BI/CH 422/622

OUTLINE:

Introduction and review
Transport
Glycogenolysis
Glycolysis
Other sugars
Pasteur: Anaerobic vs Aerobic
Fermentations — Exam-1 material
Pyruvate — Exam-2 material
Krebs' Cycle
Oxidative Phosphorylation
Electron transport
Chemiosmotic theory: Phosphorylation

Fat Catabolism — Exam-3 material
diet
storage
Fatty acid Catabolism
FOUR stages in the catabolism of lipids:
Mobilization from tissues (mostly adipose)
hormone regulated
specific lipases
glycerol
Activation of fatty acids
Fatty-acyl CoA Synthetase
Transport
carnitine
Oxidation
Rationale
Saturated FA
β-oxidation
4 steps:
dehydrogenation
hydration
oxidation
thiolase
energetics
Unsaturated FA
energetics
Odd-chain FA
Ketone Bodies
Other organelles

Protein Degradation (Catabolism)
Digestion
Inside of cells
Protein turnover
Ubiquitin
Proteosome

Amino-Acid Degradation
Dealing with the nitrogen
Ammonia
free
transamination ← know mechanism
Carbamoyl-phosphate synthetase
Urea Cycle
4 Steps
Ornithine transcarbamylase
Arginino-succinate synthetase
Arginino-succinase
Arginase
Energetics
Urea-Bi-cycle
Dealing with the carbon
Seven Families
1. ADENQ (Transaminase/deaminase Family)
2. RPH (Glu Family)
Oxidase
One-carbon (1-C) metabolism
THF
SAM
3. GSC (Pyruvate Family)
PLP uses
4. MT – 1-C metabolism (α-Ketobutyrate Family)
5. FY – oxidases (Aromatic Family)
6. KW (α-Ketoadipate Family)
7. VIL (Branched-chain AA Family (BCAA))
Convergence with Fatty acid-odd chain

Fates of the 29 nitrogen atoms in 20 AA:

9 ammonia
17 transamination
1 reduc. deamin.
2 urea

Nucleic Acid and Nucleotide Degradation
Nucleic Acids
Nucleotides
Salvage pathway
Degradation of purines
Degradation of pyrimidines
Connection of sugar metabolism

Amino Acid Degradation: the carbon "skeletons"

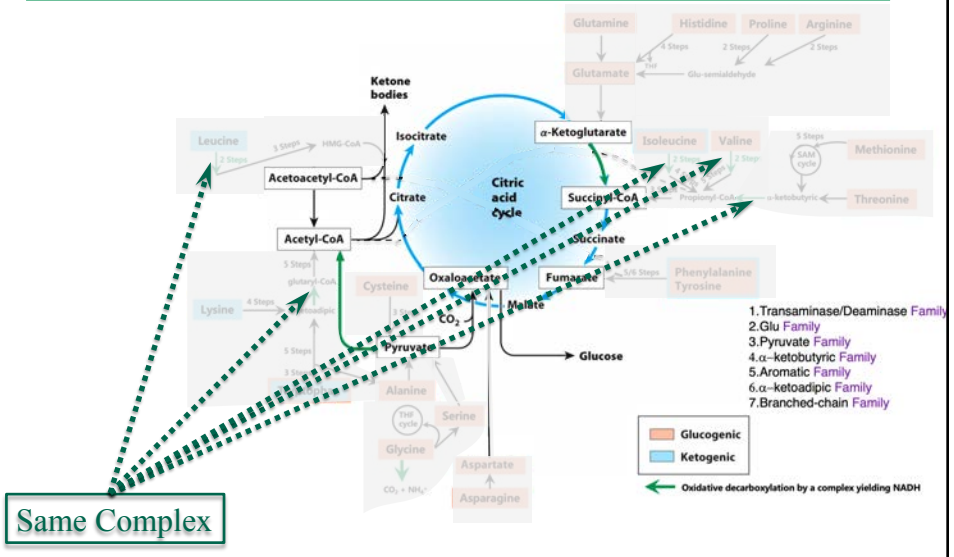
A. Concepts
1. Convergent
2. ketogenic/glucogenic
3. Reactions seen before

