mg/day

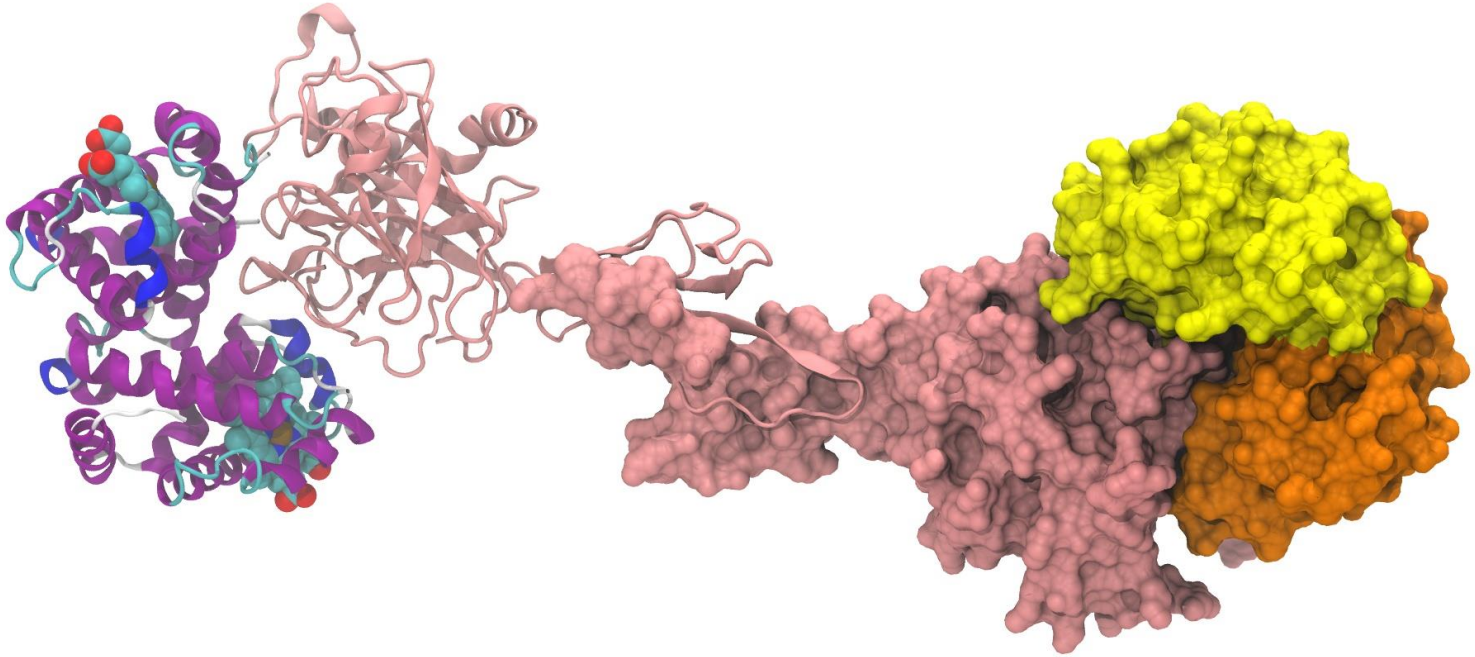


Copper is incorporated into ceruloplasmin during synthesis and is essential for oxidase activity. Within the plasma, ceruloplasmin catalyzes the oxidation of the signaling molecule NO concomitantly with cupric (Cu2+) to cuprous (Cu1+) reduction. Nitrite (NO2-) ions can therefore be used as a sink for NO production through reduction by deoxyhemoglobin, which allows for the mobilization of NO as a signaling molecule involved in hypoxic vasodilation and ischemia-reperfusion cytoprotection. In addition, nitrite acts independently as a signaling molecule necessary for cytoprotection and post-translational modifications such as iron nitrosylation and N-and S-nitrosation.

