Transformation of Aspartate into Asparagine

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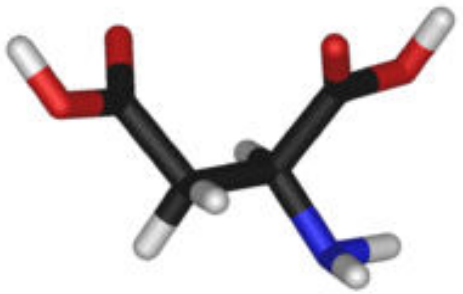
Biosynthesis of aspartate

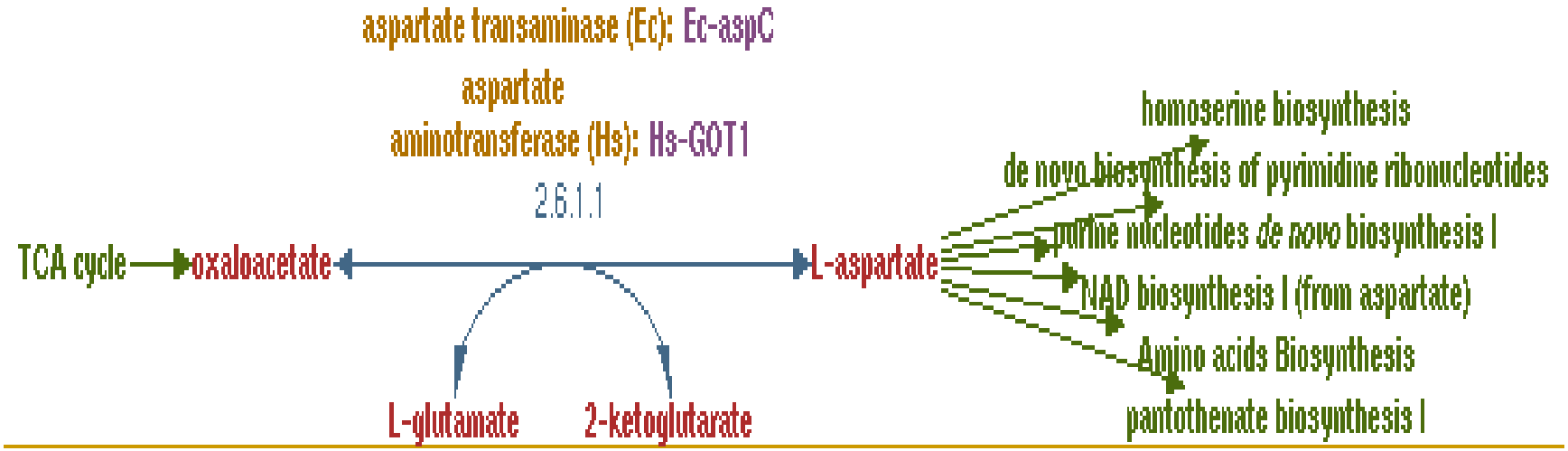
What is aspartate?

