Biosynthesis of amino acids

Plants and autotroph bacteria: Biosynthesis of all amino acids

Other living organism (e.g.: human being): They are able to biosynthesize a part of amino acids.

Non essential	Essential
Alanine	Arginine*
Asparagine	Histidine
Aspartate	Isoleucine
Cysteine	Leucine
Glutamate	Lysine
Glutamine	Methionine*
Glycine	Phenylalanine*
Proline	Threonine
Serine	Tryptophane
Tyrosine	Valine

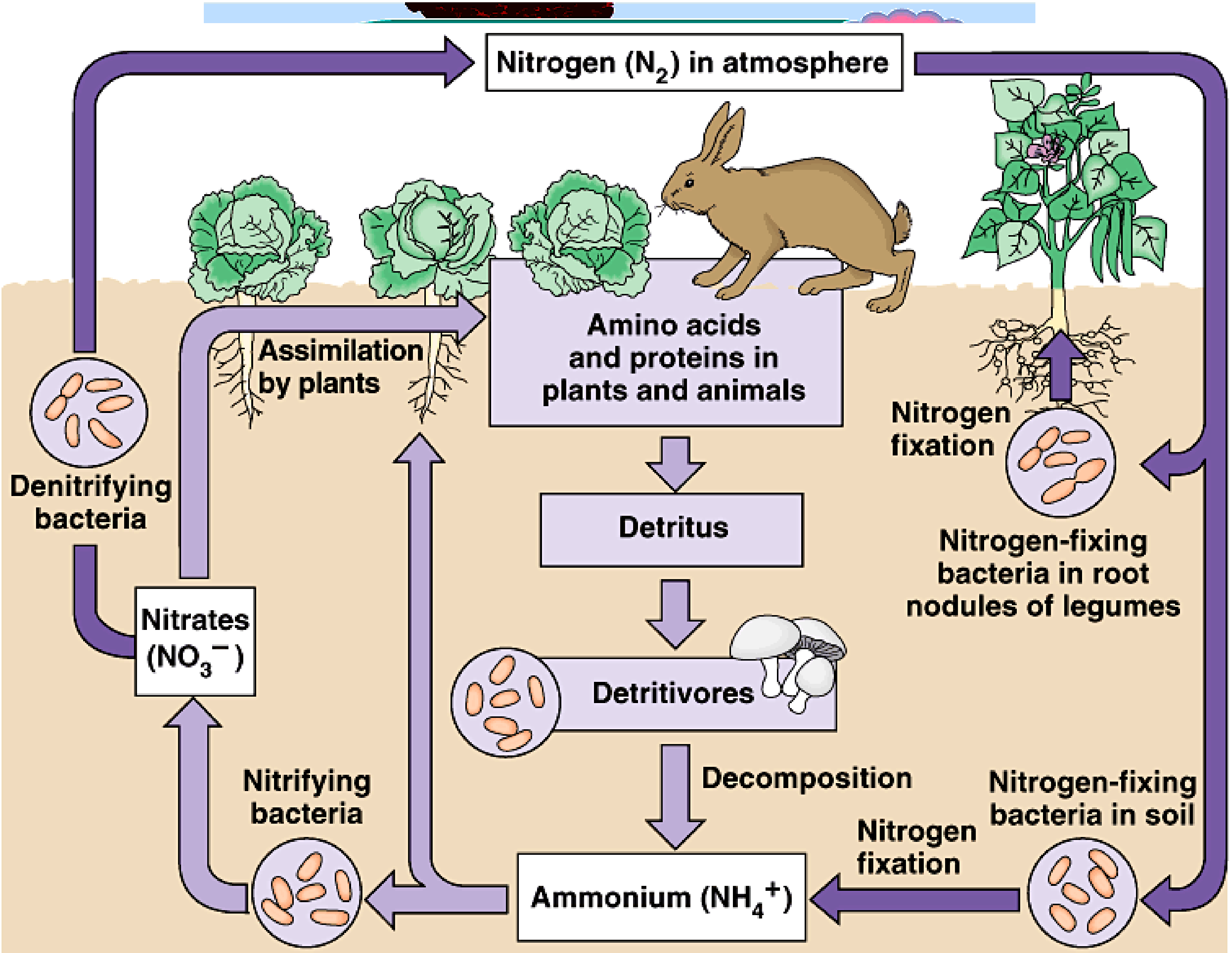
amino acid **nucleotide**

The soluble biologically available N forms are rare

↓

Strict ammonia, amino acid, nucleotide metabolism

Nitrogen cycle



The mechanism of nitrification

Only few prokaryotic species are able to fix the atmospheric nitrogen:

Cyanobacteria: soil, fresh water

Azotobacter species: soil

Rhizobium species: symbionts

$$\mathbf{N_2 + 3H_2 \longrightarrow 2\,NH_3 \qquad \Delta G^0 = -33{,}5\ kJ/mol}$$

