COMPOSITION OF URINE

By
Dr. Walaa El Gazzar

COMPOSITION OF URINE

- Normal urine contains about 50 g of solids dissolved in about 1.5 L of water per day.
- The chief organic solids are:

(I) NPN compounds

(2) Organic acids

(3) Sugars.

- The chief inorganic solids are :

(I) Sodium, (2) Potassium, and (3) Chlorides

I. NPN COMPOUNDS

- The non-protein nitrogenous (NPN) compounds include intermediary (amino acids, ammonia, and creatine) and end products (urea, uric acid, and creatinine) of protein metabolism.
- The total urinary NPN normally varies between 11 and 15, average 13 g day.

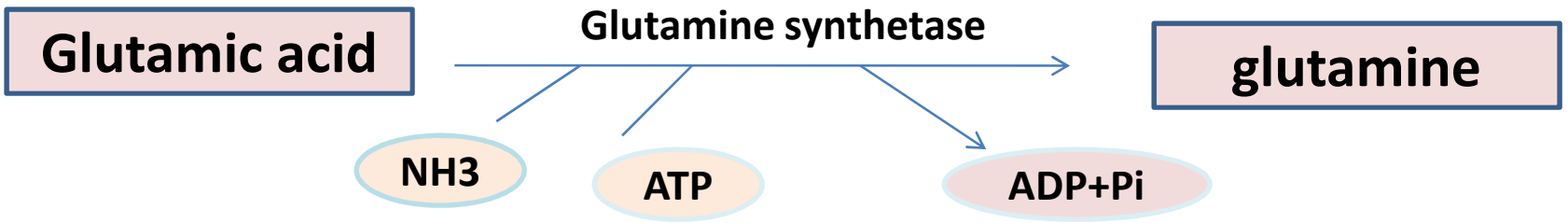
A. Urea

- Urea is the chief end product of protein metabolism in man. It is formed in the liver from the ammonia resulting from the deamination of the amino acids, and is excreted by the kidneys in the urine.
- Its excretion in the urine is more directly affected by protein intake and protein catabolism than any of the other nitrogenous compounds, which tend to remain relatively constant.

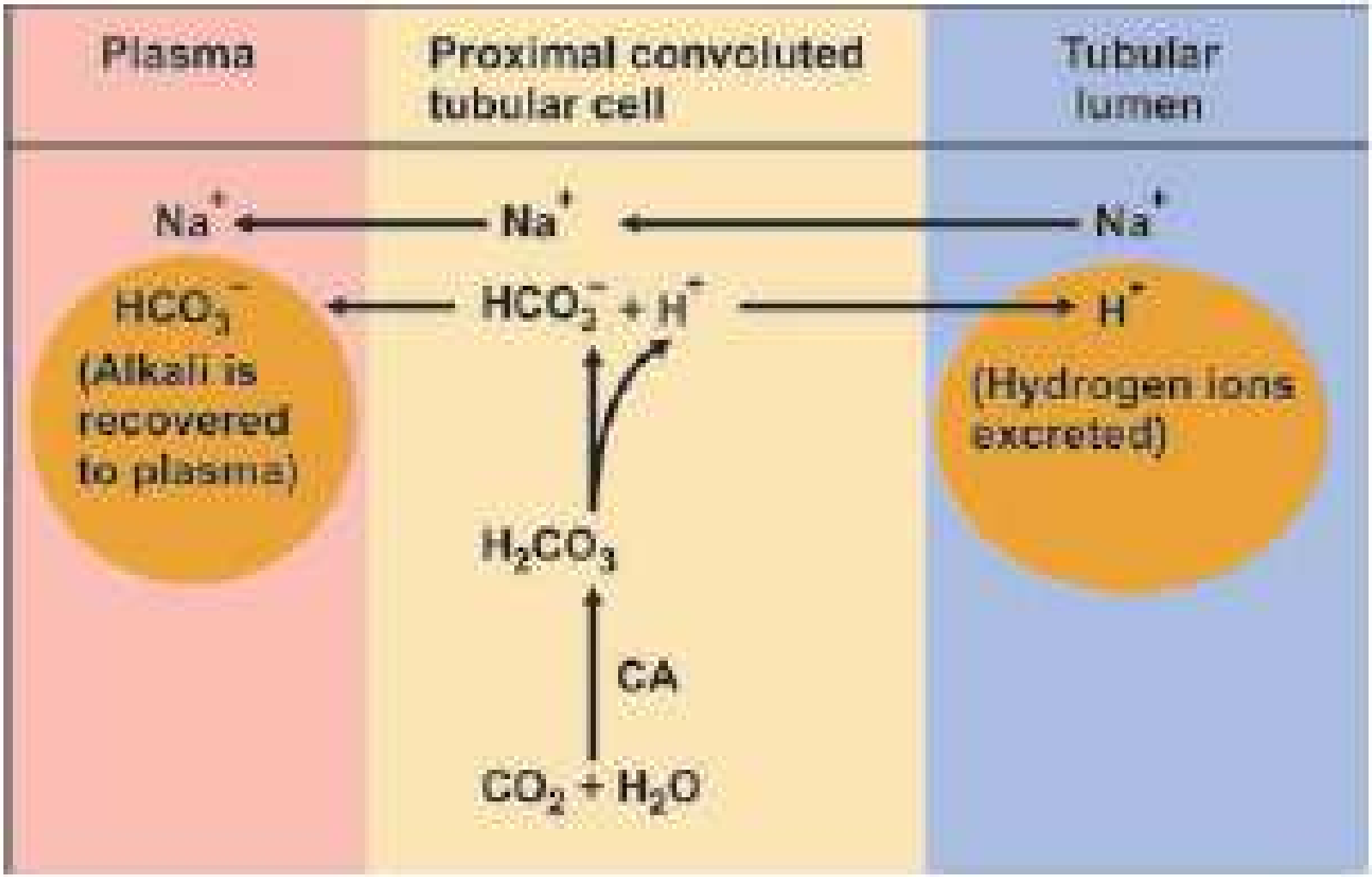
- Urinary urea is normally 20 - 30, average 24 g/day. It increases on a high protein diet and in states of increased protein catabolism (fevers, diabetes mellitus, cushing syndrome and hyperthyroidism).
- Urinary urea decreases on a low protein diet , in states of increased protein anabolism (pregnancy and lactation), in liver failure (decreased formation) and in acute renal failure (due to retention).

