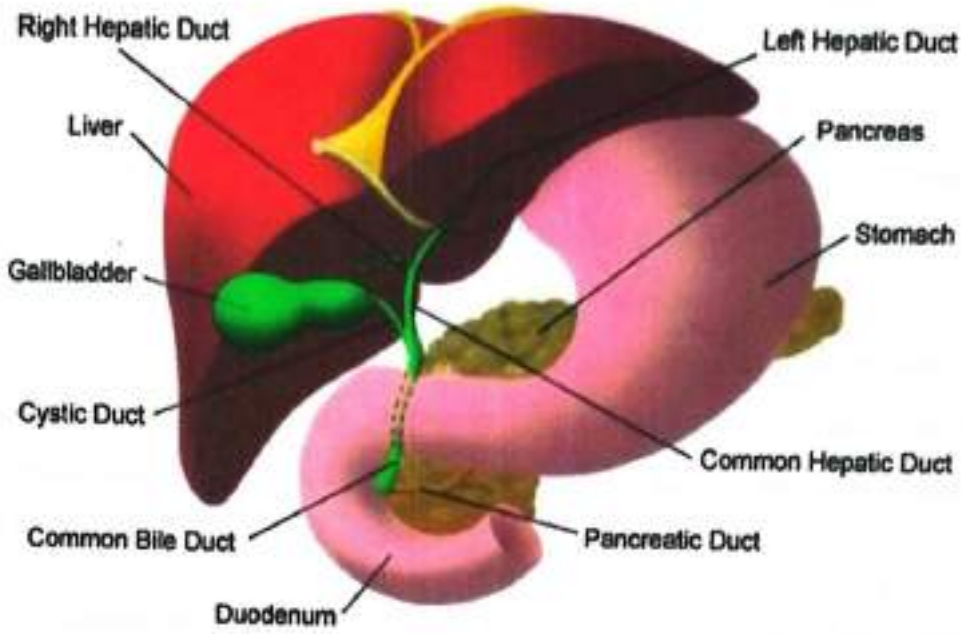
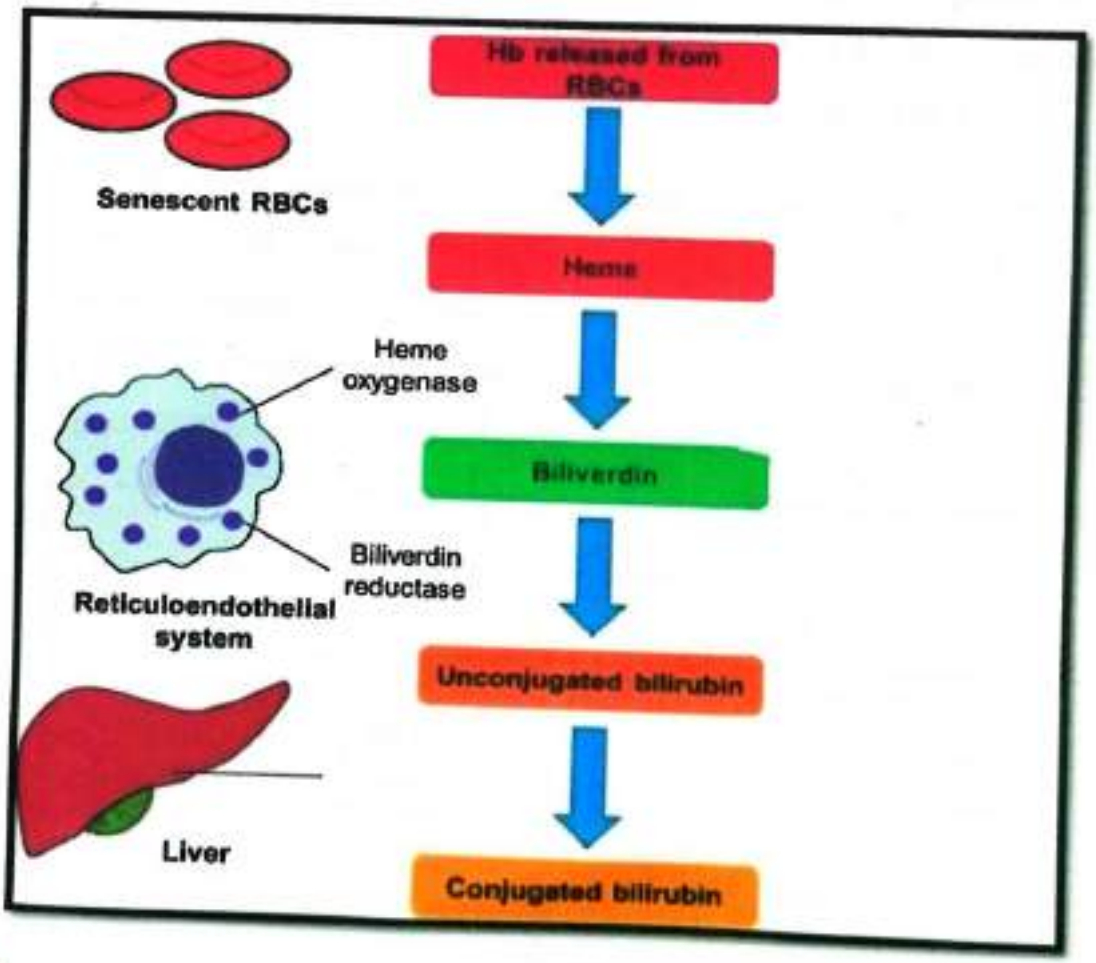
Bilirubin metabolism of the liver