$\mathbf{N \equiv N}$ **bonding energy: 930 kJ/mol**

Haber-Bosch synthesis: 400-500^{o}C and several 100 Atm pressure

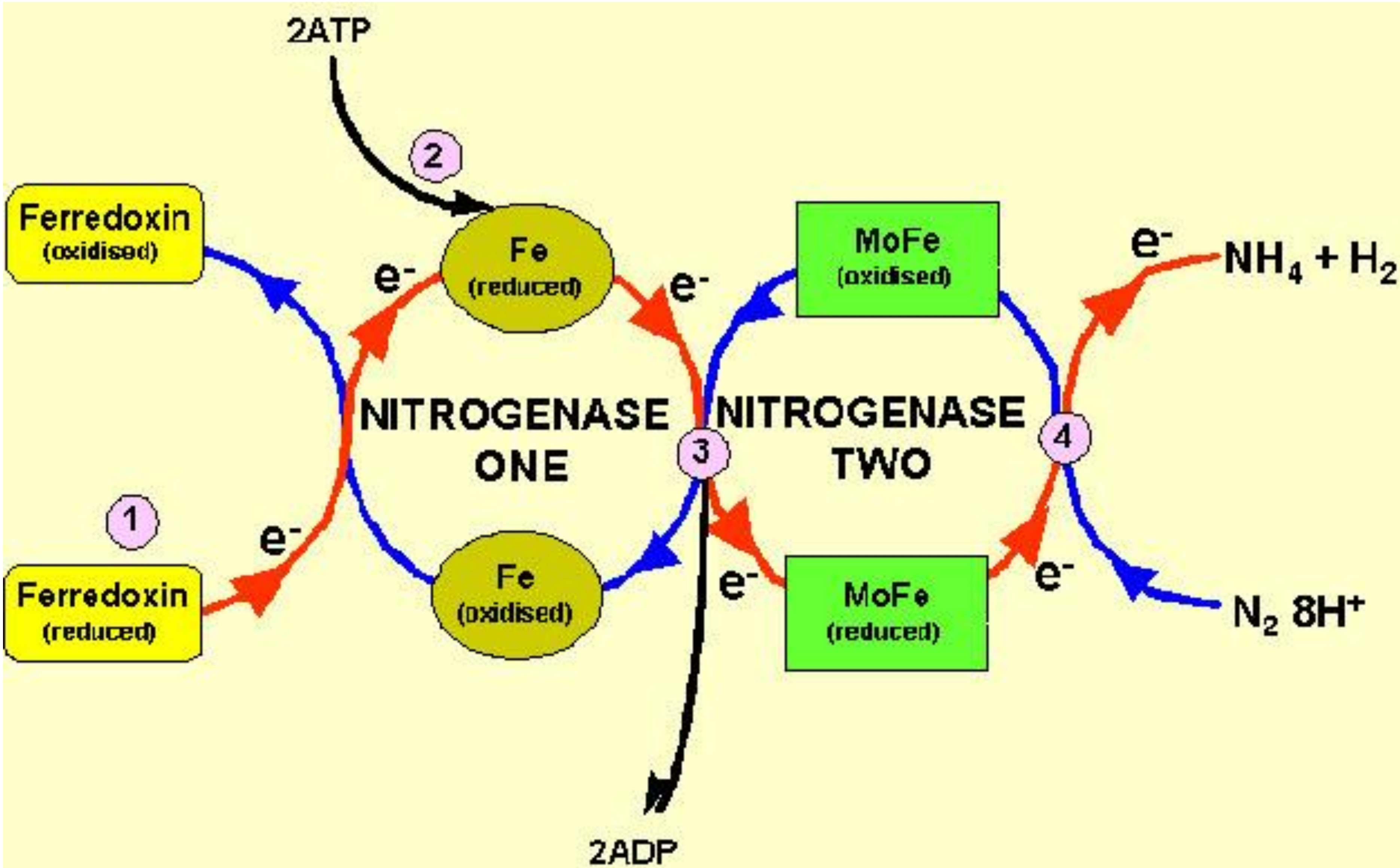
Biological N_2 fixation: biological temperature, 0,8 Atm N_2 pressure

$$\mathbf{N_2 + 8H^+ + 8e^- + 16\ ATP \longrightarrow 2NH_3 + H_2 + 16ADP + 16\ P_i}$$

