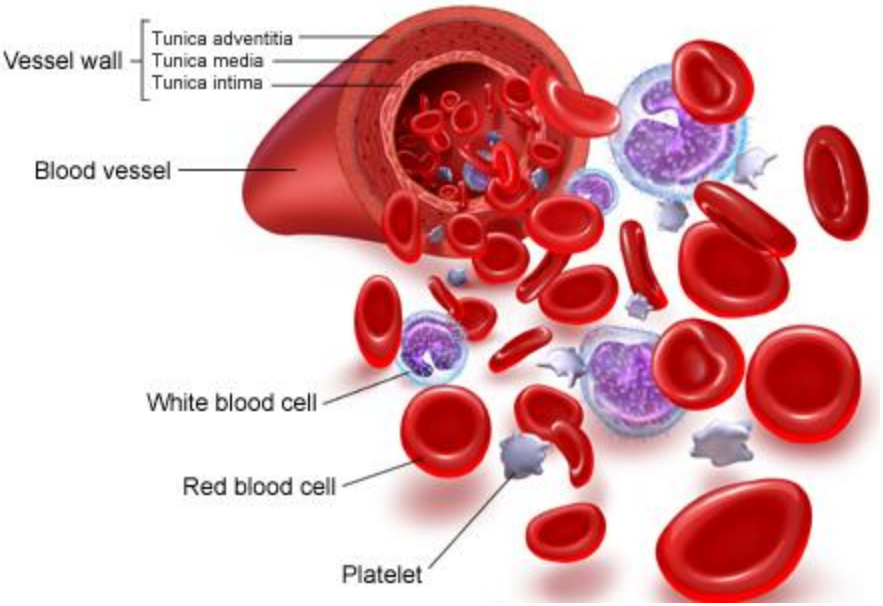
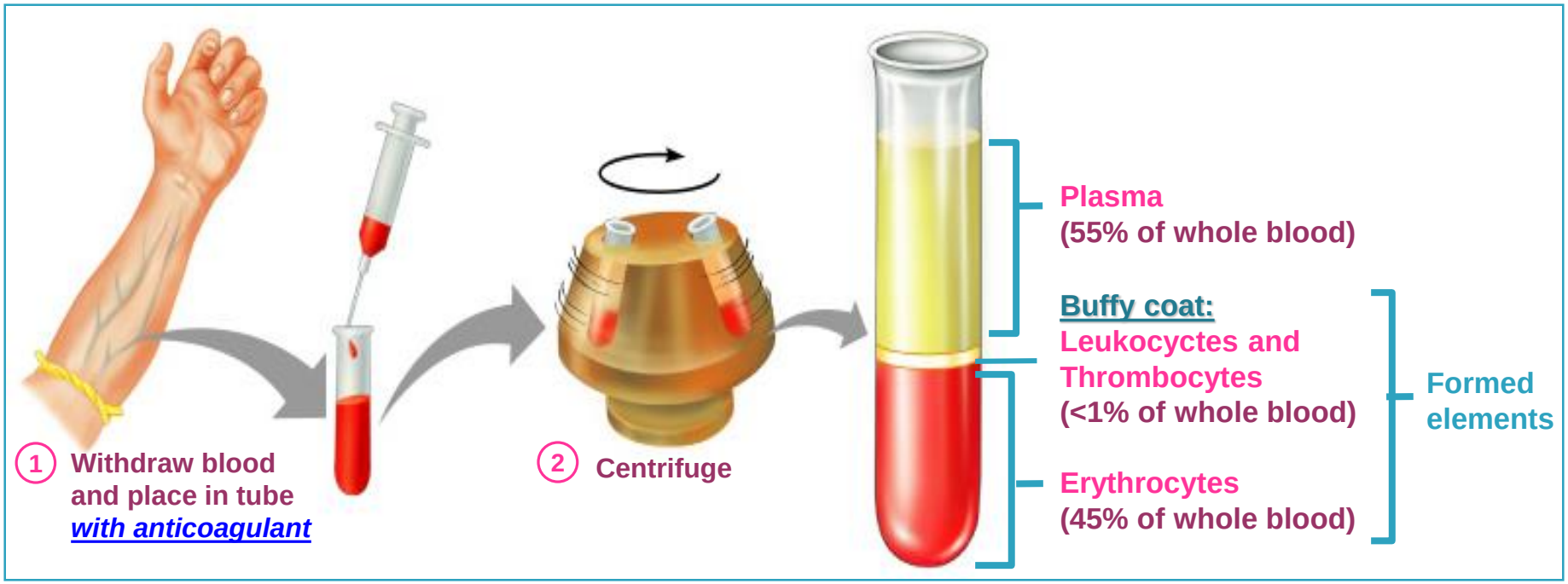
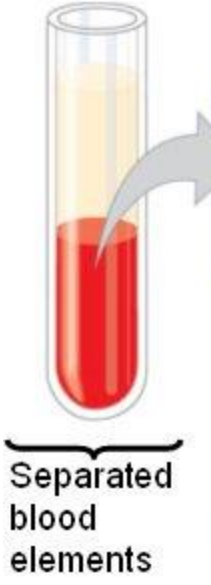


Components of Whole Blood

- Blood is a circulating tissue consisting of three types of cells suspended in a liquid known as **plasma**





Separated blood elements

Cellular elements 45%		
Cell type	**Number** per μL (mm^3) of blood	**Functions**
Erythrocytes (red blood cells)	5–6 million	Transport oxygen and help transport carbon dioxide
Leukocytes (white blood cells)	5,000–10,000	Defense and immunity
Platelets	250,000–400,000	Blood clotting

Basophil

Eosinophil

Lymphocyte

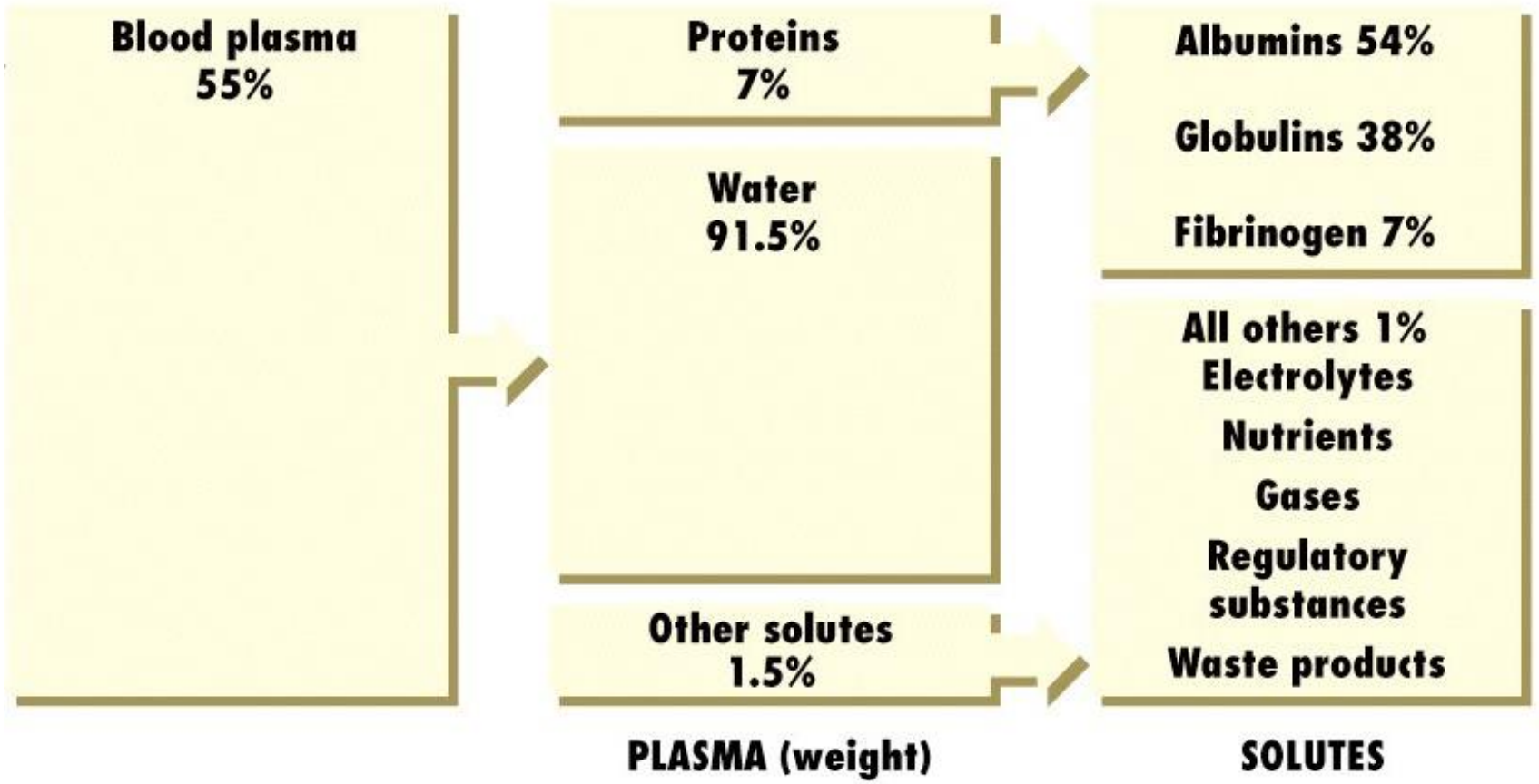
Neutrophil

Monocyte

(Macrophage in tissue)

Formed Elements

Blood plasma

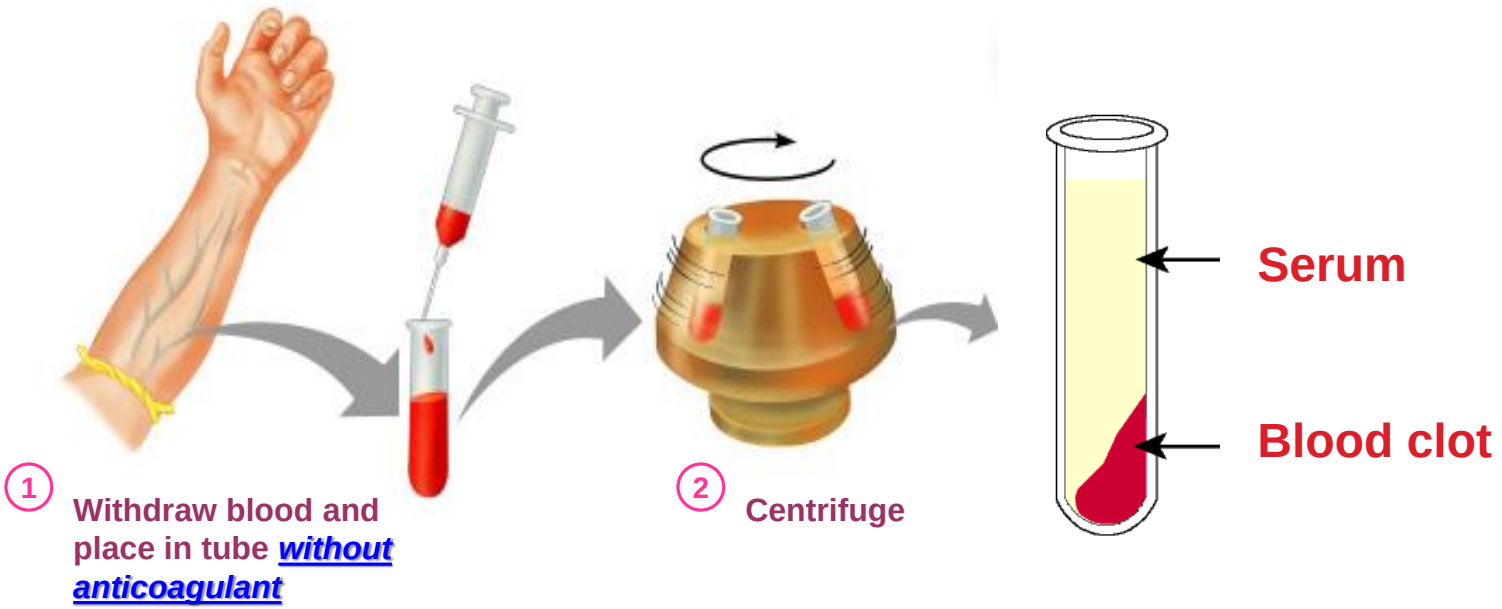


Includes over 100 different dissolved solutes

The Difference between Plasma and Serum

Serum is fluid left when blood clots

Serum = plasma – clotting factors



Physical Properties of Blood

- **Blood volume** – 4-6 liters depending on sex, size and age (~8% of Total Body Weight).

