Formation of bile

- Between one and two liters of bile are produced by liver daily .
- The bile consist 0f bilirubin , bile salts , phospholipids and cholesterol as well as electrolytes and small amounts of protein
- gallbladder reabsorbed Na, Cl, Carbonates with isosmotic amount of water → so gallbladder bile is 10 times concentrated than hepatic bile .
- At the end of their life span red blood cells broken down in reticuloendothelial system mainly in spleen -→ globin inter the general protein pool , iron is removed from heme to give bilirubin this form about 80 percent of bilirubin ,the remaining come from immature RBCs ,myoglobin and cytochromes .In adult about 180 mg of bilirubin (unconjugated) caried by albumin to the liver to be conjugated and excreted in bile .
- diseases of the hepatic cells effect conjugation ,while obstructive liver disease effect conjugated bilirubin .

  - Conjugated bilirubin is water soluble and excreted in urine -→ bilirubinuria is always pathological

Retention of bilirubin in plasma (hyperbilirubinemia) cause jaundice.

Jaundice is of 2 types :

1. Unconjugated hyperbilirubinemia

- Sever hemolysis .
- impaired conjugation because of liver disease.
- Low plasma albumin concentration .
- Displaced by high level of free fatty acids and drugs such as salicylates

It is not water soluble so not excreted in urine.

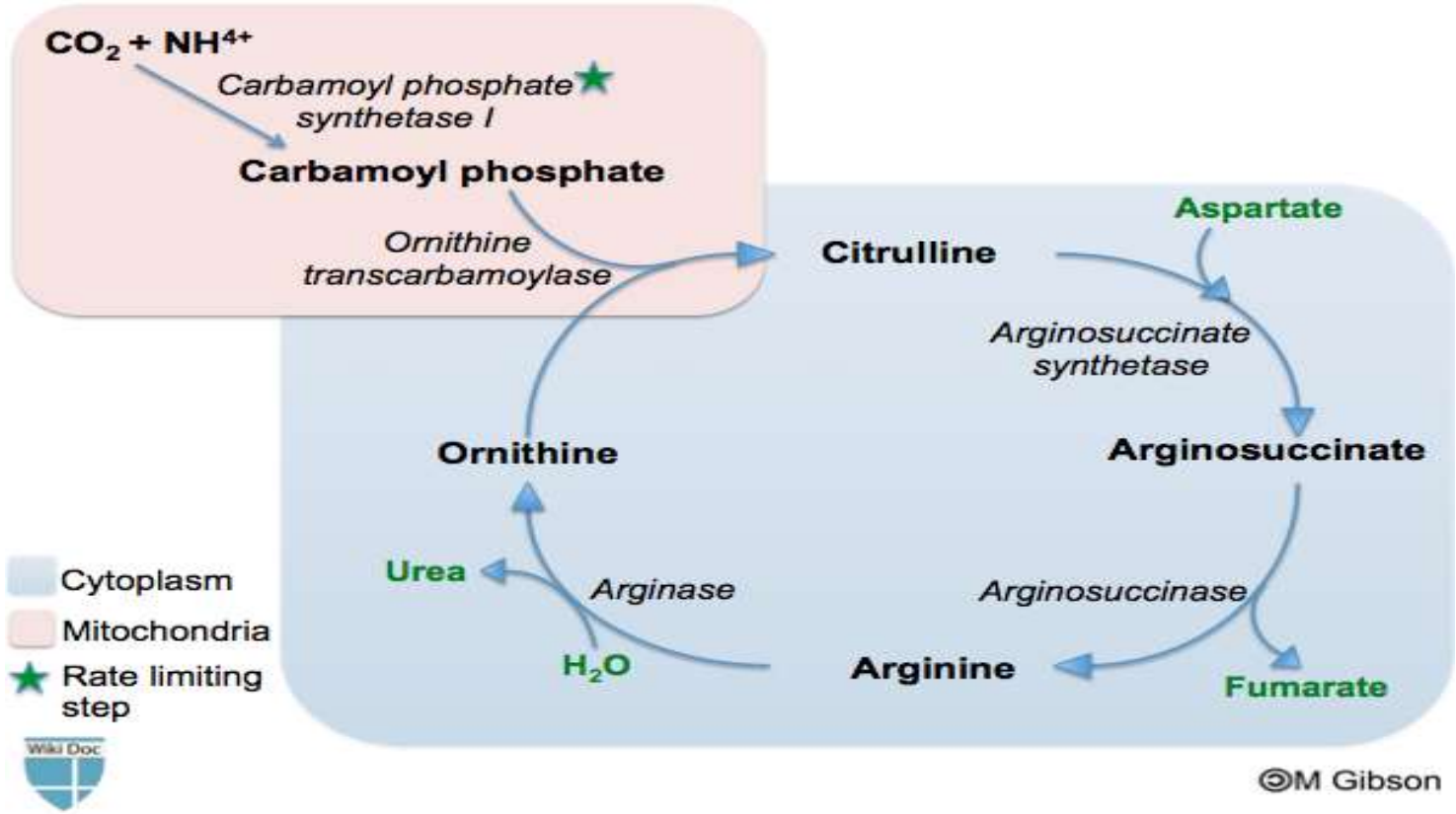
2. Conjugated hyperbilirubinemia.

