The acid base balance

1) Causes of acidosis and alkalosis

2) renal regulation of PH

Respiratory acidosis

↑CO_2 (CO_2 RETENTION) due to

- Bronchial asthma
- Chronic bronchitis
- Emphysema
- Pneumonia
- Respiratory centre inhibition
- Asphexia

↑CO_2 → ↑ blood H_2CO_3

Causes of Metabolic acidosis

1- ↑blood acids

↑production

- ↑ lactic acid in muscular exercise
- ↑ ketone bodies in Ketosis due to Diabetes mellitus
- ↑ acids from metabolism of different food stuffs (diet) as pyruvic , lactic, phosphoric and nucleic acids.

↓excretion

- failure of excretion by the kidney in <u>chronic renal failure</u>

Causes of Metabolic acidosis

1- ↑ base loss

- **Diarrhea**: Intestinal juices are alkaline being rich in Na^+ & K^+ bicarbonate
- **Vomiting**: due to low intestinal obstruction
- **Hyperkalemia**:

*↑renal tubular reabsorption of Na^+ in exchange with K^+

→ stop of Na^+/ H^+ exchange

* Na^+ reabsorption will be in the form of NaCl not $NaHCO_3$ > HCO_3^- will be excreted in the form of $KHCO_3$ in urine.

HCO_3^- loss in urine → metabolic acidosis (Alkaline urine)

↑ Cl in blood→ hyperchloremic acidosis (Acidic blood)

The alkaline urine& acidic blood is called paradoxical acidosis

Respiratory alkalosis

↑ CO_2 loss due to

- fever
- encephalitis
- high altitude
- late stages of salicylate poisoning
- hystrical hyperventilation

↓CO_2 → ↓ blood H_2CO_3

Causes of Metabolic alkalosis

1- ↑absorption of bases

- Intake of high vegetable and fruit diet: They contain Bicarbonate salts and citrate salts. Citrate salts will be transformed into bicarbonate salts by krebs cycle
- Intake of drugs containing bicarbonate & citrate salts (drugs used for treatment of hyperacidity & peptic ulcer)

Causes of Metabolic alkalosis

2- ↑loss of acids

- Prolonged suction of gastric juice
- Vomiting due to high intestinal obstruction
- Hypokalemia:

*↓renal tubular reabsorption of Na^+ in exchange with K^+

→ instead there is Na^+/ H^+ exchange

* Na^+ reabsorption will be in the form of NaHCO3 not NaCl →

Cl^- loss in urine in the form of NH4Cl→ hypochloremia and acidic urine

↑ NaHCO3 in blood→ alkalosis(alkaline blood)

