TRANSAMINATION AND UREA CYCLE

USMAN SUMO FRIEND TAMBUNAN
ARLI ADITYA PARIKESIT
SEPTIANA

BIOINFORMATICS GROUP
DEPARTEMENT OF CHEMISTRY
FACULTY OF MATHEMATIC AND SCIENCE
UNIVERSITY OF INDONESIA

What is transamination?

- Transamination

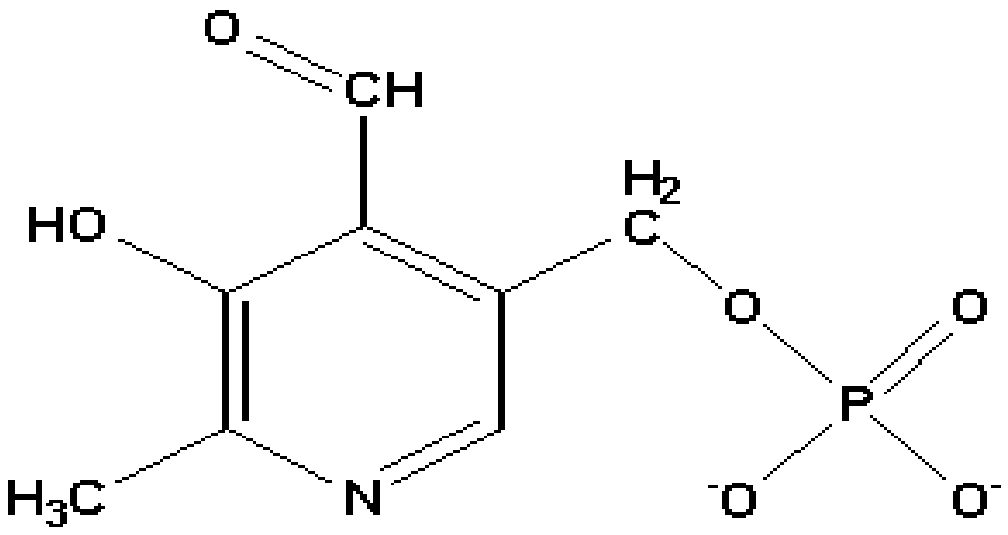
  is process by which the amino group of amino acid is transferred to an acceptor keto acid.

  * It is catalyzed by *transaminases / aminotransferases.*

- Such as :α- ketoglutarat to yield glutamate.

  oxaloacetate to yield aspartate.

- Aminotransferase utilize a coenzyme “Pyridoxal Phosphate / PLP”.
- Vitamin B_6
- Structure



Pyridoxal Phosphate (PyP; Vitamin B6)