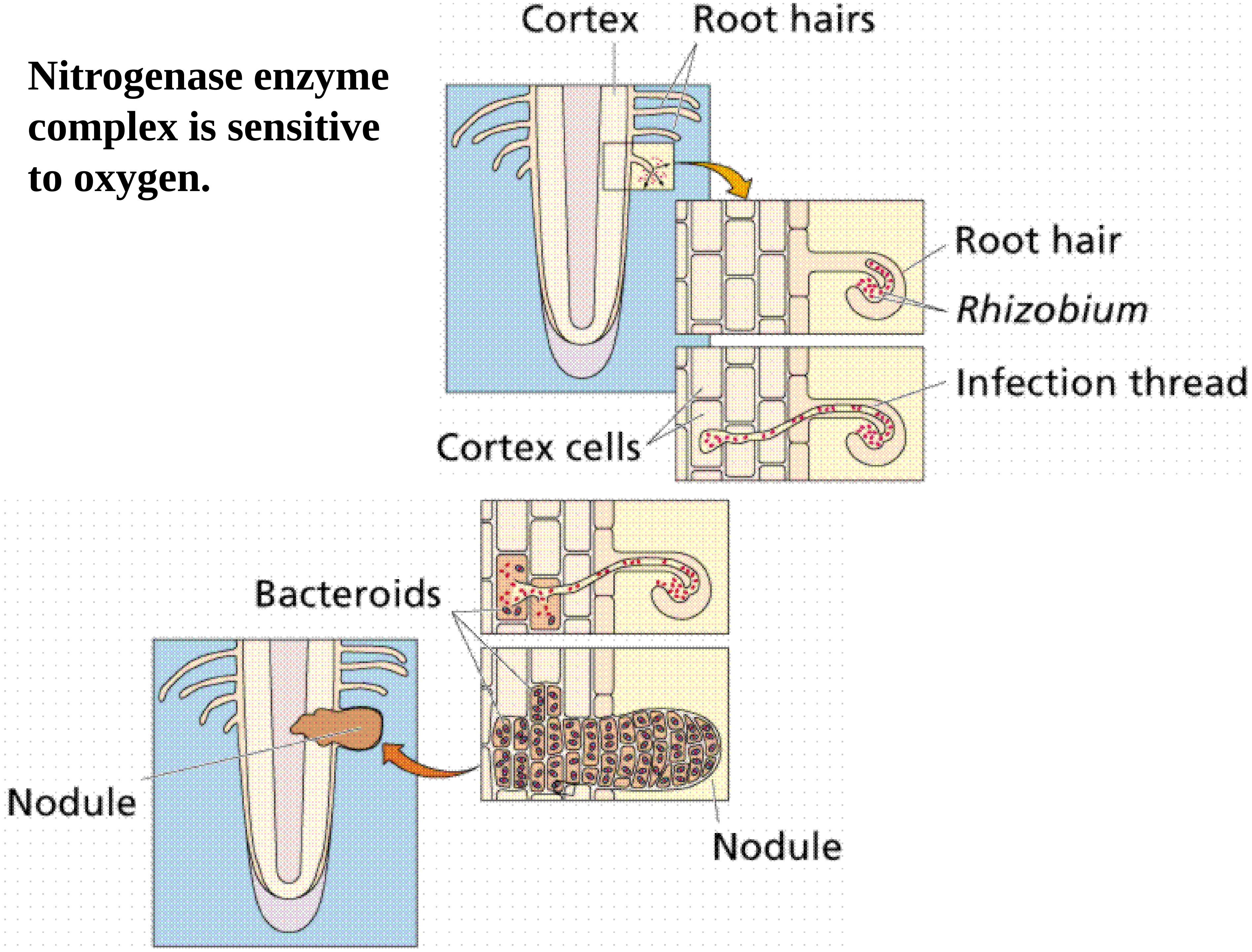
Nitrogenase enzyme complex can be found only in prokaryotes

Nitrogenase:
-Dinitrogenase reductase
-Dinitrogenase

Nitrogenase complexes of different species are highly conservative. Subunits of different nitrogenases are compatible.


2ATP
2
Ferredoxin
(oxidised)
Fe
(reduced)
MoFe
(oxidised)
e-
e-
e-
NH4 + H2
NITROGENASE
ONE
NITROGENASE
TWO
3
4
1
e-
Ferredoxin
(reduced)
Fe
(oxidised)
e-
MoFe
(reduced)
e-
N2 8H+
2ADP

Nitrogenase enzyme complex is sensitive to oxygen.