The acidic urine& alkaline blood is called paradoxical alkalosis

- Cushing syndrome: →Na& water retention & K excretion→ hypokalemia

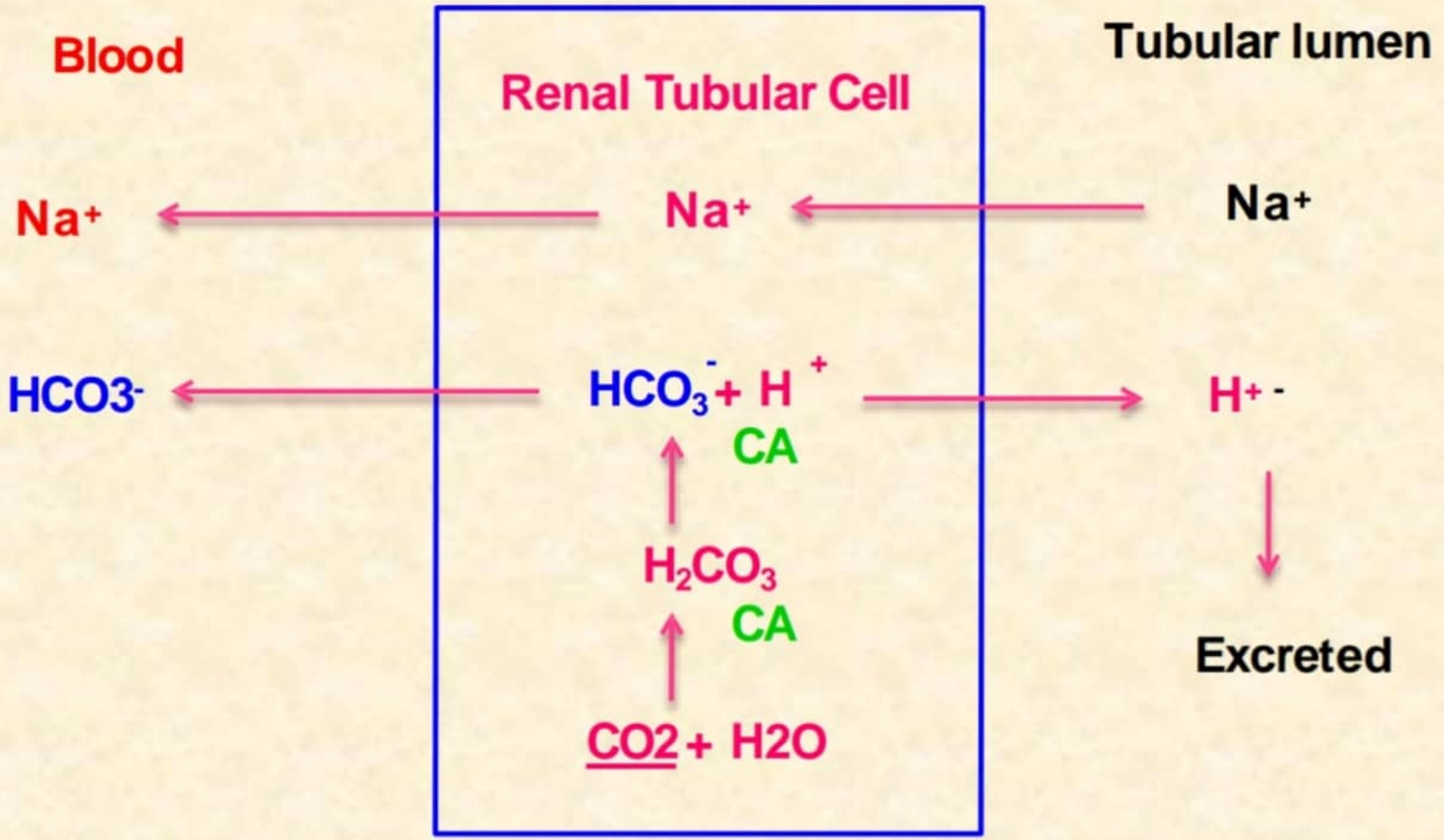
Renal mechanism for pH regulation

- The kidneys plays an important role in the regulation of pH through:
- 1-Excretion of H^+ ions
- 2-Reabsorption of Bicarbonate
- 3-Excretion of titratable acid
- 4-Excretion of ammonium ions

Excretion of H^+ ions

- Kidney is the only route through which the H^+ can be eliminated from the body.
- H^+ excretion occurs in the proximal convoluted tubules & is coupled with generation of HCO_3^-.
- Carbonic anhydrase catalyses the production of carbonic acid (H_2CO_3) from CO_2 & H_2O in renal tubular cells.
- H_2CO_3 then dissociates to H^+ & HCO_3^-
- H^+ ions are secreted into tubular lumen in exchange for Na^+
- Na^+ in association with HCO_3^- is reabsorbed into blood