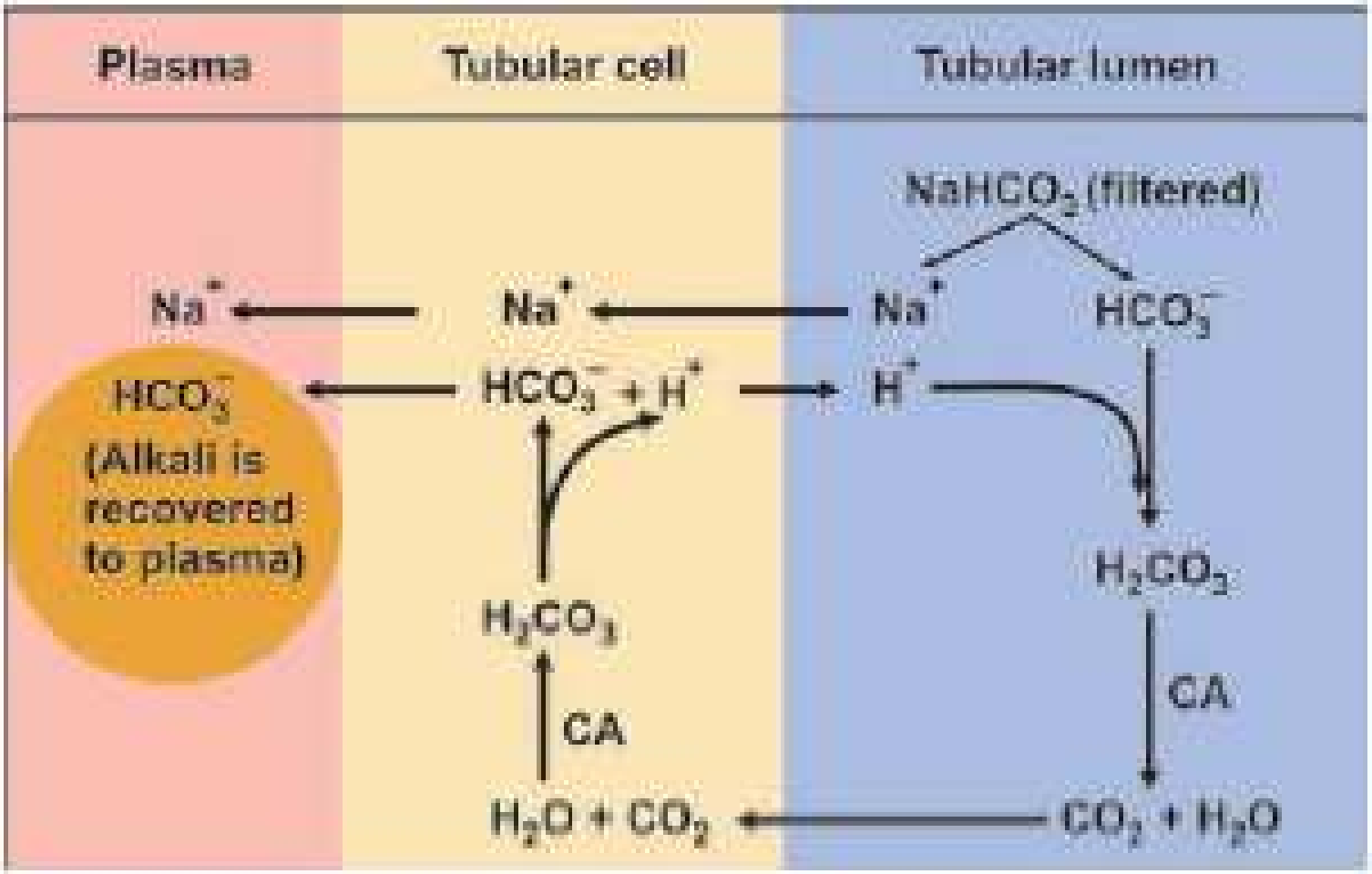
B. Ammonia

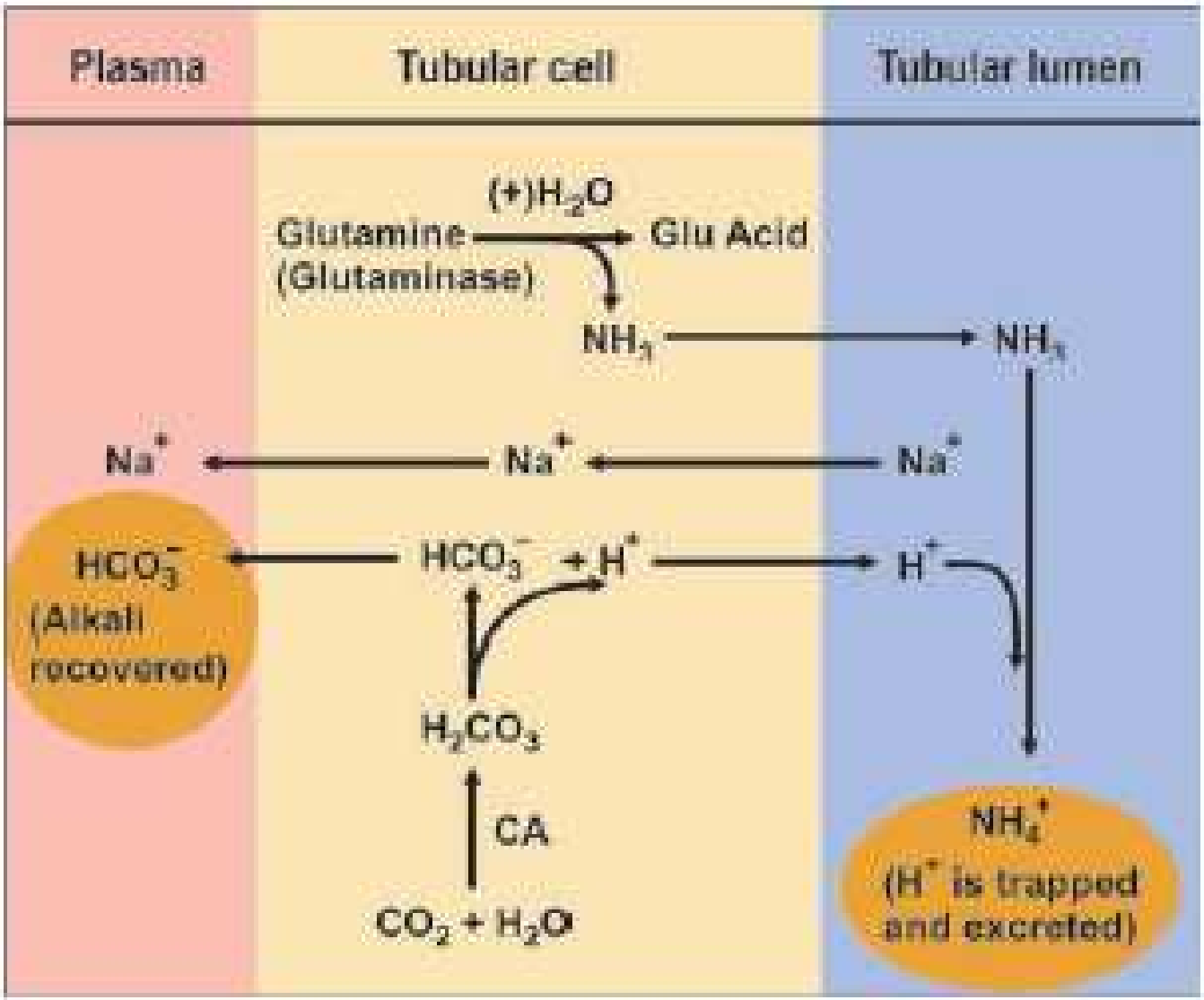
- Urinary ammonia is synthesized in the distal convoluted tubules.
- About 60% are produced by the action of the enzyme **glutaminase** on the glutamine received by the kidneys from other tissues.(The ammonia resulting from the deamination of AA in extrarenal tissues, particularly the brain, is converted to glutamine.