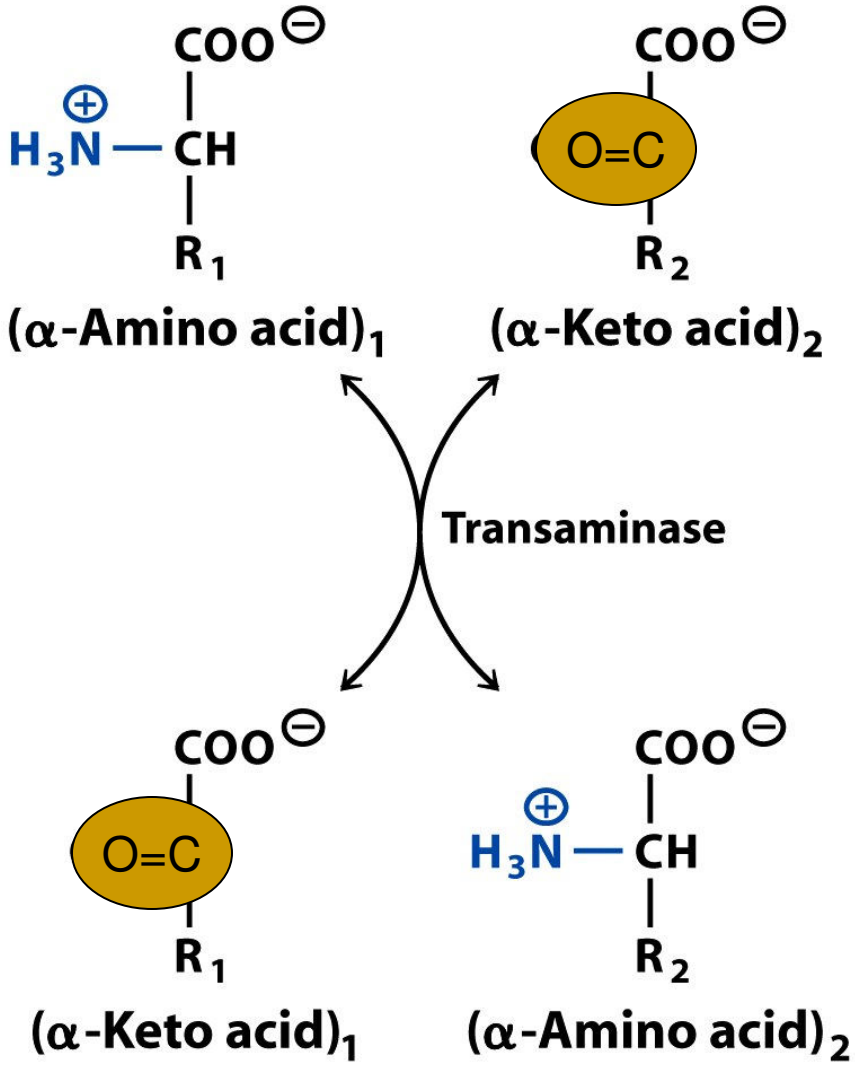
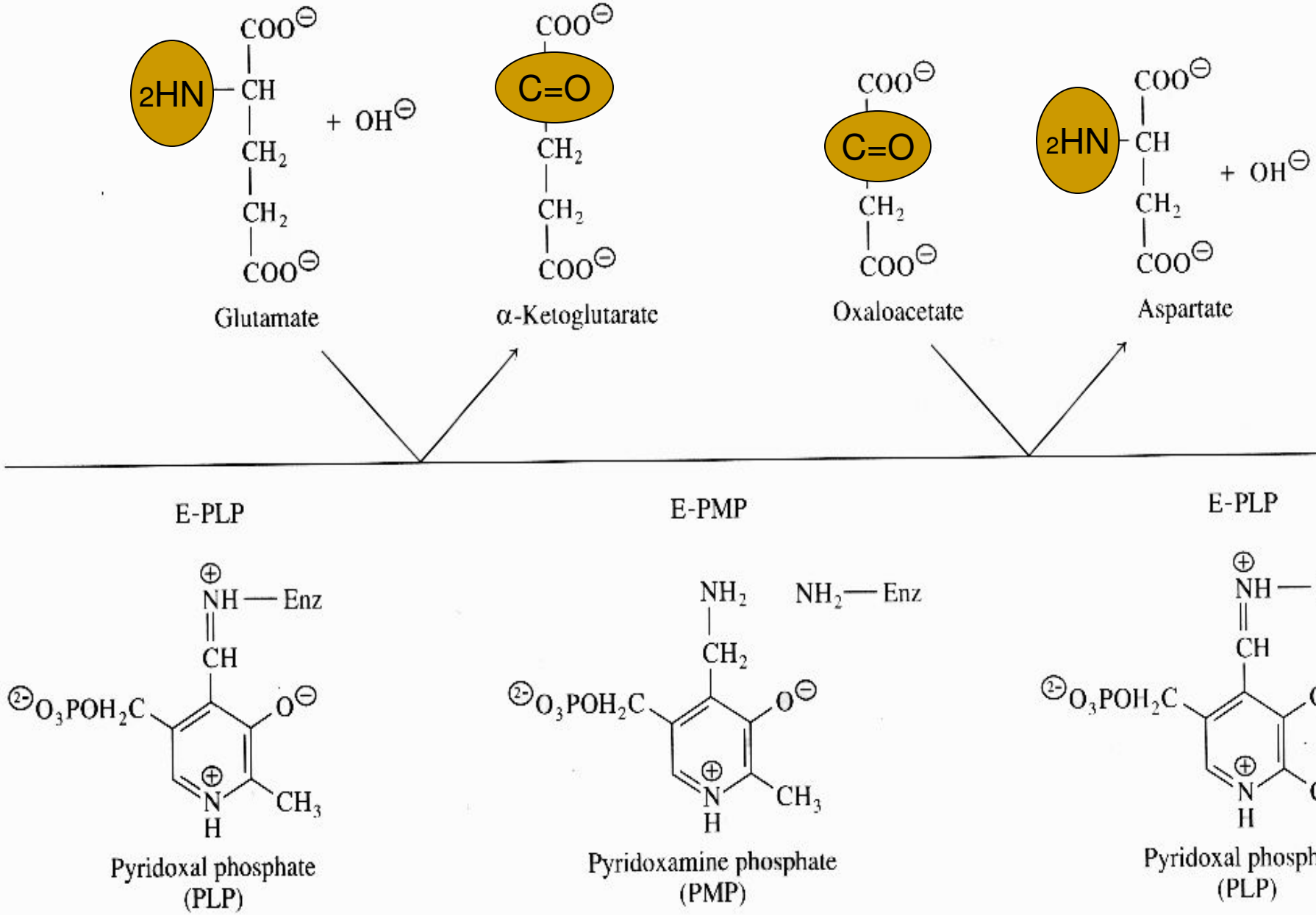


Figure 17-6 Principles of Biochemistry, 4/e


Glutamate
α-Ketoglutarate
Oxaloacetate
Aspartate
E-PLP
E-PMP
E-PLP
Pyridoxal phosphate
(PLP)
Pyridoxamine phosphate
(PMP)
Pyridoxal phosphate
(PLP)

