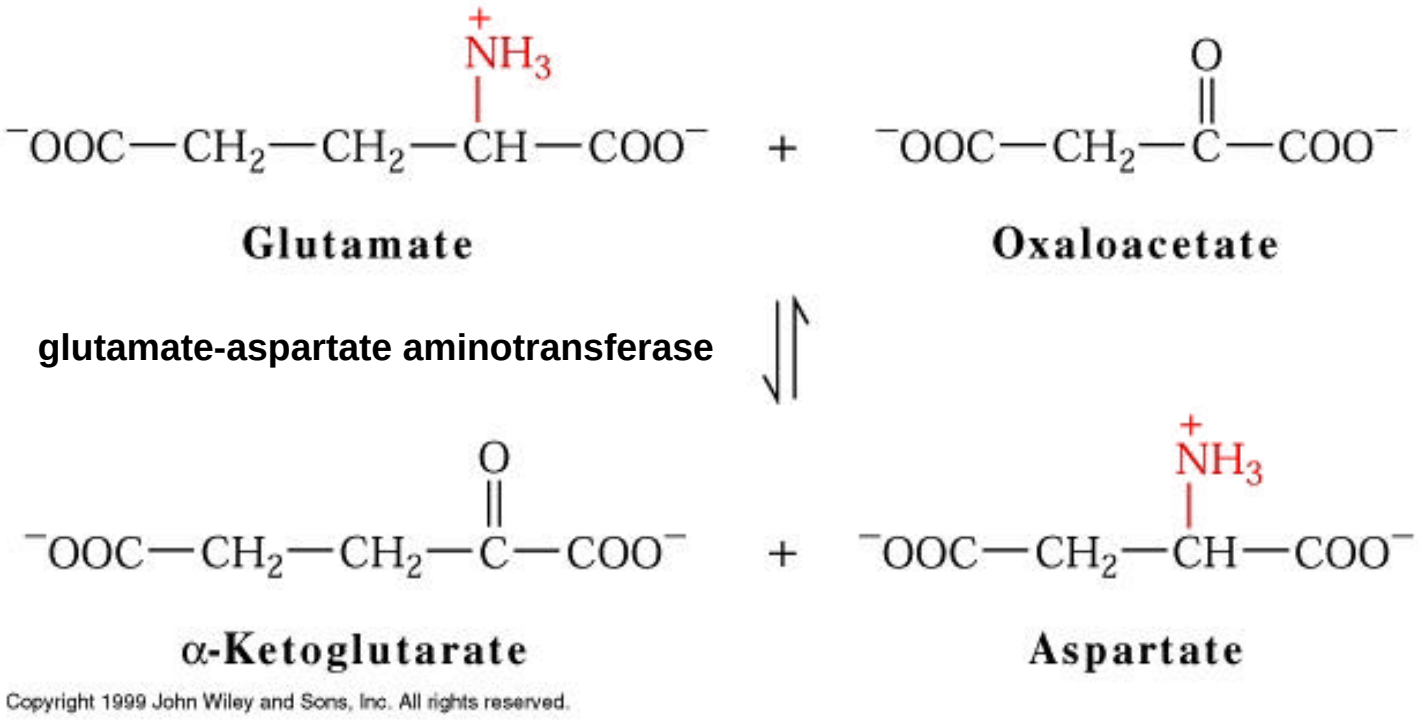
Amino Acid Metabolism (Chapter 20)

Lecture 9:

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

Quick review of the end of amino acid deamination…..

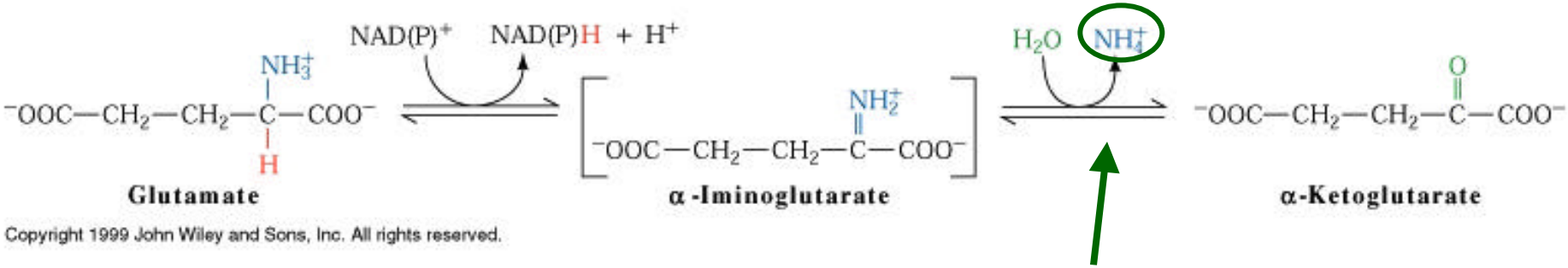
The second typical step in AA deamination involves transfer of the amino group from GLU to oxaloacetate, yeilding α-ketoglutarate and ASP:



Note that Aspartate is formed here…..

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):



Note that NH_4^+ is formed here…..

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"!).

Terrestrial and aerial species convert ammonium to less toxic waste products that require little water for excretion:

2) **UREA**

Most terrestrial vertebrates (especially mammals) —called UREOTELIC. Urea is a highly water soluble nonionic substance that **is synthesized in the liver by enzymes of the urea cycle -** happens in both the mitochondria & the cytosol. STUDY THIS!

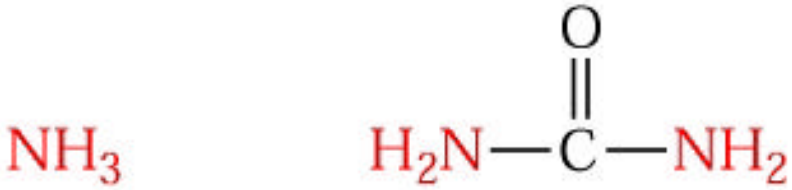
Note on urea cycle: It has 2 important AAs that are not among the 20 common in proteins: **ornithine** & **citrulline**

Urea secreted to bloodstream → KIDNEYS → excreted in URINE

3) **URIC ACID**

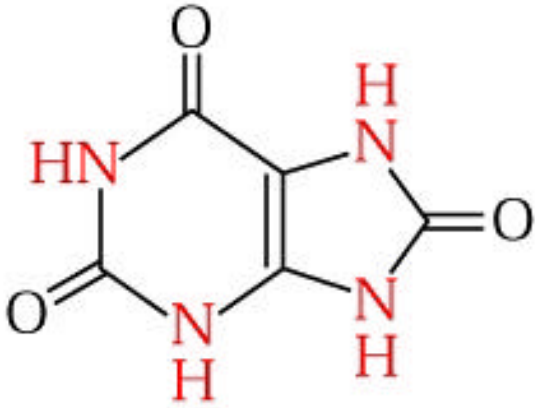
Birds & terrestrial reptiles (the white stuff: not very H_2O soluble) —called URICOTELIC.

The 3 nitrogen waste excretion products of animals from amino acid degradation (know the structures):