- Glutamine goes, via the blood, to the kidneys where it becomes hydrolyzed by **glutaminase** into **glutamic acid** and **ammonia**.
- About 40% are produced by the deamination of other amino acids in the kidneys.
- Urinary ammonia appears to be entirely concerned with the acid-base balance. In conditions of acidosis the reabsorption of Na^+ by Na^+ : H^+ exchange occurs to a limited extent being stopped when the pH of the glomerular filtrate becomes 4.8. Ammonia is secreted by the distal convolutcd tubules to neutralize this high acidity allowing Na^+ : H^+ exchange to continue and the alkali reserve to be regained.


Plasma
Proximal convoluted tubular cell
Tubular lumen
Na^+
Na^+
Na^+
HCO_3^-
(Alkali is recovered to plasma)
$HCO_3^- + H^+$
H^+
(Hydrogen ions excreted)
H_2CO_3
CA
$CO_2 + H_2O$


Plasma
Tubular cell
Tubular lumen
NaHCO3 (filtered)
Na+
Na+
Na+
HCO3−
HCO3−
(Alkali is recovered to plasma)
HCO3− + H+
H+
H2CO3
H2CO3
CA
CA
H2O + CO2
CO2 + H2O


Plasma
Tubular cell
Tubular lumen
(+)H2O
Glutamine
(Glutaminase)
Glu Acid
NH3
NH3
Na+
Na+
Na+
HCO3−
(Alkali
recovered)
HCO3− + H+
H+
H2CO3
CA
CO2 + H2O
NH4+
(H+ is trapped
and excreted)

- Urinary ammonia is normally 0.3 - 1.2, average 0.7 g/day. It markedly increases in acidosis (up to 10 g/day), and is almost absent in alkalosis. It decreases in severe nephritis due to decreased capacity of the kidneys to deaminate amino acids.
- The quantity of ammonia in the urine may increase due to hydrolysis of urea by bacteria either in the bladder (cystitis) or if the urine sample is stored without preservative.

C. AMINO ACIDS

- Most of the amino acids (about 80%) excreted in the urine are conjugated amino acids (glycine with benzoic acid and glutamine with phenylacetic acid) only a small part (about 20%) is free amino acids.
- The total urinary amino acid nitrogen normally varies between 0.5 and 1.0, average 0.7 g/day. Increased urinary amino acids (aminoaciduria) may be due to:

1. Decreased Deamination of Amino Acids:

- In liver failure the deamination of amino acids and urea formation are decreased, leading to generalized aminoaciduria. Specific aminoacidurias are caused by defective metabolism of specific amino acids, eg., phenylketonuria causes increased excretion of phenylalanine in the urine.