Conjugated bilirubin when secreted into GIT converted to stercobilin and then converted to urobilin which is excreted in urine.

Renal Function

Urea cycle defects

Liver cells play a critical role in disposing of nitrogenous waste by forming the compound urea (the primary solid component of urine) through the action of the urea cycle. When an amino acid is degraded, the ammonia nitrogen at one end of the molecule is split off, incorporated into urea, and excreted in the urine. A defect in any of the enzymes of the urea cycle leads to a toxic accumulation of ammonia in the blood. This, in turn, causes poor feeding, vomiting, lethargy, and possibly coma in the first two or three days of life (except in the case of arginase deficiency, which presents later in childhood).



Urea cycle defects are autosomal recessive, meaning they are passed on to offspring only when both parents carry the defect. One exception is ornithine transcarbamylase (OTC) deficiency, which is X-linked (and therefore causes severe disease in males who inherit the mutant X chromosome). However, OTC deficiency can also affect females who are "manifesting heterozygotes" , presenting with severe disease during infancy or later in life during times of metabolic stress—for instance, during viral illness or childbirth.

Emergency management of urea cycle disorders includes intravenous ammonia-scavenging medications and hemodialysis to decrease the blood ammonia level.

Long-term therapy consists of a low-protein diet, the provision of nutrients deficient in these disorders, and phenylbutyrate or benzoate (medications that rid the body of excess ammonia).

