

# UREA CYCLE

- The urea cycle ( also known as the ornithine cycle ) is a cycle of biochemical reactions occurring in many animals that produce urea from ammonia .
- When the nitrogen of the amino acids is converted to urea in the liver , their carbon skeletons are converted either to glucose ( in the fasting state ) or to fatty acid ( in the fed state ) .
- Ammonia travels to the liver from other tissues in the form of alanine and glutamine . It is released from amino acids in the liver by a series of transamination and deamination reactions .

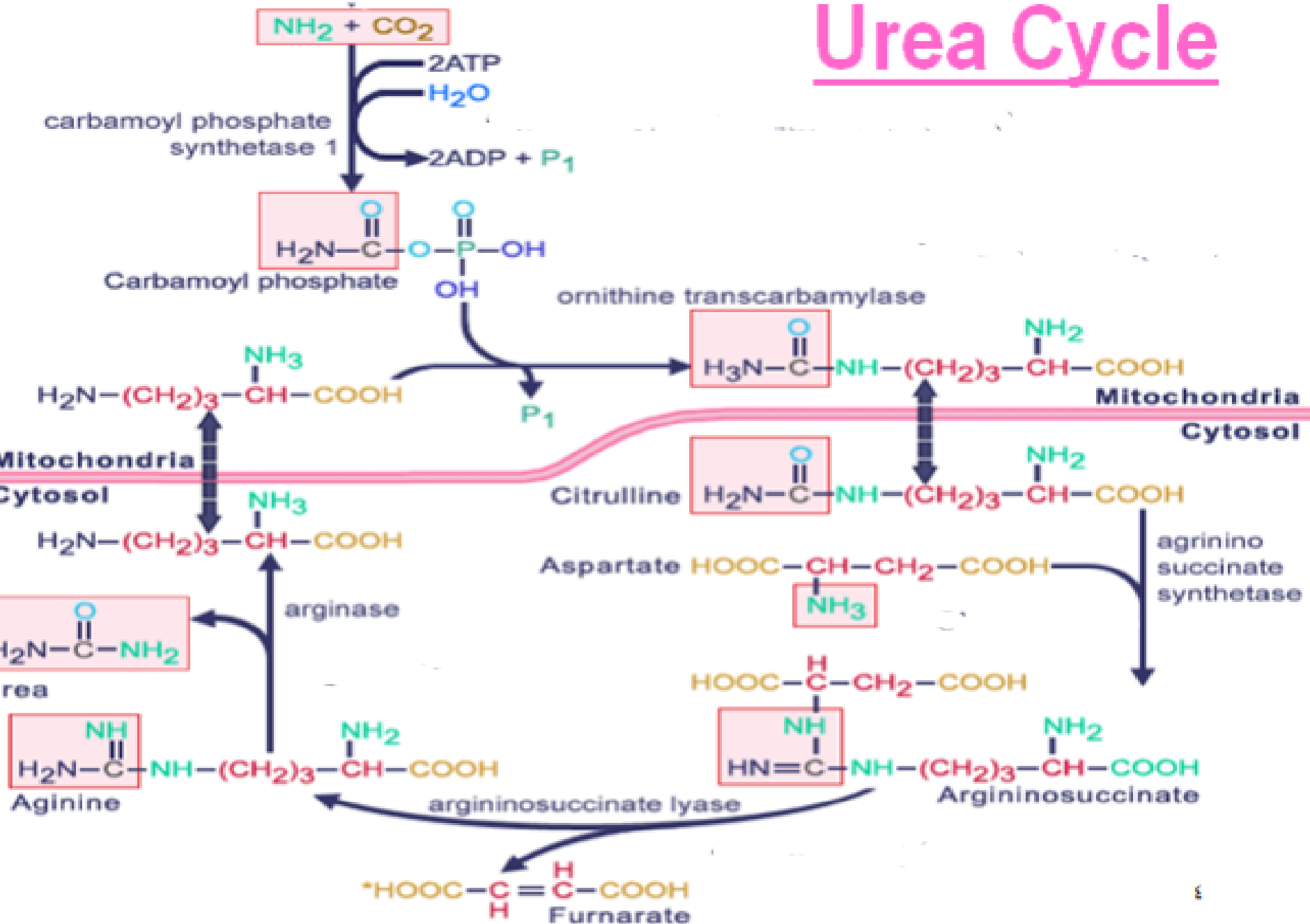
# *Urea Cycle*

1. Ammonium is toxic (  $N = 15 - 40\mu\text{M}$  , max  $70\mu\text{M}$  ) .
2. Excretion  $\text{NH}_4^+$  by kidneys important for acid-base balance.
3. Hyperammonium **> 500  $\mu\text{M}$**  plasma  $[\text{NH}_4^+] = \text{TOXIC}$   
related to inborn errors of metabolism (genetic defects) as well as induced ( liver failure ) .
- 4 . Urea is measured in the blood as blood urea nitrogen ( BUN ) ,  
BUN may be elevated in :
  - Both acute and chronic renal ( kidney ) failure .
  - Congestive heart failure lead to a low blood pressure and consequent reduced filtration rates through the kidneys .
  - urinary tract obstruction , in these hemodialysis is used to remove the soluble urea and other waste products from the blood .
- 5 . Ammonia is very toxic , particularly to the CNS .

## *Nitrogen-containing components of normal urine*

<b>End Product</b>	<b>Excreted %</b>
Urea	86.0
Creatinine	4.5
Ammonium	2.8
Uric acid	1.7
Other compounds	5.0

# Urea Cycle



# Notes

- 1. In human , uric acid is not produced from ammonia , but is synthesized from adenine and guanine found in various nucleotide . Uric acid concentration may become elevated in kidney diseases and leukemia . A painful articular disorder called gout results from deposition of uric acid salts in cartilage in the joints. ( Gout can be controlled by diet or by a drug called allopurinol which inhibit the enzyme that produce uric acid ) .**