[Infants have a larger blood volume in proportion to body weight than adults].

- **pH** – slightly alkaline 7.35 – 7.45; venous blood will have a lower pH because it has a higher concentration of CO_2.
- **Color** – arterial blood is bright red and venous blood is dark red.
- **Viscosity**– 5-6 times that of water

Functions of Blood

Transportation

- Gases
- Nutrients
- Waste products
- Hormones
- Metabolites

Regulation

- **pH:** by using blood proteins and blood solutes alkaline reserve of bicarbonate ions
- Water balance
- Electrolytes balance
- Temperature

Protection

- **Immune system:** Protect against infections by WBCs and antibodies
- **Clot formation** Preventing blood loss by platelets and fibrinogen

Complete Blood Count (CBC)

- Panel of tests that examine different components of the blood.

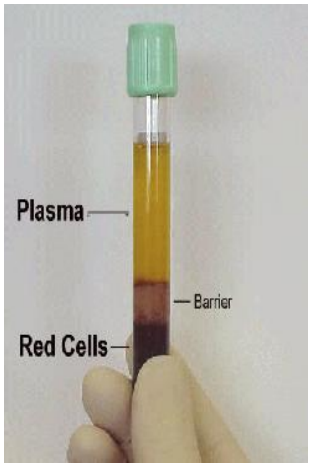
- **CBC values**:
  - **RBC count :** Actual number of RBC/ blood volume
  - **Hemoglobin (Hb):** Amount of the oxygen carrying protein in the blood
  - **WBC count:** Actual number of WBC/ blood volume
  - **WBC differential:** Types of WBC present
  - **Platelets (PLT):** actual number of PLT/Blood volume

Complete Blood Count (CBC) (cont…)

- **CBC values**:
  - **RBC indices**
    - **Mean Corpuscular Volume (MCV):** a measurement of the average size of RBCs
    - **Mean Corpuscular Hemoglobin (MCH):** the average amount of oxygen-carrying hemoglobin inside a RBC
    - **Mean Corpuscular Hemoglobin Concentration (MCHC):** the average concentration of hemoglobin inside a RBC
    - **Red Cell Distribution Width (RDW):** a variation in the size of RBCs

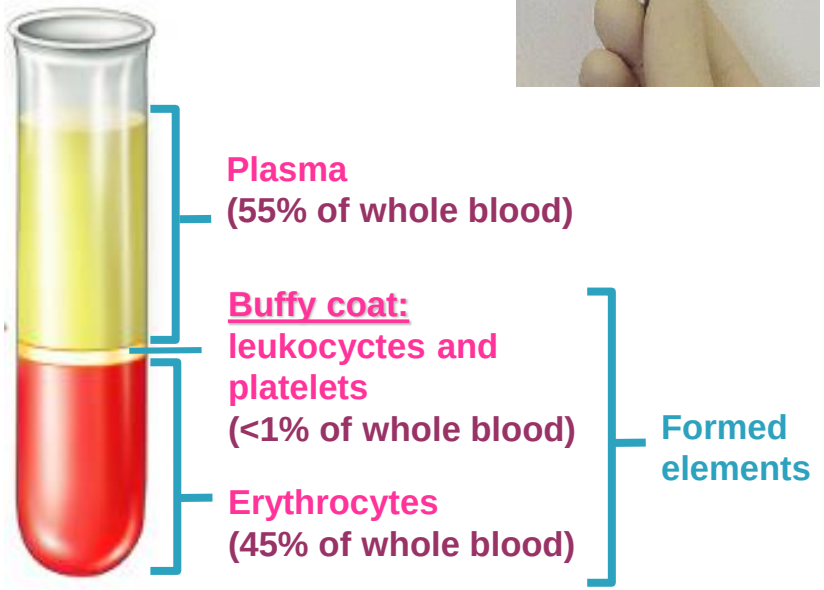
- **CBC values**:
  - **Hematocrit:** The fraction of the blood volume comprised of RBCs.

$$HCT = \frac{\text{volume of RBCs}}{\text{Total volume of blood}}\ x\ 100$$



Normal values

- Males 47% +/- 5%
- Females 42% +/- 5%



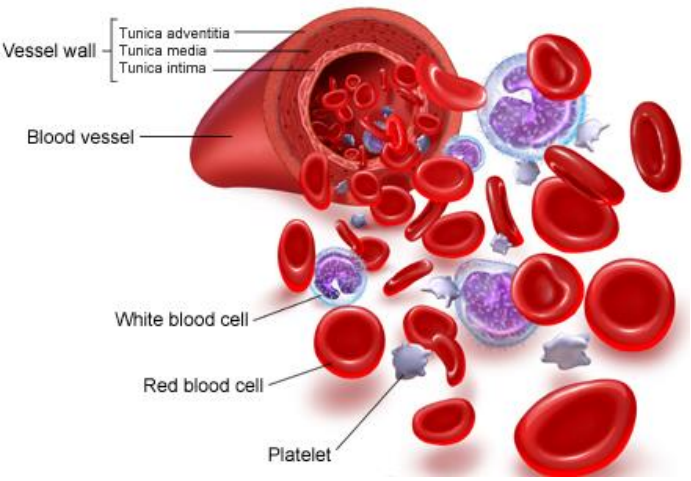
The significance of CBC

- Find the cause of symptoms such as fatigue, weakness, fever, bruising, or weight loss
- Diagnosis of anemia
- Estimation of blood loss
- Find an infection
- Diagnosis of blood diseases as leukemia
- Response to drug or radiation treatment
- Screening before surgery

The Complete Blood Cell Count

Parameter	Normal adult range	Indications
Hemoglobin	Male: 14.0 – 17.4 mg/dL Female: 12.0 – 16.0 mg/dL	Low: Anemia High: Polycythemia
Hematocrit	Male: 42% – 52% Female: 35% – 48%	Low: Anemia High: Polycythemia
RBC count	Male: 4.5 – 5.5 x 10^6/µL Female: 4.0 – 5.0 x 10^6/µL	Low: Anemia High: Polycythemia
WBC count	5.0 – 10.0 x 10^3/µL	Low: Leukopenia High: Leukocytosis
Platelet count	140 – 400 x 10^3/µL	Low: Thrombocytopenia High: Thrombocytosis
Reticulocyte count (immature RBCs)	0.5% – 1.5% 25 – 85 x 10^3/µL	Low in anemia: Low marrow output High: RBC loss
MCV	80-100 fL	
MCH	27-31 pg	
MCHC	32-36%	
RDW	11.5-14.5%	

Data extracted from: Fischbach FT. *A Manual of Laboratory and Diagnostic Tests.* Philadelphia, Pa: Lippincott Williams & Wilkins; 2003:47.



Plasma Proteins

General properties of plasma proteins

- Almost all of them are **glycoproteins** except albumin
- They have characteristic half-life in the circulation (albumin – 20 days)
- Many of them exhibit **polymorphism** (immunoglobulins, transferrin…)

General properties of plasma proteins

- Most are synthesized in the liver

  Exception: γ-globulins – synthesized in plasma cells

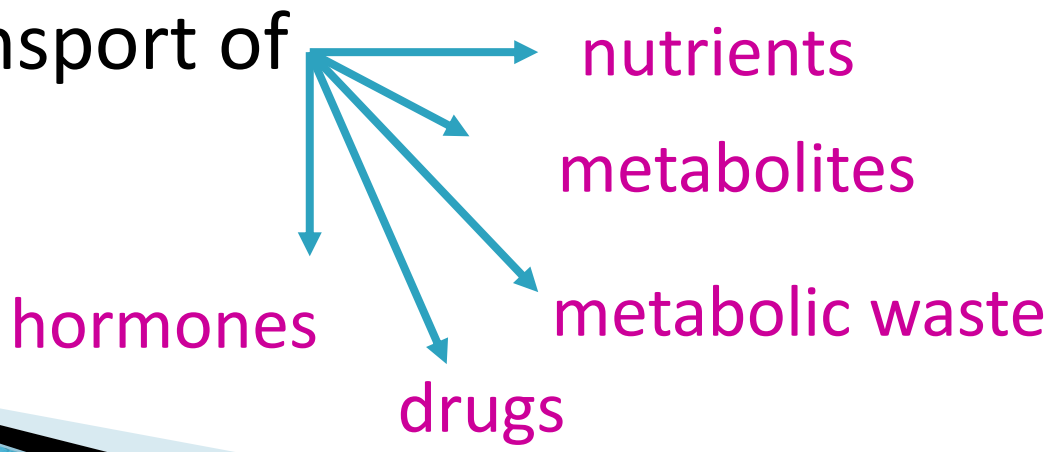
- Synthesized as pre-proteins on membrane-bound polyribosomes; then they are subjected to posttranslational modifications in ER and Golgi apparatus

Catabolism of plasma proteins

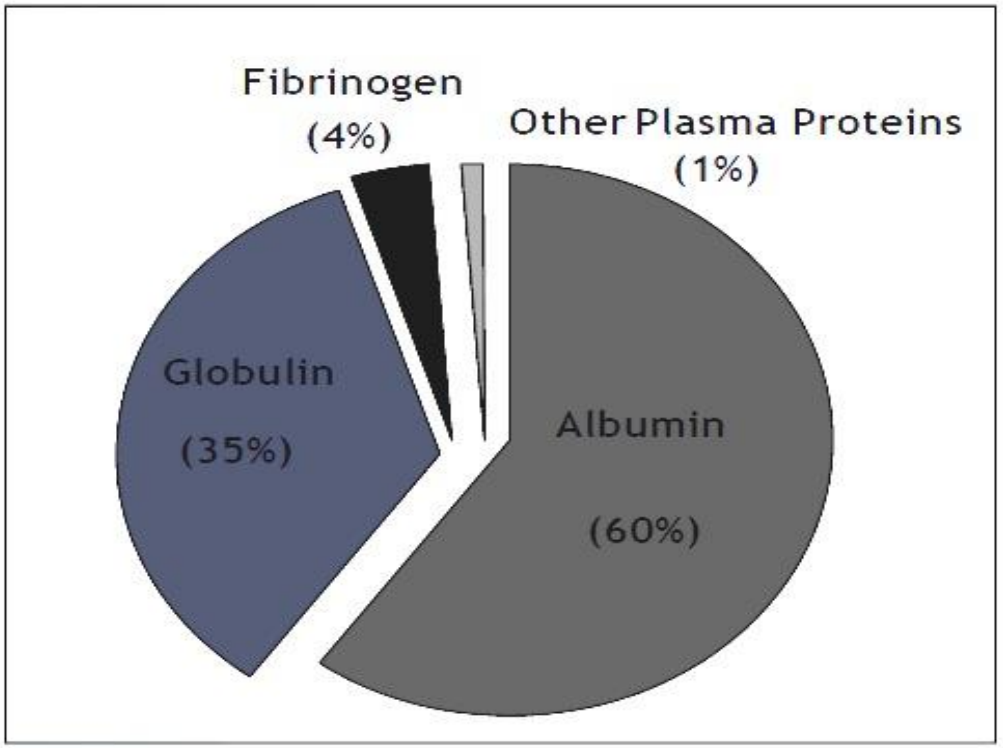
- Plasma proteins circulate not only inside the vascular system but also across the capillary bed into the interstitial fluid and back into the plasma through lymphatic vessels
- Tissue macrophages take up albumin by pinocytosis
- Albumin is broken down within the lysosomes of tissue macrophages to amino acids