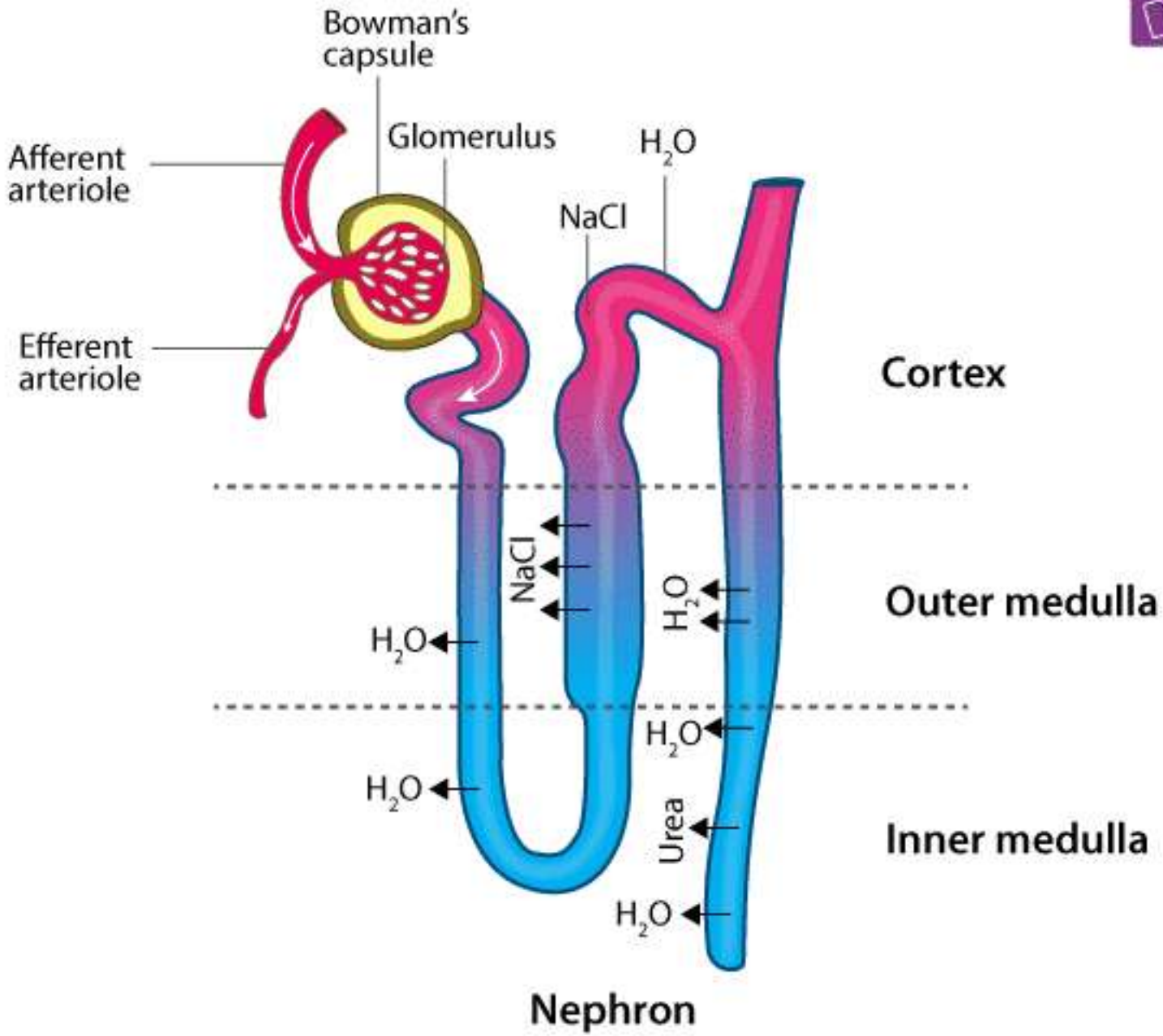
Persons with urea cycle disorders are at risk for recurrent crises ازماتwith elevated ammonia levels, especially during times of infection.

untreated or repeated episodes of high ammonia levels may cause intellectual disability and developmental impairment.

Liver transplantation can cure some of these disorders.

Urea

- Urea is synthesized in the body of many organisms as part of the urea cycle, either from the oxidation of amino acids or from ammonia .
- Urea production occurs in the liver . Urea is then dissolved into the blood (in the reference range of 2.5 to 6.7 mmol/liter) and further transported and excreted by the kidney as a component of urine. In addition, a small amount of urea is excreted (along with sodium chloride and water) in sweat.
- The cycling of and excretion of urea by the kidneys is a vital part of mammalian metabolism. Besides its role as carrier of waste nitrogen, urea also plays a role in the countercurrent exchange system of the nephrons, that allows for re-absorption of water and critical ions from the excreted urine.
- Urea is reabsorbed in the inner medullary collecting ducts of the nephrons, thus raising the osmolarity in the medullary interstitium surrounding the thin descending limb of the loop of Henle, which makes the water reabsorb.
- By action of the urea transporter 2, some of this reabsorbed urea eventually flows back into the thin descending limb of the tubule, through the collecting ducts, and into the excreted urine


Bowman's capsule
Glomerulus
Afferent arteriole
Efferent arteriole
H_2O
NaCl
Cortex
Outer medulla
Inner medulla
Urea
Nephron

Creatinine

- Creatinine is mostly derived from endogenous sources by tissue creatin breakdown ,plasma concentration in normal individual is related to muscle mass .
- The plasma creatinine concentration varies more than that of urea during the day due to protein intake in meals, however, sustained high protein diets and catabolic states probably affect the plasma creatinine concentration less than that of urea .for this reason many laboratories prefer to measure the plasma creatinine concentration to asses renal function.

its test is less precise than that of urea because of interference by bilirubin , acetoacetate , and many drugs .

Uric acid

- The purines in DNA are adenine and guanine, the same as in RNA.
- The pyrimidines in DNA are cytosine and thymine; in RNA, they are cytosine and uracil.
- **Purines are larger than pyrimidines because they have a two-ring structure while pyrimidines only have a single ring**.
- Urate is the end-product of purine metabolism in primates , including man .