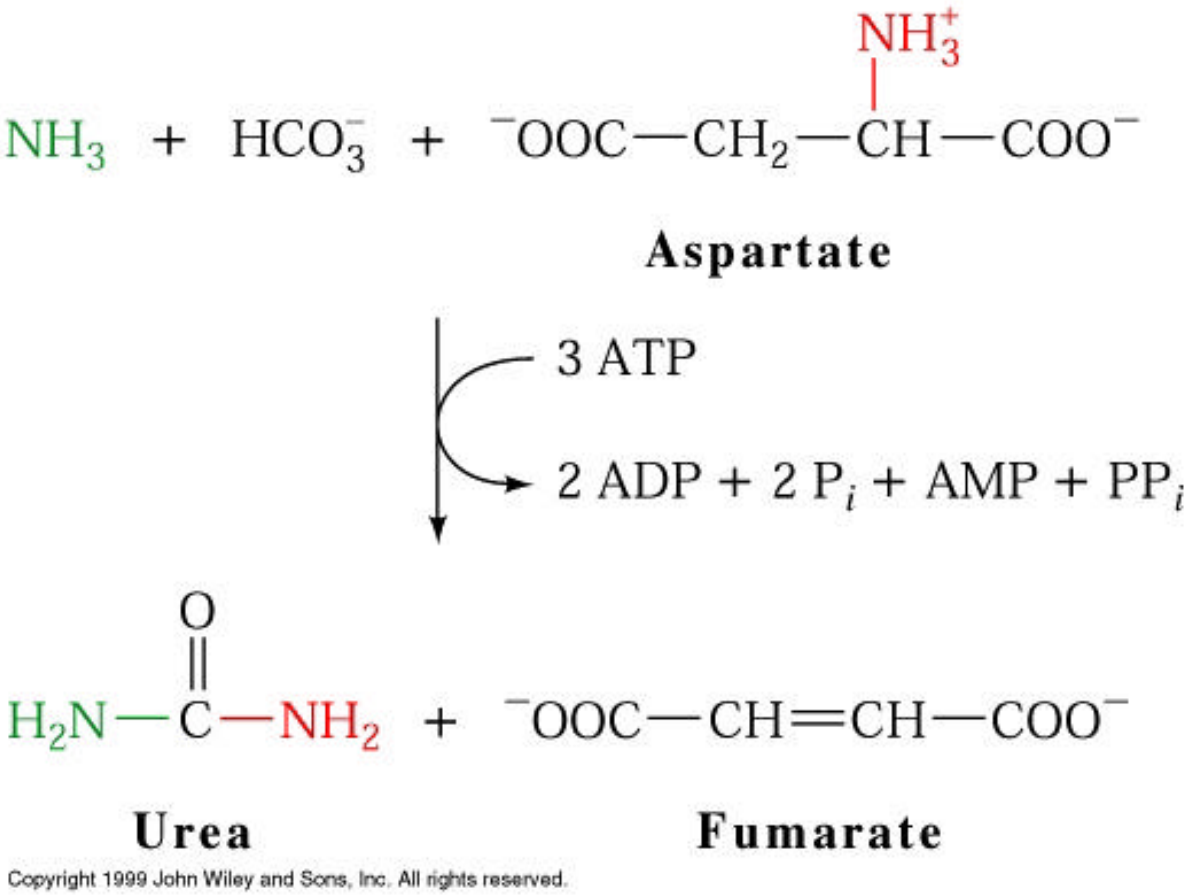
Ammonia

Urea

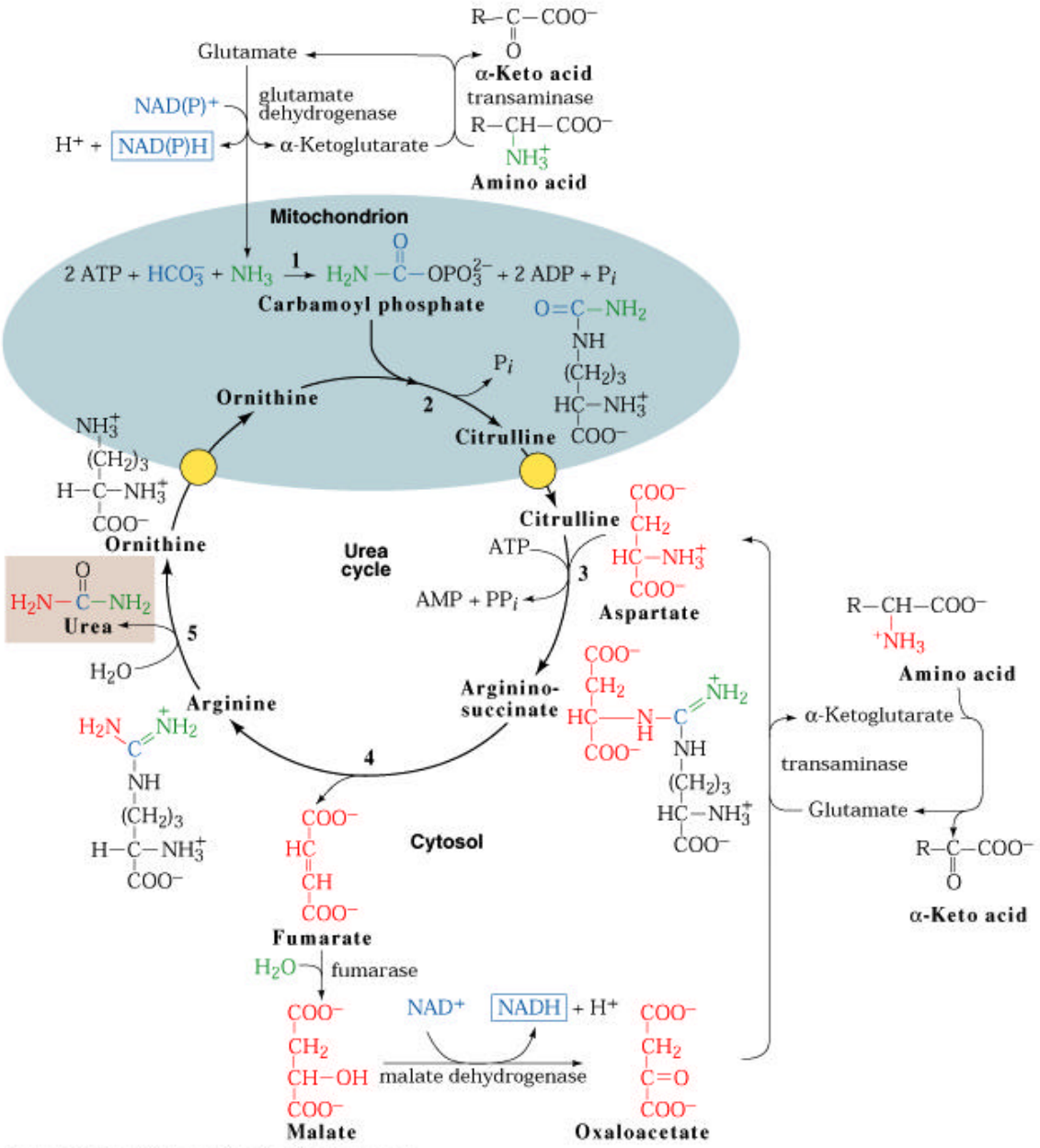


Uric acid