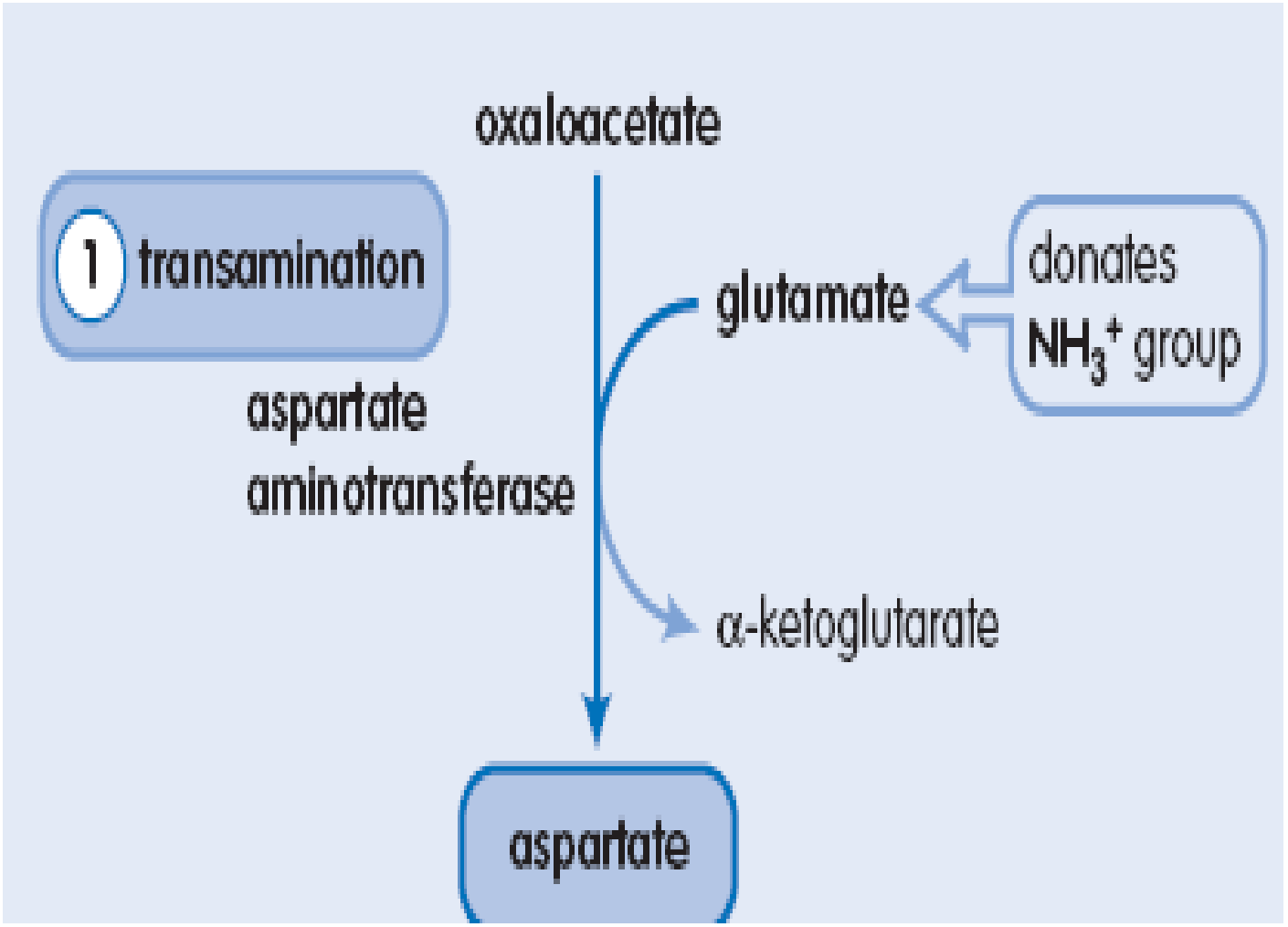
an α-amino acid with the chemical formula $HO_2CCH(NH_2)CH_2CO_2H$. The carboxylate anion of aspartic acid is known as **aspartate**