Excretion of H^+ ions

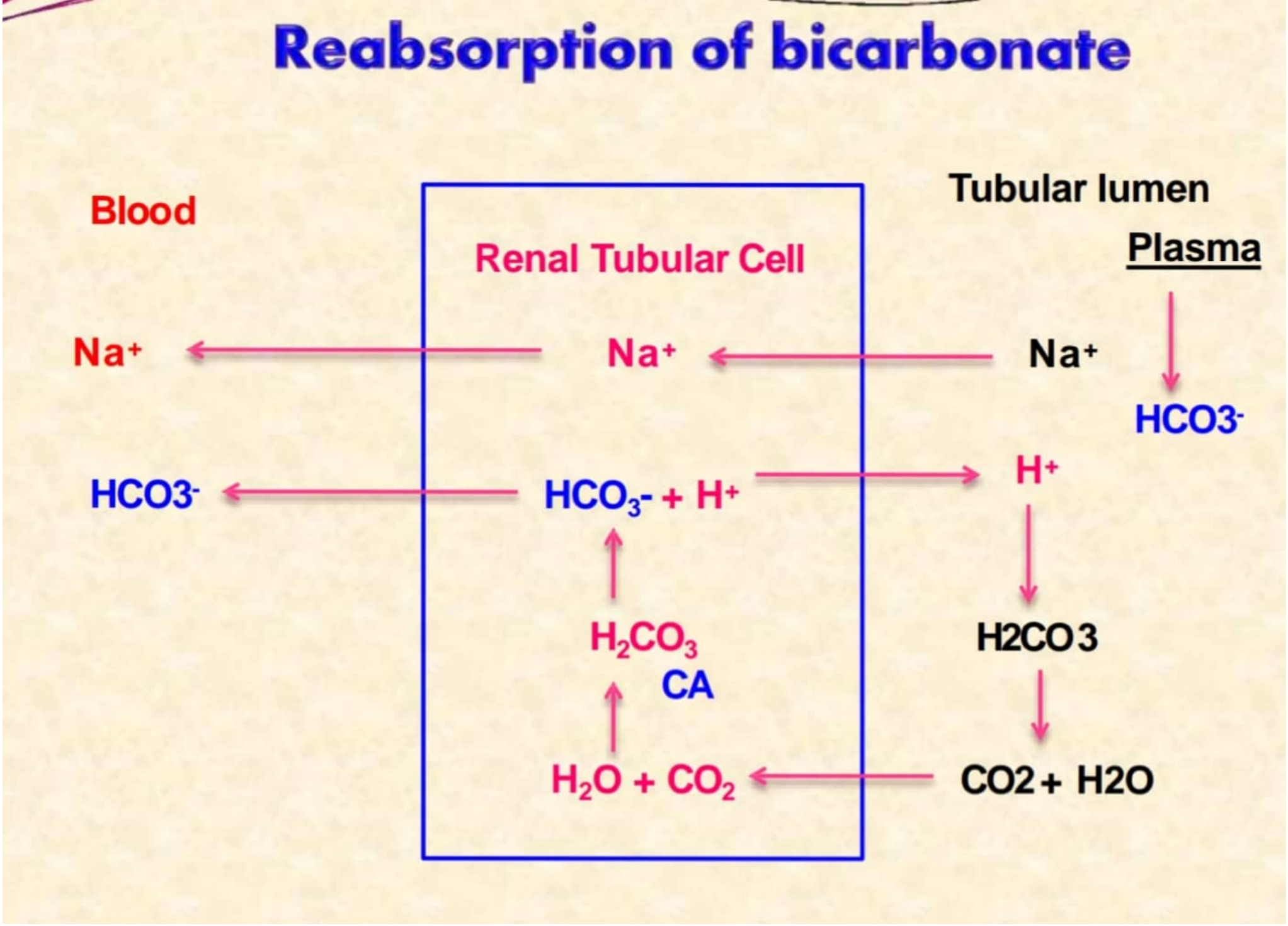


Reabsorption of Bicarbonate

- This mechanism is responsible to conserve blood HCO_3^-, with simultaneous excretion of H^+ ions.
- Bicarbonate freely diffuses from plasma into tubular lumen.
- HCO_3^- combines with H^+, secreted by tubular cells, to form H_2CO_3.
- H_2CO_3 is then cleaved to form CO_2 and H_2O.
- As the CO_2 concentration builds up in the lumen, it diffuses into the tubular cells along the concentration gradient.

- In the tubular cell, CO_2 again combines with H_2O to form H_2CO_3 which then dissociates into H^+ & HCO_3^-
- The H^+ is secreted into the lumen in exchange for Na^+.
- The HCO_3^- is reabsorbed into plasma in association with Na^+.
- Reabsorption of HCO_3^- is a cyclic process without net excretion of H^+ or generation of new HCO_3^-

Reabsorption of bicarbonate



Excretion of titratable acid

Titratable acidity is a measure of acid excreted into urine by the kidney.

Titratable acidity refers to the number of milliliters of N/10 NaOH required to titrate 1liter of urine to pH 7.4.

Titratable acidity reflects the H^+ ions excreted into urine.

H^+ ions are secreted into the tubular lumen in exchange for Na^+ ion.

This Na^+ is obtained from the base, disodium hydrogen phosphate (Na_2HPO_4).