The roots of clover: Rhizobium units

Ammonia fixation, the biosynthesis of glutamate, glutamine

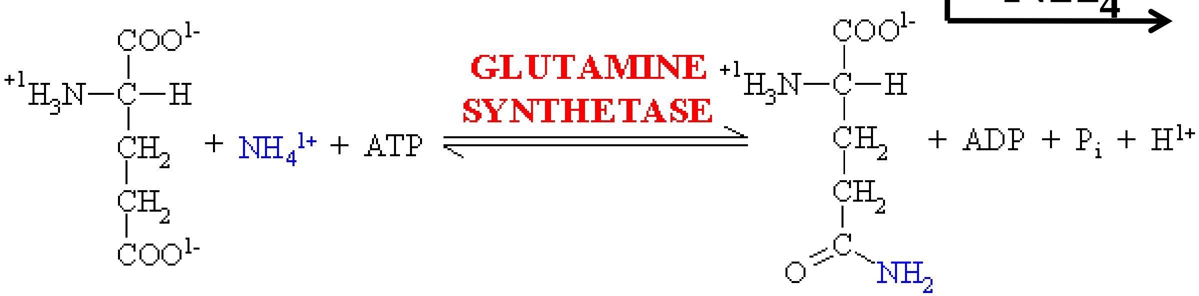
Glutamate: amino group donor for the synthesis of other amino acids (transaminase)
Glutamine: its amide nitrogen is a good amino group donor for biosynthetic processes

The concentration of these amino acids are higher than the others

1. Glutamine synthetase

Glutamate + ATP → γ-glutamil-P + ADP

$\xrightarrow{+NH_4^+}$ Glutamine + P_i + H^+



All living organism

2. Glutamate synthetase

Bacteria, plants

α-ketoglutarate + glutamine + NADPH + H^+ $\longrightarrow$ 2 glutamate + $NADP^+$

