

الكيمياء الحياتية
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المرحلة الأولى

Lec 7

Urea cycle: Urea cycle is discovered by Krebs and Hansleit(1932).

Urea cycle is the removal of excess of NH₂ derived from amino acids catabolism in the tissues and excreted in urine.

Site of synthesis: urea formation take place in liver in mammals and the enzymes isolated from liver tissues.

Urea cycle is incomplete in kidney and brain, why?

Because 1. The enzyme arginase is absent in kidney and the enzyme of forming citruline is absent.

Sources of ammonia: 1. NH₂ ——— from oxidative deamination.

2. NH₂ ——— from aspartate.

Significance of urea cycle:

1. detoxification of ammonia :toxic ammonia is converted into a nontoxic substance called urea excreted in urine.

2. biosynthesis of arginine: used for synthesis of protein.

Overall stoichiometry of the urea cycle



8 Tissues other than liver use enzymes of this pathway to make arginine.

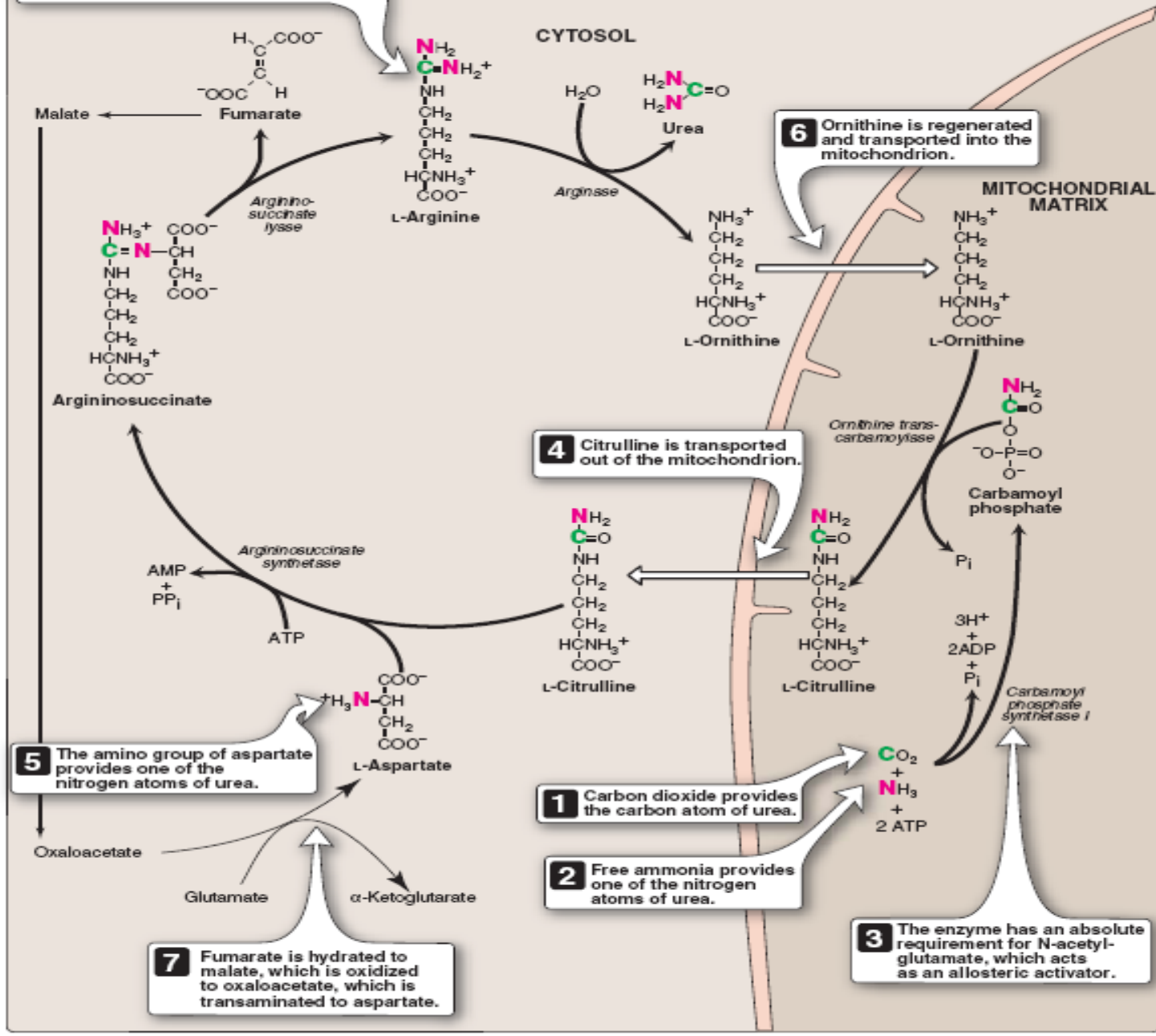


Figure 19.14
Reactions of the urea cycle.