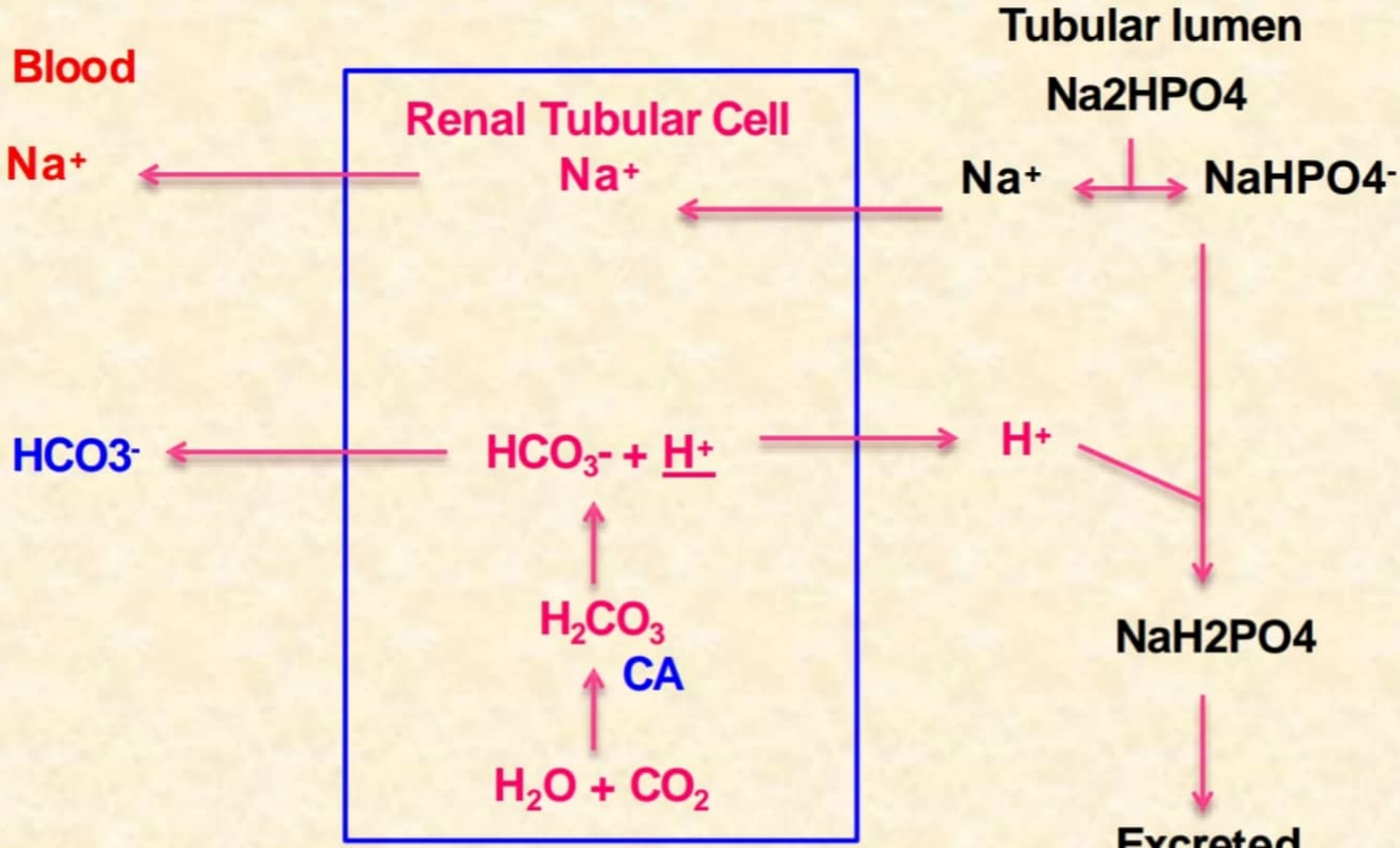
This combines with H^+ to produce the acid, sodium dihydrogen phosphate (NaH2PO4), in which form the major quantity of titratable acid in urine is present.

Tubular fluid moves down the renal tubules,

more and more H^+ ions are added, resulting in the acidification of

urine. Causes a fall in the pH of urine as low as 4.5.