Haptoglobin (Hp)

- α_2- globulin, tetramer $\alpha_2\beta_2$ chains
- Exists in 3 polymorphic forms
- Functions:
  - binds free hemoglobin and delivers it to the reticuloendothelial cells
  - complex Hb-Hp is too large to pass through glomerulus $\Rightarrow$ prevention of loss of free Hb (and Fe)

  Free Hb passes through glomerulus, enters tubules and tends to precipitate therein $\Rightarrow$ kidney damage



Causes of Hp **increase**

- Hp belongs to APRs ⇒
  - inflammation, infection
  - injury
  - malignancies

Causes of Hp **decrease**

- Hemolytic anemia:
  - half-life of Hp = 5 days **X** of complex Hp-Hb = 90 min (the complex is being rapidly removed from plasma) ⇒ Hp levels fall when Hb is constantly being released from red blood cells (as in hemolytic anemias)

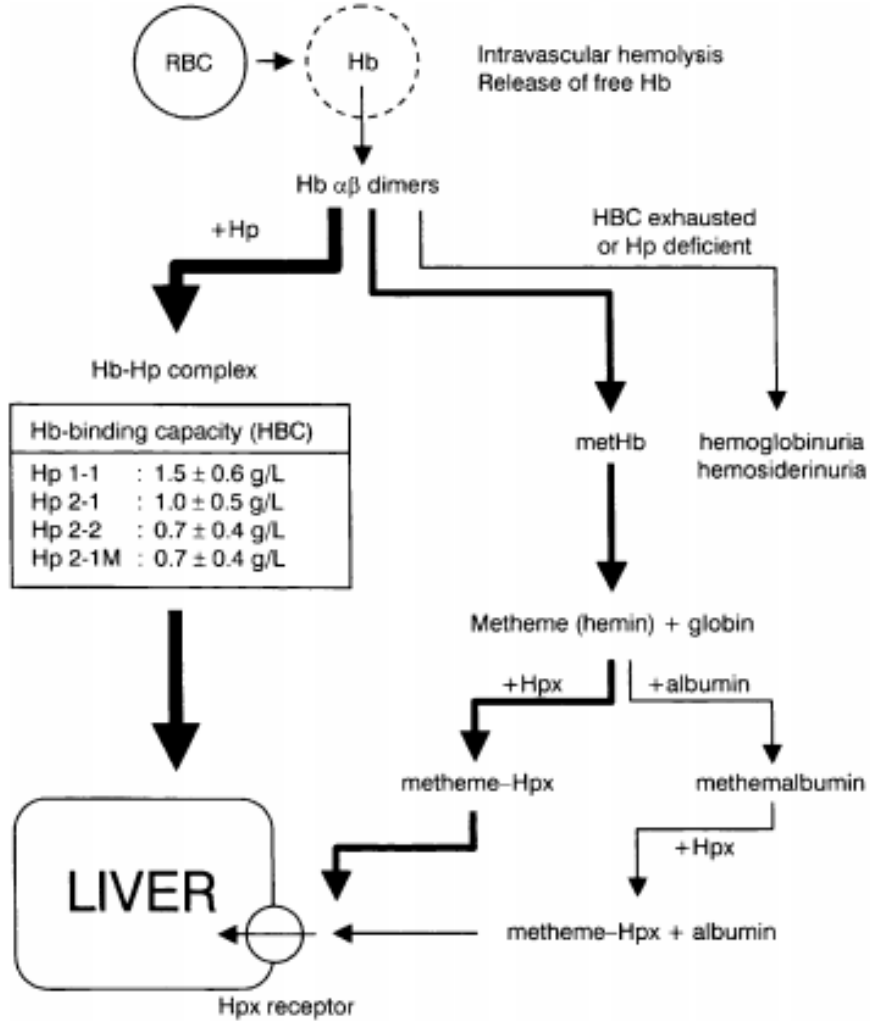


Fig. 2. Role of hemopexin in intravascular hemolysis. Initially, circulating Hp rapidly binds free Hb αβ dimers and is taken up by its hepatic receptor. HBC differs between Hp phenotypes. When HBC is exhausted, or in congenital Hp deficiency, circulating free hemin is bound by Hpx and transported to the hepatocytes by receptor-mediated endocytosis. Hpx also binds hemin bound to albumin. In massive hemolysis, free Hb passes through the glomeruli resulting in hemosiderinuria and hemoglobinuria.