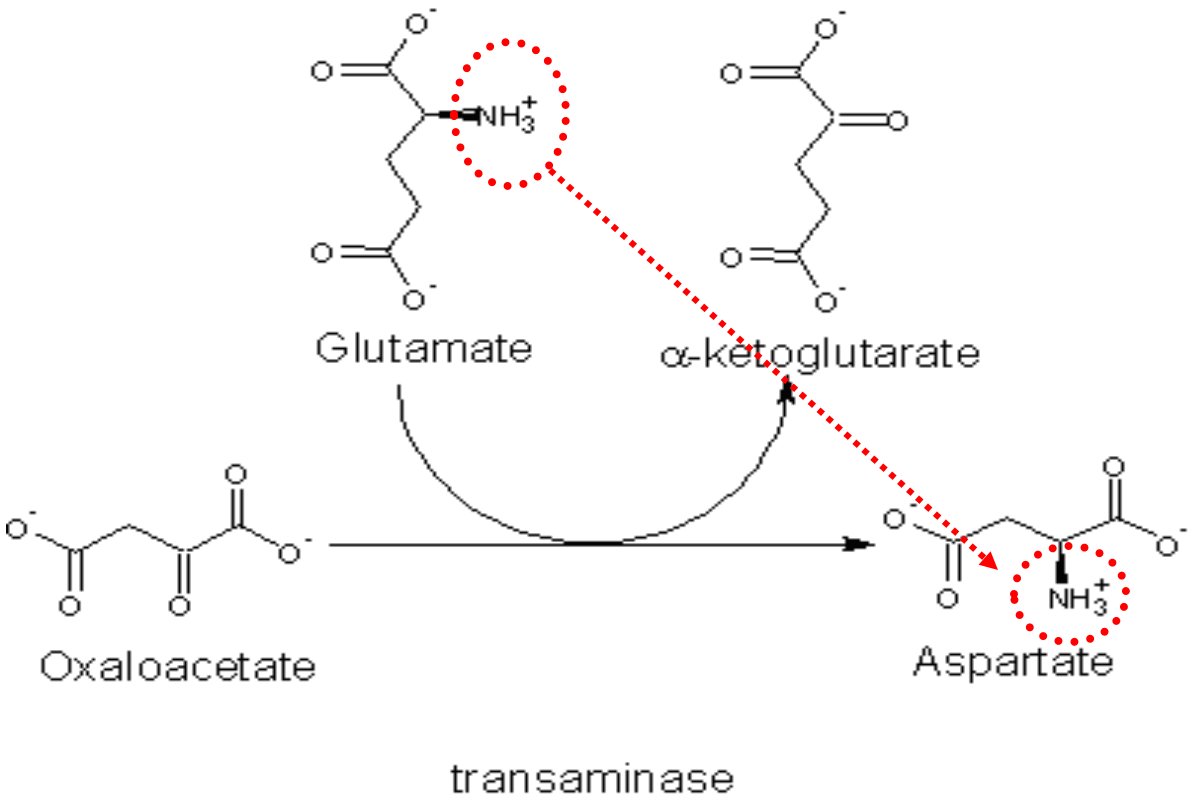


How to obtain aspartate?

Aspartic acid is non-essential in mammals, being produced from oxaloacetate by transamination.




oxaloacetate
1 transamination
aspartate
aminotransferase
glutamate
donates
NH_3^+ group
α-ketoglutarate