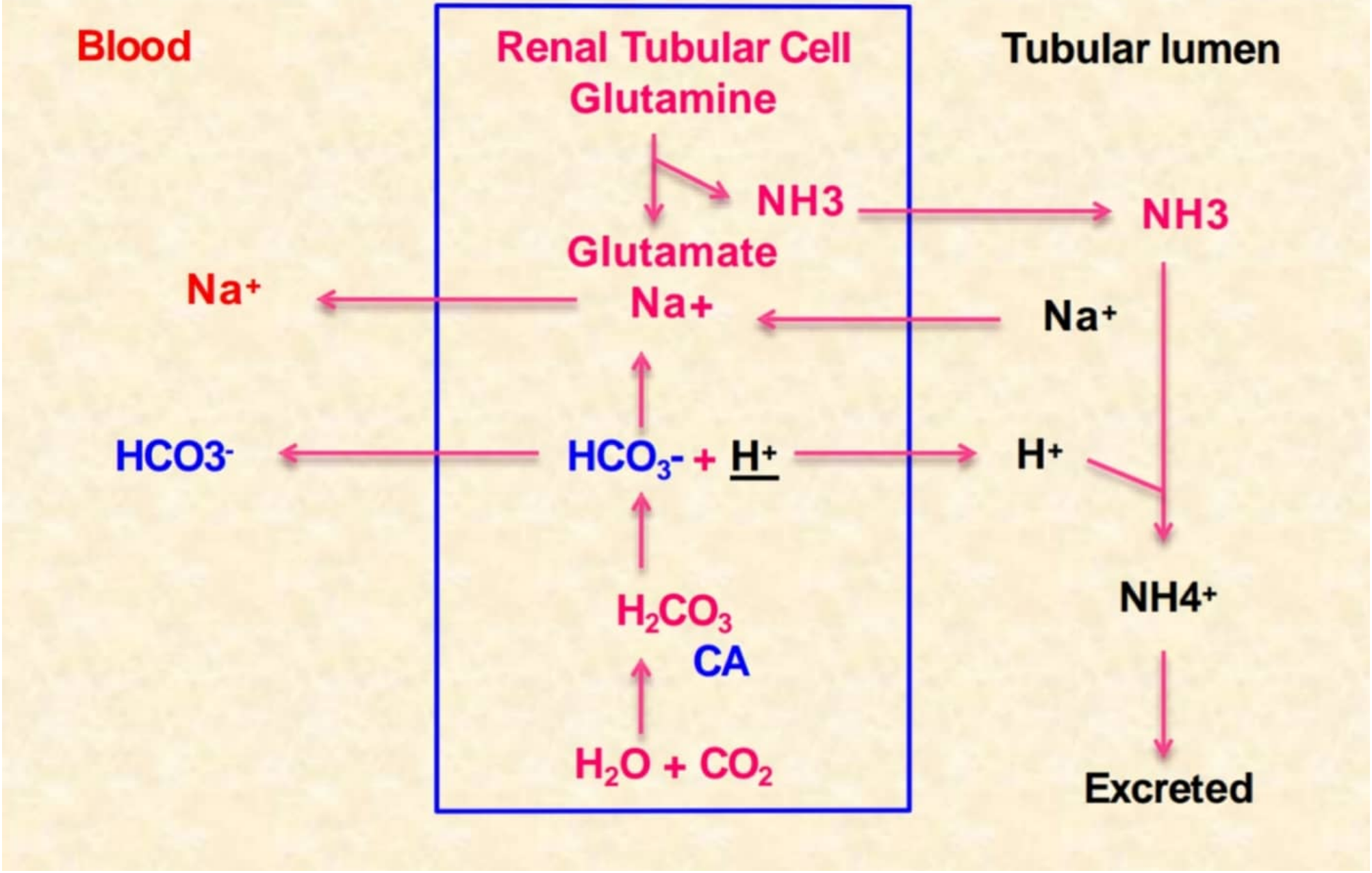
Excretion of titratable acid



Excretion of ammonium ions

- The H^+ ion combines with NH_3 to form ammonium ion (NH_4^+).
- The renal tubular cells deaminate glutamine to glutamate and NH_3 by the action of enzyme glutaminase.
- The liberated NH_3 diffuses into the tubular lumen where it combines with H^+ to form NH_4^+.
- Ammonium ions cannot diffuse back into tubular cells and excreted into urine.

Excretion of ammonium ions



Biochemical aspects of kidney function

1) Gluconeogenesis

2) creatine synthysis, abnormalites

b. Gluconeogenesis:

Definition: synthesis of glucose from ***non-carbohydrate*** precursors such as: 1- lactate. 2-glucogenic amino acids (Gln, Ala). 3-glycerol.

4-propionate.