The SEVEN (7) Families

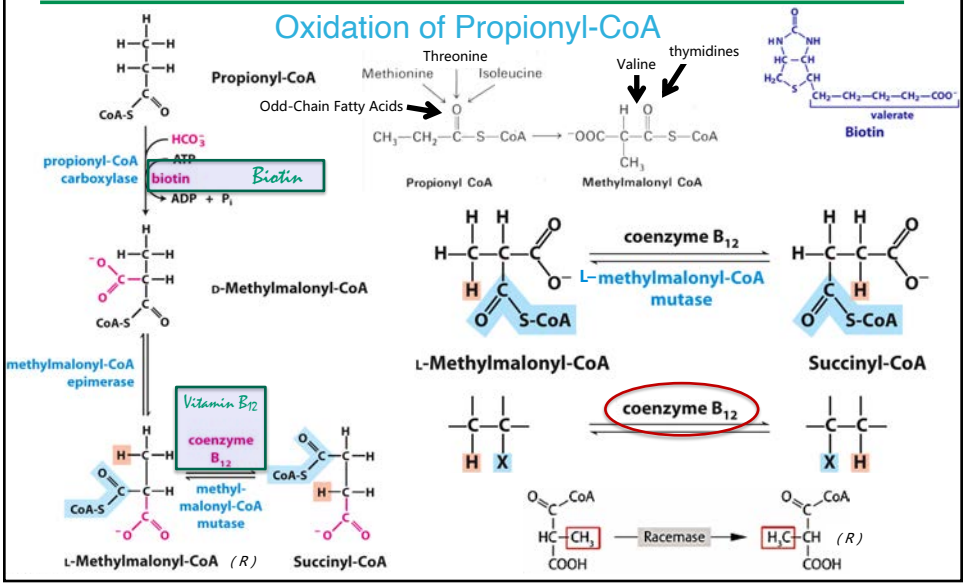
B. Transaminase (A,D,E) / Deaminase (Q,N) Family
C. Related to biosynthesis (R,P,H; C,G,S; M,T)
1. Glu Family
a. Introduce oxidases/oxygenases
b. Introduce one-carbon metabolism (1C)
2. Pyruvate Family
a. PLP reactions
3. α–Ketobutyric Family (M,T)
a. 1-C metabolism
D. Dedicated
1. Aromatic Family (F,Y)
a. oxidases/oxygenases
2. α–Ketoadipic Family (K,W)
3. Branched-chain Family (V,I,L)
E. Convergence with Fatty Acids: propionyl-CoA

Before VIL

Amino Acid Degradation

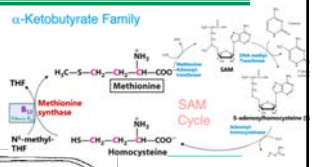


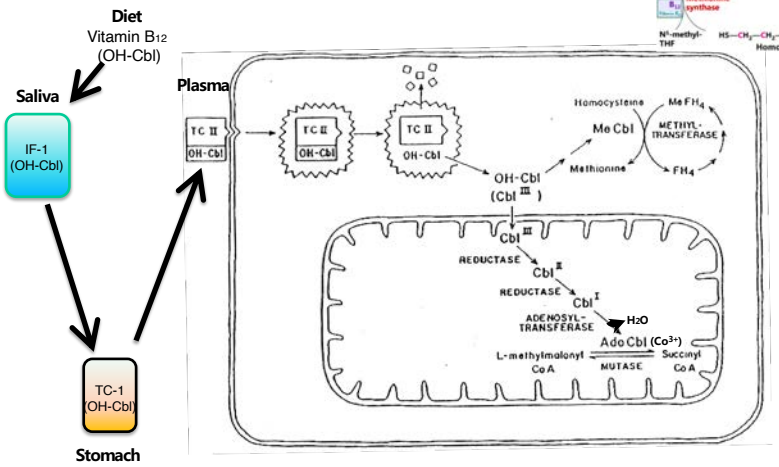
Amino Acid Degradation Meets Fatty Acid Degradation



Amino Acid Degradation Meets Fatty Acid Degradation

Only a handful of enzymes require Coenzyme B_{12} (cobalamin)





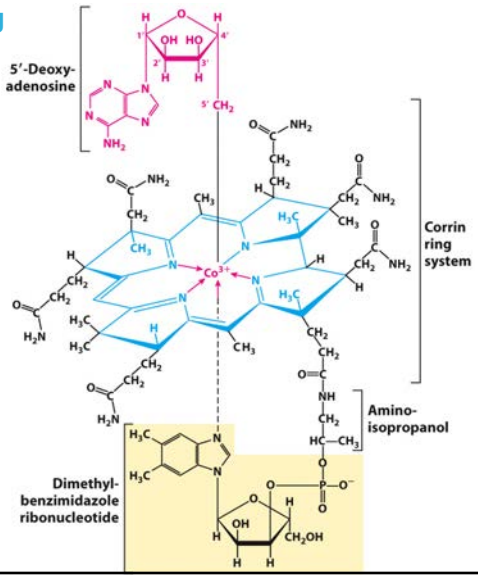
Amino Acid Degradation Meets Fatty Acid Degradation