Plasma proteins participate in:

1. Blood coagulation
2. Maintenance of homeostasis (pH, osmotic pressure)
3. Defence against infection
4. Transport of



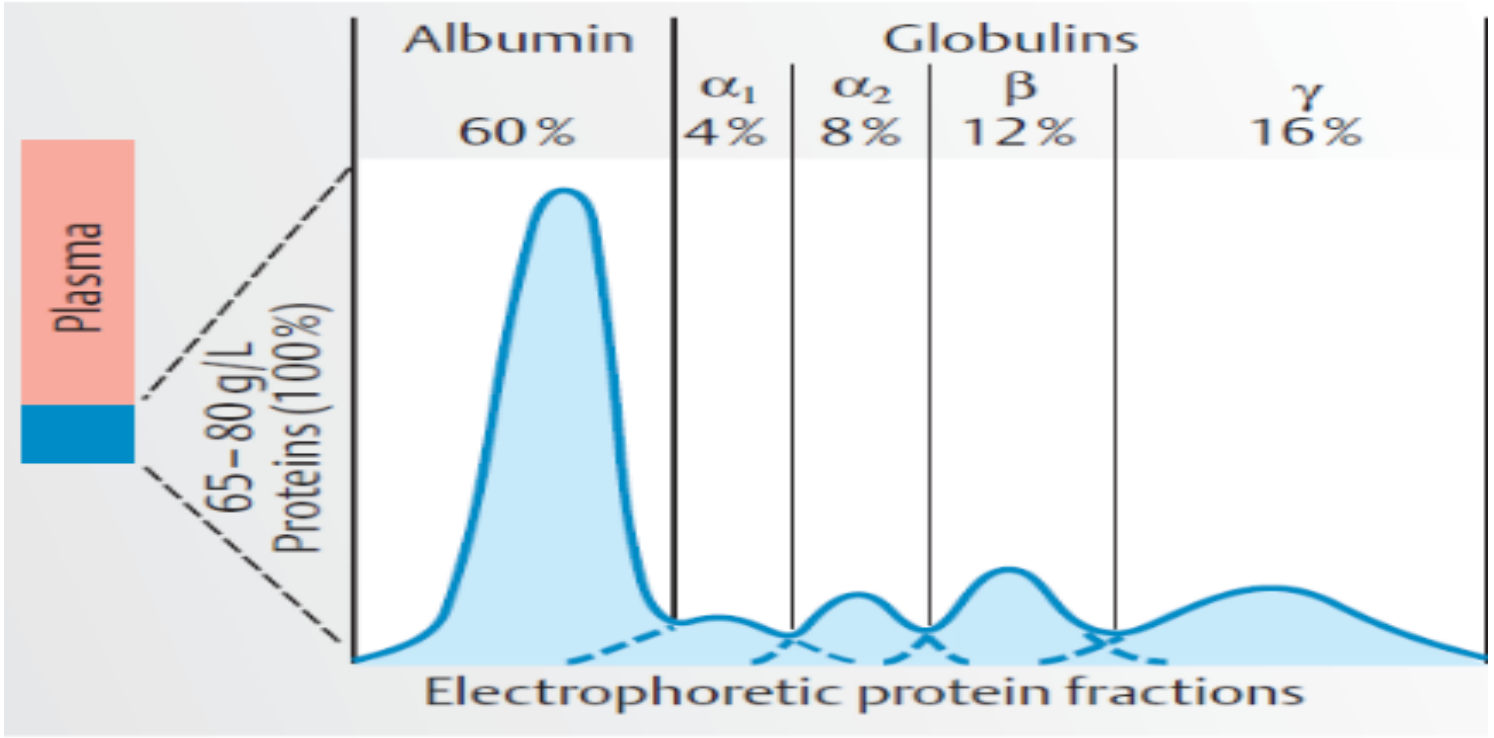
Plasma protein distribution

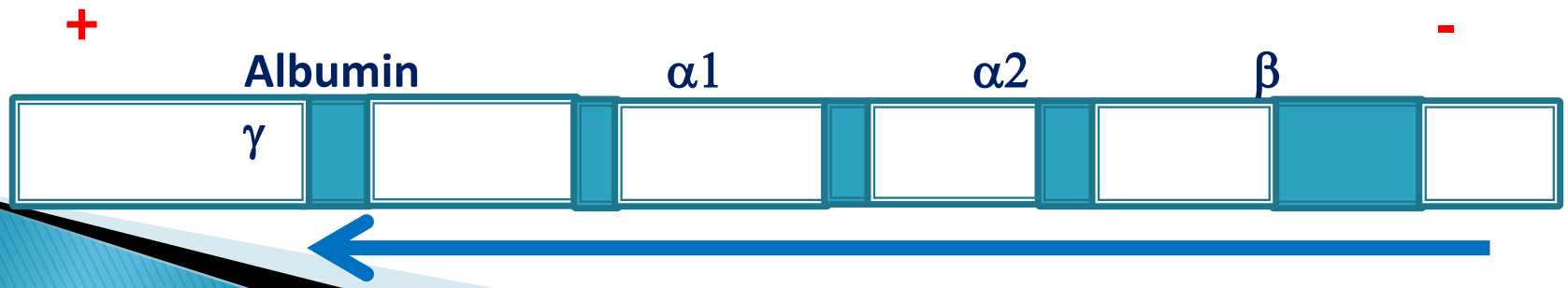


Fractions of plasma proteins

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), 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
Fibrinogens	~ 4	2 - 4.5

Electrophoresis pattern for normal serum proteins





Albumin

- It has the lowest molecular weight of almost of plasma proteins
- Liver produces about 12g albumin per day (25% of total hepatic protein synthesis and 50% of secreted protein)
- Half-life: 20 days
  - For this reason, measurement of serum albumin concentration is used to assays liver function test

Functions of Albumin

1. **Maintenance of the osmotic pressure of plasma**
   - It gives a much greater osmotic effect at the pH 7.4 of blood
   - Is responsible for about 75- 80 % of the osmotic effect of plasma because:
     - It constitutes slightly> half the plasma proteins by weight
     - It has the lower molecular weight of the major plasma proteins.

Functions of Albumin

2. **Transport:** It can bind and transport many diverse molecules and serve as low-specificity transport protein, which include:
   - free fatty acids
   - steroid hormones
   - bilirubin
   - drugs (sulfonamides, aspirin)
   - Ca^{2+}, Cu^{2+}

Causes of Albumin Deficiency

- Liver diseases (cirrhosis) – decrease in the ratio of albumin to globulins
- Protein malnutrition
- Excessive excretion by kidneys (renal disease) (**proteinuria**)
- Mutation causing **analbuminemia** (little or no circulating albumin)
  - There will be a reduction in osmotic pressure, leading to enhanced fluid retention in tissue spaces (edema).

Transferrin

- Beta globulin
- Concentration in plasma: 3 g/l
- **Functions:**

1. **Transport of iron**: from catabolism of heme and from food (gut) to the sites where iron is required, i.e. to the bone marrow and other organs
2. 2 moles of **Fe^{3+}** per 1 mole of transferrin

Causes of transferrin deficiency:

- Burns
- Infections
- Malignancies
- Liver and kidney diseases
- Pregnancy

Ferritin

- Intracellular protein; only small portion in plasma
- **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.

Ceruloplasmin

- α2-globulins
- 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 copper

    $\Rightarrow$ Albumin may be more important in copper transport (donates copper to tissues more readily)

Causes of ceruloplasmin deficency

- **Liver diseases**, in particular **Wilson´s disease**:
  - **Genetic disease** in which copper fails to be excreted into the bile and accumulates in liver, brain, kidney, and red blood cells
  - **Cause:** mutations in the gene encoding for copper-binding ATPase
  - **Consequences:** accumulation of copper in liver, brain, kidneys… ⇒ liver disease, neurologic symptoms

Causes of ceruloplasmin increase

- Inflammatory states
- Carcinomas, leukaemia
- Rheumatoid arthritis

Haptoglobin

- α_2- globulin, tetrameric
- **Functions:**
  - **binds free hemoglobin** and delivers it to the reticuloendothelial cells
  - **complex Hb-Hp** is too large to pass through glomerulus

    ⇒ prevention of loss of free Hb in the urine

    ⇒ kidney damage

Causes of Hp increase

- Inflammation, infection
- Injury
- Malignancies

Causes of Hp decrease

- **Haemolytic anaemia**

  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 haemolytic anaemia)

Hemopexin

- β-globulins
- Binds free heme and transfers it to the liver

$\Rightarrow$ prevent its urinary excretion

transferrin
ferritin
ceruloplasmin
haptoglobin
hemopexin

act as antioxidants: remove Fe^{2+} (iron) and thus **prevent the Fenton reaction**:

$$H_2O_2 + Fe^{2+} \rightarrow Fe^{3+} + \underbrace{OH\cdot}_{\text{Free radicals}} + OH^-$$

Free radicals

↓

Oxidative stress
cellular damage
eventual cellular death

α1- Antitrypsin

- A glycoprotein with 394 a.a (52 kDa)
- Synthesized by hepatocytes and macrophages
- Major component (>90 %) of the α_1-fraction
- Highly polymorphic, the most common is M type
- **Function:** principal **plasma inhibitor of serine protease** (inhibits trypsin, elastase)

α1- Antitrypsin

- Genetic deficiency of α1-Antitrypsin
  - Synthesis of the defective α1-Antitrypsin occurs in the liver but it cannot secrete the protein
  - α1-Antitrypsin accumulates in hepatocytes and is deficient in plasma

α1- Antitrypsin

- Deficiency has a role in **emphysema** – proteolytic damage of the lung
- Methionine involved in antitrypsin (AT) binding to proteases is oxidized by smoking

  ⇒ AT no longer inhibits proteases

  ⇒ increased proteolytic damage of the lung, particularly devastating in patients with AT-deficiency

α1 Fetoglobulin(AFP)