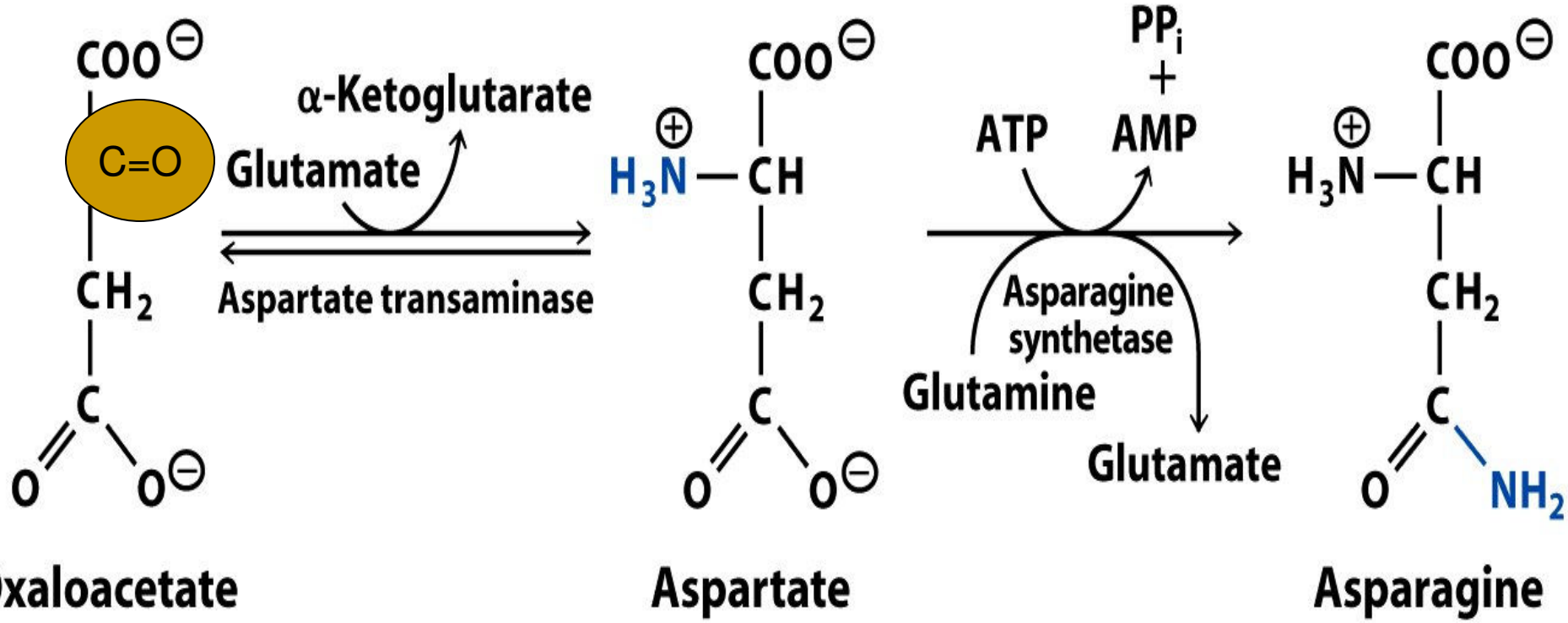
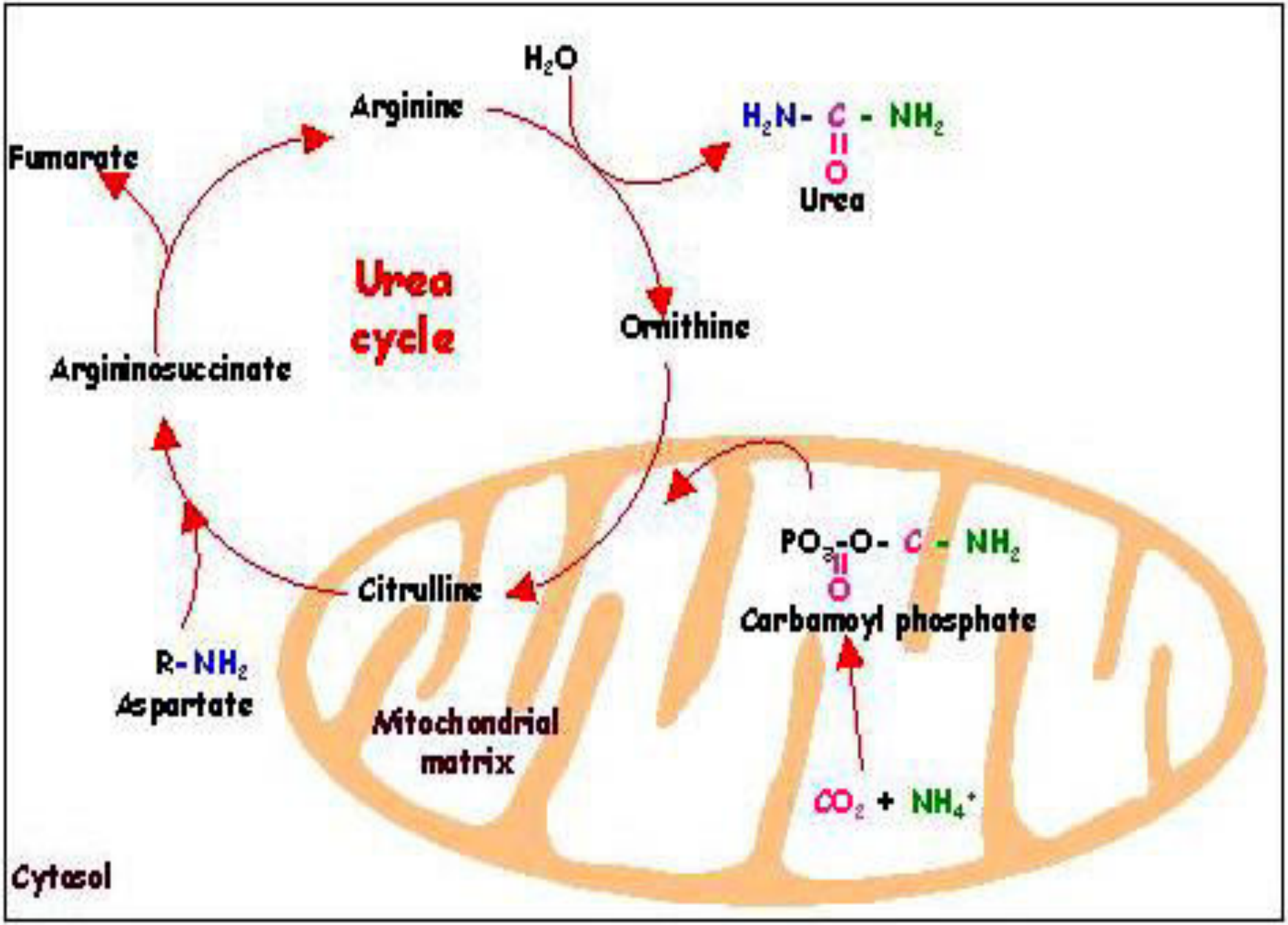
