Amino Acid Metabolism
(Chapter 20)

Lecture 8:

Nitrogen Fixation (20.7);
Nitrite Assimilation (not in text?);
Protein Digestion in the Gut (**5.3b**, 11.5, 20.2);
Amino Acid Degradation in Cells (**20.2**);

Next: The Urea Cycle (20.3)
Breakdown of AAs (20.4)
AA Biosynthesis (20.5)

Amino acid roles:

1) protein monomeric units (primary purpose)
2) energy metabolites (about 10% of energy)
3) precursors of many biologically important nitrogen-containing compounds such as:
    - HEME
    - physiologically active AMINES
        [(nor)epinephrine, dopamine, GABA (γ-aminobutyric acid), serotonin, histamine]
    - GLUTATHIONE
    - NUCLEOTIDES
    - nucleotide COENZYMES

Amino acid metabolism is intimately intertwined with **nitrogen acquisition** (see 20-7). All organisms need bioavailable sources of nitrogen for proteins and nucleic acids. The major form of nitrogen in the atmosphere is N_2, an ***extremely*** stable compound: the **N ≡ N** triple bond has a bond energy of 945kJ/mol.

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N_2 is converted to metabolically useful forms (is "fixed") only by a few species of prokaryotes, called diazatrophs. Diazatrophs of the genus *Rhizobium* live symbiotically in the root nodules of legumes, where they convert N_2 to NH_3 (ammonia) in a process called NITROGEN FIXATION:

$$N_2 + 8\,H^+ + 8\,e^- + 16\,ATP + 16\,H_2O \xrightarrow{\text{NITROGENASE}} 2\,NH_3 + H_2 + 16\,ADP + 16\,P_i$$

But, less than 1% of N entering the biosphere comes from N-fixation. Another oxidized form of nitrogen, NO_3^- (nitrate ion) is also found in the soils and oceans. It is converted to NH_4^+ through...

NITRATE ASSIMILATION: **The reduction of NO_3^- to NH_4^+ (ammonium ion) occurs in green plants, various fungi, and certain bacteria in a two-step pathway:**

(1) The 2-electron reduction of nitr<u>a</u>te to nitr<u>i</u>te:

$$NO_3^- + 2\,H^+ + 2\,e^- \rightarrow NO_2^- + H_2O$$

This reaction is catalyzed by **nitr<u>ate</u> reductase**, a soluble α2-type homodimer protein that has an unusual molybdenum-containing cofactor (named "**MoCo**") that is involved in the transfer of the electrons to nitrate.

(2) This is followed by the 6-electron reduction of nitrite to ammonium:

$$NO_2^- + 8\,H^+ + 6\,e^- \rightarrow NH_4^+ + 2\,H_2O$$

This reaction is catalyzed by **nitr<u>ite</u> reductase**.

THESE REACTIONS ALSO REQUIRE LARGE ENERGY INPUTS (not shown).

NH_3/NH_4^+ can be incorporated into the amino acids glutamate by glutamate dehydrogenase (20-2B) and glutamine by glutamine synthetase (20-5A).

No animals are capable of either N-fixation or nitrate assimilation, so they (we!) are totally dependent on plants and microorganisms for the synthesis of organic nitrogenous compounds, such as amino acids and proteins, to provide this essential nutrient.

Dietary protein digestion:

Most amino acids which we eat are in the form of **proteins,** which must be digested into **amino acid monomers**. This digestion occurs in the gut:

stomach:	pancreas to small intestine:	intestinal wall:
pepsin	trypsin	dipeptidases
	chymotrypsin	
	carboxypeptidase A	
	carboxypeptidase B	
	elastase	

Monomers (free amino acids) pass through the wall and into the bloodstream and are taken up by cells. Excess dietary amino acids are converted to common metabolites that are precursors of glucose, fatty acids, and ketone bodies (metabolic fuels).