3. L-glutamate dehydrogenase

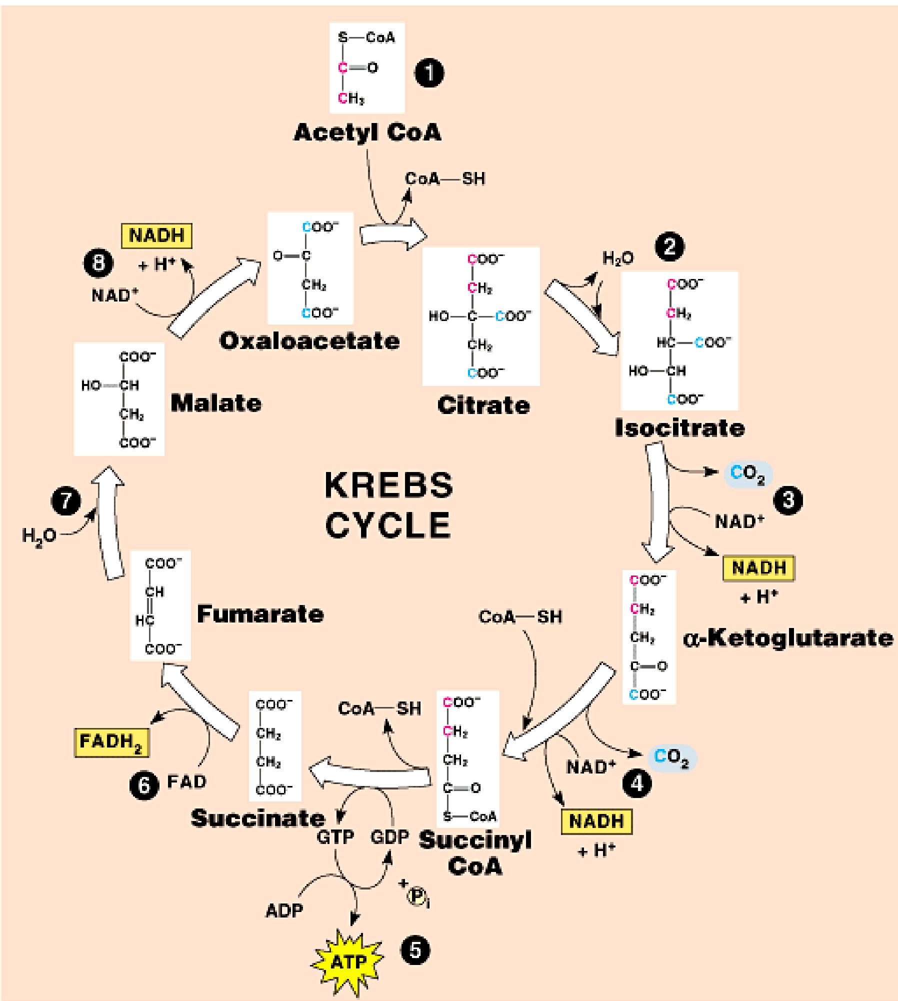
Minor pathway

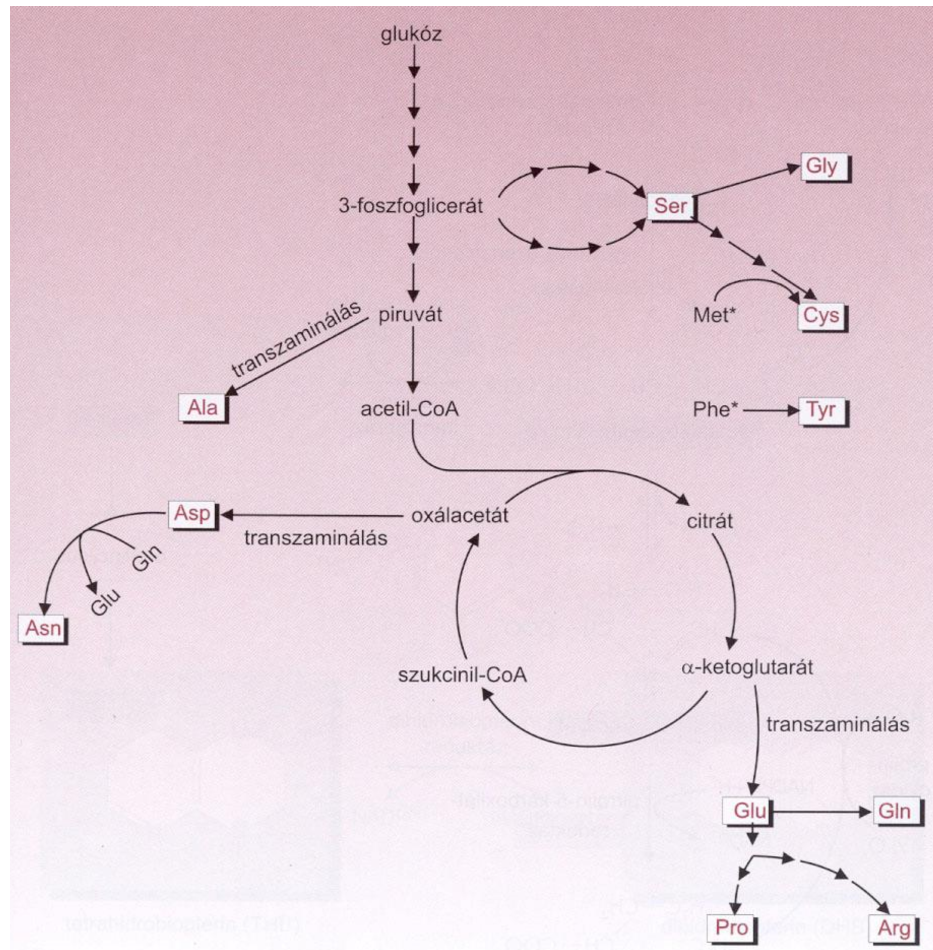
All living organism

α-ketoglutarát + NH_4^+ + NADPH $\longrightarrow$ L-glutamát + $NADP^+$ + H_2O

Carbon chain: comes from the carbohydrate metabolism.

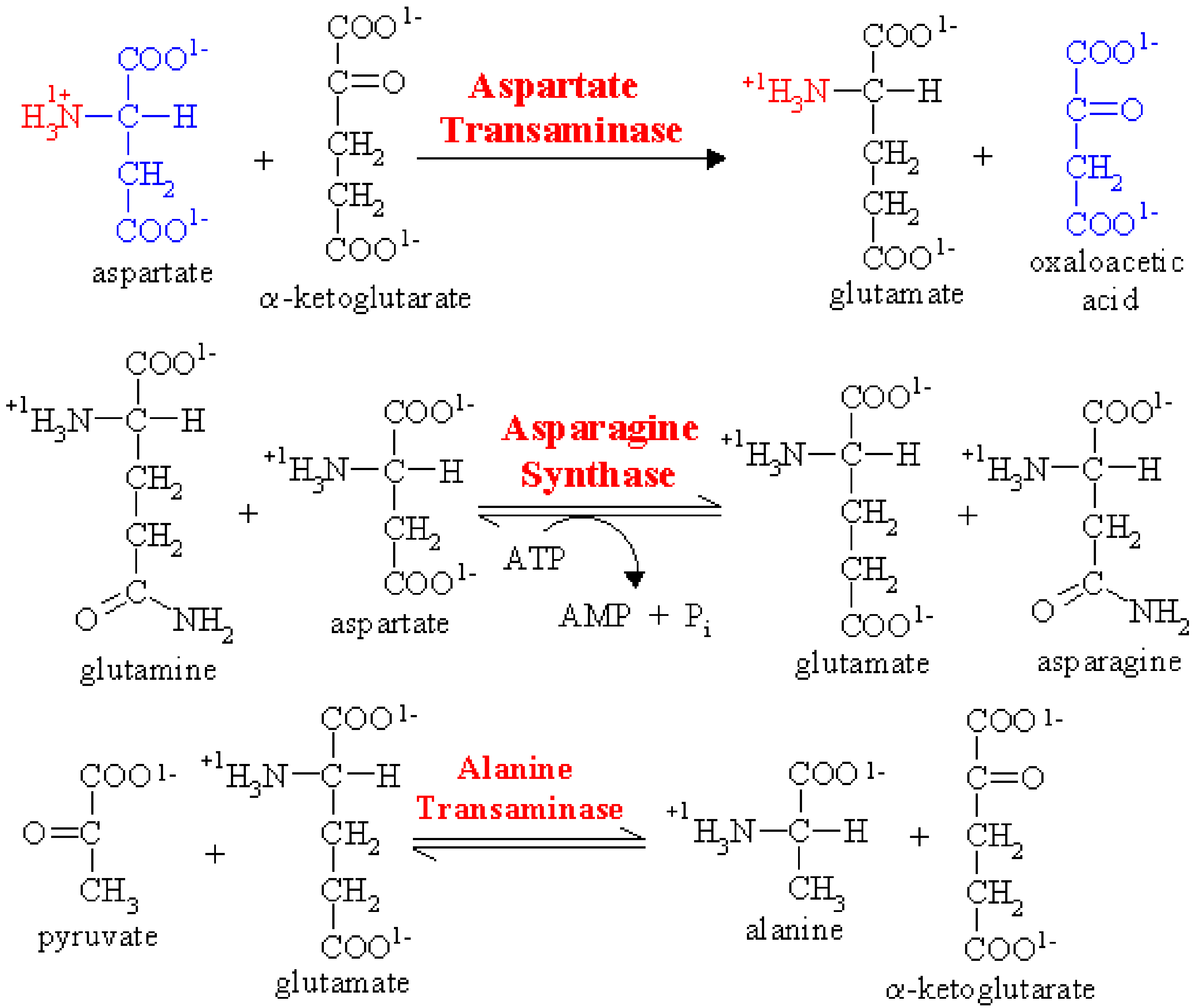
α-keto acids from the catabolism of carbohydrates