Comparison between haptoglobin and hemopexin

	Hemopexin	Haptoglobin
Molecular mass (kDa)	60	Hp 1-1: 86 Hp 2-1: 86–300 Hp 2-2: 170–900
Reference range in adults (g/l)	0.4–1.5	0.3–2.0
Binding capacity	~ 6 mg/l heme	~ 1 g/l hemoglobin
Congenital deficiencies	Not described	Rare in Caucasians (1/1000) Common in blacks (up to 30%)
Plasma half-life (days)	7	5.4
Half-life of the complex	7–8 h	< 10 min
Recycled after complexation	Yes	No
Acute phase responsiveness	Low (↑)	High (↑ ↑ ↑)

Delanghe JR, Langlois MR: **Hemopexin: a review of biological aspects and the role in laboratory medicine.** ***Clinica Chimica Acta 2001, 312(1-2):13-23.***

Plasma proteins as antioxidants

Transferrin

Ferritin

Ceruloplasmin

Haptoglobin

Hemopexin (binds heme and transfers it to the liver)

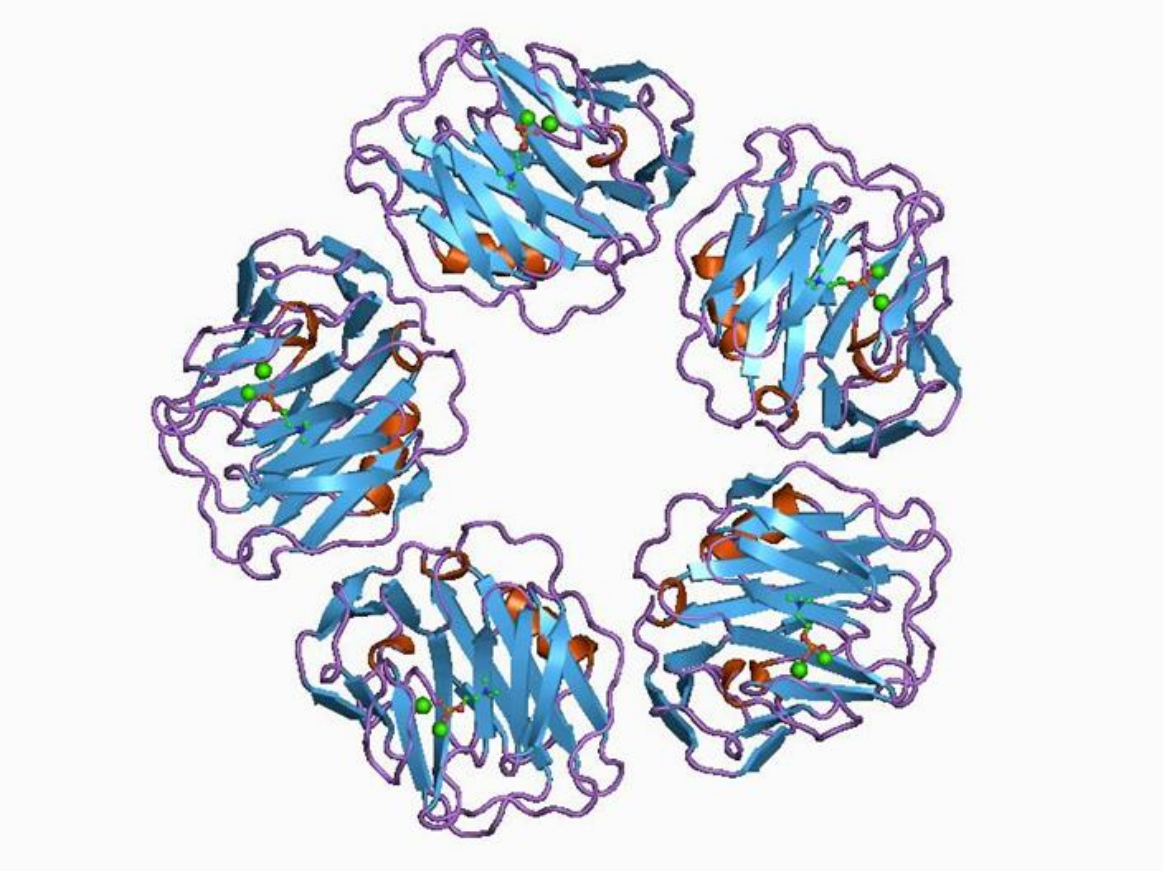
act as antioxidants:

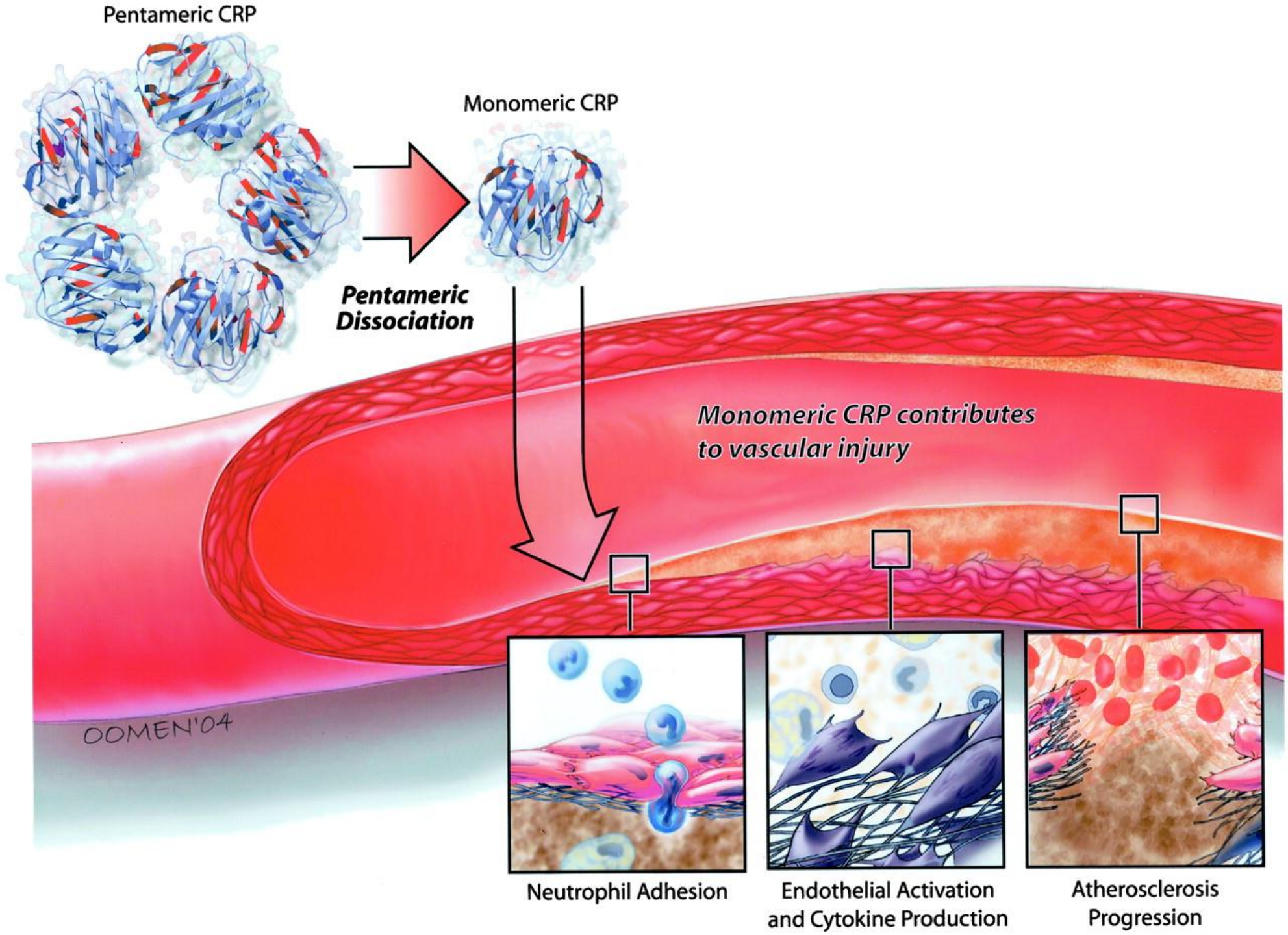
remove Fe^{2+} and thus prevent the Fenton reaction:

$$H_2O_2 + Fe^{2+} \rightarrow \mathbf{HO^{\bullet}} + OH^- + Fe^{3+}$$

C-reactive protein (CRP)