Amino acid degradation (section 20-2):

There are 3 common stages of amino acid degradation:

1) DEAMINATION = amino group removal: amino groups converted to
   - A) ammonia or
   - B) the amino group of aspartate.
2) Incorporation of ammonia or aspartate nitrogen into UREA for excretion (20.3).
3) Conversion of the AA carbon skeletons (i.e., the α-keto acids that result from deamination) to the common intermediates (20.4)

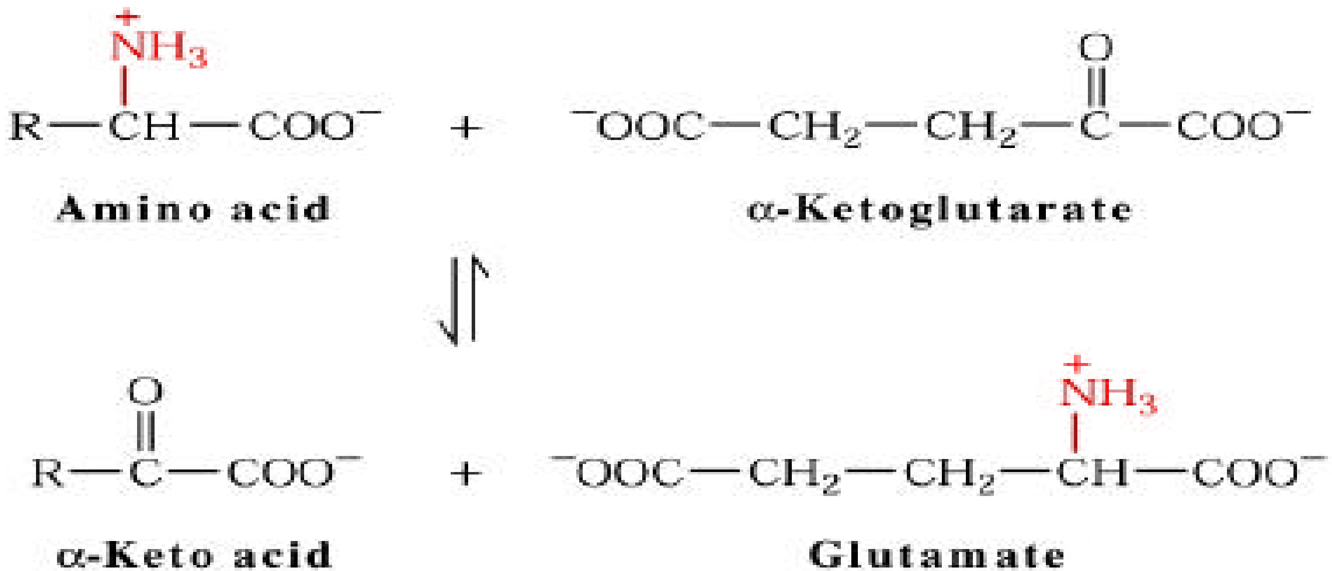
AMINO ACID DEAMINATION

The first step in AA breakdown usually is removal of an α-amino group. Most AAs are deaminated by "**TRANSAMINATION" — the transfer of the amino group to an α-keto acid. The OVERALL STOICHIOMETRY of a generalized transamination reaction is**:

amino $acid_1$ + α-keto $acid_2$ α-keto $acid_1$ + amino $acid_2$

The acceptor—**α-keto $acid_2$**—is usually **α-ketoglutarate** (or **oxaloacetate** to a lesser extent). The enzymes that catalyze these reactions are now generally referred to as **aminotransferases** (the older name — still in use — is **transaminases**).

Typical first transamination reaction:



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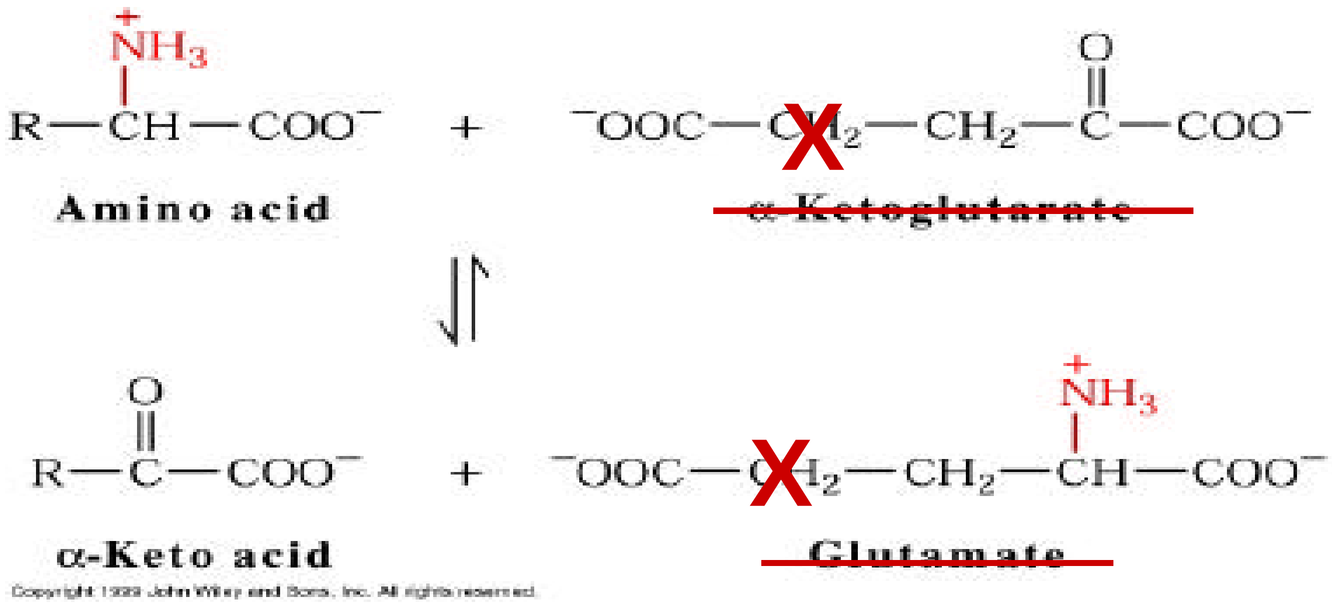
The usual AA acceptor is α-ketoglutarate, producing GLUTAMATE and the new α-keto acid.

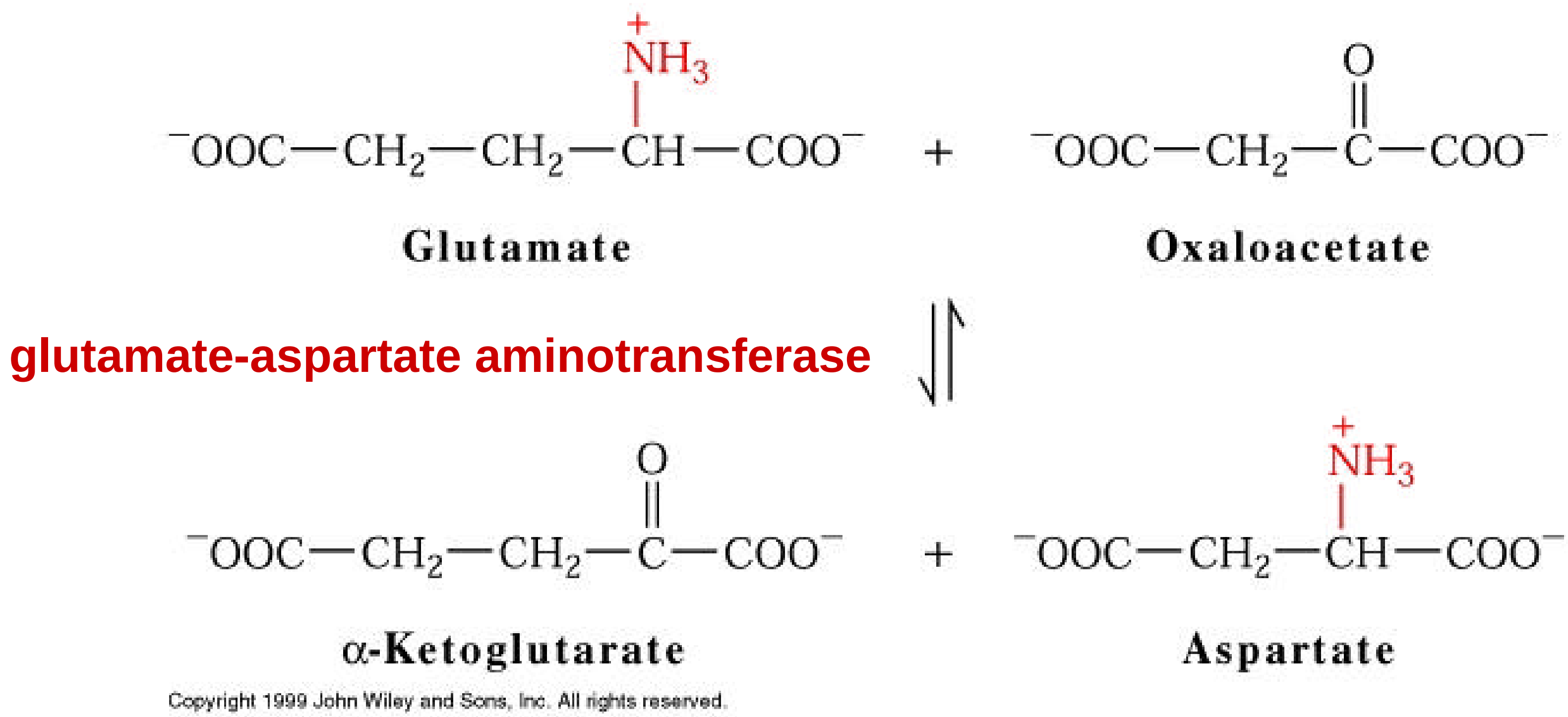
What is produced if oxaloacetate is the acceptor?