Kidney Functions:

- **Kidney functions are measure of 1. glomerular filtration rate 2. and study tubular function.**
- **Kidney functions test are:**
- **1. blood urea. 2. serum creatinin 3.creatinine clearance.**

1. Blood Urea

Urea is the end product of protein metabolism. It consist of 2NH_3 and CO_2 .

Normal blood urea in healthy fasting adult = 15- 40 mg/ dl

Uremia: increase in blood urea above normal value .

- **Increase in blood urea occur in:**
- **severe burns , hemorrhage , obstruction to urine flow, acute glomerulonephritis , renal tuberculosis.**

- **Decrease in blood urea:**

Severe liver damage , in pregnancy (physiological condition).

Fate of urea : Urea diffuses from liver  to the blood  then to the kidney (filtered and excreted in urine).

A portion of urea diffuse from blood to the intestine also.

Ammonia(NH₃):

Normal blood level = 40-70 microgram/ dl

- = 0.1- 0.2 mg / dl

Hyperammonaemia: increase level of ammonia in the blood more than normal value.

Ammonia increase in : 1. hepatic disease (liver cirrhosis) cause severe reducing in urea synthesis.

2. genetic defects in urea cycle enzymes cause decrease in urea level and increase in NH₃ concentration.

Why ammonia is toxic?

1. it raise intracellular PH.
2. in mitochondria excess of NH_3 will favour the reverse reaction of L- glutamate dehydrogenase



In brain the toxicity is due to:

- Low level of alpha keto glutarate cause depletion in CAC \longrightarrow
- Cause inhibition in respiration of brain \longrightarrow Fatal (high level of NH_3 in tissues and blood).

NH_3 is removed from the body by several methods:

- 1. Amination of keto acid.
- 2. Amidation of glutamic acid to form glutamine.
- 3. formation of urea cycle.

Toxicity affect CNS(central nervous system) cause:

- 1. weakness**
- 2. unsteadness**
- 3. tremors**
- 4. seizures**
- 5. decerebrate rigidity**
- 7. coma**
- 8. death**

serum creatine and creatinine:

Creatine: is normal constituent of the body, consist of amino acids glycine , arginine and methionine.

Creatin present: 1- 2 % in liver , blood , brain.

98% is present in muscle, as free and phosphorylated.

(phosphorylated creatine in muscle equal to 80%.

In whole blood : normal creatine level varies from 2- 7 mg/ dl

In male : 0.2- 0.6 mg/dl

In female: 0.35- 0.9 mg/dl

Urinary excretion:

- **In healthy people**, creatine is excreted as creatinine form in urine.
- **In male:** 1.5- 2.0 mg in 24 hrs in urine.
- **In female:** 0.8- 1.5 mg in 24 hrs in urine.

Increase in urine in case of(normal case).

1. muscular persons.
2. after severe exercise.

Creatinuria: excretion of creatine in urine it is occur in

1. pregnancy
2. myopathese disease.
3. children: reason probably lack of ability to convert creatine to creatinine
4. in wasting disease, malignancies.

Uric acid:

It is the chief end product of purine metabolism.

The ingestion of food high in nucleoprotein such as glandular organs produces a marked increase in urinary uric acid.

Diets like milk , eggs , cheese, with low purine contents, cause no increase in urinary uric acid

Uric acid present in body water. In normal subjects about 1130 mg of uric acid is present.

Plasma contains higher concentration of uric acid compared to other compartment contain water.

Normal range of uric acid:

in male: 3- 7 mg/dl

in female: 2- 6 mg/dl

- **Normally 500- 600** mg of uric acid is synthesized. Some is excreted in urine ,some is excreted in bile and some is converted to ammonia and urea by the intestinal bacteria.

- **Clinical disorder:**

Gout: Gout is chronic disorder characterized by excess of uric acid in blood (**hyperuricemia**). This occur due to deposition of **sodium monourate** in **tophi** structure.

Recurring attacks of acute arthritis; These are due to deposition of **imonosodium urate** in and around the affected joints.