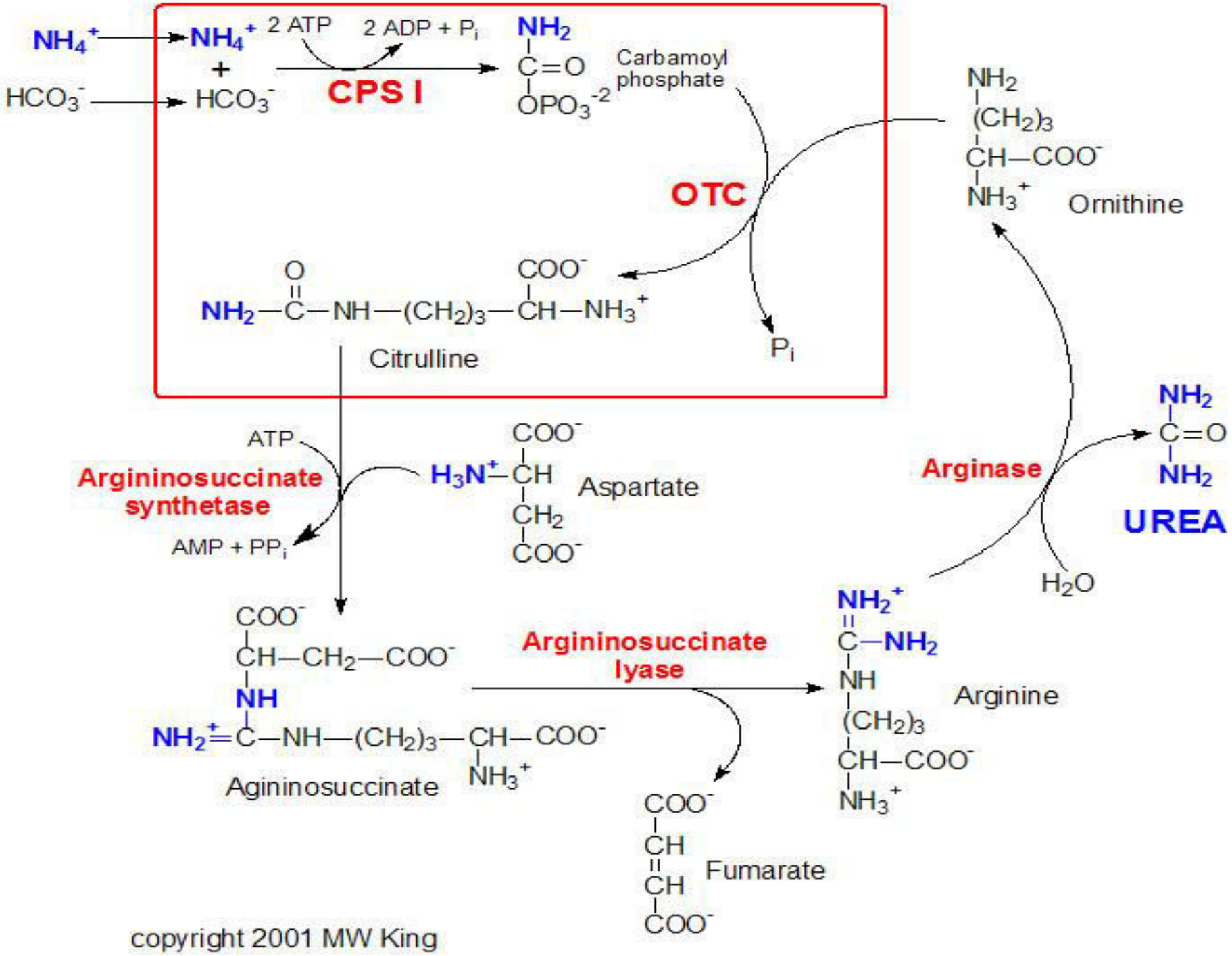