aspartate



The equation:

$$\text{Oxaloacetate} + \alpha\text{-amino acid} \longrightarrow \text{L-aspartate} + \alpha\text{-keto acid}$$

Oxaloacetate is the intermediate phase in TCA cycle

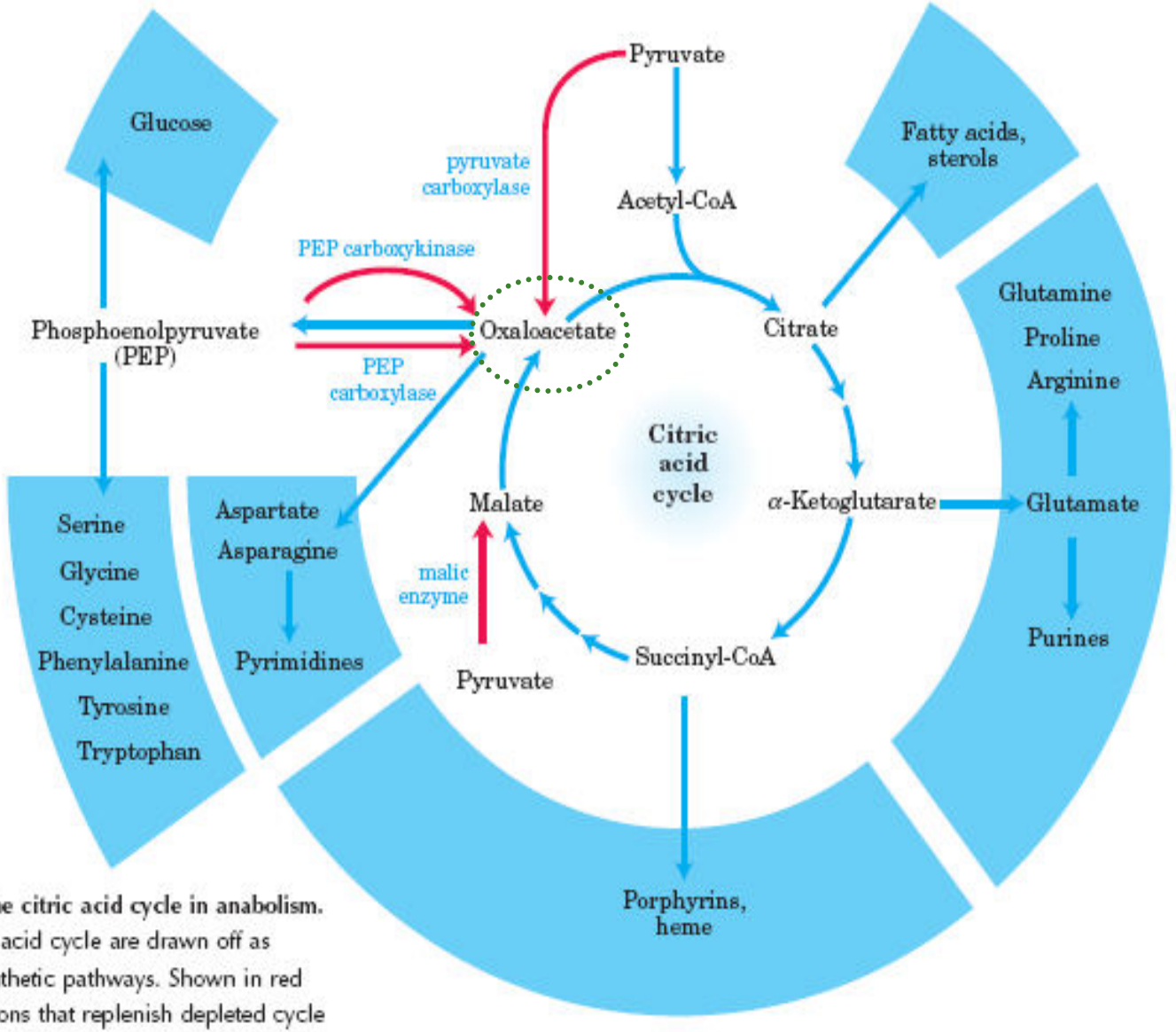
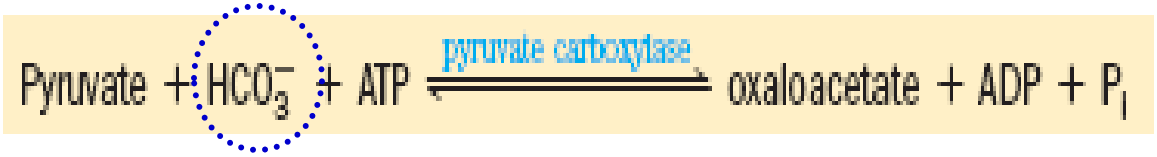