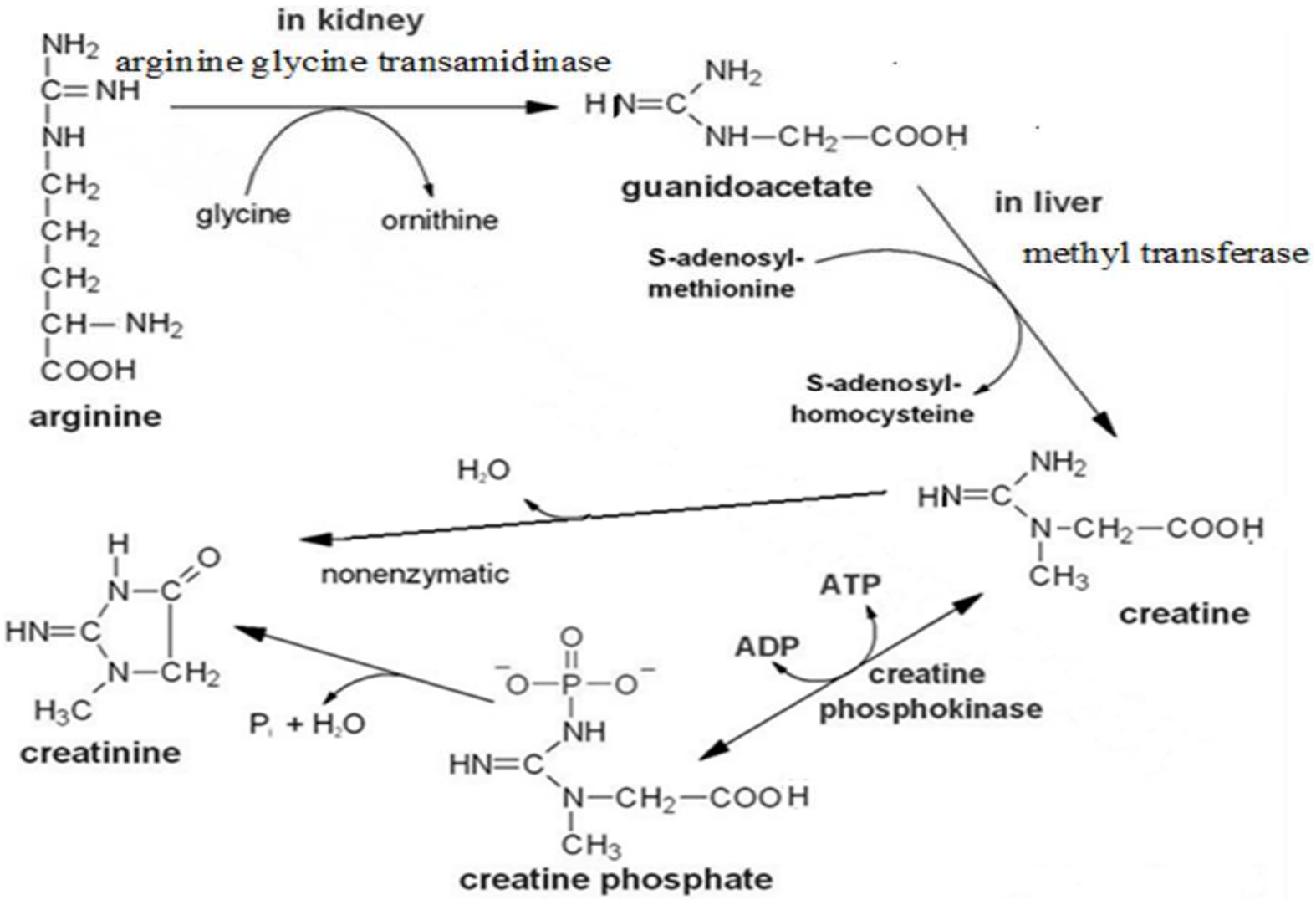
2. Inability of the Kidneys to reabsorb Amino Acids:

- In sever nephritis and in fanconi syndrome the kidneys fail to reabsorb all amino acids, leading to generalized aminoaciduria. In cystinuria kidneys fail to reabsorb cystine, ornithine, arginine and lysine, leading to their excretion in the urine.

3. Ingestion of certain toxic substances:

- These include benzoic acid, phenylacetic acid, and bromobenzene. which are respectively, conjugated with glycine, glutamine, and cysteine, leading to the excretion of large amounts of these amino acids in the urine.