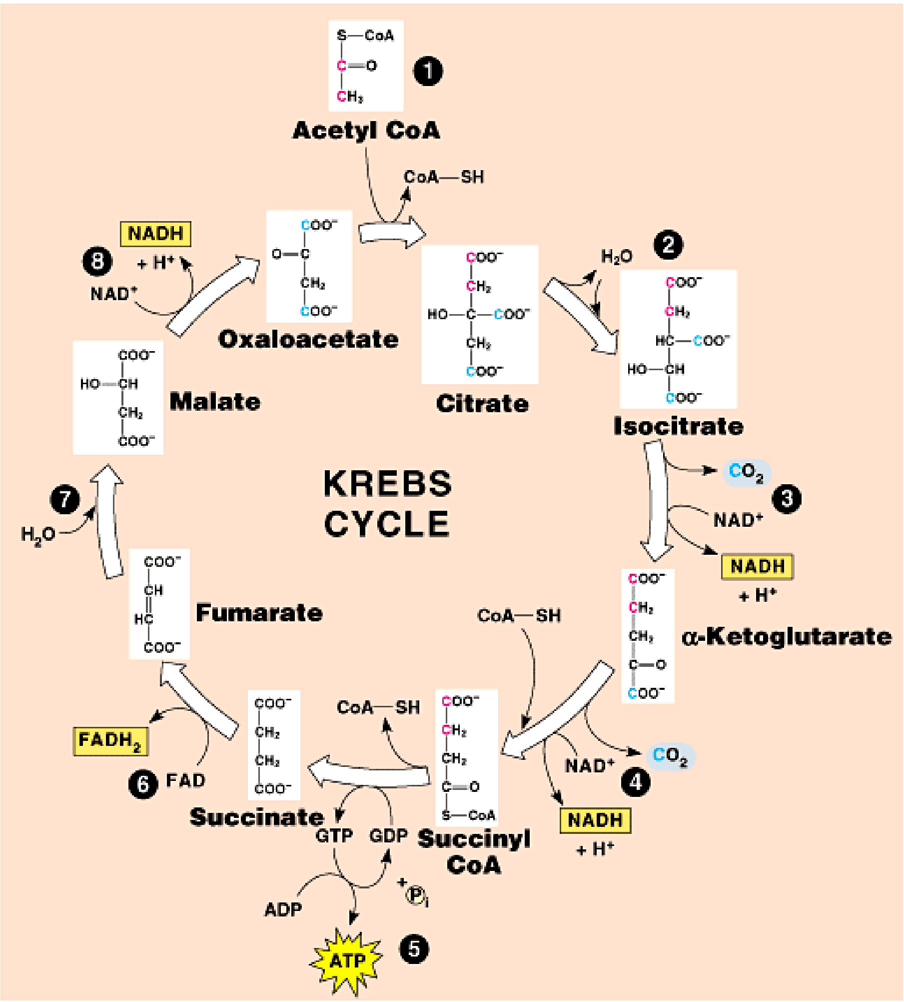


The finishing step: transamination

Transamination interconverts pairs of α-amino acids and α-keto acids



Transamination is readily reversible, and aminotransferases also function in amino acid biosynthesis.