Figure 17-10 Principles of Biochemistry, 4/e

UREA CYCLE

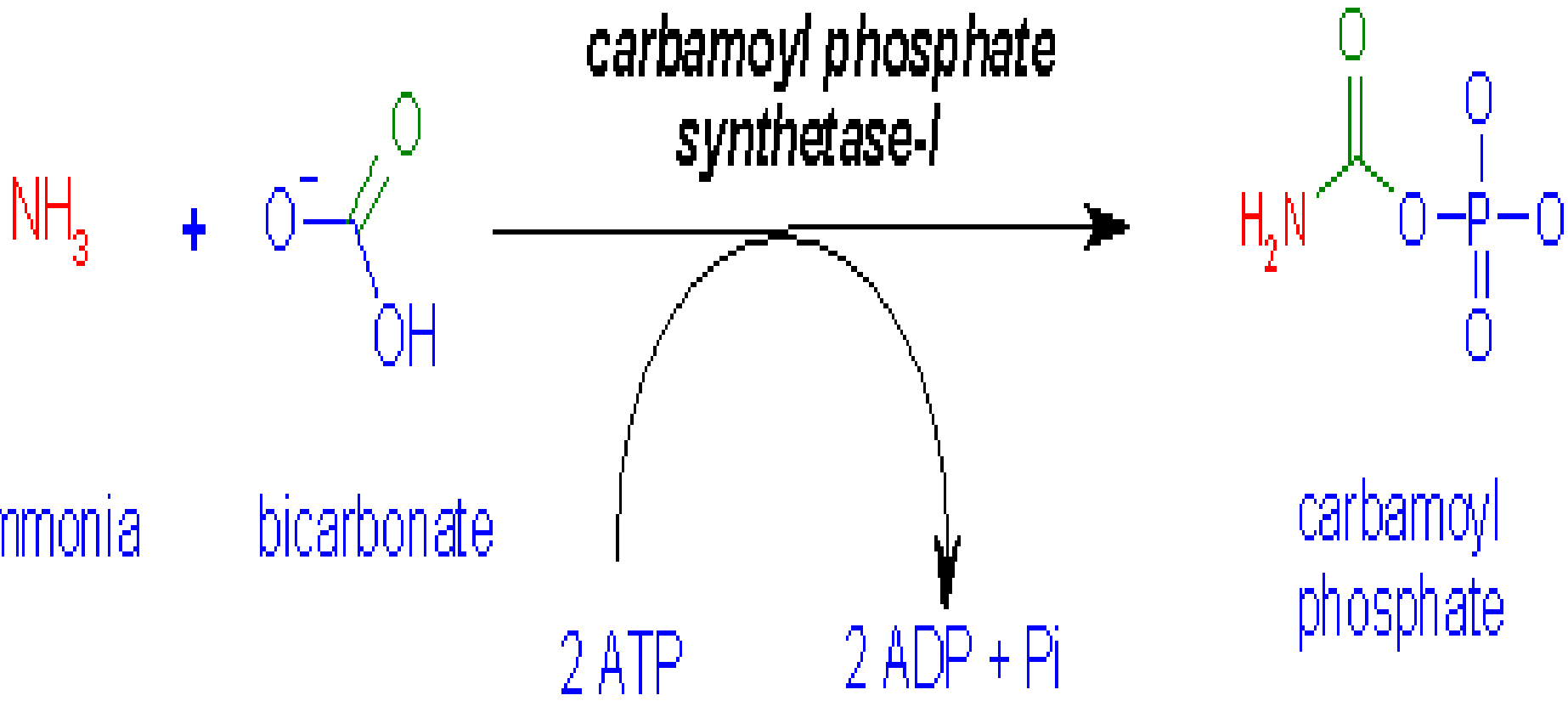
- How is the process of urea cycle?


H2O
Arginine
H2N- C - NH2
O
Urea
Fumarate
Urea cycle
Ornithine
Argininosuccinate
PO3-O- C - NH2
O
Carbamoyl phosphate
Citrulline
R-NH2
Aspartate
Mitochondrial matrix
CO2 + NH4+
Cytosol