Complex Cobalt-Containing Compound: Coenzyme B_{12}

Nobel Prize

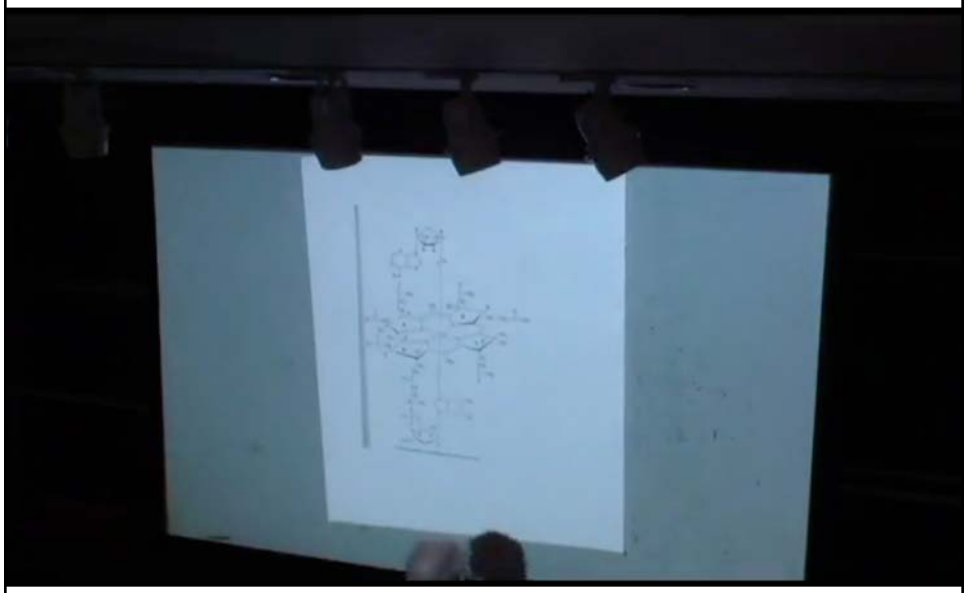
Alexander R. Todd
1957

Dorothy Hodgkin
1964



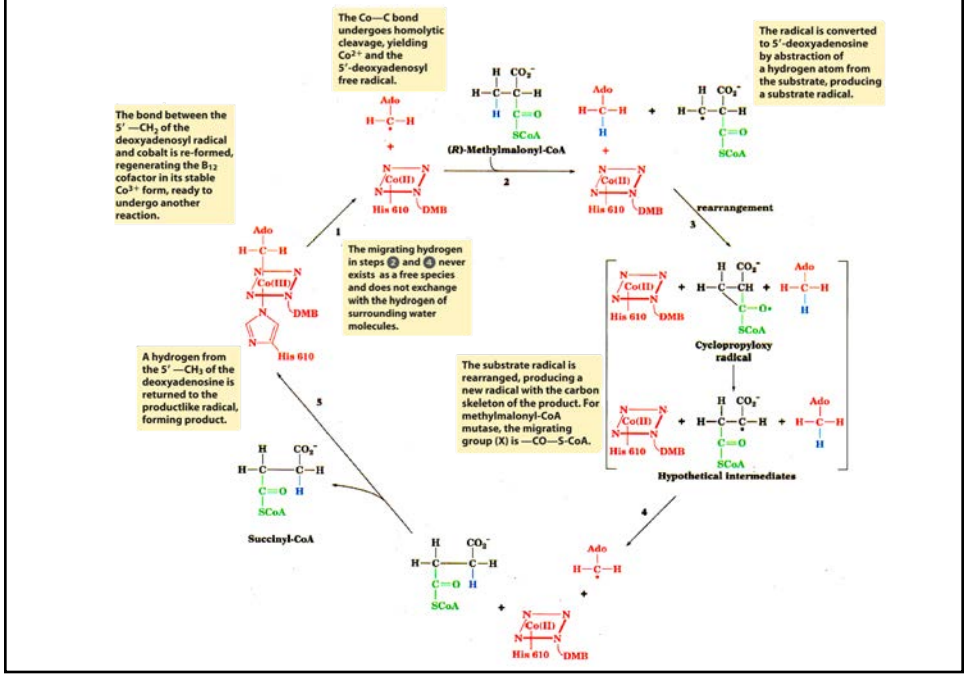
Amino Acid Degradation Meets Fatty Acid Degradation