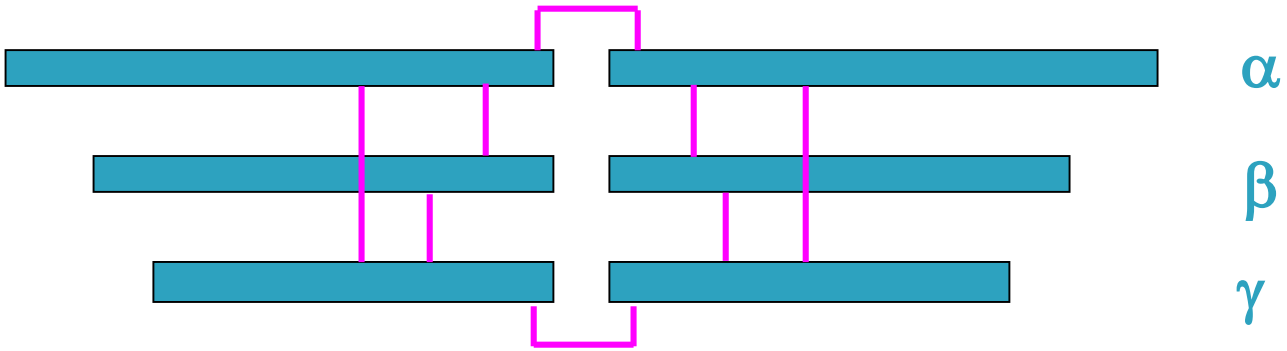
- Major protein in the human fetal plasma and amniotic fluid (glycoprotein)
- AFP levels decrease gradually during intra-uterine life and reach adult levels at birth
- Very low amounts in adults
- Function is unknown but it may protect fetus from immunologic attack by the mother or has same function of albumin in adult
- Sequences of fetoglobulin and albumin are homologous

α1 Fetoglobulin(AFP)

- Elevated maternal AFP levels are associated with:
  - Neural tube defect, anencephaly
- Decreased maternal AFP levels are associated with:
  - Increased risk of Down's syndrome
- AFP is a tumor marker for:
  - Hepatoma and testicular cancer

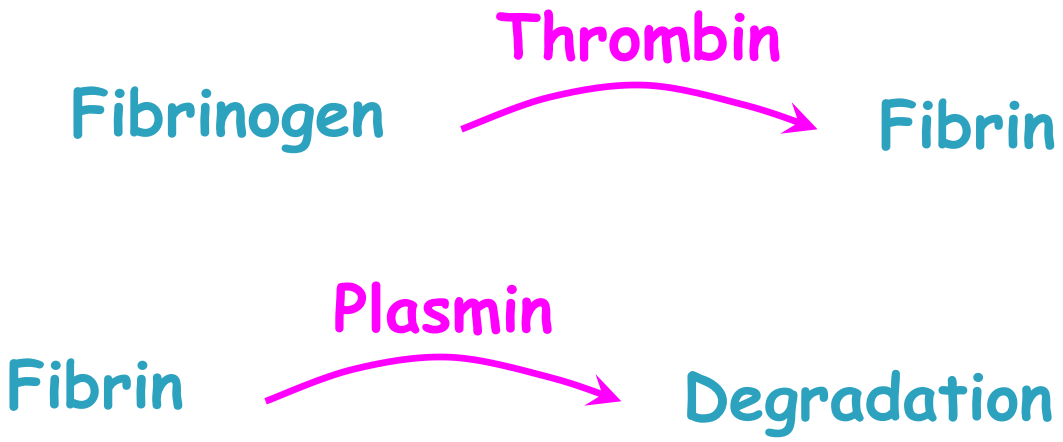
Fibrinogen

- Structure
  - MW 340 000
  - 6 polypeptide chains, 2α (67,000), 2β (56,000), 2γ (47,000)



Fibrinogen

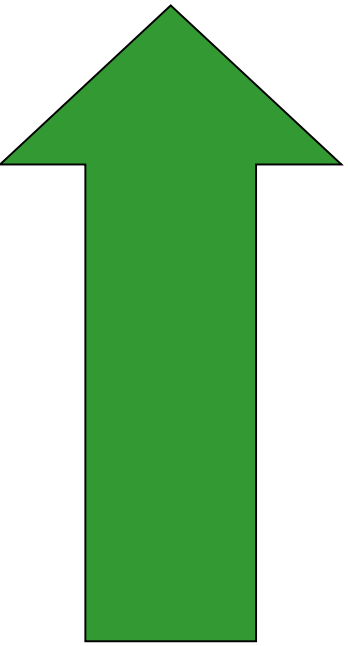
- **Function**
  - Blood coagulation (clotting)



Acute phase reactants (APRs)

- Class of proteins whose plasma levels change (increase or decrease) during **acute inflammatory response**
- APRs concentration changes in:
  1. infection
  2. surgery
  3. injury
  4. cancer

Types of APRs



Positive

α1-antitrypsin

C-reactive protein (CRP): ~1000-fold increase!

fibrinogen

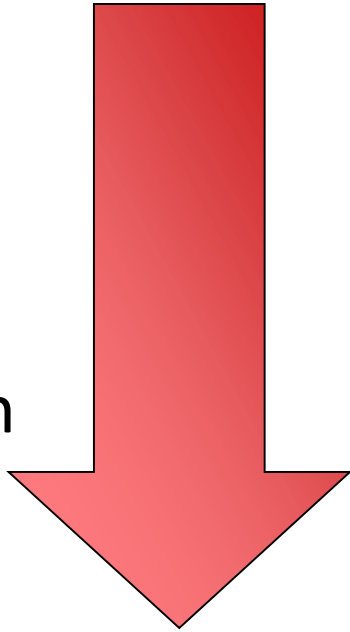
haptoglobin (HP)

C3, C4

Negative

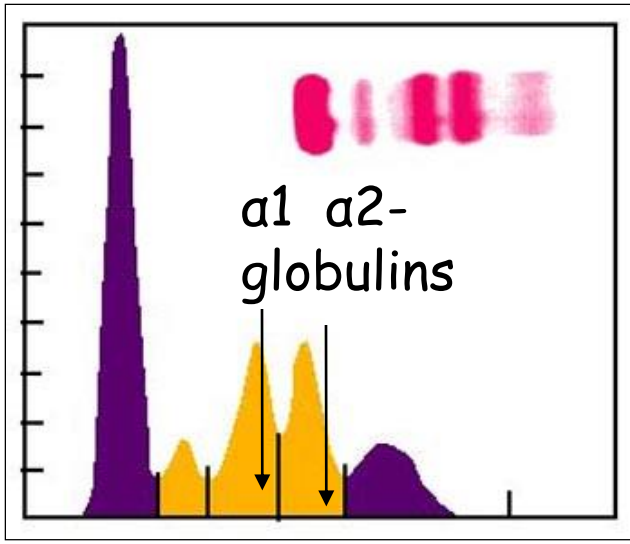
albumin

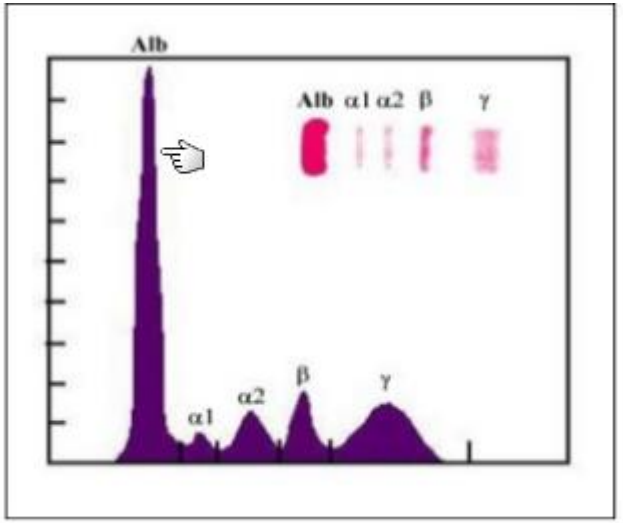
transferrin



Acute inflammatory response

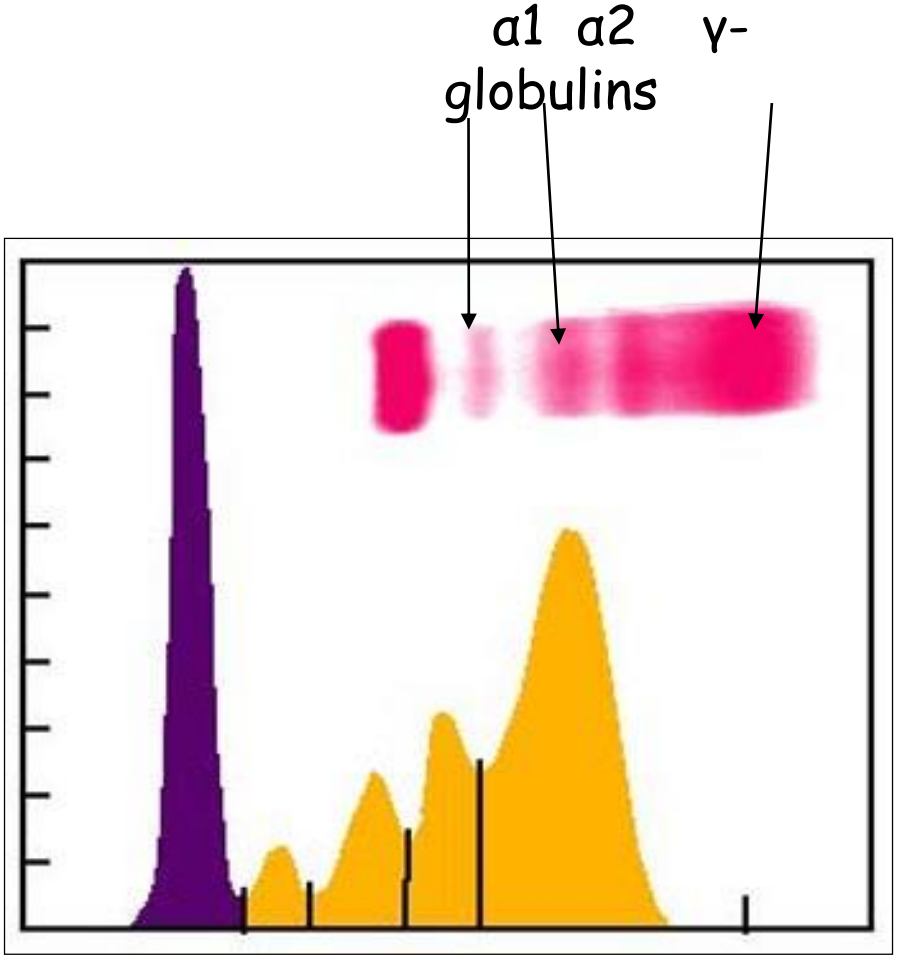
- Immediate response occurs with stress or inflammation caused by infection, injury or surgical trauma
  - Normal or ↓ albumin
  - ↑ α1 and α2 globulins