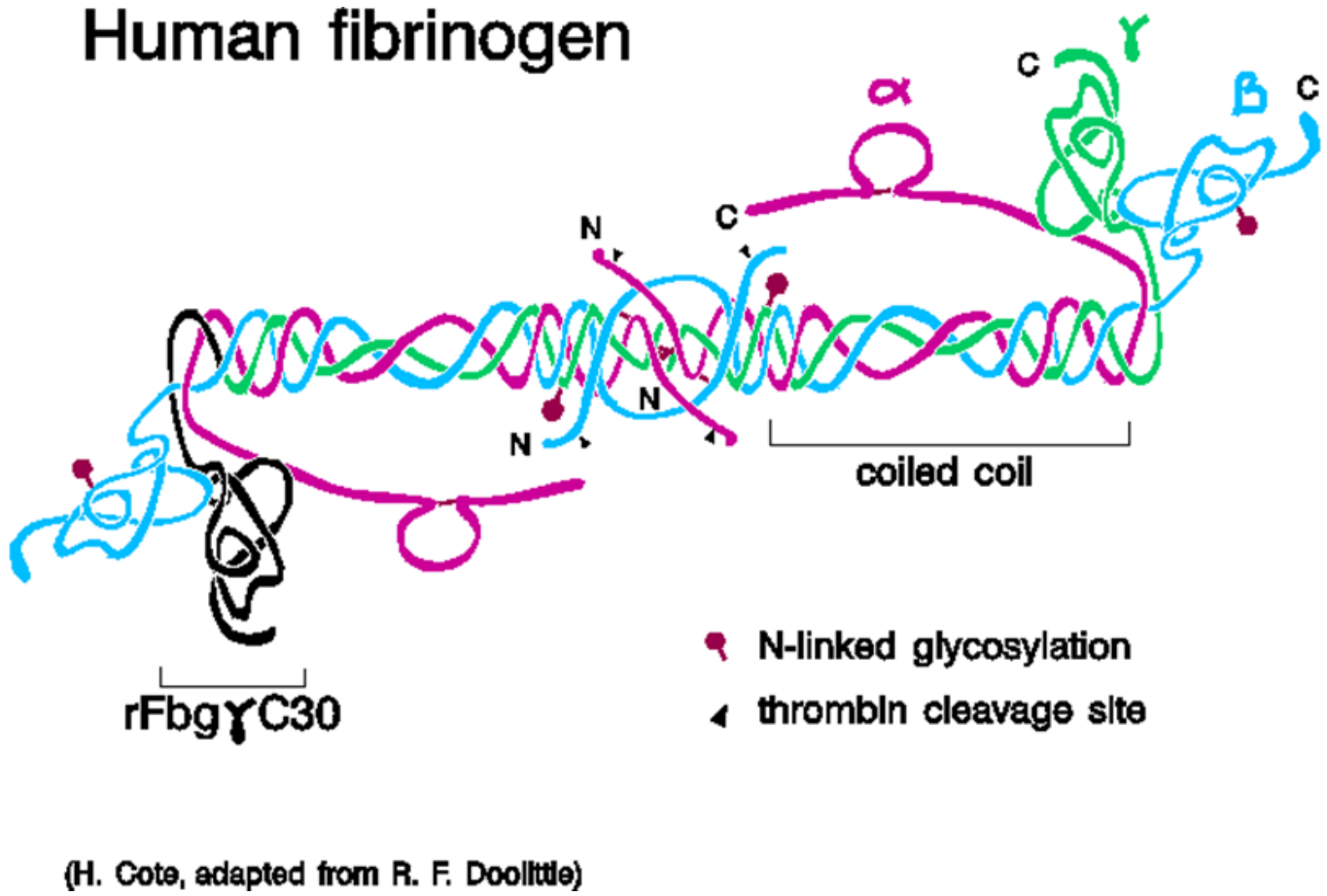
- Belongs to β_2-globulin, the levels of which rise in response to inflammation
- Acute-phase reactant
- Its physiological role is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria)
- plasma concentration levels of CRP rapidly increase within 2 hours of acute insult, reaching a peak at 48 hours (bacterial, viral, fungal infection, rheumatic diseases, malignity, tissue necrosis)