Site: in ***liver*** (90%) & ***kidney cortex*** (10%)

Importance:

1. Gluconeogenesis is important when the dietary supply of glucose does not satisfy the metabolic demands.

- Under these conditions, glucose is required by the ***CNS***, the ***RBC***, ***renal medulla*** and possibly, other tissues which cannot obtain all their energy requirements from fatty acids or ketone body oxidation.

2. gluconeogenesis may be important in the removal of excessive quantities of glucose precursors from the blood (lactic acid after severe exercise for example).

- The ability of the kidney to convert certain organic acids to glucose, a neutral substance, is an example of a ***nonexcretory mechanism in the kidney for pH regulation***.

Gluconeogenesis: liver vs renal cortex

- Although the biosynthetic pathways are similar, there are several important differences in the factors, which regulate gluconeogenesis in the two organs.

1. The **liver** utilizes predominately pyruvate, lactate and ***alanine.*** The **kidney cortex** utilizes pyruvate, lactate, and ***glutamine***.
2. ***Hydrogen ion*** activity has little effect upon hepatic gluconeogenesis, but it has marked effects upon renal gluconeogenesis.

- Thus, when intracellular fluid pH is reduced (acidosis), the rates of gluconeogenesis in slices of renal cortex are markedly increased.

Protein metabolism: b. Creatine: synthesis

- It is present in muscle as creatine phosphate **(CP)** which is a high-energy phosphate compound.

Synthesis: It is synthesized from:

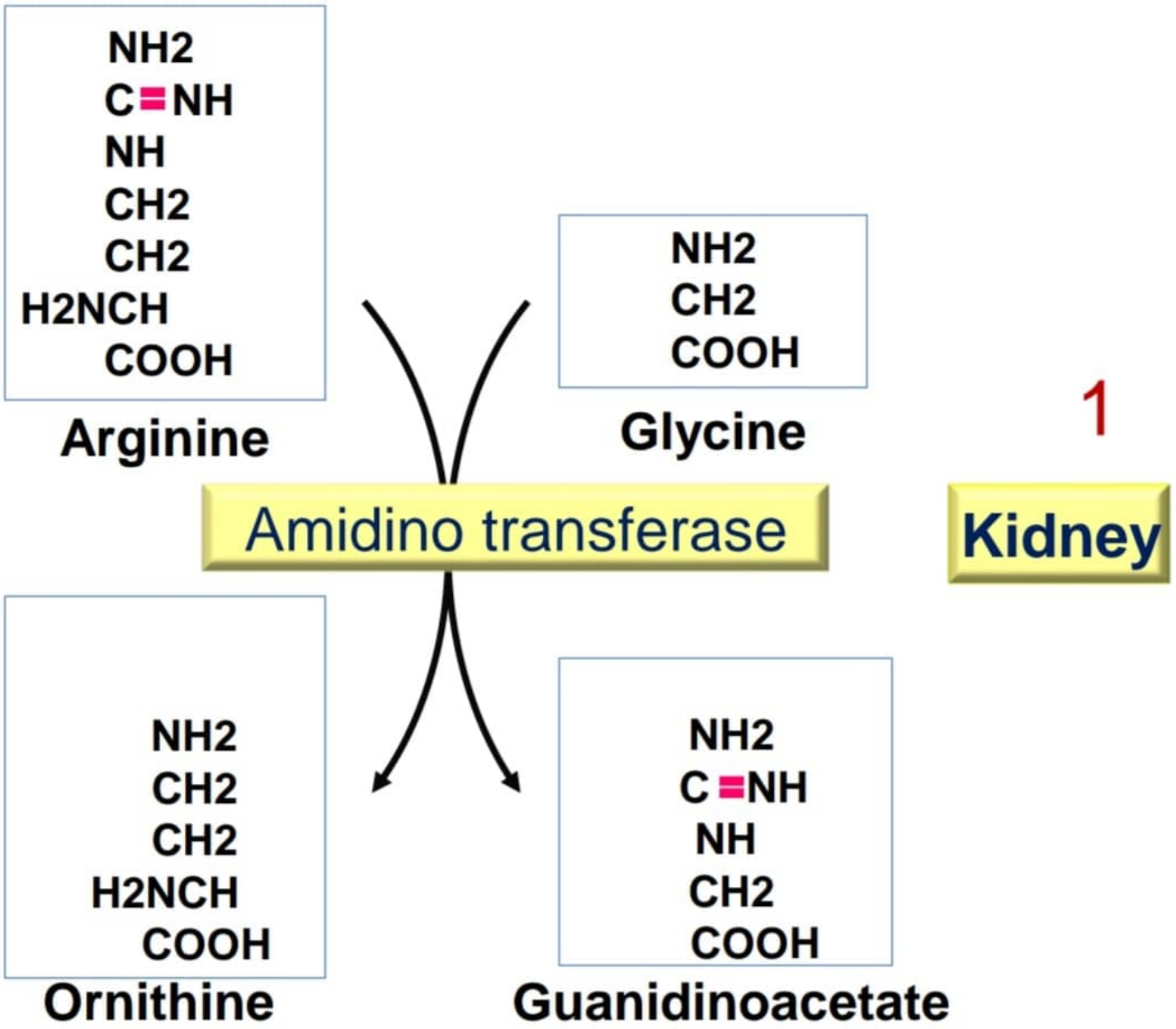
1. ***Glycine.***
2. The guanidino group of ***arginine***.
3. The methyl group of S-adenosylmethionine ***(SAM).***