FIGURE 16-15 **Role of the citric acid cycle in anabolism.** Intermediates of the citric acid cycle are drawn off as precursors in many biosynthetic pathways. Shown in red are four anaplerotic reactions that replenish depleted cycle intermediates (see Table 16–2).

The synthesis of oxaloacetate from pyruvate by using pyruvate carboxylase

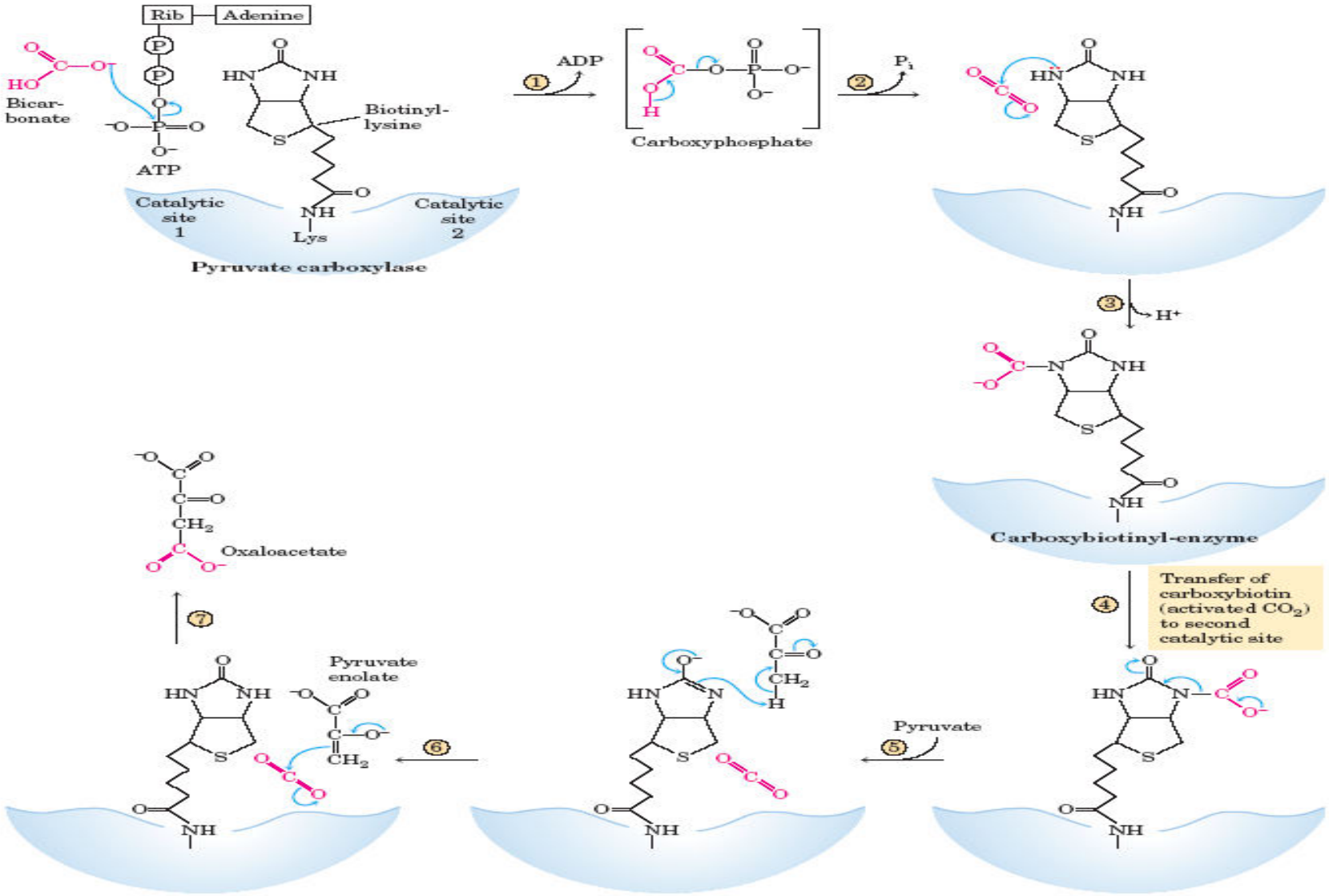
Place: liver and kidney



This reaction is catalyzed by pyruvate carboxylase, an enzyme activated by Acetyl-CoA, indicating a lack of oxaloacetate.

Enzyme pyruvate carboxylase requires the vitamin **Biotin** which is the prosthetic group of the enzyme.

Biotin is a specialized carrier of one-carbon groups in their most oxidized form: CO_2.


Rib
Adenine
Bicar-
bonate
ATP
Biotinyl-
lysine
Catalytic
site
1
Catalytic
site
2
Lys
Pyruvate carboxylase
ADP
Carboxyphosphate
P_i
H^+
Carboxybiotinyl-enzyme
Transfer of
carboxybiotin
(activated CO_2)
to second
catalytic site
Pyruvate
Pyruvate
enolate
Oxaloacetate

The production of pyruvate (glycolysis)

1. Glucose + ATP ⟶ glucose 6 phosphate + ADP
2. Glucose 6 phosphate ⇌ fructose 6 phosphate
3. Fructose 6 phosphate + ATP ⟶ fructose 1,6 bisphosphate + ADP
4. Fructose 1,6 bisphosphate ⇌ dihydroxyacetone phosphate + glyceraldehyde 3 phosphate
5. Dihydroxyacetone phosphate ⇌ glyceraldehyde 3 phosphate
6. Glyceraldehyde 3 phosphate + P_i + NAD^+ ⇌ 1,3 bisphosphoglycerate + NADH + H^+ [2x]
7. 1,3 Bisphosphoglycerate + ADP ⇌ 3 phosphoglycerate + ATP [2x]
8. 3 Phosphoglycerate ⇌ 2 phosphoglycerate [2x]
9. 2 Phosphoglycerate ⇌ phosphoenolpyruvate + H_2O [2x]
10. Phosphoenolpyruvate + ADP ⟶ pyruvate + ATP [2x]

Overall equation of glycolysis:

glucose + 2ADP + 2Pi +2NAD^+ → 2 pyruvate + 2ATP + 2NADH + 2H^+ +2H_2O

Net equation of aspartate synthesis from glucose :

Glycolysis:

$$\text{glucose} + \cancel{2ADP} + \cancel{2Pi} + 2NAD^{+} \rightarrow 2\ \cancel{\text{pyruvate}} + \cancel{2ATP} + 2NADH + 2H^{+} + 2H_2O$$

Production of oxaloacetate:

$$\cancel{2\text{Pyruvate}} + 2HCO_3^{-} + \cancel{2ATP} \xrightarrow{\text{pyruvate carboxylase}} \cancel{2\text{Oxaloacetate}} + \cancel{2ADP} + \cancel{2Pi}$$