Pentameric CRP
Monomeric CRP
Pentameric Dissociation
Monomeric CRP contributes to vascular injury
OOMEN'04
Neutrophil Adhesion
Endothelial Activation and Cytokine Production
Atherosclerosis Progression

Fibrinogen

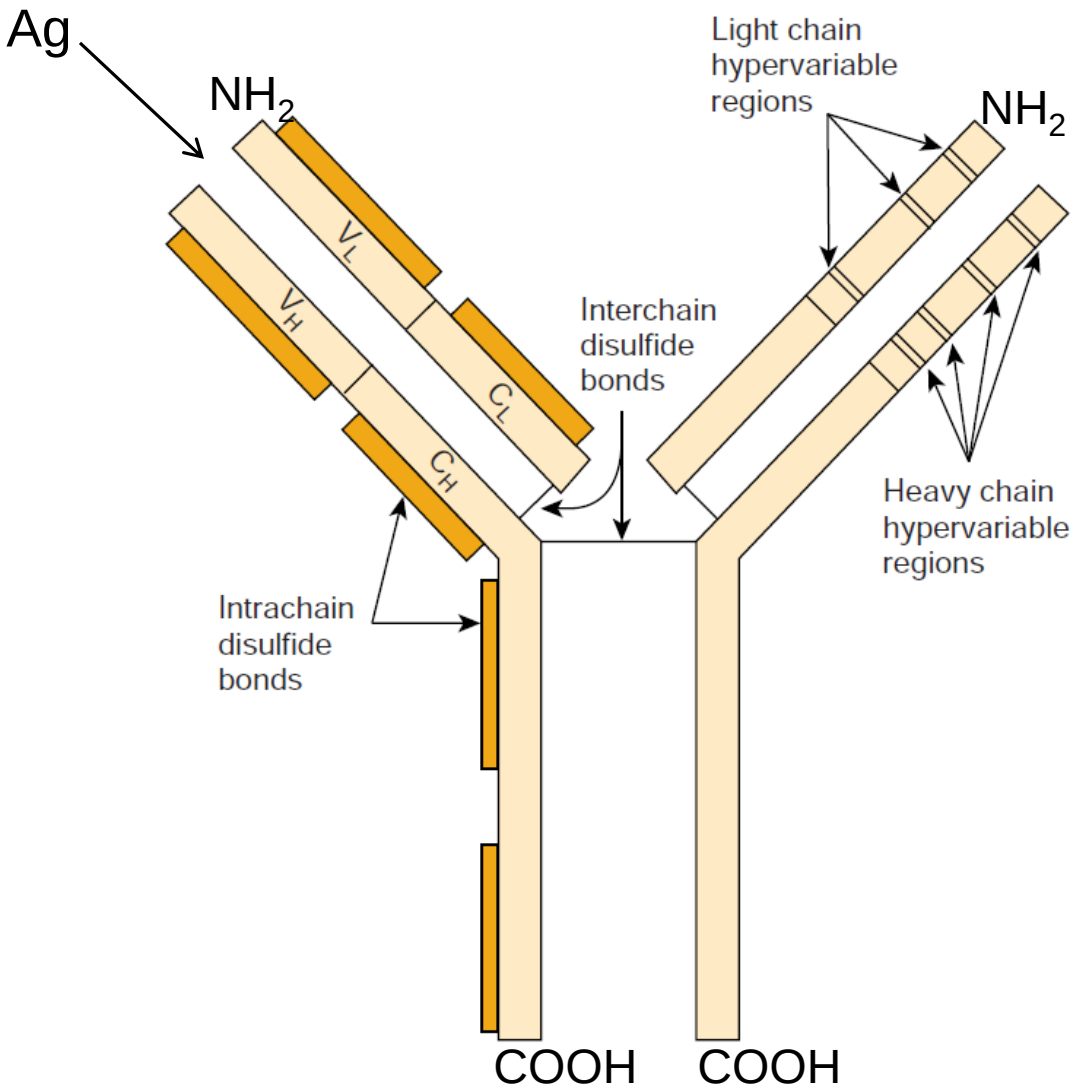
- Glycoprotein, belongs to β_2-globulins (Mr 340 000)
- Concentration in plasma - 1.5 – 4.5 g/l
- component of the coagulation cascade – fibrin precursor
- acute-phase reactant ⇒ ↑ acute inflammation