D. Creatine and Creatinine



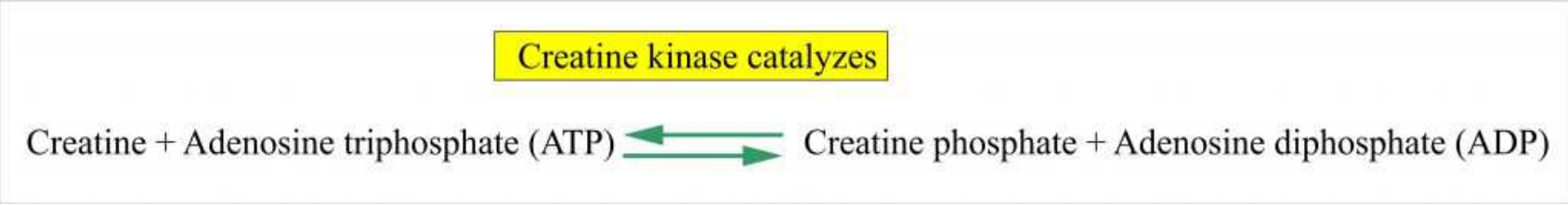
- **Creatine** is methyl guanido acetic acid. It is a NPN compound.
- It is widely distributed in our tissues: mainly (98%) in muscles as phosphocreatine (= phosphagen).
- **Creatinine** is creatine anhydride, it is the excretory product of creatine.
- The transamidinase reaction occurs in the kidney.
- The methyl transferase reaction occurs in the liver.

- The creatine goes via blood to different tissues mainly to the muscles (98% of the body creatine).
- Androgen (male sex hormones e.g. testosterone) increase the uptake and retention of creatine by muscles, that is why androgen deficiency leads to creatinuria and decreased muscle creatine.
- Adults excrete very little creatine in the urine (< 50 mg/day in males and < 100 mg/day in females.

Function :

❖ Creatine forms creatine phosphate (phosphagen) which is the main storage form of energy in the cells .

❖ During muscular exercise, ATP is consumed rapidly to ADP. ATP is formed quickly at the expense of creatine phosphate by reversal of the CPK reaction. This occurs before glycoysis starts to produce ATP. i.e. maintain ATP during 1st few minutes of muscle contraction.



FATE AND EXCRETION

- Creatine phosphate spontaneously and irreversibly loses Phosphate, forming creatinine. Creatine itself loses water to form the Same product but at a Slower rate.
- The two reactions result in the steady production of a Constant amount of **creatinine** that is proportional to the total amount of phosphocreatine + creatine in the body, which is in turn proportional to the muscle mass of the organism.
- The creatinine formed goes via the blood to the kidneys to be excreted in the urine.

- The plasma creatinine level varies between **0.6- 1.2 mg/dl**., depending on muscle bulk (higher in males than in females).

- Higher levels are Observed in renal failure.