The Vitamin B_{12} Story

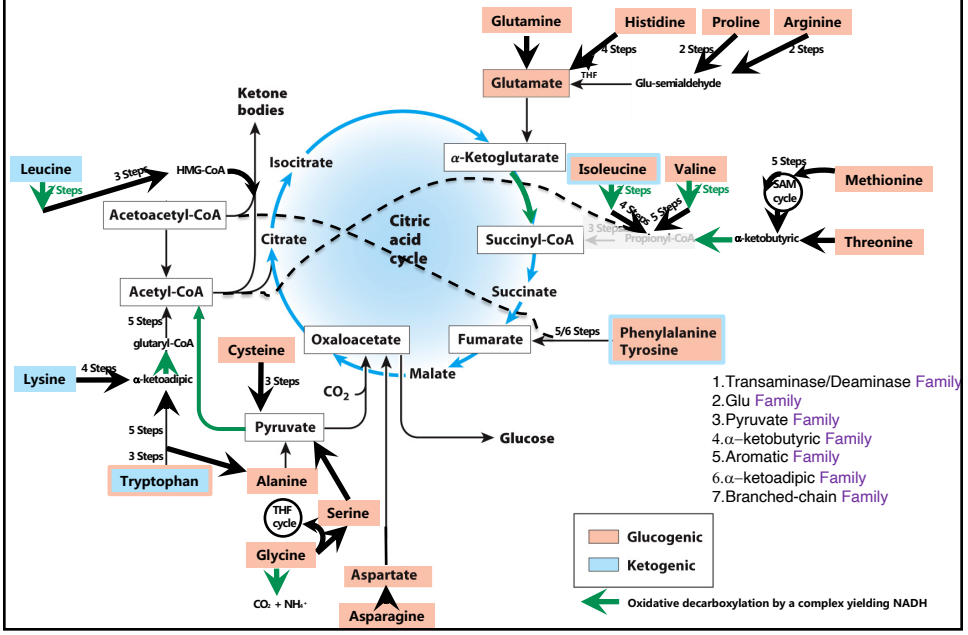


Dr. Kornberg: **Lecture 16 02.27.17 (28:19-29:33) VitB-12 1.3 min**

Amino Acid Degradation Meets Fatty Acid Degradation

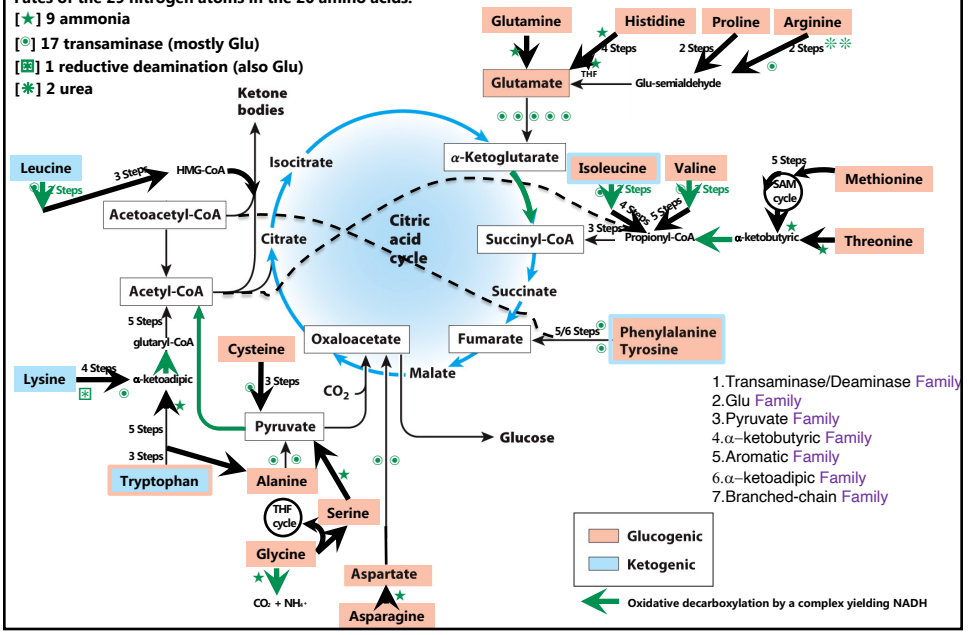


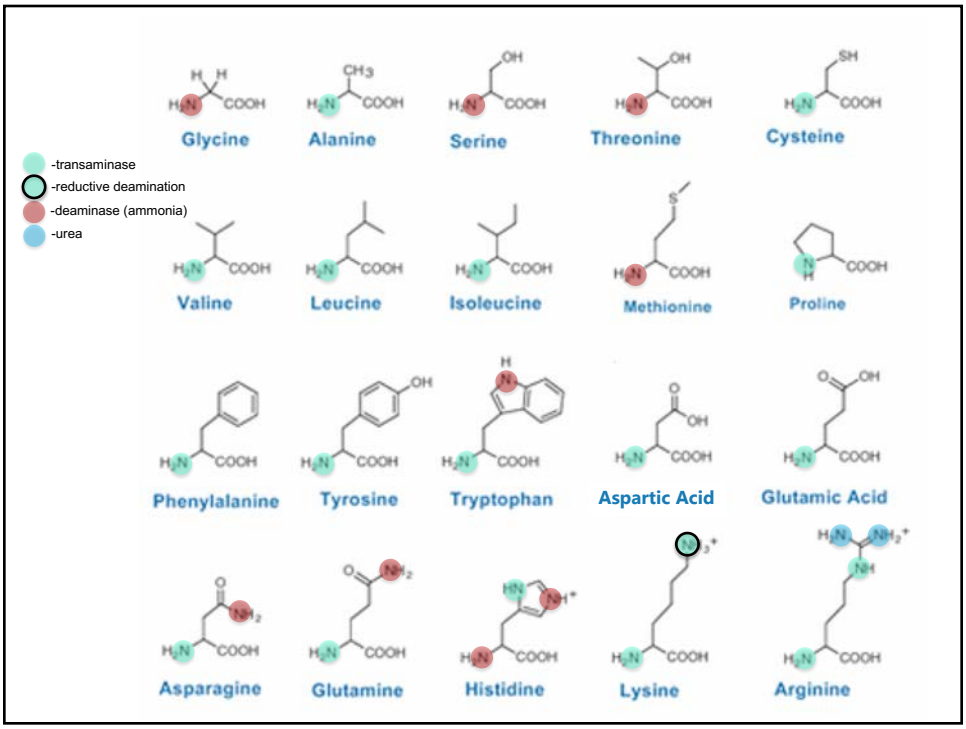
Amino Acid Degradation: Overview



Amino Acid Degradation: Overview

Fates of the 29 nitrogen atoms in the 20 amino acids:
[★] 9 ammonia
[⊙] 17 transaminase (mostly Glu)
[⊞] 1 reductive deamination (also Glu)
[✳] 2 urea





Amino Acid Degradation: Overview

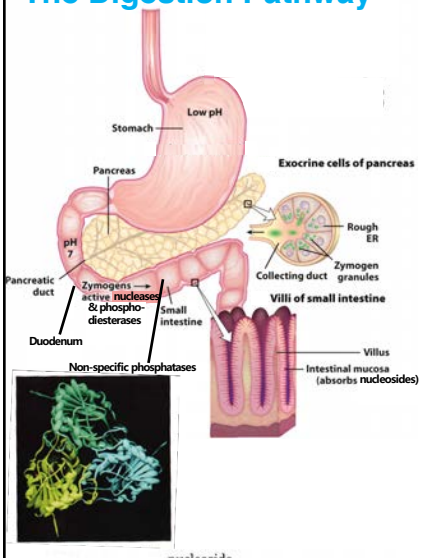
We learned that:

- amino acids from protein are an important energy source in carnivorous animals
- the first step of AA catabolism is transfer of the NH_3 via PLP-dependent aminotransferase usually to α-ketoglutarate to yield L-glutamate
- in most mammals, toxic ammonia is quickly recaptured into carbamoyl phosphate and passed into the urea cycle
- amino acids are degraded to pyruvate, acetyl-CoA, α-ketoglutarate, succinyl-CoA, and/or oxaloacetate
- amino acids yielding acetyl-CoA are ketogenic