Carbon chain: go back to the carbohydrate metabolism and to the citrate cycle.

Amino group: All the amino nitrogen from amino acids that undergo transamination can be concentrated in glutamate.

Urea biosynthesis occurs in four stages:

1.Transamination
2. oxidative deamination of glutamate
3. ammonia transport
4. reactions of the urea cycle

1. All the amino nitrogen from amino acids that undergo transamination can be concentrated in glutamate.

2. Release of nitrogen as ammonia is catalyzed by hepatic L-glutamate dehydrogenase (GDH),

3. Glutamine synthase fixes ammonia as glutamine. Hydrolytic release of the amide nitrogen of glutamine as ammonia, catalyzed by glutaminase.

4. Reactions of the urea cycle

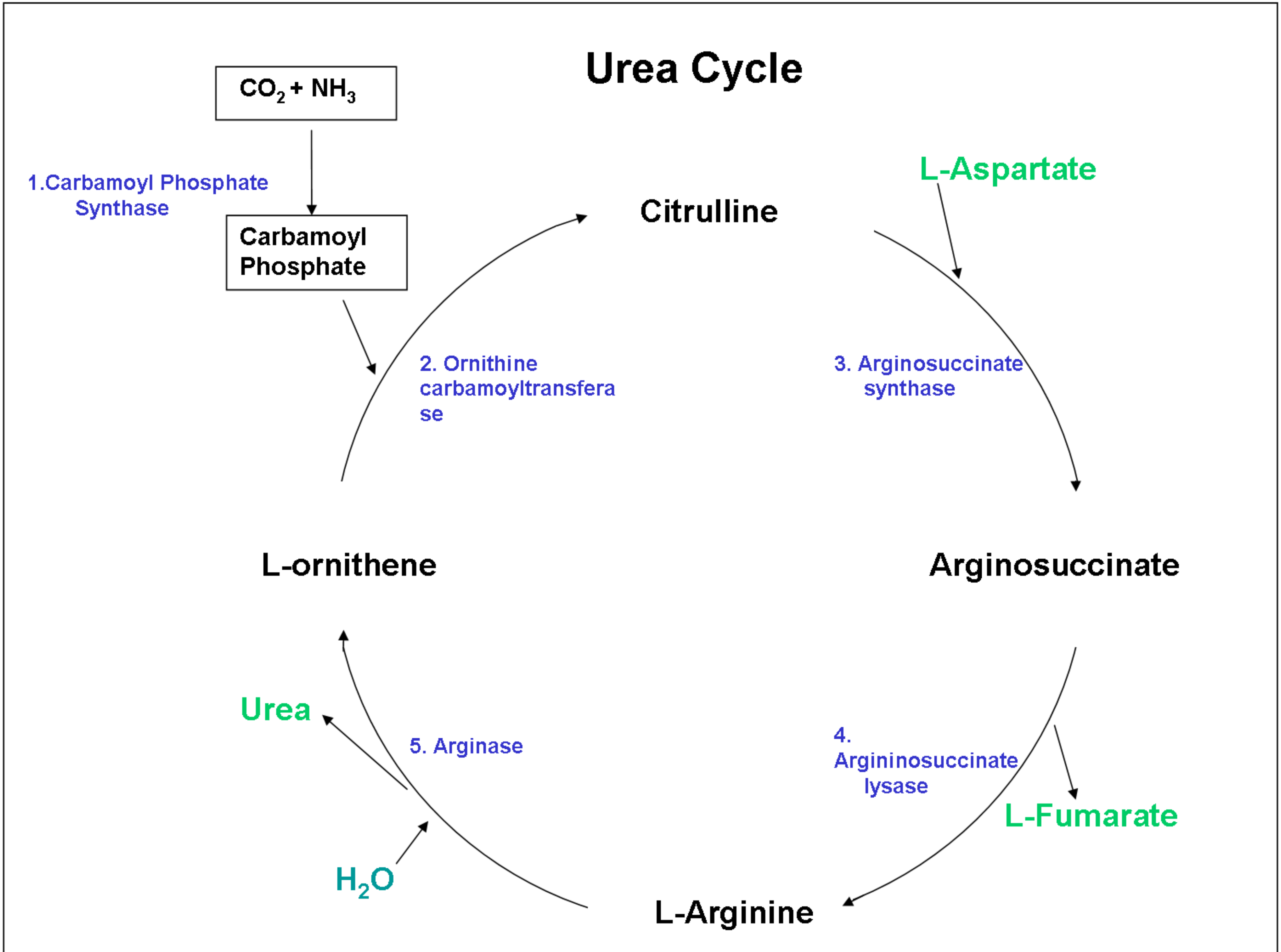
1. Condensation of CO_2, ammonia, and ATP to form carbamoyl phosphate