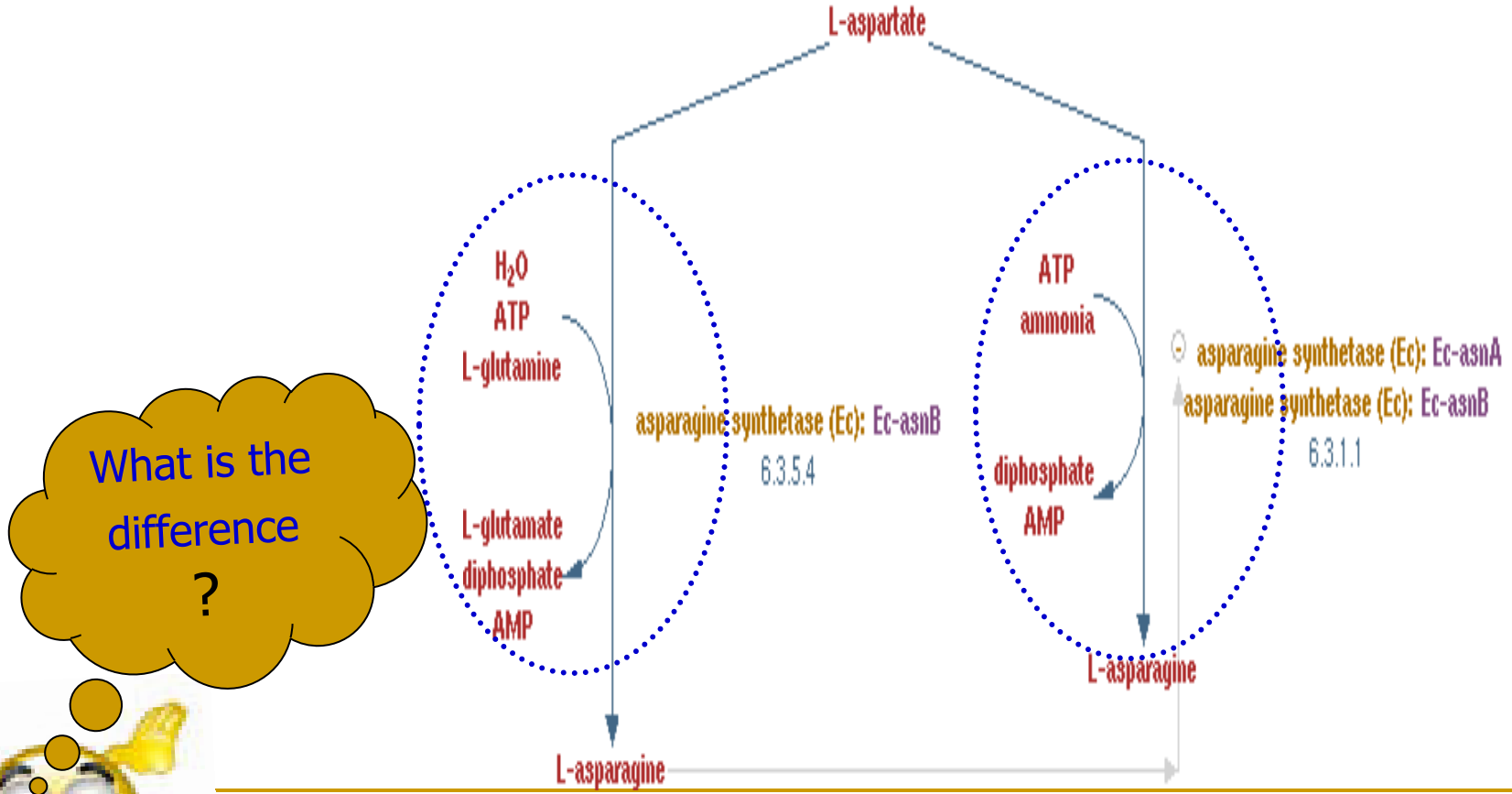
Transamination:

$$\cancel{2\text{Oxaloacetate}} + 2\ \alpha\text{-amino acid} \leftrightarrow 2\text{L-aspartate} + 2\ \alpha\text{-keto acid}$$

$$\text{Glucose} + 2\ NAD^{+} + 2\ \alpha\text{-amino acid} + 2HCO_3^{-} \rightarrow 2\text{L-aspartate} + 2NADH + 2H^{+} + 2H_2O + 2\ \alpha\text{-keto acid}$$

TRANSFORMATION OF ASPARAGINE

There are two routes for transforming aspartate to asparagine at the expense of ATP.
In both eukaryotes and prokaryotes, asparagine is biosynthesized from aspartate by amidation using asparagine synthetase.



BACTERIA

In some bacteria the enzyme can use glutamine, or ammonia as amide donor

Bacteria (*E. coli*) have two kind of asparagine synthetase

Asparagine synthetase A (AsnA) is catalyzing the ammonia-dependent conversion of aspartate to asparagine.