Immunoglobulins

- Antibodies produced by B cells in response to antigen stimulation of the organism
- React specifically with antigenic determinants

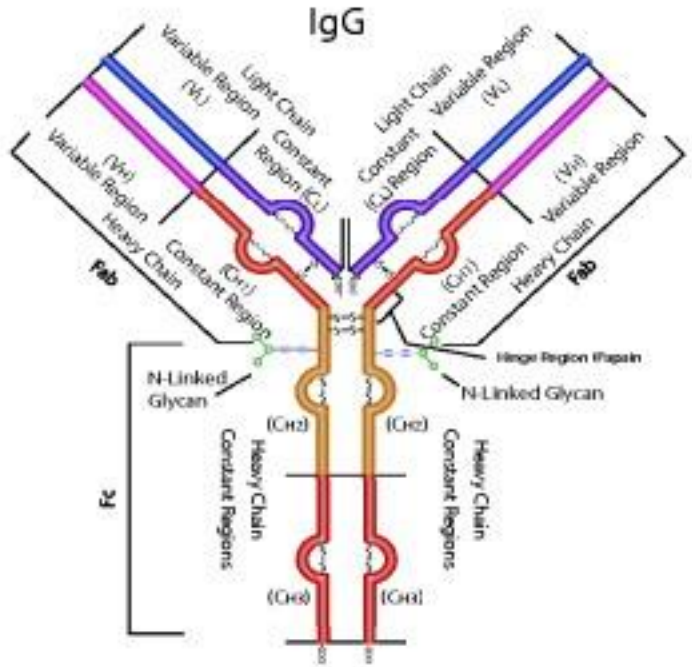
- Structure:
  - consist of a minimum of 4 polypeptide chains - 2 heavy (H) a 2 light (L) linked by disulfide bridges
    - light chains contain constant (C) and variable (V) region