What is produced if oxaloacetate is the acceptor?
It is one C shorter than α-ketoglutarate, so produces…..



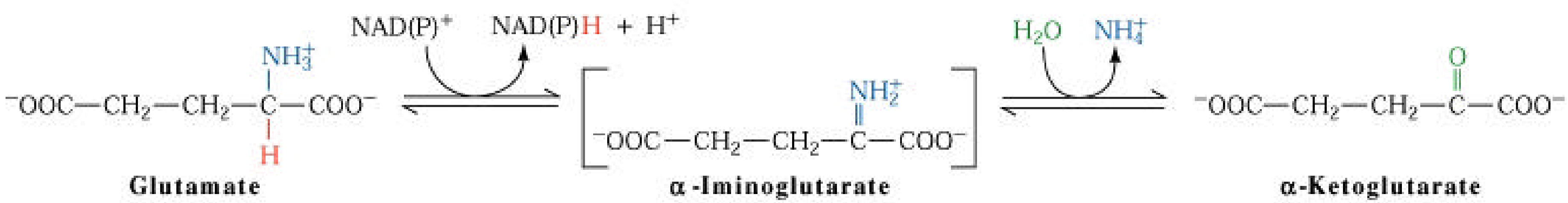
ASPARTATE

The second typical step in AA deamination involves transfer of the amino group from GLU to oxaloacetate, yeilding α-ketoglutarate and ASP:



Oxidative deamination (20.2b):

The transamination steps do not result in any NET deamination. GLUTAMATE is oxidatively deaminated by GLUTAMATE DEHYDROGENASE, yielding NH_3 and regenerating α-ketoglutarate (p. 619):



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Urea Cycle (20.3):

Animals are the only organisms that normally have a dietary excess of N, but...↑ **[NH_4^+] is toxic to animals**, so it must be gotten rid of. Excess N from AA breakdown is excreted from animals in one of 3 forms, depending on the availability of water:

Ammonia (book shows it as NH_3 or NH_4^+).
Aquatic animals simply release it into the surrounding water where it gets diluted to non-toxic concentrations. Animals that do this are called **AMMONOTELIC** (from the Greek, meaning "end"!—they did not know metabolism, so I don't think that this refers to the "end product"!!).