Asparagine synthetase B (AsnB) is catalyzing the glutamine-dependent and ammonia-dependent conversion of aspartate to asparagine. The amino-terminal cysteine of AsnB is important for its glutamine-dependent activity, but not for its ammonia-dependent activity

AsnA is the more active of two asparagine synthetase activities in *E. coli (Humbert, R, and Simoni, R. D. (1980) J. Bacteriol).*

MAMMALS

The mammalian enzyme uses cellular glutamine as amide donor.

The transformation of aspargine from aspartate in mammals

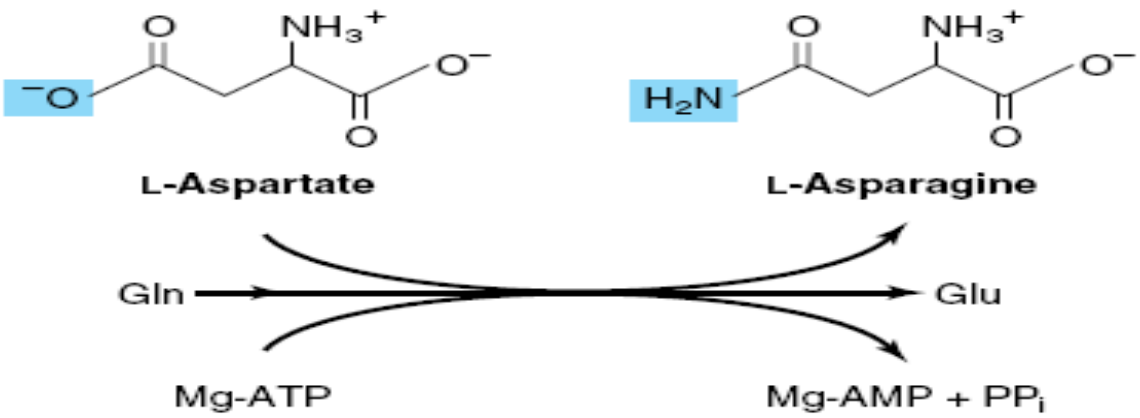


Figure 28–4. The asparagine synthetase reaction. Note similarities to and differences from the glutamine synthetase reaction (Figure 28–2).

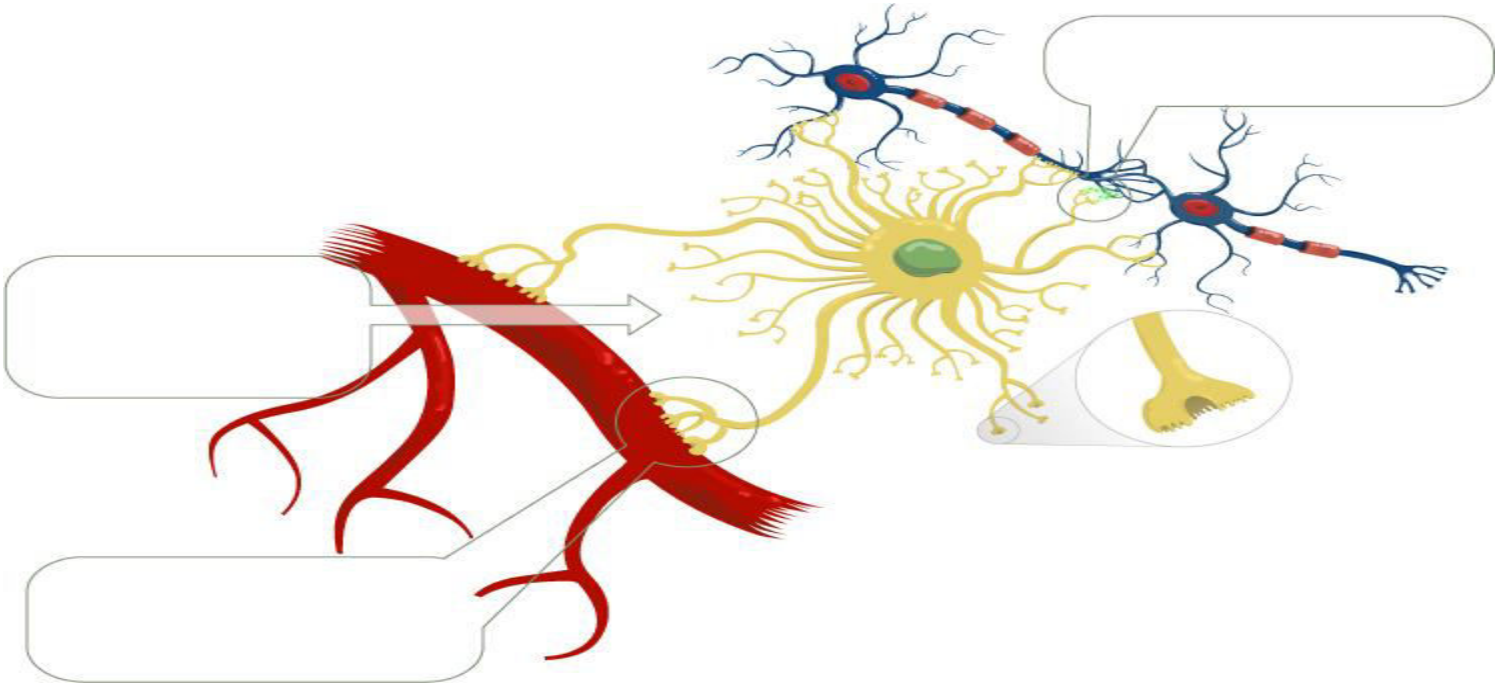
Ammonia is quite toxic to animal tissues