L-3





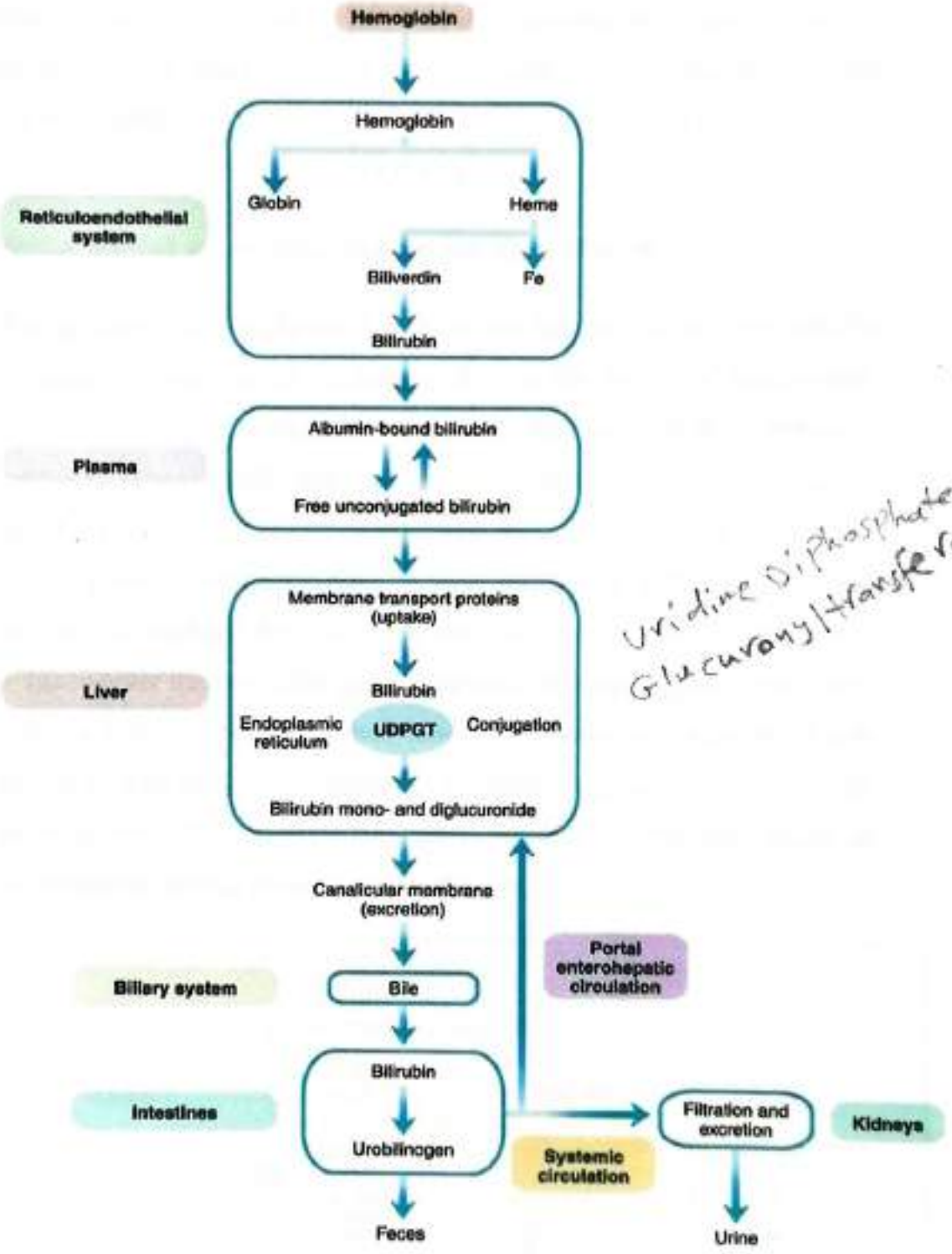
Bilirubin is an organic anion. It is mainly derived from the degradation of ageing erythrocytes in the spleen, liver (hepatocytes, Kupffer cells), kidneys and bone marrow.