- amino acids yielding other end products are glucogenic
- genetic defects in amino-acid degradation pathways result in a number of human diseases
- amino acid catabolism is dependent on a variety of cofactors, including THF, ado-Met (SAM), Cbl, biotin, and **PLP**

Nucleic-Acid Degradation

Nucleic-Acid Degradation

The Digestion Pathway

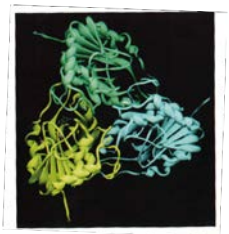


$$\text{Nucleoside} + P_i \xrightarrow{\text{nucleoside phosphorylase}} \text{base} + \text{ribose-1-P}$$

- Ingestion of food always includes nucleic acids.
- As you know from BI 421, the low pH of the stomach does not affect the polymer.
- In the duodenum, zymogens are converted to nucleases and the nucleotides are converted to nucleosides by non-specific phosphatases or nucleotidases.
- Only the non-ionic nucleosides are taken up in the villi of the small intestine.
- **In the cell**, the first step is the release of the ribose sugar, most effectively done by a non-specific nucleoside phosphorylase to give ribose 1-phosphate (Rib1P) and the free bases.
- Most ingested nucleic acids are degraded to Rib1P, purines, and pyrimidines.