2. L-Ornithine transcarbamoylase catalyzes transfer of the carbamoyl group of carbamoyl phosphate to ornithine, forming citrulline and orthophosphate

3. Argininosuccinate synthase links aspartate and citrulline via the amino group of aspartate

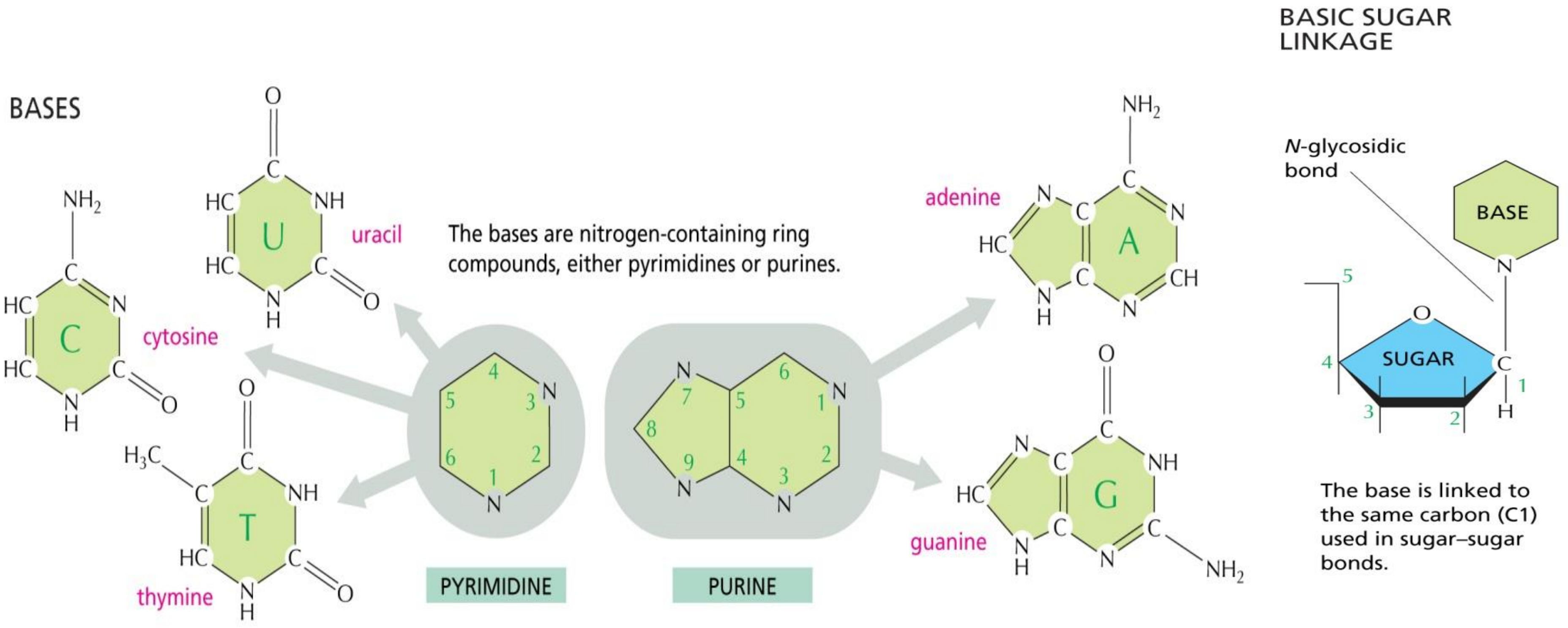
4. Cleavage of argininosuccinate, catalyzed by argininosuccinase or argininosuccinate lyase

5. Hydrolytic cleavage of the guanidino group of arginine, catalyzed by liver arginase, releases urea. The other product, ornithine, reenters liver mitochondria for additional rounds of urea synthesis.


Urea Cycle
$CO_2 + NH_3$
1.Carbamoyl Phosphate Synthase
Carbamoyl Phosphate
Citrulline
L-Aspartate
2. Ornithine carbamoyltransfera se
3. Arginosuccinate synthase
L-ornithene
Arginosuccinate
Urea
5. Arginase
4. Argininosuccinate lysase
L-Fumarate
H_2O
L-Arginine

Nucleotides

Nucleosides are derivatives of purines and pyrimidines that have a sugar linked to a ring nitrogen.
Numerals with a prime (eg, 2′ or 3′) distinguish atoms of the sugar from those of the heterocyclic base.



Human tissues can synthesize purines and pyrimidines from amphibolic intermediates.
Ingested nucleic acids and nucleotides are degraded in the intestinal tract to mononucleotides, which may be absorbed or converted to purine and pyrimidine bases.