The oxidation of haem, (a complex consisting of iron and protoporphyrin which is derived from haemoglobin), is effected by haem oxygenase to produce biliverdin. This is converted to bilirubin by biliverdin reductase. The reaction speed of this process is governed by the haem oxygenase. This enzyme complex contains the inducible cytochrome P 450, which accelerates bilirubin production when the haemoglobin level is elevated.

Bilirubin an apolar, water-insoluble lipophile substance is potentially toxic. It is bound to serum albumin and transported to the sinusoidal membrane of the liver cell as a bilirubin-albumin complex. (fig.)

Jaundice, also known as icterus, is a yellowish or greenish pigmentation of the skin and whites of the eyes due to high bilirubin levels. Jaundice in adults is typically a sign indicating the presence of underlying diseases involving abnormal heme metabolism, liver dysfunction, or biliary tract obstruction.

Category	Definition
Pre-hepatic/hemolytic	The pathology occurs prior to the liver metabolism, due to red blood cell rupture.
Hepatic/hepatocellular	The pathology is due to damage of parenchymal liver cells.
Post-hepatic/ obstructive	The pathology occurs after bilirubin conjugation in the liver, due to obstruction of the biliary tract and/or decreased bilirubin excretion.

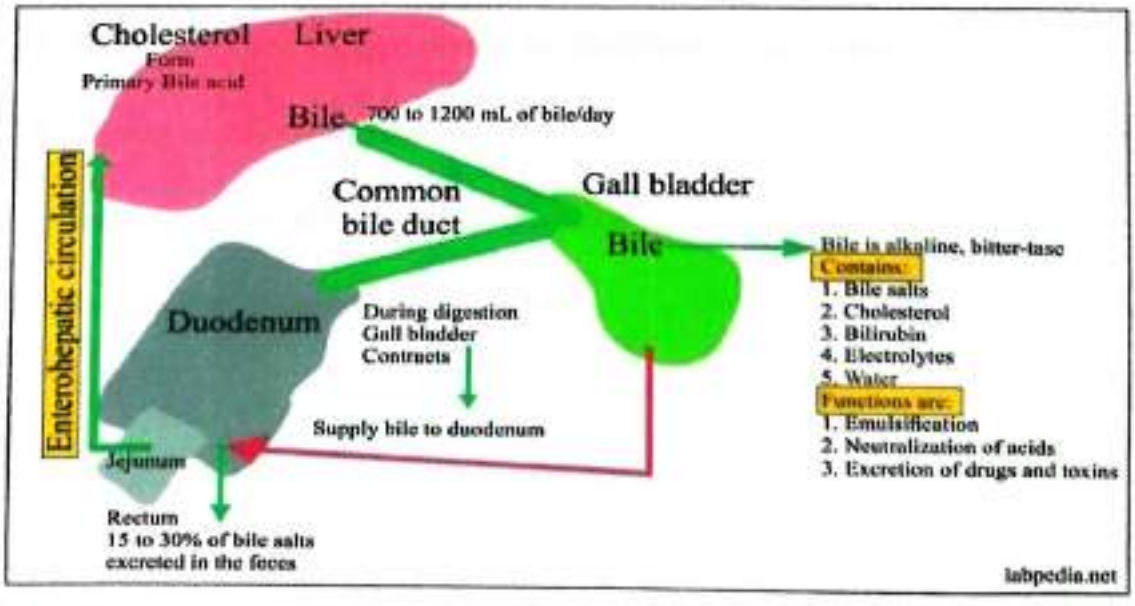


The binding capacity of albumin is exceeded only at a serum bilirubin concentration of >45 mg/dl. In the case of decreased albumin binding (e. g. in acidosis) or oversaturated binding capacity, there is a danger of toxic cell damage due to the diffusion of unbound bilirubin into the cells (in

some cases accompanied by kernicterus). Neonates and premature babies are at particular risk because of their immature blood-**cerebrospinal fluid barrier (BBB)** . Albumin-bound bilirubin can function as an **antioxidant** to intercept free radicals and/or O2 radicals.