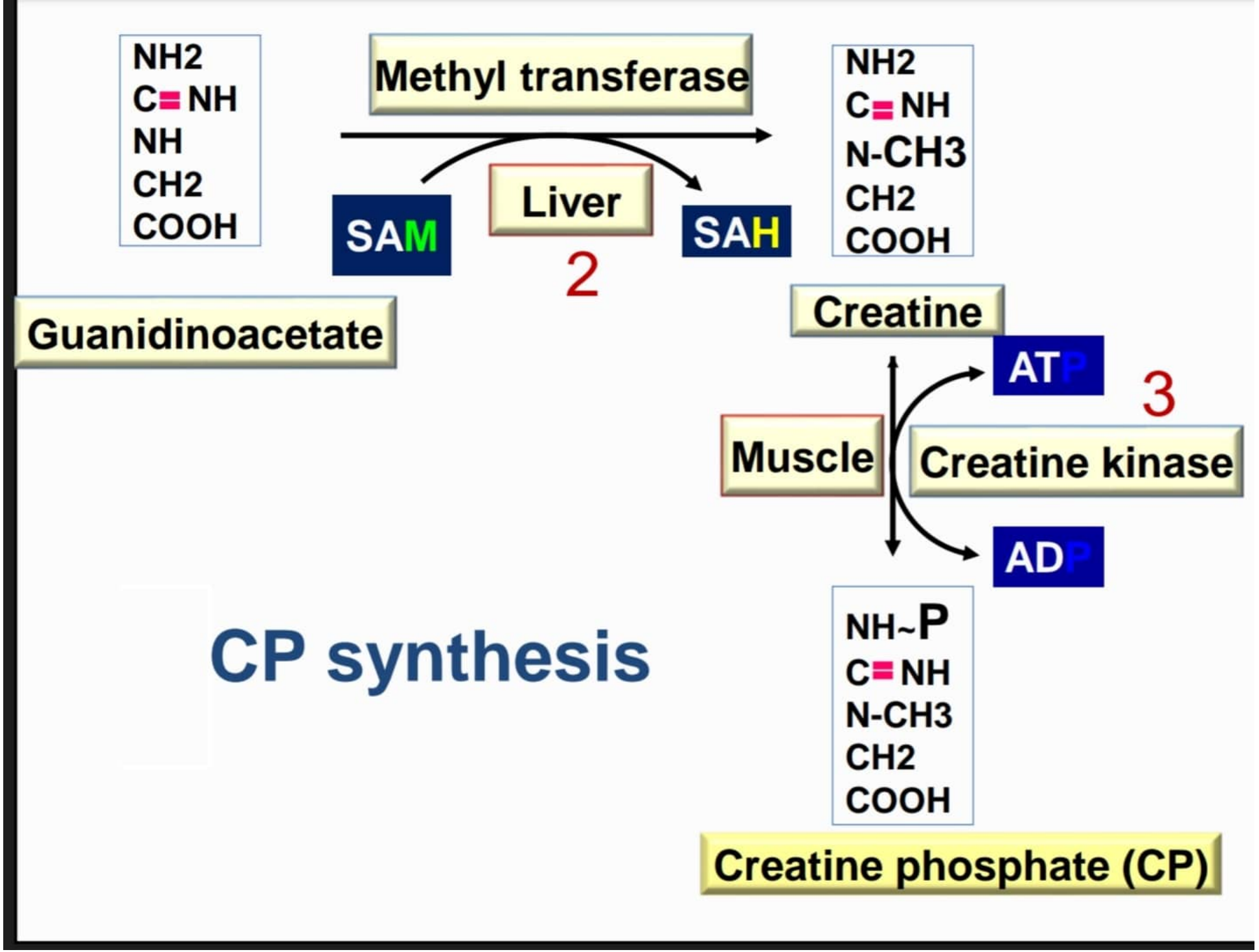
- Creatine formed in the ***liver*** is transported by blood to muscles where it is phosphorylated to phosphocreatine (phosphagen).