It is because of the, poor solubility of urate , it can cause hyperuricemia and gout , the purines (adenine and guanine) are constitutes both RNA and DNA .the purines are derived from ingested nucleic acids or synthesized de novo from small molecules .

Causes of hyperuricemia :-

1- increase rate of urate formation .

a- increase synthesis of purines .

b- increase intake of purines .

C- Increased turnover of nucleic acids.

2- reduced rate of excretion .

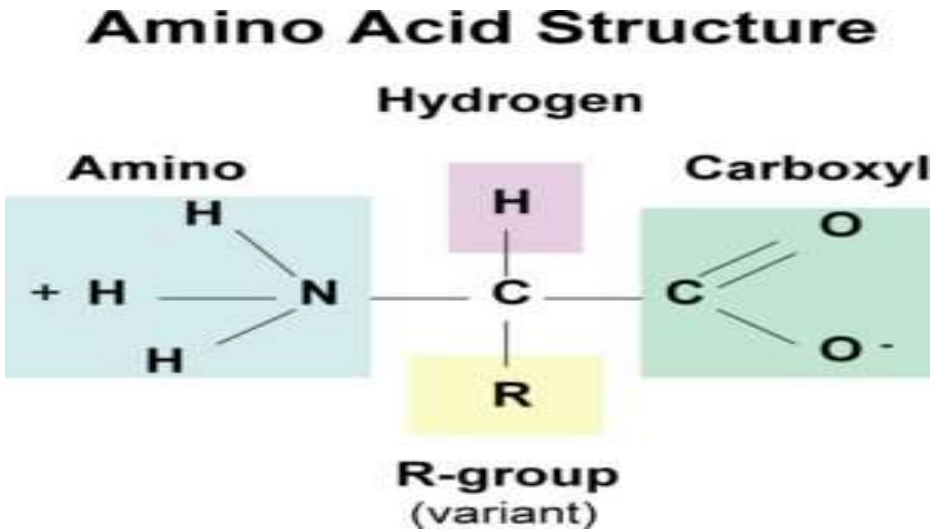
What are Amino Acids?

Amino acids constitute a group of neutral products clearly distinguished from other natural compounds chemically, mainly because of their ampholytic properties as they contain both acidic (COOH) and basic (NH2) groups(They can react with both alkalis and acids to form salts), and biochemically, mainly because of their role as protein constituents.

Proteins are biosynthesized from 20 amino acids in a system involving strict genetic control. Thus, amino acids are the basic unit of proteins. More than 300 amino acids are found in nature but only 20 amino acids are standard and present in protein because they are coded by genes.

Structure of Amino acids

All 20 of the common amino acids are alpha-amino acids. They contain a carboxyl group, an amino group, and a side chain (R group), all attached to the α-carbon.



Classification of amino acids on the basis of nutrition

Essential	Conditionally Non-Essential	Non-Essential
Histidine	Arginine	Alanine
Isoleucine	Cystine	Asparagine
Leucine	Glutamine	Aspartate
Lysine	Glycine	Glutamate
Methionine	Proline	Serine
Phenylalanine	Tyrosine	
Threonine		
Tryptophan		
Valine		

Plasma proteins: make up about 7% of plasma.

1- The liver synthesizes and releases more than 90% of the plasma proteins, including all albumins, fibrinogen, and most globulins.

2- Albumins: (about 60% of total plasma protein) they are responsible for maintain normal plasma osmotic pressure. Also act as carrier molecules for free fatty acids, some drugs and steroid hormones.

3- Globins: which include alpha, beta, and gamma globulins, make up around 36% of the plasma proteins.

* The alpha and beta globulins are produced by the liver, and are mostly transport proteins that bind to fat-soluble vitamins, lipids, and metal ions (e.g. transferrin carries the mineral iron), also play role in transportation of some hormones, (e.g. thyroglobulin carries the hormone thyroxin)

* The gamma globulins are antibodies is synthesized from B lymphocytes during the immune response.

4- Fibrinogen, which makes up around 4% of the plasma proteins, is the largest, in size, of the plasma proteins and important for blood coagulation.

Under certain conditions fibrinogen molecules interact to form large, insoluble strands of fibrin.

Fibrin provides the basic framework for a blood clot.

4- Clotting factors. These are responsible for coagulation of blood.