The overall reaction of the UREA CYCLE:



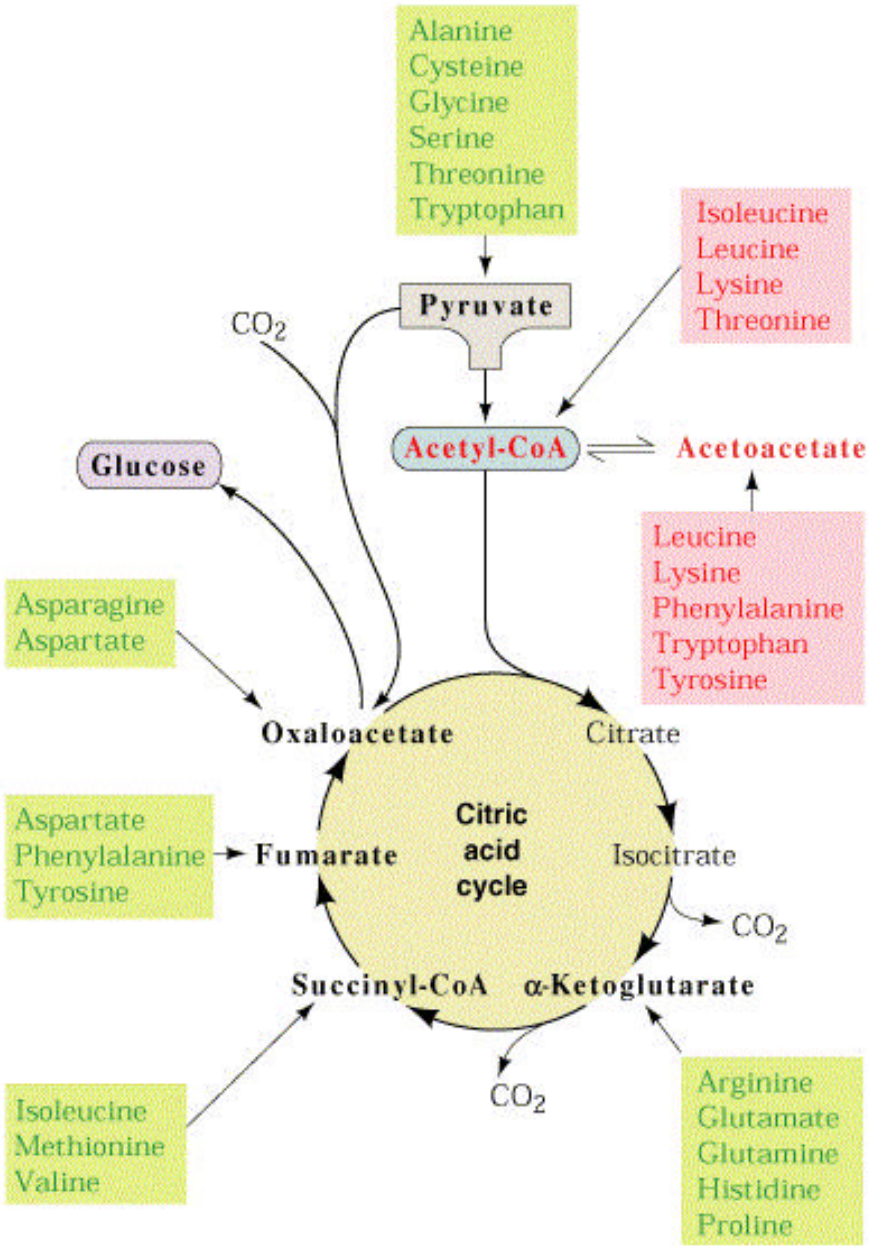
The 2 N of urea are contributed by ammonia and aspartate.