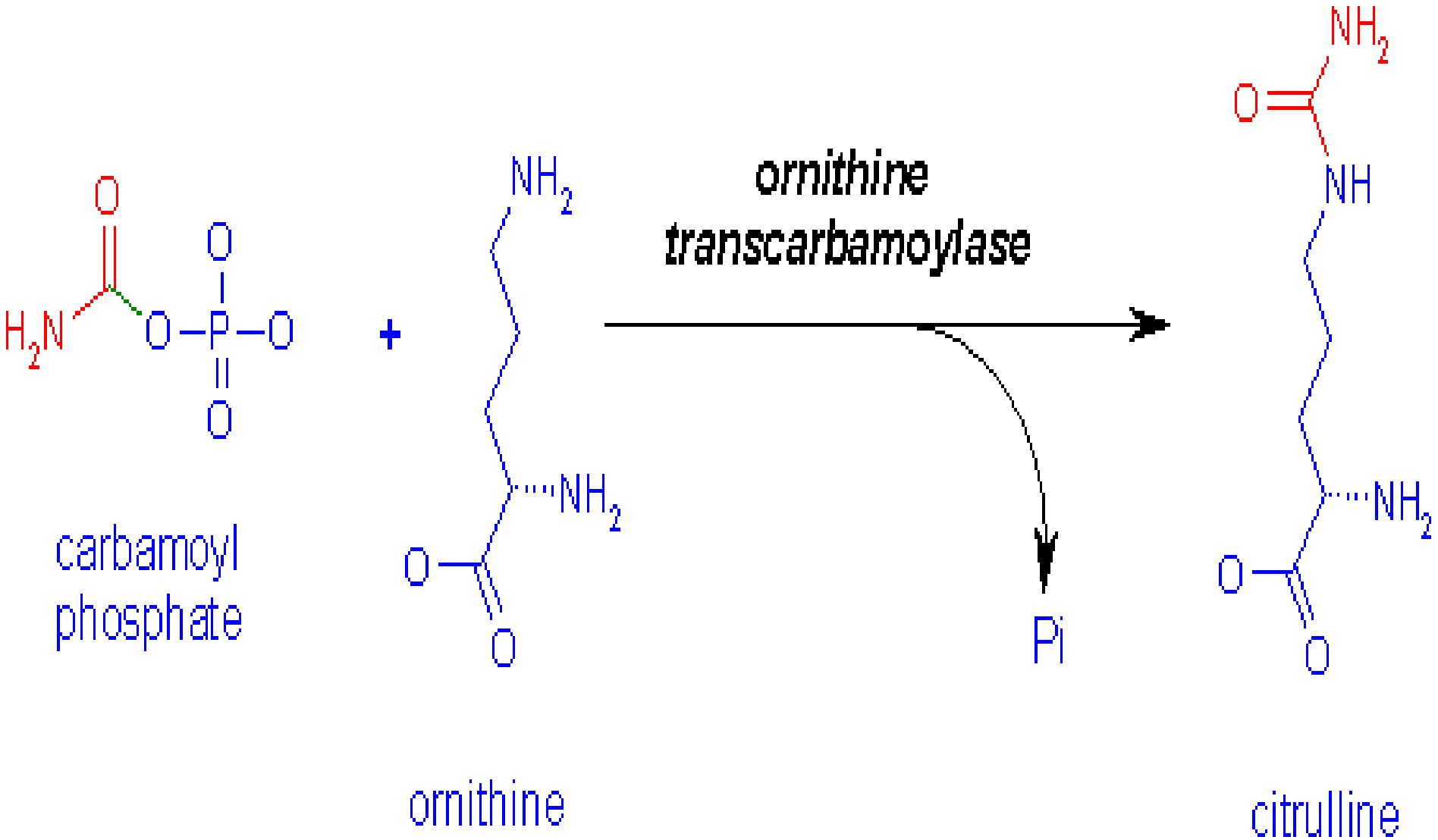

NH4+
HCO3-
2 ATP
2 ADP + Pi
CPS I
Carbamoyl phosphate
OTC
Ornithine
Citrulline
Pi
ATP
Argininosuccinate synthetase
AMP + PPi
Aspartate
Arginase
UREA
H2O
Argininosuccinate lyase
Agininosuccinate
Arginine
Fumarate
copyright 2001 MW King