Nucleotide Degradation: Overview

Fate of Nucleic Acids:



Purine Nucleoside Phosphorylase

Nucleotides

P_i

Nucleosides

P_i → αD-Rib 1-P & αD-dRib 1-P

Bases

Purine & Pyrimidine Salvage Pathway

Oxidation

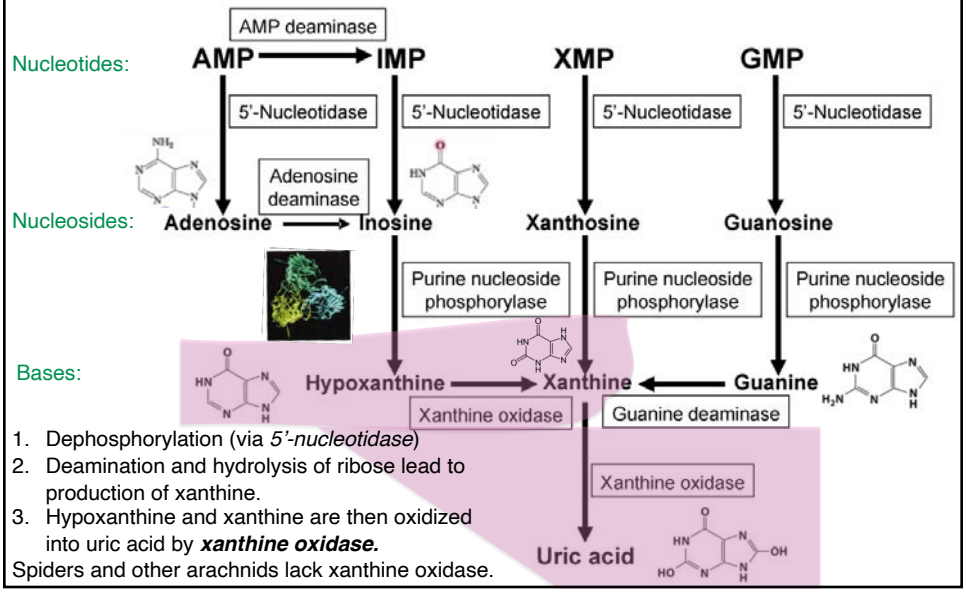
The Salvage Pathways are in competition with the *de novo* biosynthetic pathways, and are both ANABOLISM

Once broken down to the nitrogenous bases they are either:

1. Salvaged for recycling into new nucleic acids (most cells; from internal, not ingested, nucleic acids).
2. Oxidized (primarily in the intestine and liver) by first converting to nucleosides, then to
   - –Uric Acid (purines)
   - –Acetyl-CoA & succinyl-CoA (pyrimidines)
   - –Both yield ammonia