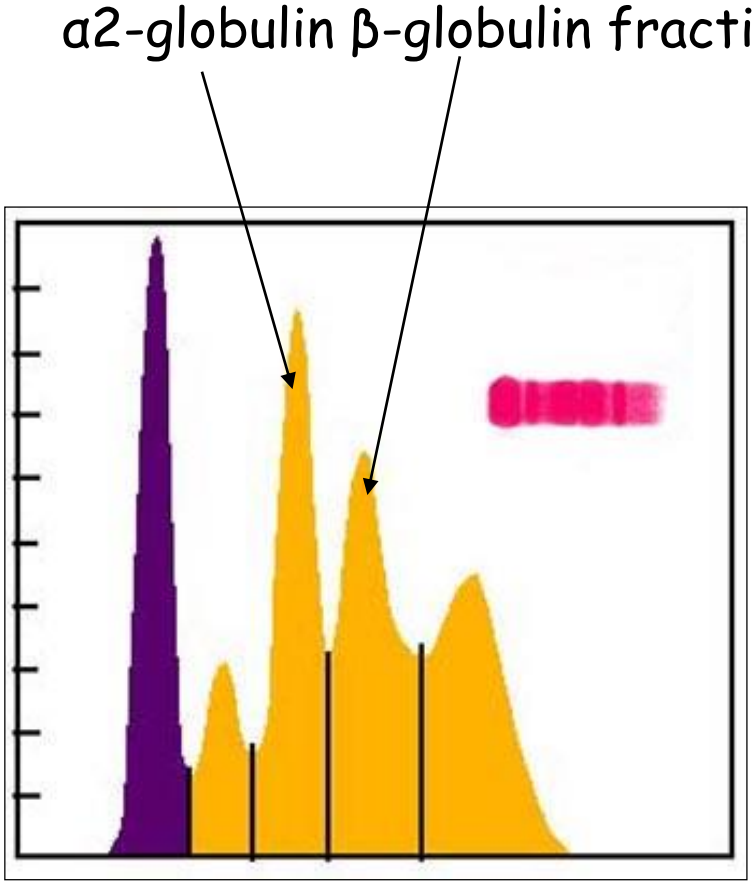
Chronic inflammatory response

- Late response is correlated with chronic infection (autoimmune diseases, chronic liver disease, chronic infection, cancer)
  - Normal or ↓ albumin
  - ↑α1 or α2 globulins
  - ↑↑ γ globulins



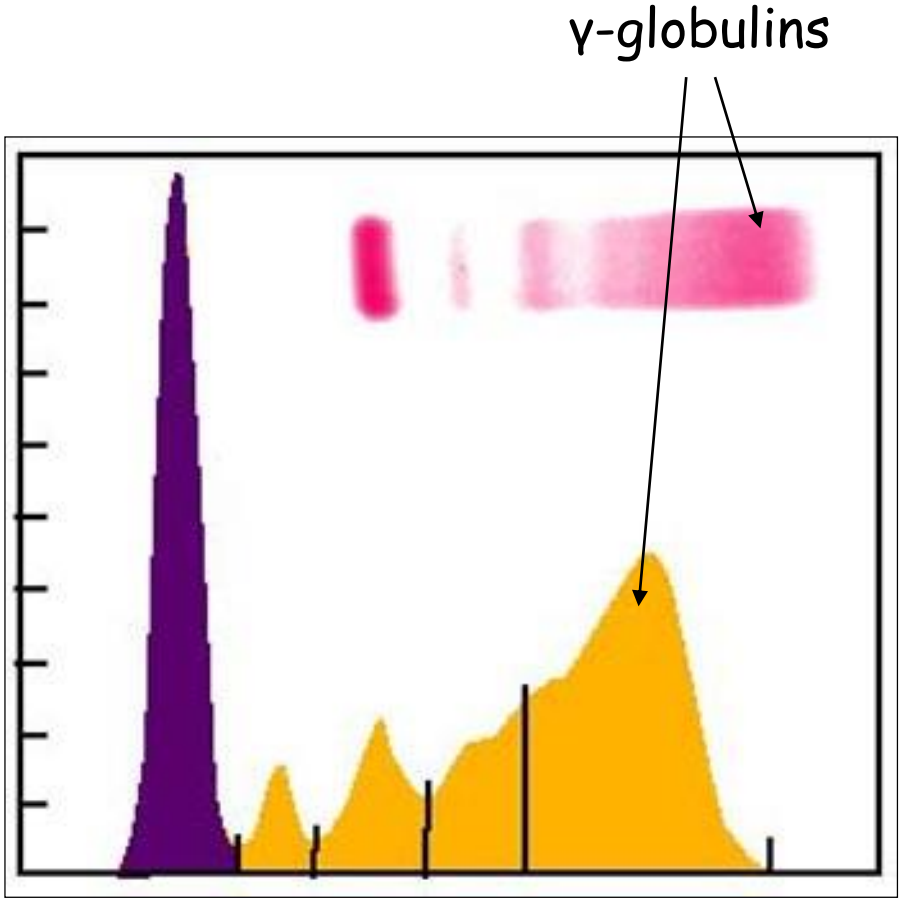
Nephrotic syndrome

- The kidney damage illustrates the long term loss of lower molecular weight proteins
  - ↓ albumin and IgG – they are filtered in kidney
- Retention of higher mwt proteins
  - ↑↑ α2-macroglobulin and ↑β-globulin)



Liver damage - Cirrhosis

- Cirrhosis can be caused by chronic alcohol abuse or viral hepatitis
  - ↓ albumin
  - ↓ α1, α2 and β globulins
  - ↑ Ig A in γ-fraction



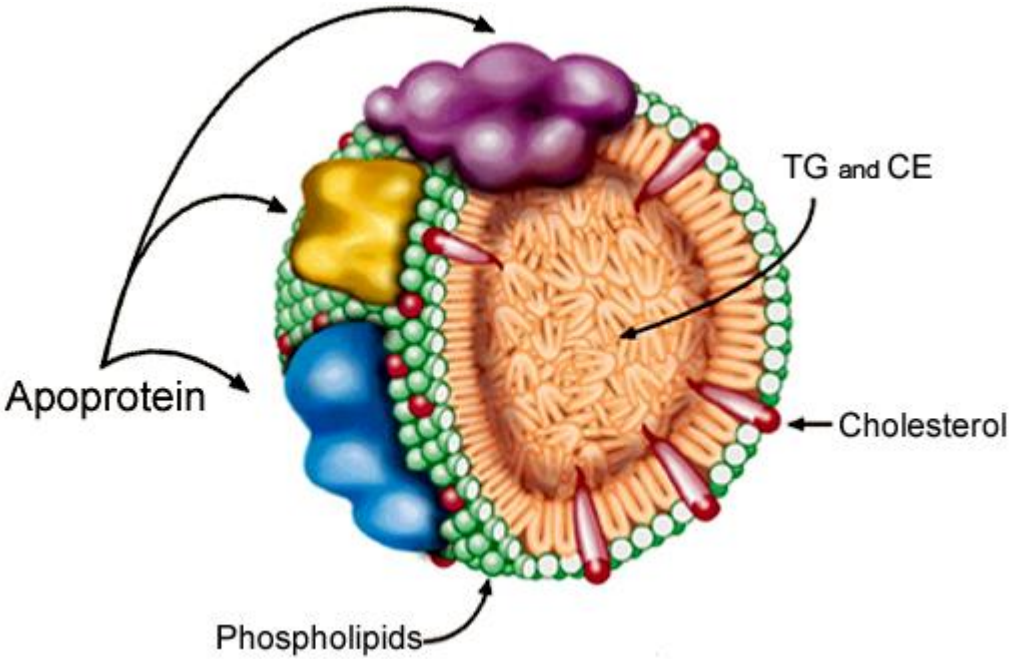
Lipid transport in blood

- The plasma lipoprotein are spherical macromolecular complex of lipids and specific proteins (apolipoproteins)

- Lipoproteins function both to keep their component lipid soluble as they transport them in the plasma (to and from the tissues)

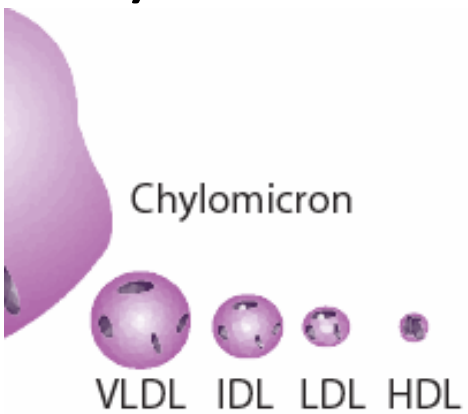
Plasma Lipoproteins Structure

- **LP core**
  - Triglycerides
  - Cholesterol esters
- **LP surface**
  - Phospholipids
  - Proteins
  - cholesterol



Lipoprotein classes

1. Chylomicrons
2. very low density lipoproteins (VLDL)
3. intermediate density lipoproteins (IDL)
4. low density lipoproteins (LDL)
5. high density lipoproteins (HDL)



They are identified and classified on basis of:

- Chemical composition
- Physical properties including density and floatation characteristics
- Mobility upon electrophoresis

Chemical composition

Lipoprotein / Chemical %	Chylomicron	VLDL	LDL	HDL
Triglyceride	90	65	10	2
Cholesterol	5	13	43	18
Phospholipid	4	12	22	30
Protein	1	10	25	50

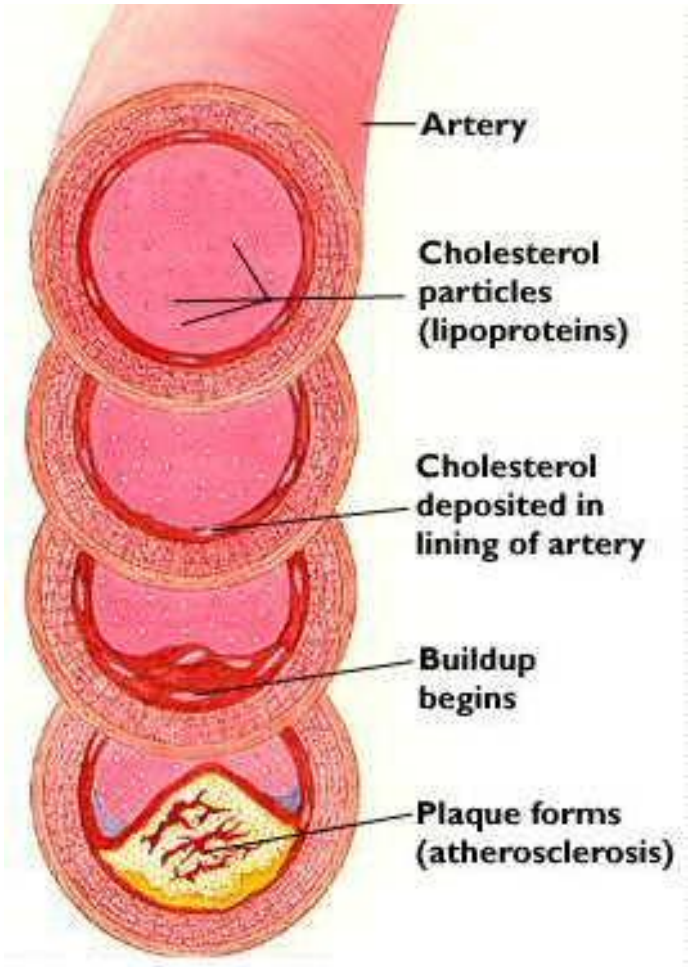
Properties and functions of human lipoproteins

Increasing density

Lipoprotein class	Density (g/mL)	Diameter (nm)	Source and function
HDL α-lipoprotein	1.063-1.21	5 – 15	Liver Removes "used" cholesterol from tissues and takes it to liver → good cholesterol
LDL β-lipoprotein	1.019 – 1.063	18 – 28	Formed in circulation by partial breakdown of IDL. Delivers cholesterol to peripheral tissues
IDL	1.006-1.019	25 - 50	Synthesized from VLDL during VLDL degradation Triglyceride transport and precursor to LDL
VLDL pre-β lipoprotein	0.95 – 1.006	30 - 80	Liver transport mainly TG from liver to peripheral tissues
Chylomicron	< 0.95 Least dense	100 – 500 Large sized	Intestine Transport of dietary TG from intestine to liver