Five Step of Urea Cycle

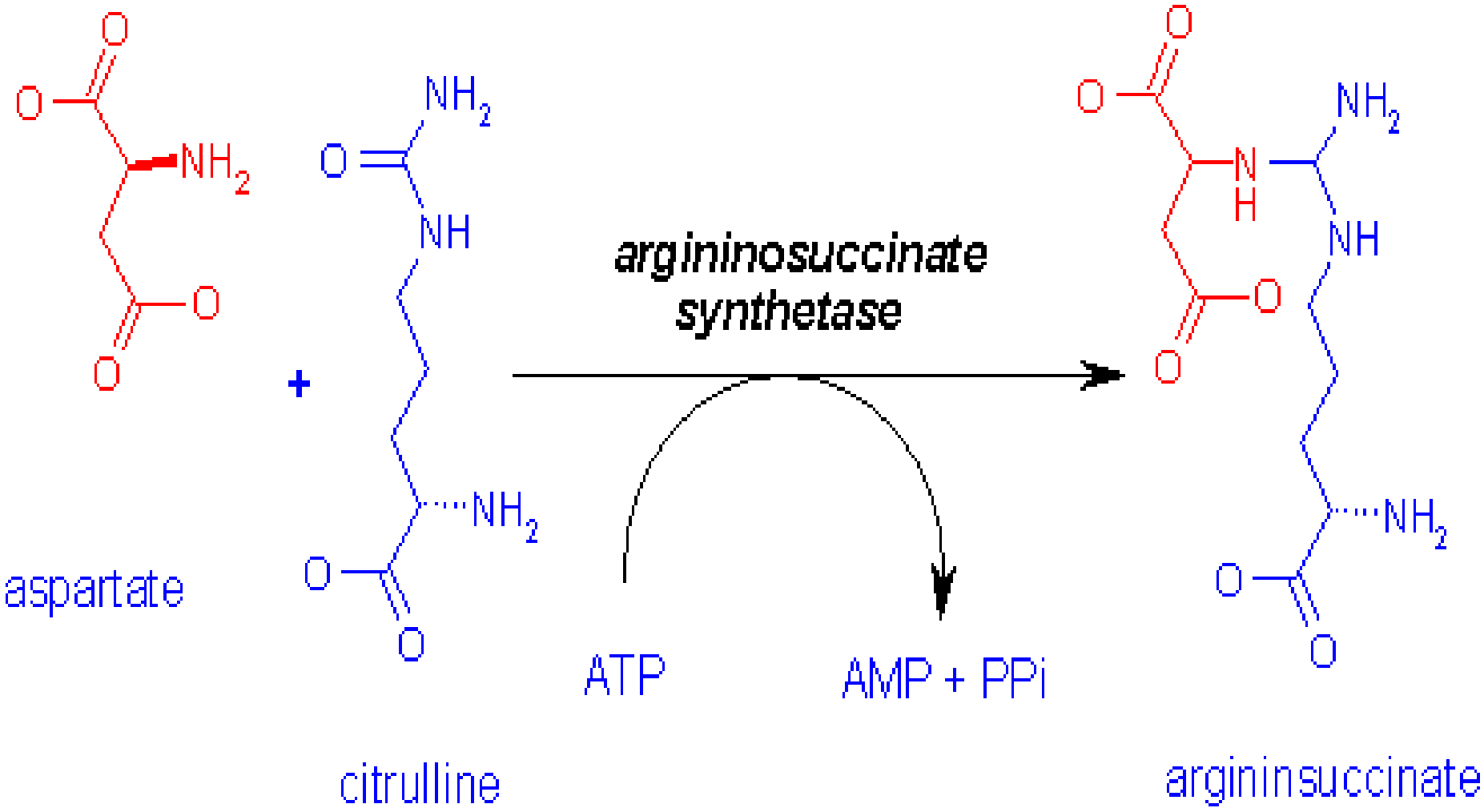
STEP 1



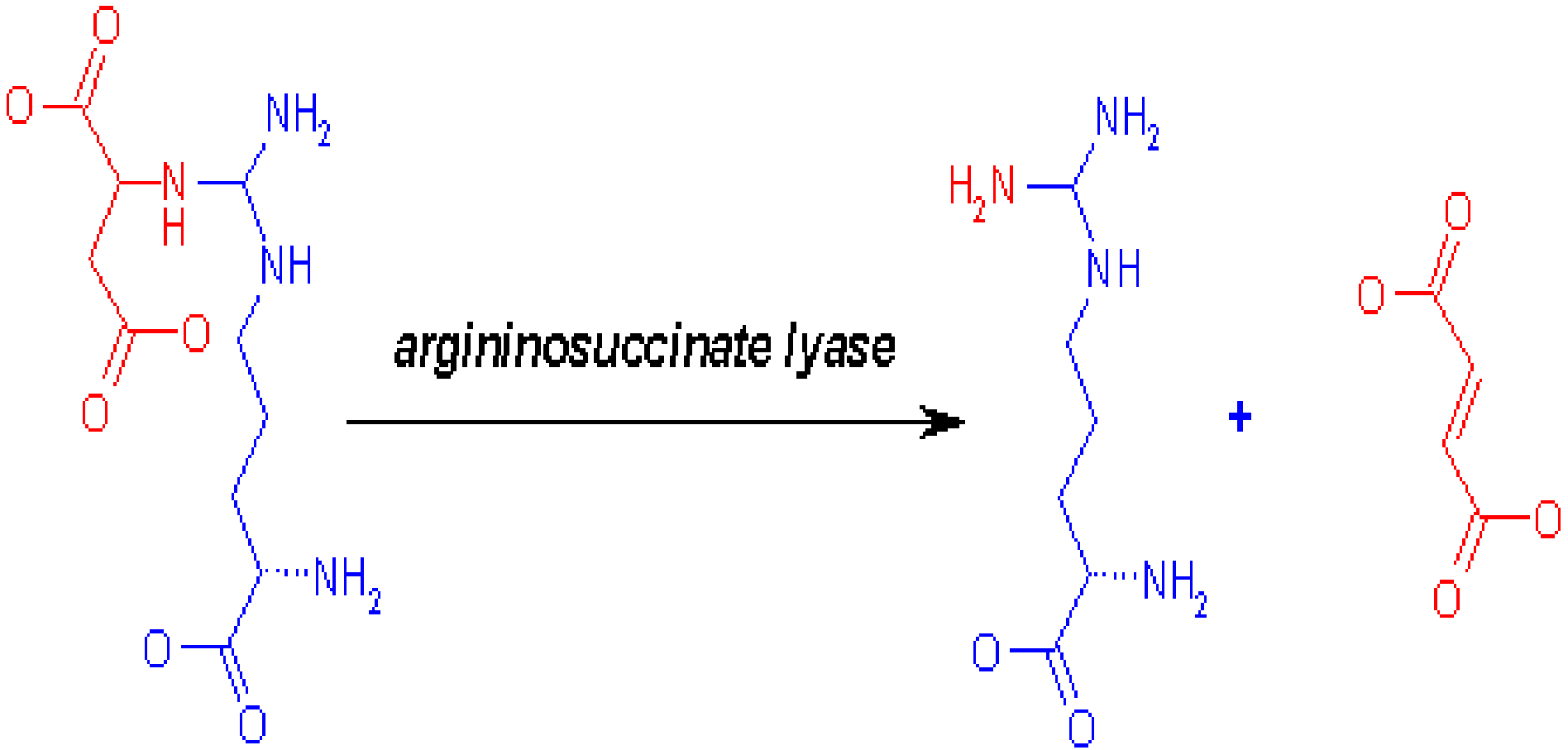
Step 2


ornithine
transcarbamoylase
carbamoyl
phosphate
ornithine
Pi
citrulline

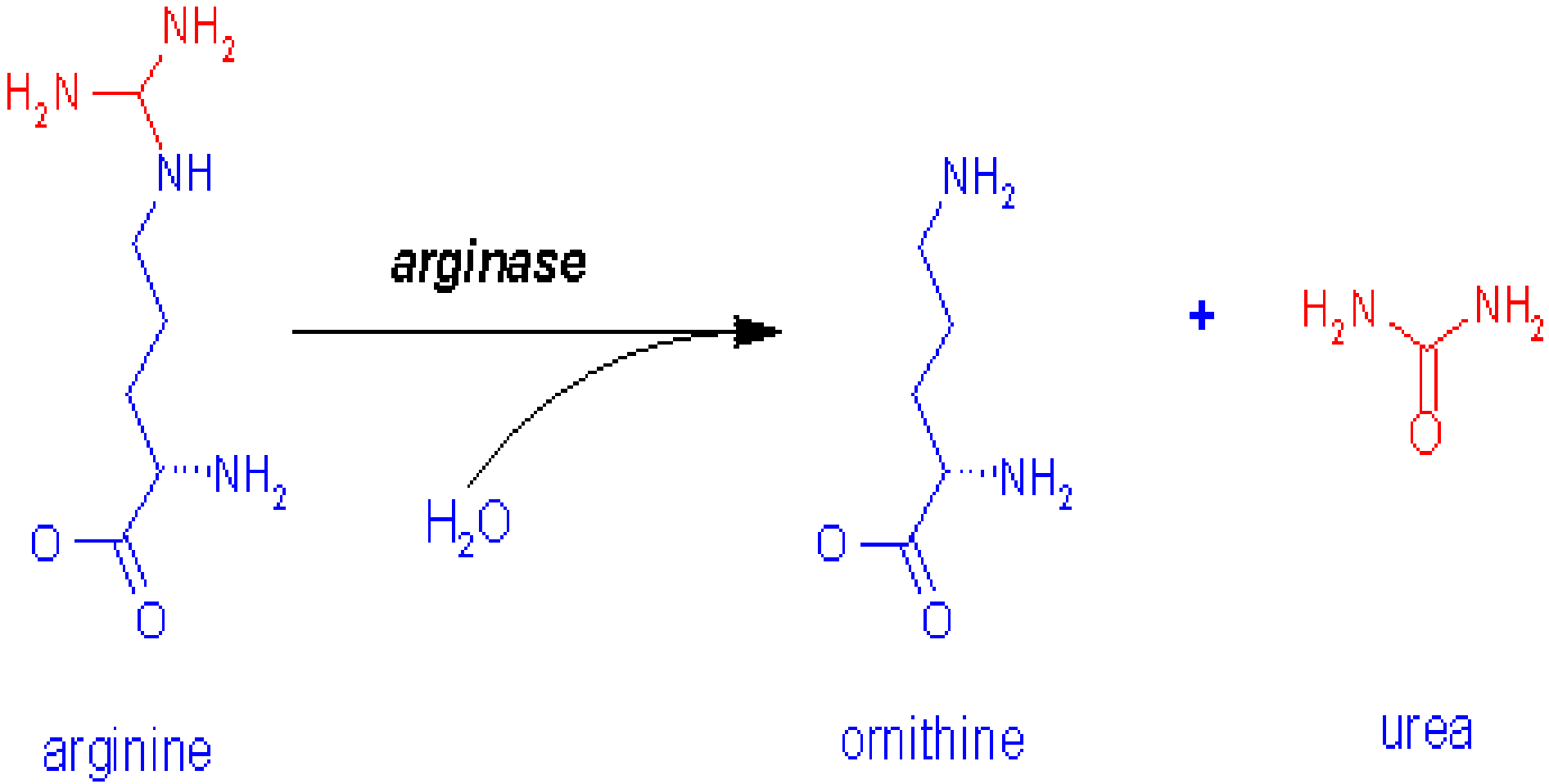
Step 3


argininosuccinate synthetase
aspartate
citrulline
ATP
AMP + PPi
argininsuccinate

Step 4


argininosuccinate lyase
argininsuccinate
arginine
fumarate

Step 5


NH2
H2N
NH
NH2
O
O
arginase
H2O
NH2
NH2
O
O
+
H2N
NH2
O
arginine
ornithine
urea

Urea Cycle Disorder

No	Urea Cycle Disorder (UCD)	Enzymes deficiency	Symptoms/Comments
1.	Type I Hyperammonemia, CPSD	Carbamoylphosphate synthetase I	with 24h - 72h after birth infant becomes lethargic, needs stimulation to feed, vomiting, increasing lethargy, hypothermia and hyperventilation; without measurement of serum ammonia levels and appropriate intervention infant will die: treatment with arginine which activates N-acetylglutamate synthetase

Urea Cycle Disorder

2.	N-acetylglutamate synthetase Deficiency	N-acetylglutamate synthetase	Severe hyperammonemia, mild hyperammonemia associated with deep coma, acidosis, recurrent diarrhea, ataxia, hypoglycemia, hyperornithinemia: treatment includes administration of carbamoyl glutamate to activate CPS.

Urea Cycle Disorder

3.	Type 2 Hyperammonemia OTCD	Ornithine transcarbamoylase	most commonly occurring UCD, only X-linked UCD, ammonia and amino acids elevated in serum, increased serum orotic acid due to mitochondrial carbamoylphosphate entering cytosol and being incorporated into pyrimidine nucleotides which leads to excess production and consequently excess catabolic products: treat with high carbohydrate, low protein diet, ammonia detoxification with sodium phenylacetate or sodium benzoate

Urea Cycle Disorder

4.	Classic Citrullinemia, ASD	Argininosuccinate synthetase	episodic hyperammonemia, vomiting, lethargy, ataxia, siezures, eventual coma: treat with arginine administration to enhance citrulline excretion, also with sodium benzoate for ammonia detoxification