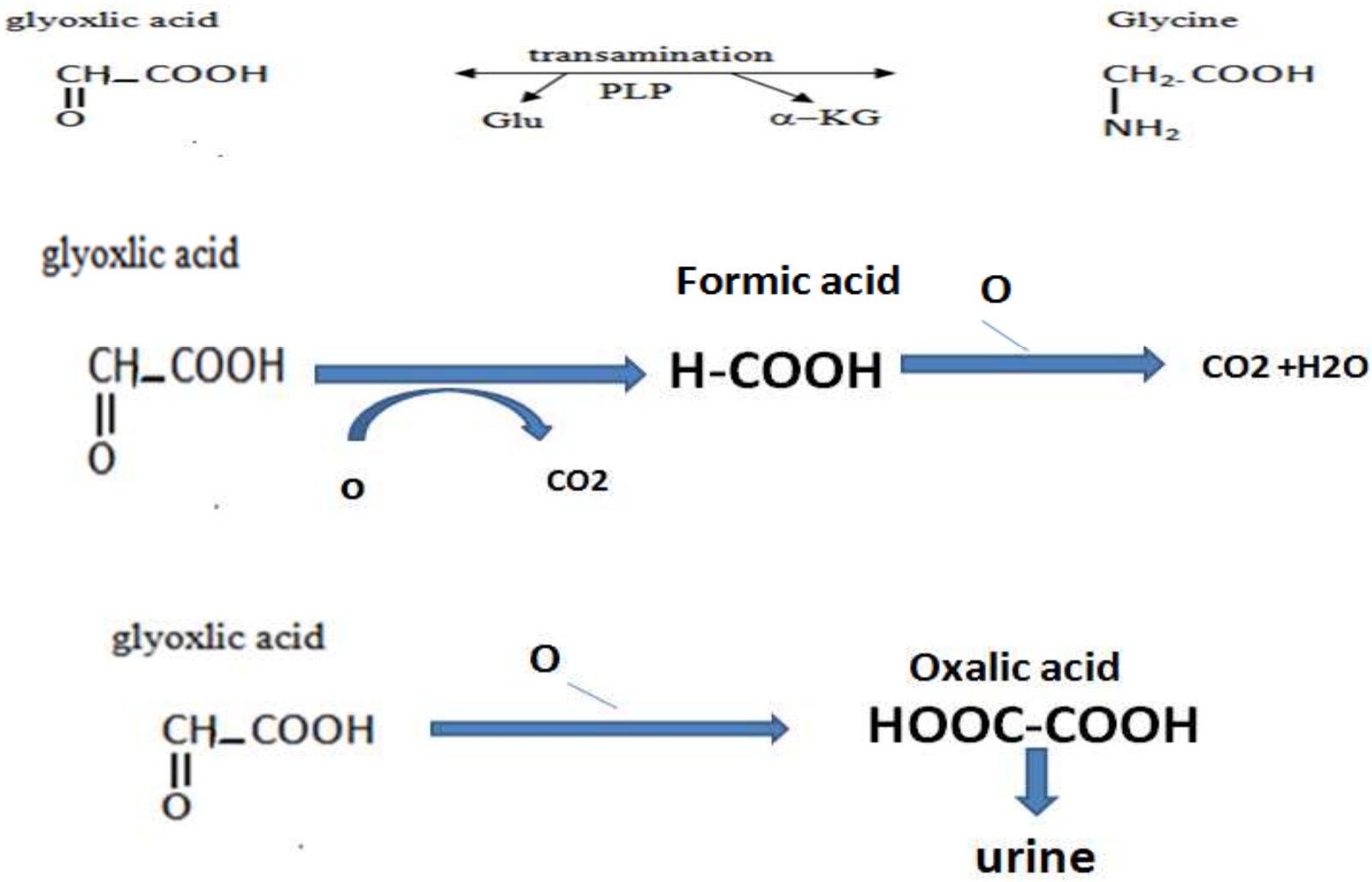
- Creatinine is excreted in the urine in an amount that is directly proportional to the muscle mass, averaging 1.5 g/day in males and 1.0 g/day in females.

II. Organic Acids

A. Oxalic acid

- Urinary oxalic acid is mostly exogenous, being derived from foods containing oxalates (spinach, artichokes, tomatoes, strawberries, mangoes, apricots and peaches). A small part is endogenous, being derived from the metabolism of glycine or from the metabolism of ascorbic acid.
- Very small amounts of oxalates are normally excreted in the urine (10 - 30 mg/day), mostly in the form of calcium oxalate.
- Increased urinary oxalates (hyperoxaluria) may be dietary, due to the ingestion of foods rich in oxalates or the intake of large amounts of vitamin C. It also occurs in an error in glycine metabolism called "primary hyperoxaluria“ .
- Hyperoxaluria leads to the formation of calcium oxalate stones in the renal tract.

Fate of glyoxylic acid



Primary hyperoxaluria:

- Congenital disease caused by decreased metabolism of glyoxylic acid either by oxidative decarboxylation to formic acid or transamination to glycine .
- Accumulated glyoxylic acid is oxidized to oxalic acid. There is excretion of large amounts of oxalate in urine. Oxalate reacts with calcium forming the insoluble Ca-Oxalate that leads to the formation of Ca-Oxalate stones in the urinary tract.

B. Lactic acid

- Lactic acid is the end product of glycolysis in erythrocytes and in muscles during exercise. It mostly goes to the liver where it becomes converted to glucose. Little lactic acid is excreted in the urine (50 200 mg / day).

C. Citric acid

- The citric acid in urine is mostly derived from intermediary metabolism. Some citric acid is excreted in the urine 200- 1200 mg/day.

D. Ketone bodies:

- The ketone bodies include acetone, acetoacetic acid, and β-hydroxybutyric acid. They are formed in the liver as intermediates in the metabolism of fatty acids. Small amounts of ketone bodies (less than 15 mg/day on an average diet, and up to 100 mg/day on a high fat diet), mostly β - hydroxybutyric acid, are excreted in the urine. Their excretion markedly increases in ketosis.