Bile acid metabolism of the liver

The primary bile acids are formed in the hepatocytes as liver-specific degradation products of cholesterol due to the action of microsomal, peroxisomal and mitochondrial enzymes; they are linked to cytosolic proteins. The initial enzyme in the biosynthesis, cholesterol-7α-hydroxylase, is also the rate-determining one. This enzyme, a cytochrome P 450 mixed-function oxidase, is localized in the SER. Its enzymatic activity is regulated by a negative feedback mechanism, in which bile acids re-enter the liver after passage through the enterohepatic circulation. After a possible second hydroxylation, the enzymatic removal of side chains as well as the introduction of a carboxylic group take place in the mitochondria. Two primary bile acids are thus synthesized. Twice as much **cholic acid** as **chenodeoxycholic acid** is produced.



Functions of bile acids

The essential functions of bile acids are found in cholesterol metabolism, digestion and resorption of fats in the intestine, and regulation of bile flow.

1. Cholesterol metabolism

a. reduction in excess cholesterol through degradation of cholesterol to bile acids by solubilization of cholesterol in the bile

b. regulation of cholesterol synthesis in the liver and intestine

c. regulation of cholesterol output into the bile

2. Digestion and resorption of dietary fats

a. by formation of micelles; Micelles help the body absorb lipid and fat soluble vitamins.They help the small intestine to absorb essential lipids and vitamins from the liver and gall bladder.

b. by stabilization and activation of enzymes (e. g. pancreatic lipase, phospholipase)

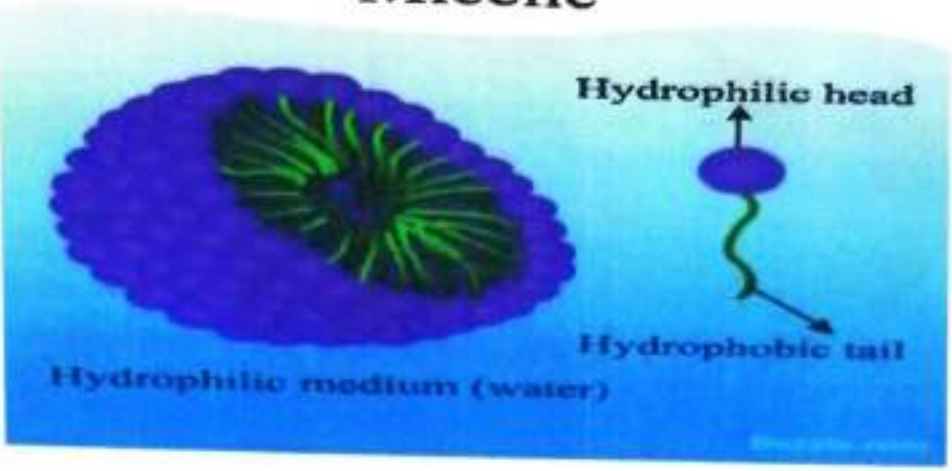
3. **Effects on the bile flow due to osmotic water movement**

4. **Effects on bile secretion**

5. **Emulsification of fat-soluble vitamins**

6. **Stimulation of intestinal motility**

Micelle



Amino acid and protein metabolism of the liver

Human protein metabolism is essentially dependent on 20 amino acids. These amino acids lend themselves to various classification criteria, which also give hints regarding their **biochemical functions**:

1. according to their metabolic characteristics into **ketogenic** and **glucogenic** amino acids