Nucleotide Degradation

Catabolism of Purines

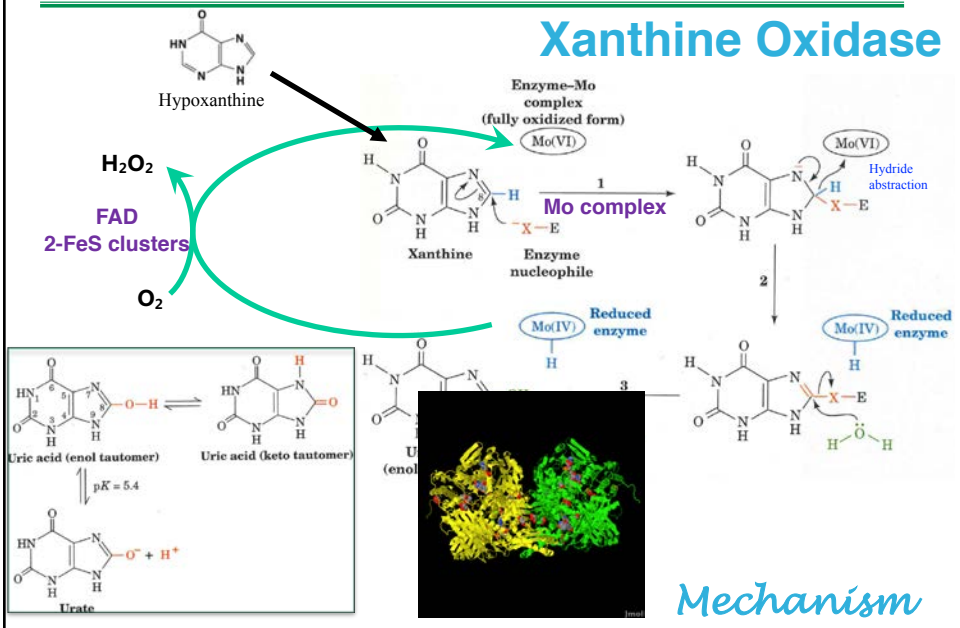


1. Dephosphorylation (via *5'-nucleotidase*)
2. Deamination and hydrolysis of ribose lead to production of xanthine.
3. Hypoxanthine and xanthine are then oxidized into uric acid by ***xanthine oxidase.***

Spiders and other arachnids lack xanthine oxidase.

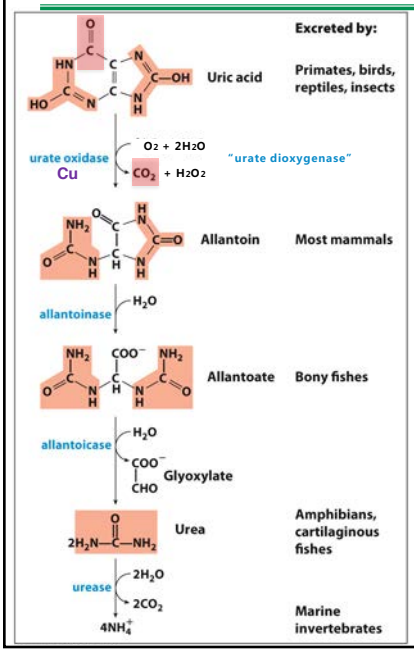
Nucleotide Degradation

Xanthine Oxidase



Mechanism

Nucleotide Degradation

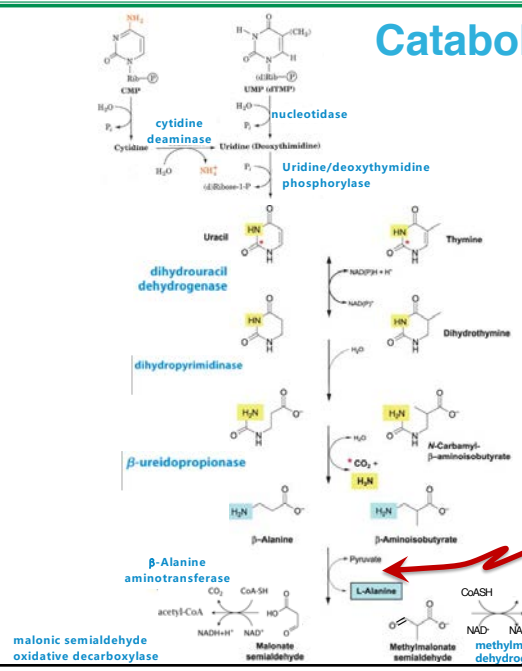


- Degree of further oxidation of uric acid is organism dependent.
- Birds and insects don't excrete amino-acid nitrogen as urea, but as uric acid to conserve water.

Conversion of Uric Acid to Allantoin, Allantoate, and Urea

Nucleotide Degradation

Catabolism of Pyrimidines



- Leads to NH_4^+ and urea
- T is degraded to succinyl-CoA.
- U & C are degraded to acetyl-CoA