- 2. Role of Urea cycle : rid the body of toxic  $\text{NH}_4^+$  therefore permitting the use of amino acids as an energy source .**
- 3. Liver major site of urea synthesis , major source of arginase , ( small amounts in small intestine) and is the only tissue with the complete set of all 5 enzymes required .**

- 4 . Normal value of the blood urea is 3.3 – 7.5 mmole/l while the normal value of serum uric acid is 180 – 420 mmole / l .**
- 5 . Any disease or condition that adversely affects liver mitochondria can also produce an increased level of ammonia in the blood such condition include cirrhosis , alcoholism and hepatitis .**
- 6 . Carbamoyl phosphate synthetase is the rate limiting enzyme of the urea cycle .**
- 7 . Symptoms of hyperammonemia with in 3 – 5 days include feeding intolerance , vomiting , irritability , seizures and coma .**

8 . Synthesis of one mole of carbamoyl phosphate requires 2 mole of ATP . One ATP serves as the phosphoryl donor for formation of the mixed acid anhydride bond of carbamoyl phosphate . The second ATP provides the driving force for synthesis of the amide bond of carbamoyl phosphate .

9 . The normal nitrogen balance is a state where the amount of nitrogen ingested each day is balanced by the amount excreted resulting no net change in the amount of the body nitrogen .

# Nitrogen balance

Under some conditions, the body is either in negative or positive nitrogen balance. In negative nitrogen balance, more nitrogen is excreted than ingested, this occurs in starvation and certain diseases.

A diet deficient in essential amino acids also leads to negative nitrogen balance since body proteins are degraded to provide the deficient essential amino acids. Negative nitrogen balance also occurs in injury when there is net destruction of tissue and in major trauma or illness.

Positive nitrogen balance occurs in pregnancy and during feeding after starvation and occurs in growing children who are increasing their body weight.