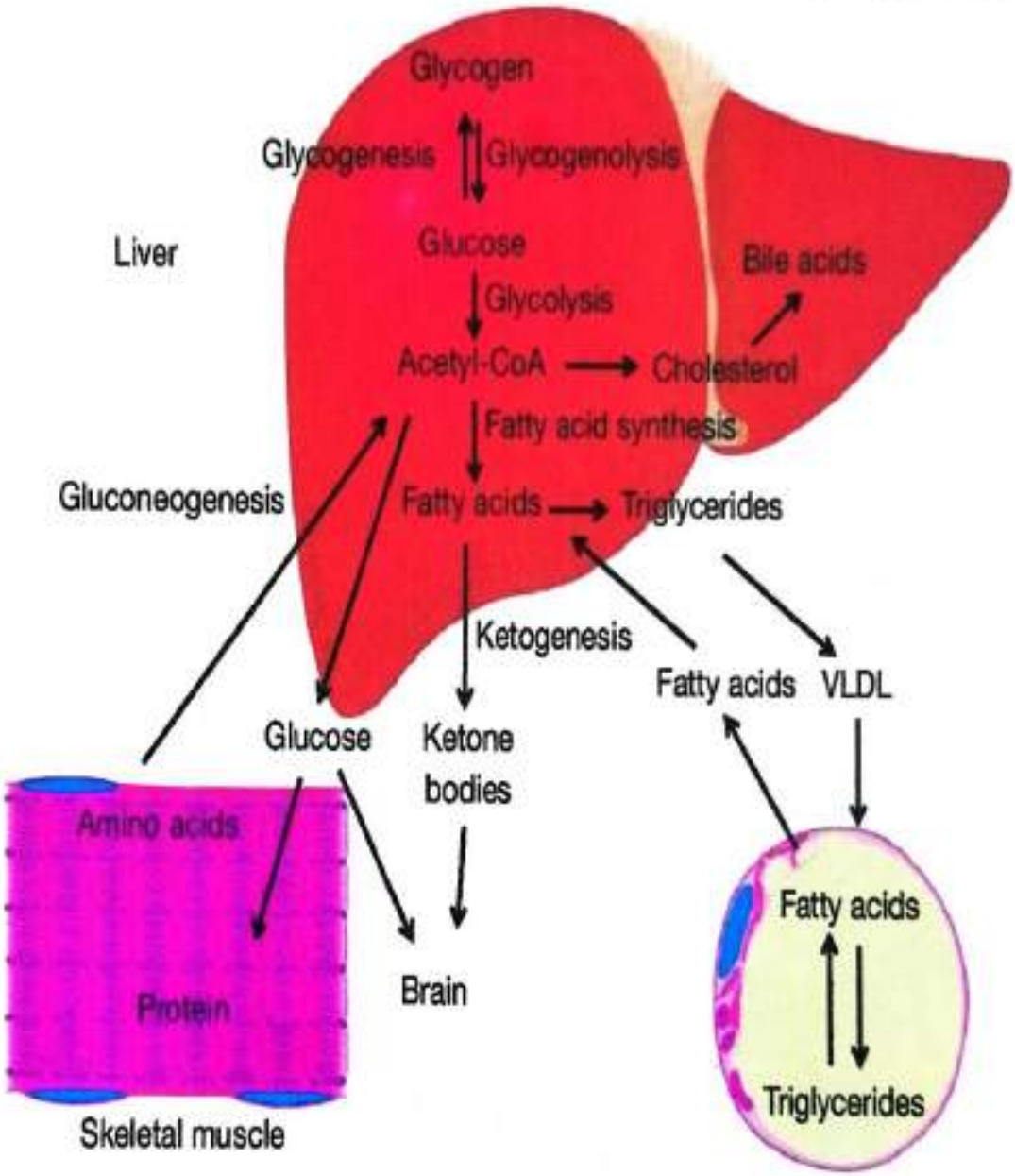
2. according to their chemical structure into **α-**, **β-** and **γ-**amino acids

3. according to their configuration into D- and L-amino acids

4. according to their isoelectric point into **neutral**, **acidic** and **basic** amino acids as well as **amphoteric** amino acids.

5. according to the polarity of their side chains into **polar** amino acids and **nonpolar** amino acids

6. according to their biosynthesis in the human organism into **8 essential**, **10 non-essential** and **2 semi-essential** amino acids.


Glycogen
Glycogenesis
Glycogenolysis
Liver
Glucose
Bile acids
Glycolysis
Acetyl-CoA
Cholesterol
Fatty acid synthesis
Gluconeogenesis
Fatty acids
Triglycerides
Ketogenesis
Fatty acids
VLDL
Glucose
Ketone bodies
Amino acids
Protein
Brain
Fatty acids
Triglycerides
Skeletal muscle