Excess AAs are **not stored** (as amino acids) or **excreted** (as amino acids), but rather excess amino acids are degraded by **20 different pathways** (I will not expect you to know the 20 different pathways, only the general information that I will give you later). Do understand that these 20 pathways **converge to just 7 common metabolic intermediates that feed into the TCA (= citric acid or Krebs) cycle:**

pyruvate
α-ketoglutarate
succinyl-CoA
fumarate
oxaloacetate
acetyl-CoA ← Ketone bodies!
acetoacetate

Fig. 20.11
Amino acid degradation



Note that some AAs are both glucogenic and ketogenic:

Ile
Phe
Thr **Both glucogenic & ketogenic**
Trp
Tyr

Leucine & lysine are the only purely ketogenic amino acids

All others are glucogenic.

Section 20.5: Amino acid biosynthesis

Organisms show great differences in their capacity to synthesize the 20 amino acids commonly found in proteins. Most plants and microorganisms can make all of their nitrogenous metabolites, including all of the amino acids, from inorganic forms of N such as NH_4^+ and NO_3^-. In these organisms, the α-amino group for all amino acids is derived from glutamate, usually by transamination of the corresponding α-keto acid analog of the amino acid. Thus, in many cases amino acid biosynthesis is simply a matter of synthesizing the appropriate α-keto acid carbon skeleton, followed by transamination using glutamate.

The **predominant amino acid/α-keto acid pair in such reactions is glutamate and α-ketoglutarate**, to that **glu** is the primary amino donor for the **synthesis** of amino acids. These transamination reactions are catalyzed by **aminotransferases** ; they are named according to their amino acid substrates (ex: **glutamate-aspartate aminotransferase**).

Most mammals can synthesize only about 10 of the 20 common amino acids. Relating to human diet, the AAs are classified into (TABLE 20.3):

Essential:	**Non-essential:**
Arg*	**Ala**
His	**Asn**
Ile	**Asp**
Leu	**Cys**
Lys	**Glu**
Met	**Gln**
Phe	**Gly**
Thr	**Pro**
Trp	**Ser**
Val	**Tyr**

NONESSENTIAL: the organism **can** synthesize the α-keto analog.
ESSENTIAL: the organism **cannot** synthesize their carbon skeletons, so must obtain these AAs in the diet.

must get in diet	mammals synthesize (varies)
<u>Essential</u>	<u>Non-essential</u>
Arg * (children only)	Ala
His * (children only)	Asp
Ile	Asn
Leu	Cys
Lys	Glu
Met	Gln
Phe	Gly
Thr	Pro
Trp	Ser
Val	Tyr (is readily formed from Phe)

[Eskimos? (Western white male is standard "human" in medicine)]

Milk/most meats have all

- Beans ↑ Lys, ↓ Met]
- Wheat ↓ Lys, ↑ Met]

Balanced diet

(each day, not necessarily each meal)

Pathways of amino acid biosynthesis vary greatly across species (unlike lipid & carbohydrate metabolism, which are almost universal in animals)

Excess dietary amino acids cannot be stored (as amino acids) for future use. Nor are they excreted unused. Instead, they are converted to common metabolic intermediates that can either be oxidized by the TCA cycle or used to form GLUCOSE. [So....what happens when we eat too much protein? Converted to glucose.... and then what?.....eventually stored as.....?.....FAT!]