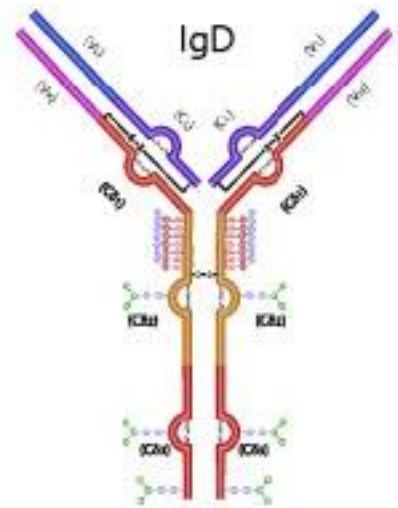


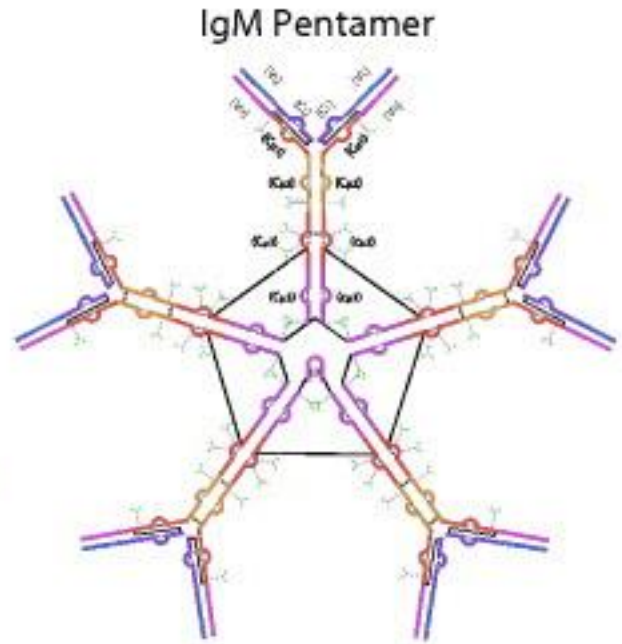
IgG

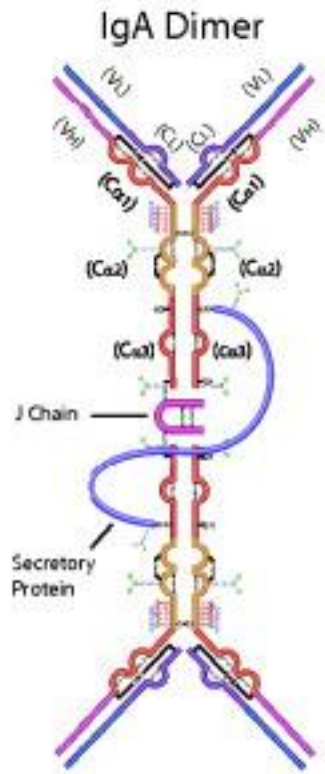
Table 43.1 The Five Classes of Immunoglobulins

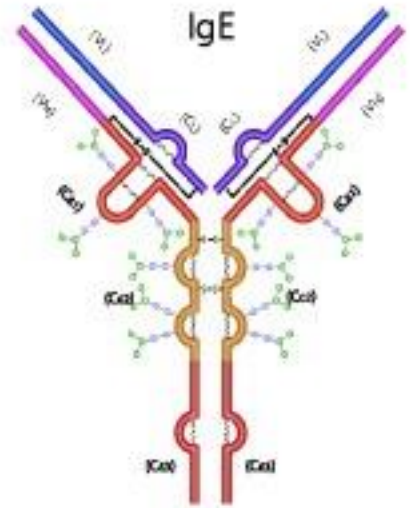
IgM (pentamer) 	IgMs are the first circulating antibodies to appear in response to an initial exposure to an antigen; their concentration in the blood then declines rapidly. Thus the presence of IgM usually indicates a current infection. IgM consists of five Y-shaped monomers arranged in a pentagonal structure. The numerous antigen-binding sites make it very effective in agglutinating antigens and in reactions involving complement. IgM is too large to cross the placenta and does not confer maternal immunity.
IgG (monomer) 	IgG is the most abundant of the circulating antibodies. It readily crosses the walls of blood vessels and enters tissue fluids. IgG also crosses the placenta and confers passive immunity on the fetus. IgG protects against bacteria, viruses, and toxins in the blood and lymph, and triggers action of the complement system.
IgA (dimer) 	IgA is produced by cells in mucous membranes. The main function of IgA is to prevent the attachment of viruses and bacteria to epithelial surfaces. IgA is also found in many body secretions, such as saliva, perspiration, and tears. Its presence in the first milk produced helps protect the infant from gastrointestinal infections.
IgD (monomer) 	IgD antibodies do not activate the complement system and cannot cross the placenta. They are mostly found on the surfaces of B cells, probably functioning as antigen receptors that help initiate the differentiation of B cells into plasma cells and memory B cells.
IgE (monomer) 	IgE molecules are slightly larger than IgG and represent only a small fraction of the antibodies in the blood. The tails attach to mast cells and basophils and, when triggered by an antigen, cause the cells to release histamine and other chemicals that cause an allergic reaction.











Plasma enzymes

1. Plasma specific enzymes:

   cholinesterase,

   plasma superoxid dismutase,

   lecithin-cholesterol acyltransferase,

   Serin proteases – inactive zymogens of coagulation factors and factors of fibrinolysis (faktor II - prothrombin, factor VII, IX, XIII) and complement system components, non-specific immune system (components C1 – C9).

Plasma enzymes (cont.)

Enzyma name	**abbreviation**	**Causes leading to increased levels**
Alanine aminotransferase	ALT	liver and biliary tract disease pancreatic disease decompensated heart defects
Aspartate aminotransferase	AST	liver diseases myokardium damage disease of skeletal muscle and myocardium
Alkaline phosphatase	ALP	liver and biliary tract disease bone diseases
Creatin kinase	CK	disease of skeletal muscle and myocardium
Lactate dehydrogenase	LD_{1-5}	Myocardium disease (LD_1, LD_2) and muscle disease hepatopathy
γ-glutamyl transferase	GMT	liver and biliary tract disease and pancreatic disease