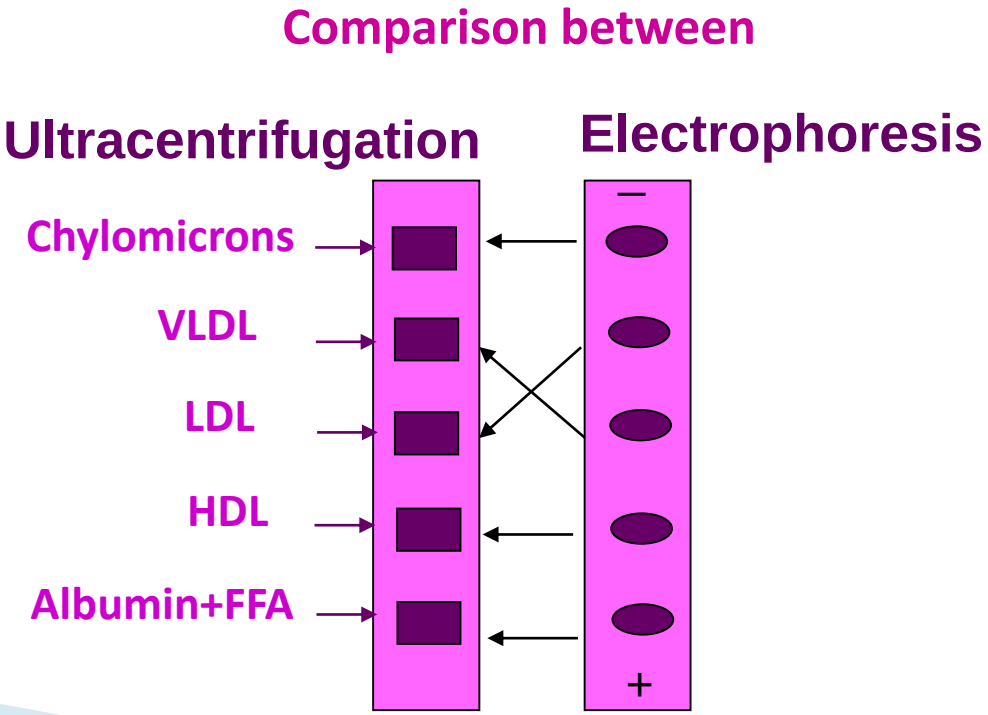
- Note that
  - **high LDL** values are **bad**
  - **high HDL** values are **good**
- High LDL Cholesterol and Low HDL Cholesterol

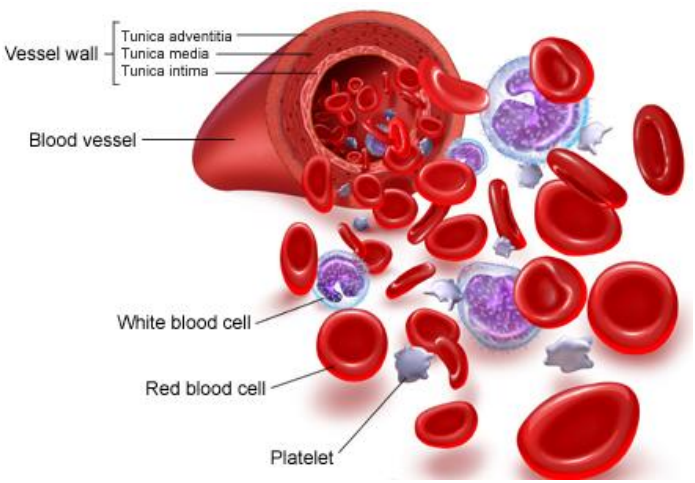
→Atherosclerosis



Separation of lipoproteins

- Plasma lipoproteins are separated by 2 methods (ultracentrifugation, electrophoresis) into different fractions





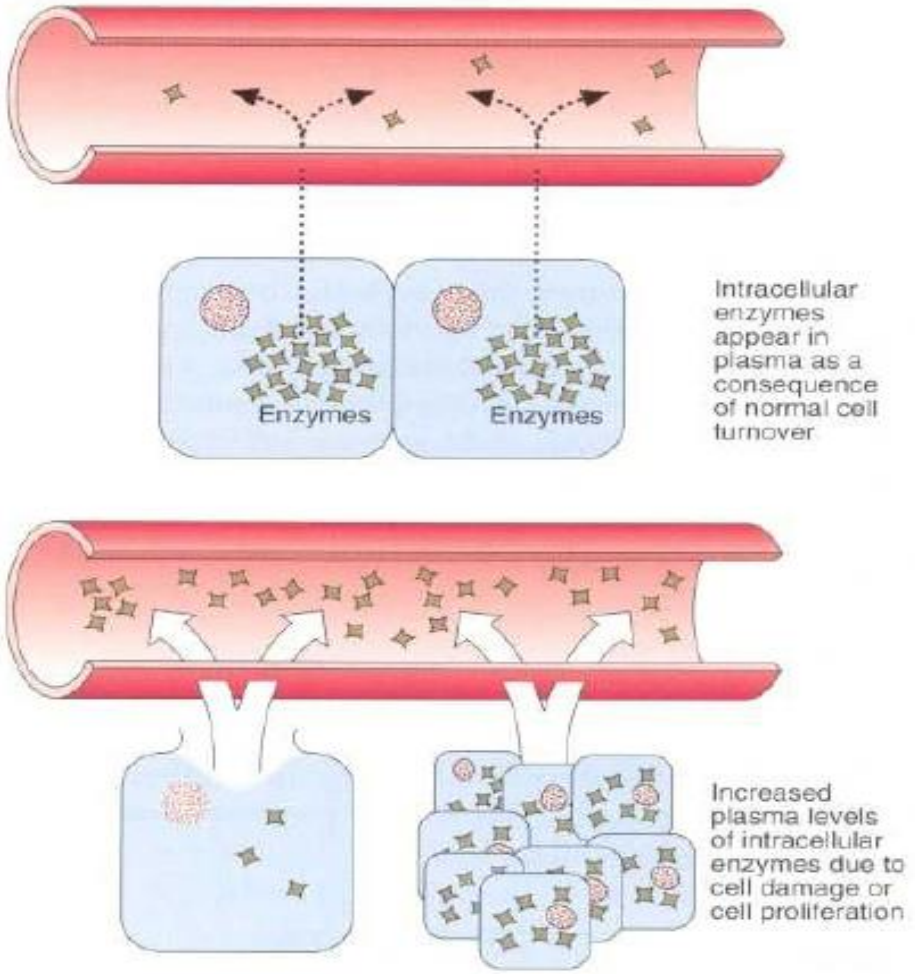
Plasma enzymes

- Blood plasma contains many enzymes which are classified into:

1. Functional plasma enzymes
2. Non functional plasma enzyme

Differences between functional and non functional enzymes

	Functional plasma enzymes	Non functional plasma enzymes
Concentration in plasma	Present in plasma in higher concentrations in comparison to tissue	Normally, Present in plasma in very low concentrations in comparison to tissue
Function	Have known functions	No known functions
Substrate	Their substrates are always present in plasma	Their substrates are absent from plasma
Site of synthesis	liver	Different organs .g. liver heart, skeletal muscles and brain
Effect of disease	Decrease in liver disease	Increase in different organ diseases
Examples	Clotting factors e.g. Prothrombin Lipoprotein lipase, Pseudocholinesterase	ALT, AST, CK, LDH, alkaline phosphatase, acid phosphatase and lipase



- Small amounts of intracellular enzymes are present in the blood as a result of normal cell turnover.
- 'Normal' plasma enzyme levels reflect the balance between the rate of synthesis and release into plasma during cell turnover, and the rate of clearance from the circulation.
- The presence of elevated enzyme activity in the plasma may indicate tissue damage that is accompanied by increased release of intracellular enzymes

Source of non functional enzymes

- **Cell damage** with the release of its content of enzymes into blood e.g. Myocardial infarction and viral hepatitis
- **Obstruction of normal pathways** e.g. Obstruction of bile duct increases alkaline phosphatase
- **Increase of the enzyme synthesis** e.g. bilirubin increases the rate of synthesis of alkaline phosphatase in obstructive liver disease
- **Increased permeability** of cell membrane as in hypoxia

- **Measurement of non functional enzymes is important medically for:**

1. **Diagnosis of diseases** as disease of different organs cause elevation of different plasma enzymes

2. **Prognosis of the disease** we can follow up of the treatment by measuring plasma enzymes before and after treatment

Disadvantages of enzyme assays in diagnosing tissue damage

- Lack of specificity to a particular tissue or cell type. Many enzymes are common to more than one tissue.

- This problem may be obviated to some extent in 2 ways:
  - **First**, different tissues may contain (and thus release when they are damaged) two or more enzymes in different proportions
  - **Second**, some enzymes exist in different forms (isoforms)

Isoenzymes

- Isoenzymes are a group of enzymes that catalyze the same reaction but they differ in amino acid sequence
- Isoenzymes can be:
  - produced by different genes (= true isozymes)
  - produced by different posttranslational modification (= isoforms)
- found in different compartments of a cell
- found in different tissues of an organism
- can be oligomers of various subunits (monomers)

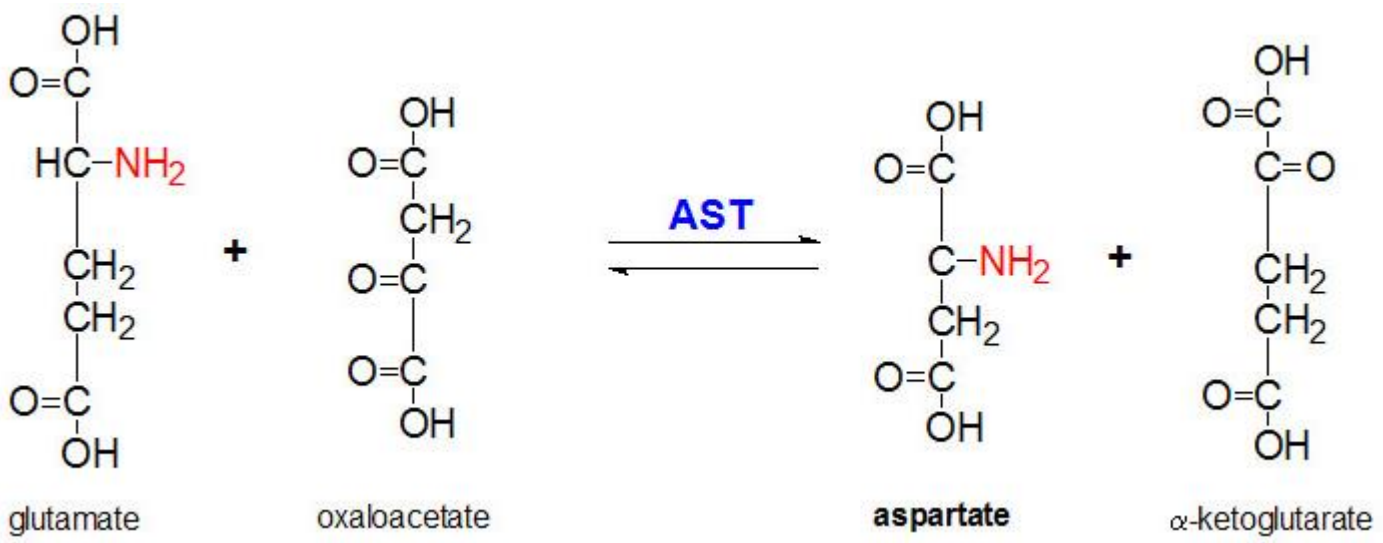
Isoenzymes

- They differ in:
  - electrophoretic mobility
  - enzymatic properties
  - physical properties (e.g heat stability)
  - biochemical properties such as amino acid composition, immunological reactivities