➢ During ***rest*** (relaxed muscle), creatine is phosphorylated to store energy.

➢ In ***contracting muscle*** the reaction is reversed to supply ***ATP*.**

Synthesis of Creatine Phosphate: 1




NH2
C=NH
NH
CH2
COOH
Methyl transferase
SAM
Liver
SAH
2
NH2
C=NH
N-CH3
CH2
COOH
Guanidinoacetate
Creatine
ATP
3
Muscle
Creatine kinase
ADP
NH~P
C=NH
N-CH3
CH2
COOH
CP synthesis
Creatine phosphate (CP)

Creatine in urine

- At normal plasma levels, **creatine** is almost completely reabsorbed by renal tubules, thus it is not excreted in significant amounts in urine of normal adult.
- Under normal physiological and some pathological conditions, creatine excretion in urine increases.

Causes of physiological creatinuria:

- In ***young children***. - In ***pregnant*** females and early postpartum period. - prolonged administration of ***androgens***, which reflects increased muscle mass.

Causes of pathological creatinuria:

- All conditions of **muscle wasting** as in:

- Starvation. ***- Hyperthyroidism.*** ***- Diabetes mellitus.***

- Fevers. - Degenerative muscle diseases ***(myopathies)***

Urine analysis

1)volume and specific gravity of urine

2) crystals in urine

Urine analysis

I. Physical properties of urine

- *Volume, Colour, Odour, Reaction, Aspect, Deposits, Specific Gravity.*

• Volume

- Normal urine volume is ***600 - 2 000 ml/day***.
- Normally, more urine is secreted during the day than at night.

Increased volume:

❖ ***Physiological increase***: - After excessive fluid intake.

❖ ***Abnormal increase(polyuria):*** More than 3 L/day

- Diabetes mellitus (may reach 5 L/day)
- Diabetes insipidus (10-15 L/day)

Urine analysis

I. Physical properties of urine: Volume

Decreased volume:

Physiological decrease: in summer due to increased sweating

Abnormal decrease (Oliguria): Less than 200 ml/day

- acute nephritis.
- heart failure.
- hemorrhage.

Anuria: *No urine* at all. In late stages of renal failure and heart failure.

Specific gravity

- urinary specific gravity (SG) is a measure of the concentration of solutes in the urine. It measures the ratio of urine density compared with water density and provides information on the kidney's ability to concentrate urine.
- Measured by:
  - urinometer
  - refractometer
  - dipsticks

Specific gravity

Normal :- 1.010- 1.030.

- Increase in Specific Gravity - Low water intake, Diabetes mellitus, Albuminuruia, Acute nephritis.
- Decrease in Specific Gravity - Absence of ADH, Renal Tubular damage.
- Fixed specific gravity (isosthenuria)=1.010

In chronic renal failure

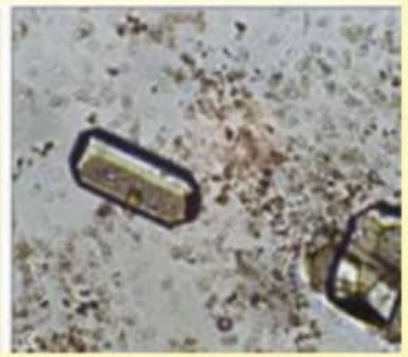
Urine analysis

microscopic examination: Crystals

Crystals in acidic urine:

- **Calcium oxalate:**
  - Shape: envelope shaped or in the form of dumb-bells.
  - Color: colorless.

- **Uric acid:**
  - Shape: various forms e.g. rosettes or barrels.
  - Color: brownish or colorless.



Crystals in alkaline urine

- **Triple phosphate:**
  - Shape: prismatic
  - Color: colorless