Like reaction converting Orn to glutamate semialdehyde

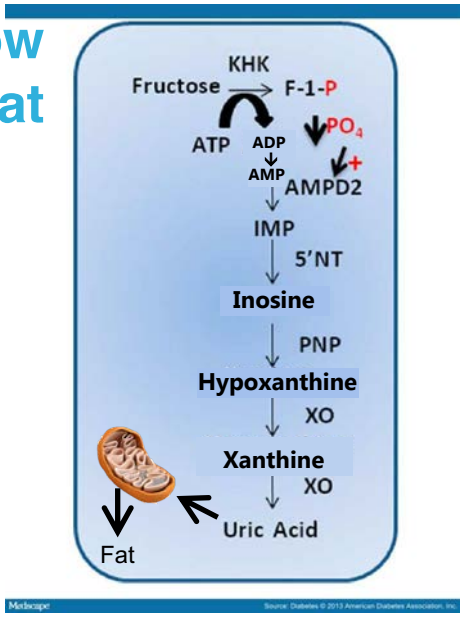
Val

Like reaction putting CoA on isobutryl-semialdehyde in Val degradation

Nucleotide Degradation

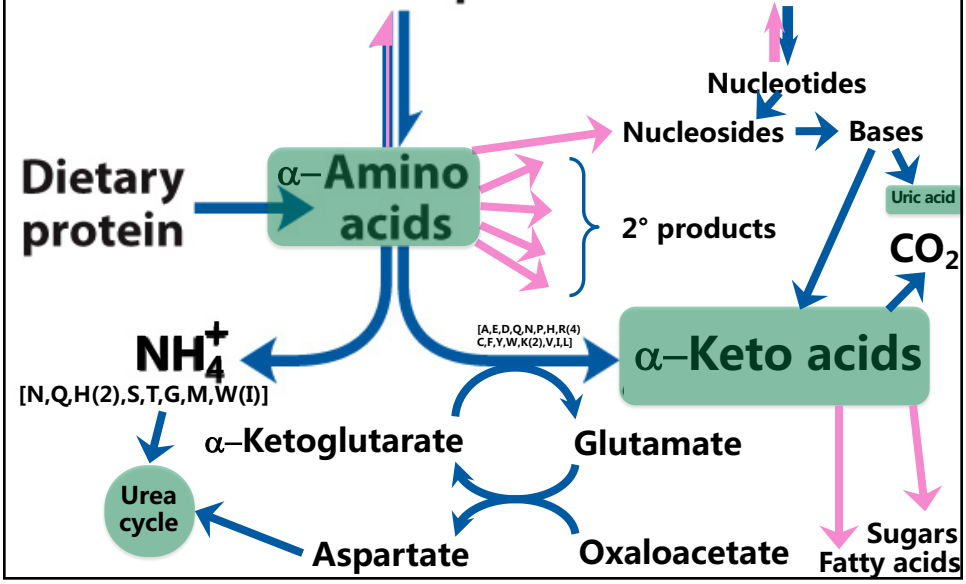
Hyperuricemia: how sugar "becomes" fat

- The interesting connection between sugar metabolism and nitrogen metabolism
- What is even more interesting is that this metabolism is connected to fat metabolism as well
- The production of Uric Acid converts liver mitochondria to fatty acid synthesis by unknown mechanisms.



Nitrogen Metabolism

Catabolism
Anabolism

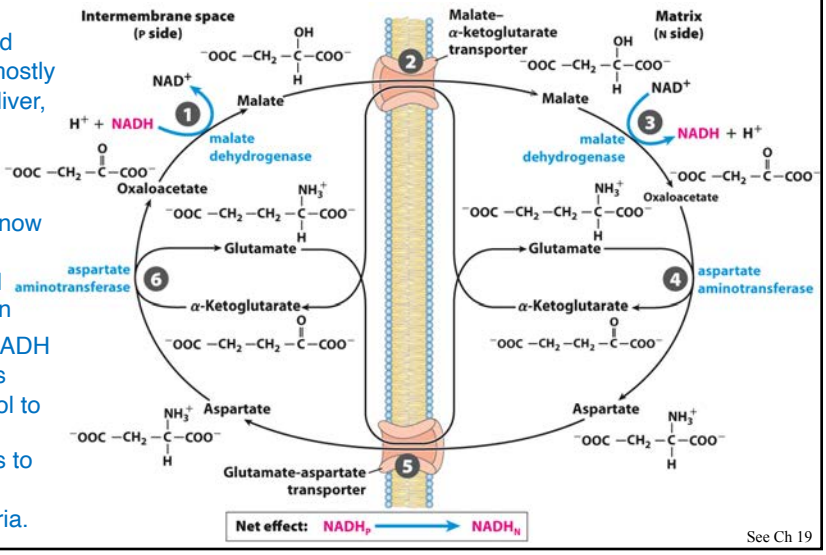


Oxidative Phosphorylation

Malate-Aspartate Shuttle

Converting Cytosolic Electron Carriers (NADH) to the Mitochondria

- This more complicated shuttle is mostly present in liver, heart, and kidney.
- Can be discussed now that we did amino-acid degradation
- It moves NADH equivalents form cytosol to NADH equivalents to the mitochondria.



See Ch 19

End of Material for Exam 3