Urea Cycle Disorder

5.	Argininosuccinic aciduria, ALD	Argininosuccinate lyase (argininosuccinase)	episodic symptoms similar to classic citrullinemia, elevated plasma and cerebral spinal fluid argininosuccinate: treat with arginine and sodium benzoate

Urea Cycle Disorder

6.	Hyperargininemia, AD	Arginase	rare UCD, progressive spastic quadriplegia and mental retardation, ammonia and arginine high in cerebral spinal fluid and serum, arginine, lysine and ornithine high in urine: treatment includes diet of essential amino acids excluding arginine, low protein

Hyperammonemia

* It occurs because deficiencies of the enzyme involved in metabolism of waste nitrogen.

- *Hyperammonemia* is treated by either

  decreasing ammonia production in the gastrointestinal tract or by increasing ammonia removal from the blood by the liver and skeletal muscle.

- *Common causes of hyperammonemia :*

  a. genetic defects in the urea cycle

  b. organic acidemias ("secondary urea cycle dysfunction), as well as genetic or acquired disorders resulting in significant hepatic dysfunction.

Conclusion

- *Transamination is the process by which amino group of amino acid is transferred to an acceptor keto acid .*
- *Urea cycle*

  Five key compound:

  1. *carbamoyl phosphate (CP).*
  2. *citrulline*
  3. *argininosuccinate*
  4. *arginine*
  5. *ornithine*

Conclusion

Five key enzymes:

1. *CPS (carbamoyl phosphate synthetase)*
2. *OTC (ornithine transcabamoylase)*
3. *ASS (argininosuccinate synthetase)*
4. *ASL (argininosuccinate lyase)*
5. *ARG (arginase)*

- *Hyperammonemia occurs commonly because defective detoxification in the liver due to a various inborn errors of metabolism and rarely due to excess production in kidneys and intestine. Acute and chronic liver disease resulting in hyperammonemia are also known .*

Reference

http://themedicalbiochemistrypage.org/nitrogen-metabolism.html#urea

http://en.wikipedia.org/wiki/Transamination

http://www.encyclopedia.com/doc/108-transamination.html

www.yourdictionary.com/transamination