E. Hippuric Acid

- Hippuric acid is the product of detoxication of benzoic acid, by conjugation with glycine. Benzoic acid is present in many fruits and vegetables, especially in plums and prunes. It is used as preservative in some food products, such as jams and ketchup. It also results from the action of intestinal bacteria on phenylalanine. The amount of hippunc acid excreted in the urine is related to the dietary intake of benzoic acid as well as to intestinal putrefaction. It normally ranges between 0.1 and 1.0 g/day.

III. Sugars

- Normally not more than 1 g of sugars is excreted in the urine per day. they cannot be detected by the ordinary tests of Fehling and Benedict. The chief sugar is glucuronic acid (about 0.5 g/day). which is present in urine conjugated with xenobiotics. In addition, smaller quantities of glucose , lactose, and L-arabinose may be present in urine.
- ***Xenobiotics are foreign organic substances, which are substances not normally metabolized in the body. Xenobiotics of medical importance include drugs, toxins, food additives.***

IV. Proteins

- Urine of normal subjects contains small amounts of glycoproteins, which are derived from the mucous glands of the renal tract. Tracts of albumin (< 30 mg /day) are excreted in urine. They cannot be detected by the heat coagulation test.

ABNORMAL CONSTITUENTS

I. Proteinuria :

- This is the presence of detectable amounts of proteins in the urine. It may be:

A- Prerenal Proteinuria

1. Albuminuria: This occurs in heart failure due to increased renal venous pressure.
2. Bence Jones Proteinuria: this is an abnormal globulin, composed of light chains only, formed by malignant plasma cells (multiple myeloma). It precipitates at 60°C, redissolves at 100 C, and reprecipitates on cooling.

3. Myoglobinuria: Myoglobinuria occurs in crush syndrome and in myocardial infarction due to release of myoglobin from crushed skeletal muscles and heart, respectively.
4. Hemoglobinuria: Hemoglobin appears in the blood plasma and in the urine if intravascular hemolysis occurs, e.g,, in hemolytic anemia and in malaria.

B-Renal Proteinuria

- This is due to kidney affection. Albumin, having a higher plasma concentration and a lower molecular weight, appears in the urine in higher concentrations that globulins, and hence the name albuminuria.

1. False Albuminuria (Functional Albuminuria):

- This is not pathological; no organic lesion is detectable in the kidneys. It is intermittent, occurring only when the renal venous pressure increases, e.g., during muscular exercise and on assumption of the erect posture (orthostatic), and disappears on lying down. Thus, it is absent in the morning sample, and only present in the day samples.

2. Microalbuminuria:

- Albumin is detected by ordinary tests only if urinary albumin exceeds 200 mg/d. Levels between 20 and 200 mg/L, called microalbuminuria, can only be detected by special tests. It is an early sign of glomerular affection in uncontrolled diabetes mellitus.

3. True Albuminuria :

- This is pathological. It is more commonly due to lesions of the renal glomeruli (glomerulonephritis and nephrosis) than lesions of the renal tubules (pyelonephritis).

B-Postrenal Proteinuria

- This is caused by inflammation, tumors, or stones of the renal tract, leading to the secretion of mucus and the passage of blood (albumin, globulins, and hemoglobin) in the urine.

II. Glycosuria:

- This term has long been used to indicate the presence of detectable amounts of glucose in the urine. More properly, it should be used to indicate the presence of any sugar in the urine, these include glucose, fructose, galactose, pentoses, or lactose.

III. Chyluria

- Chyluria is the presence of absorbed fat (chylomicrons) in the urine. It rarely follows the ingestion of large amounts of fats, particularly in severe diabetic patients (decreased clearance of chylomicrons and VLDL due to decreased activity of lipoprotein lipase),
- it may also be caused by an abnormal connection between the intestinal lymphatics and the urinary tract. This may be congenital and may be caused by filariasis. The urine acquires a milky appearance that disappears upon shaking with ether.

IV. Choluria

- Choluria is the appearance of bile in the urine. It includes:

1. Bilirubin and Bile Salts: Bilirubin and bile salts appear in the urine in obstructive Jaundice, due to obstruction of the biliary passages and regurgitation of bile into the blood
2. Urobilinogen: Urobilinogen is normally present in the urine in very small amounts (less than 4 mg/day). It markedly increases hemolytic jaundice.

V. Ketonuria

- Ketonuna is the presence of delectable amounts of ketone bodies in the urine.