- Because isoenzymes are originated from different tissues, their determination give more information than measurement of total enzyme activity in plasma

Abnormal plasma enzyme activities

- **Aspartate Transaminase (AST)/ Serum Glutamate oxaloacetate (SGOT)**



Diagnostic Significance

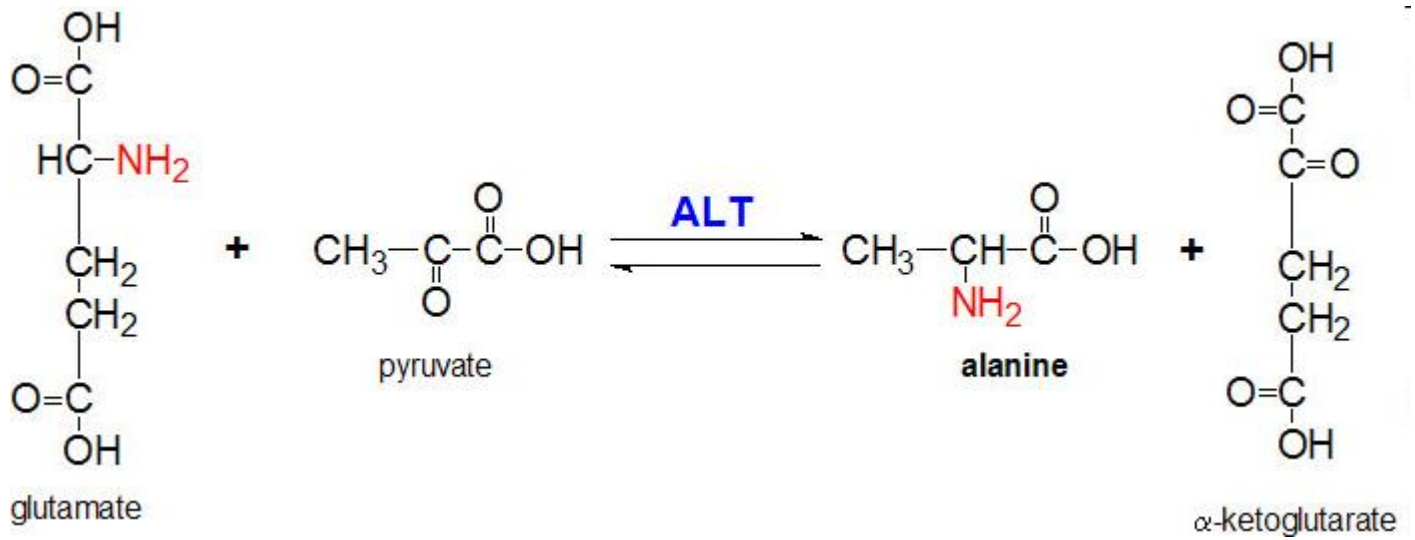
- The clinical use of AST is limited mainly to the evaluation of hepatocellular disorders and skeletal muscle involvement.
- Post AMI (Acute Myocardial Infarction)
  - Rises 6 – 8 hours
  - Peaks at 24 hours
  - Returns to normal by day 5
- AST levels are highest in acute hepatocellular disorders, viral hepatitis, cirrhosis.
  - Viral hepatitis may reach 100 x ULN (Upper limit of Normal)

Diagnostic Significance

- There are two isoenzyme fractions located in the cell cytoplasm and mitochondria,
  - the cytoplasmic isoenzyme is predominant in serum
  - while the mitochondrial one may be increased following cell necrosis.
- Isoenzyme analysis of AST is not routinely performed in the clinical laboratory.

Abnormal plasma enzyme activities

- **Alanine Transaminase (ALT)/ glutamate pyruvate transaminase (GPT)**

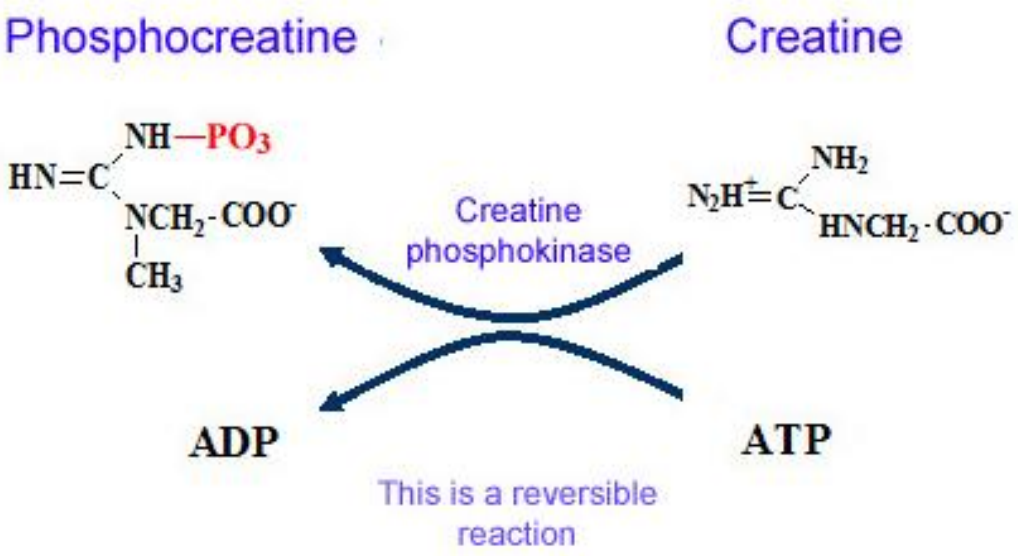


Alanine aminotransferase (ALT)

- Very high values are seen in acute hepatitis, either toxic or viral in origin.
- Both ALT and AST are increased in liver diseases, but ALT >AST.
- Moderate increase may be seen in chronic liver disease such as cirrhosis, and malignancy in liver.
- (AST/ALT) in normal conditions is 1.33 ± 0,42.

Abnormal plasma enzyme activities

- **Creatine Kinase (CK, CPK)**



Creatine Kinase (CK)

- High concentrations of CK in:
  - **skeletal muscle**
  - **cardiac muscle**
  - **brain tissue**
- Increased plasma CK activity is associated with damage to these tissues

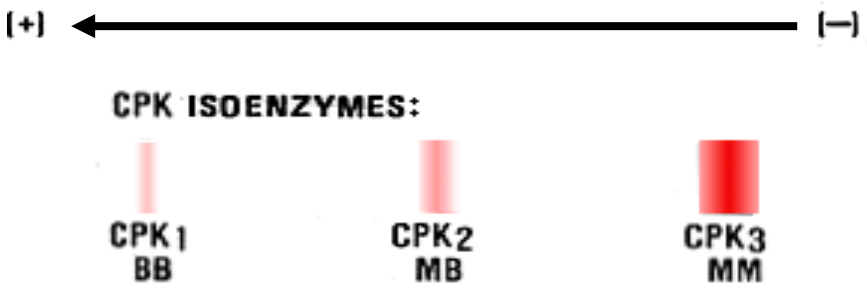
- ↑ CK is especially useful to diagnose:
  - AMI
  - Skeletal muscle diseases (Muscular Dystrophy)

Creatine Kinase isoenzymes

- CK occurs in 3 isoenzymes, each is a dimer composed of 2 subunits (B & M): **CK1** = **BB**, **CK2** = **MB** and **CK3** = **MM**
- Normal serum consists of:
  - Approximately 94% to 100% CK-MM
  - Values for the MB isoenzyme range from undetectable to trace (<6% of total CK).
  - CK-BB is also present in small quantities
- Cardiac muscle CK is 80% CK-MM and 20% CK-MB

Creatine Kinase isoenzymes

- Each CK isozyme shows a characteristic electrophoretic mobility.



Diagnostic Significance

- The value of CK isoenzyme separation can be used principally in detection of myocardial damage.
  - increased CK – MB (> 6% of the total CK activity) is a strong indication of AMI
- Post AMI
  - CK-MB increases 4 – 8 hours
  - Peaks at 12 - 24 hours
  - Returns to normal 48 - 72 hours