Ammonia is especially toxic to the brain and can cause confusion, lethargy, and sometimes coma.

in brain astrocytes:

❖↑ NH_4 ↑ glutamine → water intake to maintain osmotic balance.

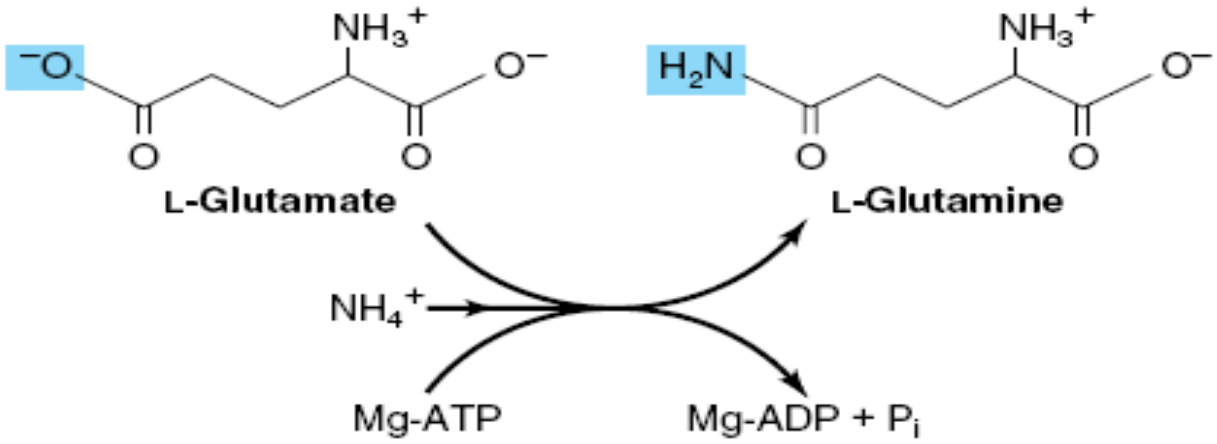
❖↓ glutamate ↓ neurotransmitters as well as changes in cellular osmotic balance.



Astrocytes are star-shaped glia that hold neurons in place, get nutrients to them, and digest parts of dead neurons. But because astrocytes cannot generate action potentials, they haven't received a lot of attention, until recently.

It has been discovered that astrocytes can indeed communicate with neurons and modify the signals they send or receive. That means astrocytes are much more involved than we thought in the processing of information, and in the signaling that occurs at the synapse.

The free ammonia produced in tissues is combined with glutamate to yield glutamine by the action of **glutamine synthetase.**



(1) Glutamate + ATP ⟶ γ-glutamyl phosphate + ADP

(2) γ-Glutamyl phosphate + NH_4^+ ⟶ glutamine + P_i + H^+

Sum: Glutamate + NH_4^+ + ATP ⟶ glutamine + ADP + Pi + H^+ (22–1)

What have we learned?

1. Aspartate can be synthesize from glucose.

   Glucose + 2 NAD^+ + 2 α-amino acid + 2HCO_3^- ⟶ 2L-aspartate
   + 2NADH + 2H^+ +2H_2O + 2 α-keto acid

2. There are two routes for transforming aspartate to asparagine at the expense of ATP using asparagine synthetase.
   - ✓ Using glutamine as amide donor
   - ✓ Using ammonia as amide donor

   in mammals : glutamine as amide donor
   in bacteria : glutamine, or ammonia as amide donor

References

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- http://biocyc.org/META/NEW-IMAGE?type=PATHWAY&object=ASPARAGINESYN-PWY

end of the show, thank to finish