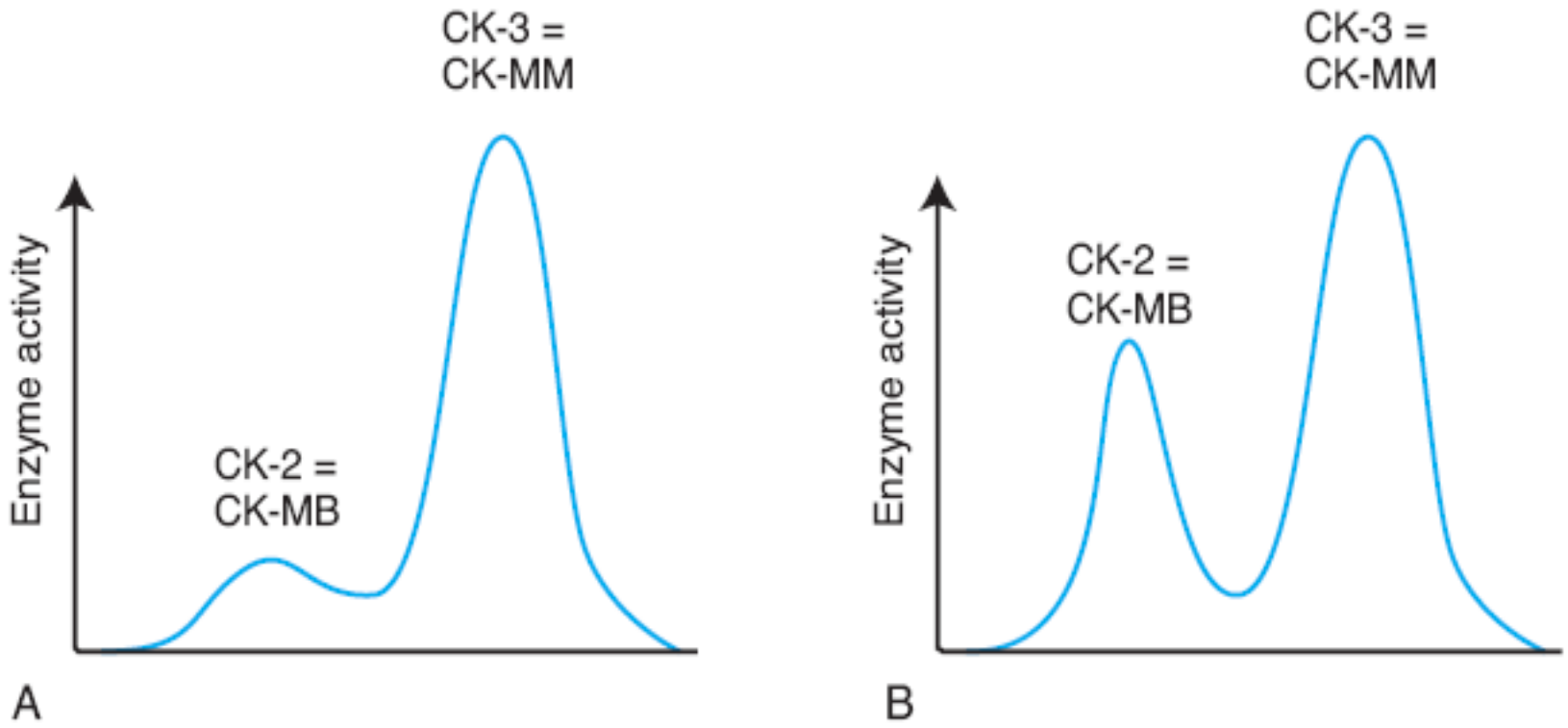
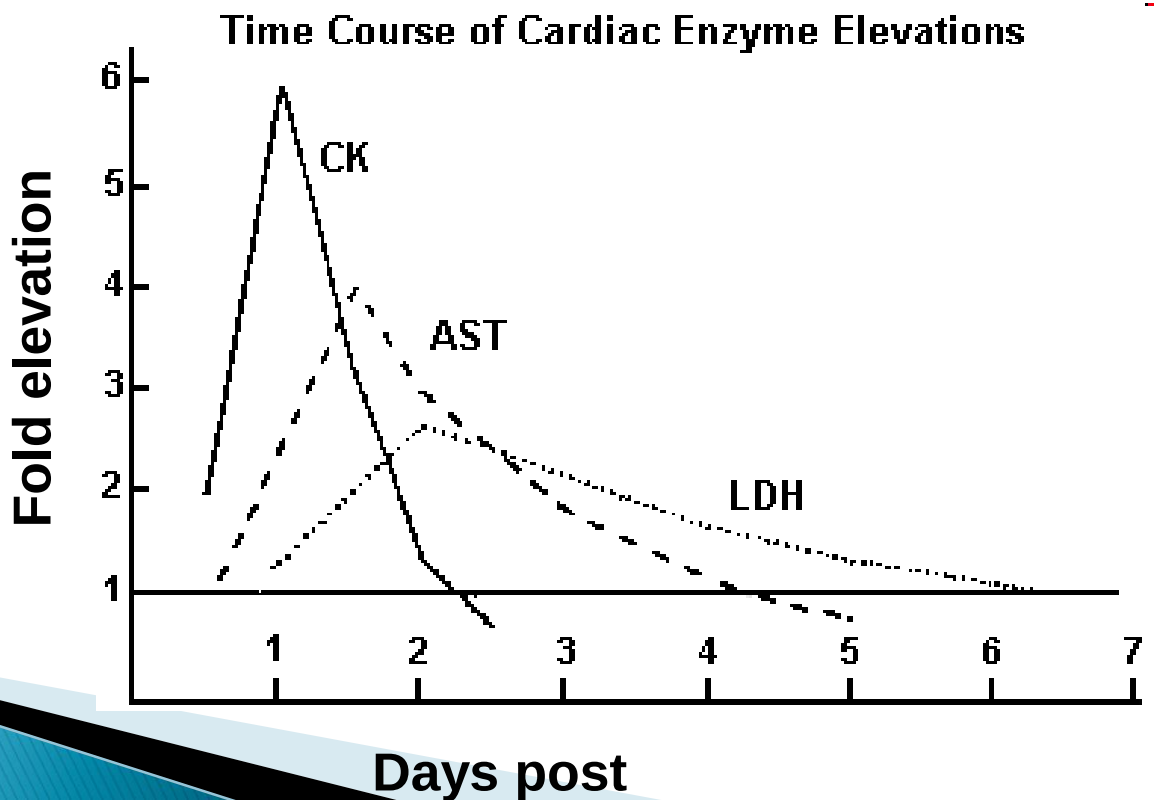


Figure 8–1. Electrophoretic separation of the CK isoenzymes in the serum of (*A*) a healthy individual and (*B*) a patient with acute myocardial infarction. Isoenzymes are numbered on the basis of their electrophoretic mobility, with the most anodal form receiving the lowest number.

Cardiac Disorders

- The **CK** rise the earliest, the **LDH** rise is latest
- The **LDH** elevations are present longer than those of **CK** and **AST**



Abnormal plasma enzyme activities

- **α-Amylase**
  - hydrolyses alpha-bonds of large alpha-linked polysaccharides such as starch and glycogen, yielding glucose and maltose
  - It is used as a marker to detect acute pancreatitis and appendicitis

Abnormal plasma enzyme activities

- **Gamma-glutamyl-transferase (GGT)**

Carboxypeptidase which cleaves C-terminal glutamyl groups and transfers them to peptides and other suitable acceptors

Abnormal plasma enzyme activities

- **Alkaline Phosphatase (ALP)**
  - Widely distributed throughout the body
  - High levels are seen is liver, bone, placenta and intestine
  - Physiological increases are been in pregnancy, due to the placental isoenzyme, and in childhood (when bones are growing), due to the bone isoenzyme.

Diagnostic Significance

- In hepatobiliary obstruction, hepatocytes lining the biliary ducts induces the ALP synthesis.
- High levels of ALP is indicative of extrahepatic obstruction rather than intrahepatic obstruction
- In bones, the enzyme is derived from osteoblasts. Hence increased in bone diseases like rickets, osteomalacia, neoplastic diseases with bone metastates and healing fractures

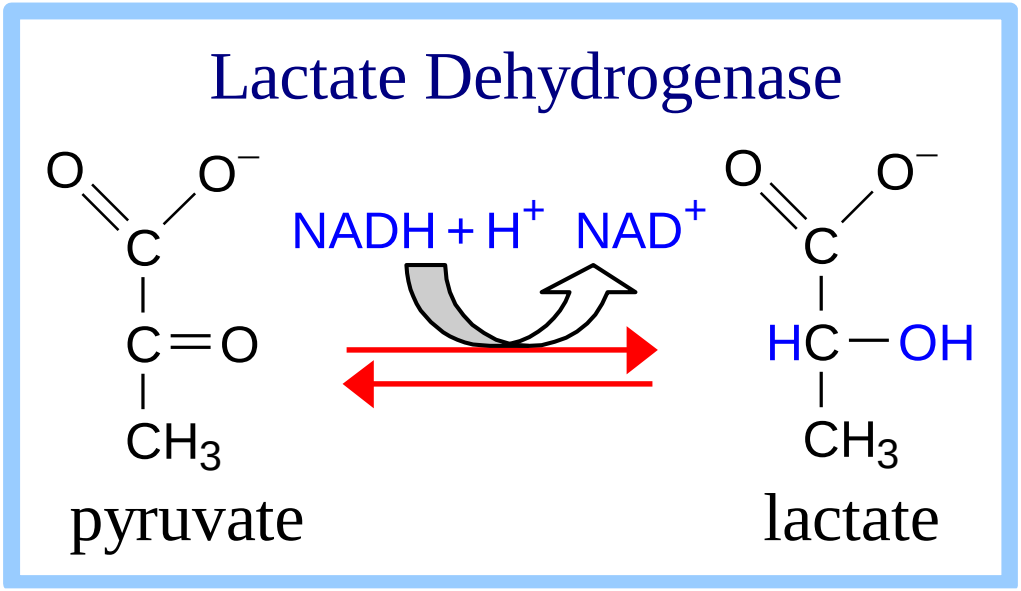
Abnormal plasma enzyme activities

Acid Phosphatase (ACP)

- ACP is secreted by prostate cells, RBC, platelets and WBC.
- The main source of ACP is prostate gland and so can be used as a marker for prostate disease.
- Different forms of acid phosphatase are found in different organs, and their serum levels are used as a diagnostic for disease in the corresponding organs.

Abnormal plasma enzyme activities

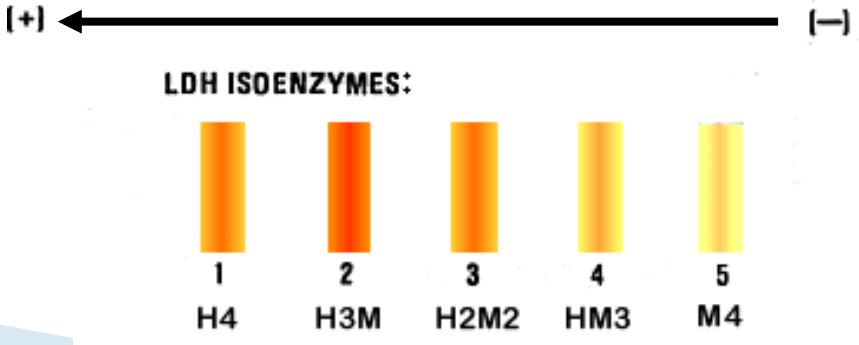
- **LDH**



  - High activities in heart, liver, muscle, kidney, and RBC
  - Lesser amounts: Lung, smooth muscle and brain

Abnormal plasma enzyme activities

- LDH occurs in 5 isoenzymes:
  - LDH1 (H4): Cardiac , RBCs
  - LDH2 (H3M): Cardiac , RBCs
  - LDH3 (H2M2): Lung, spleen, pancreas
  - LDH4 (HM3): Hepatic
  - LDH5 (M4): Skeletal muscle



Diagnostic Significance

- LDH is elevated in a variety of disorders:
  - in cardiac,
  - hepatic,
  - skeletal muscle,
  - and renal diseases,
  - as well as in several hematologic and neoplastic disorders
- The highest levels of LD-1 are seen in pernicious anemia and hemolytic disorders
- LD-3 with pulmonary involvement
- LD-5 predominates with liver & muscle damage

Diagnostic Significance

- In healthy individuals
  - LD-2 is in highest quantity then LD-1, LD-3, LD-4 and LD-5
- Heart problems:
  - If problem is not MI, both LD1 and LD2 rise, with LD2 being greater than LD1
  - If problem is MI, LD1 is greater than LD2.

Diagnostic Significance

- LDH-6 has been present in patients with arteriosclerotic cardiovascular failure
- Its appearance signifies a grave prognosis and impending death
- It is suggested, that LDH-6 may reflect liver injury secondary to severe circulatory insufficiency

Abnormal plasma enzyme activities

- **Lipase**

  It is highly elevated in acute pancreatitis and this persists for 7-14 days. Thus, lipase remains elevated longer than amylase.

Intracellular Distribution of Diagnostic Enzymes

Liver	Heart	Pancreas	Salivary Glands	Bone	Muscle	Biliary Tract	Prostate
LDH_5 ALT AST	LDH_1 AST CK	LPS AMS	AMS	ALP	CK	ALP GGT	ACP

Major Enzymes of Clinical Significance

Disease	Enzyme
Cardiac Disorders	**AST-LDH1-CK**
Hepatocellular Disorders Viral hepatitis: Hepatitis B & Hepatitis C. Toxic hepatitis: caused by chemicals & Toxins	**ALT-AST-LDH5**
Skeletal Muscle Disorders	**CK-AST**
Biliary tract disorders	**ALP- GGT**
Bone Disorders	**ALP**
Acute Pancreatitis	**Lipase-AMS**
Salivary Gland Inflammation	**AMS**