BB 422/622

OUTLINE:

Introduction and review
Transport
Glycogenolysis
Glycolysis
Other sugars
Pasteur: Anaerobic vs Aerobic

Exam-1 material

Fermentations
Pyruvate
Krebs' Cycle
Oxidative Phosphorylation
Electron transport
Chemiosmotic theory: Phosphorylation

Exam-2 material

Fates of the 29 nitrogen atoms in 20 AA:

9 ammonia
17 transamination
1 reduc. deamin.
2 urea

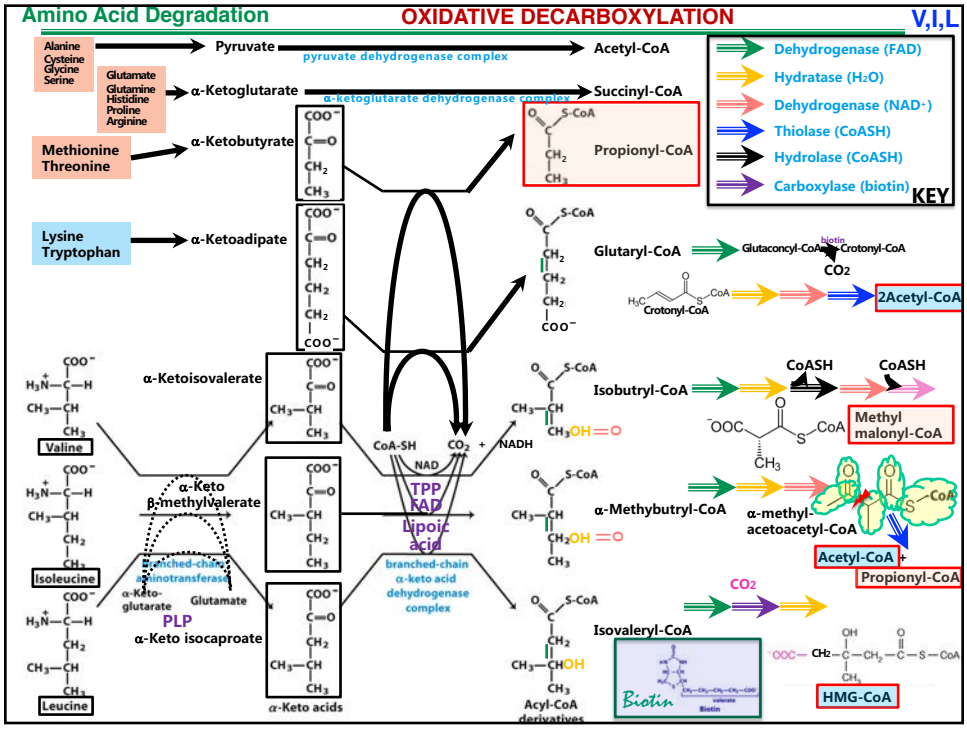
Exam-3 material

Fat Catabolism
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

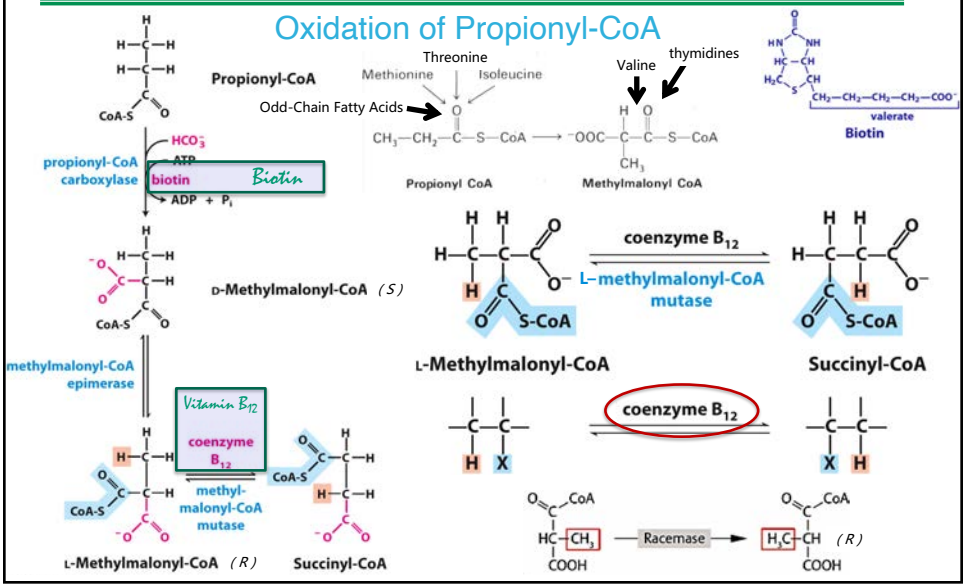
Protein Degradation (Catabolism)
Digestion
Inside of cells
Protein turnover
Ubiquitin
Proteosome
Amino-Acid Degradation
Dealing with the nitrogen
Ammonia
free
know mechanism → transamination
Carbamoyl-phosphate synthetase
Urea Cycle
5 Steps
Ornithine transcarbamylase
Arginino-succinate synthetase
Arginino-succinase
Arginase
Energetics
Urea Bi-cycle
Dealing with the carbon

Seven Families
1. ADENQ (Trans-/de- aminase 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-KetoB Fami)
5. FY – oxidases (Aromatic Family)
6. KW (α-Ketoadipate Family)
7. VIL (Branched-chain AA Family)
Propionyl-CoA

Nucleic-Acid Degradation
nucleotide to bases
salvage vs oxidation
purine
pyrimidine

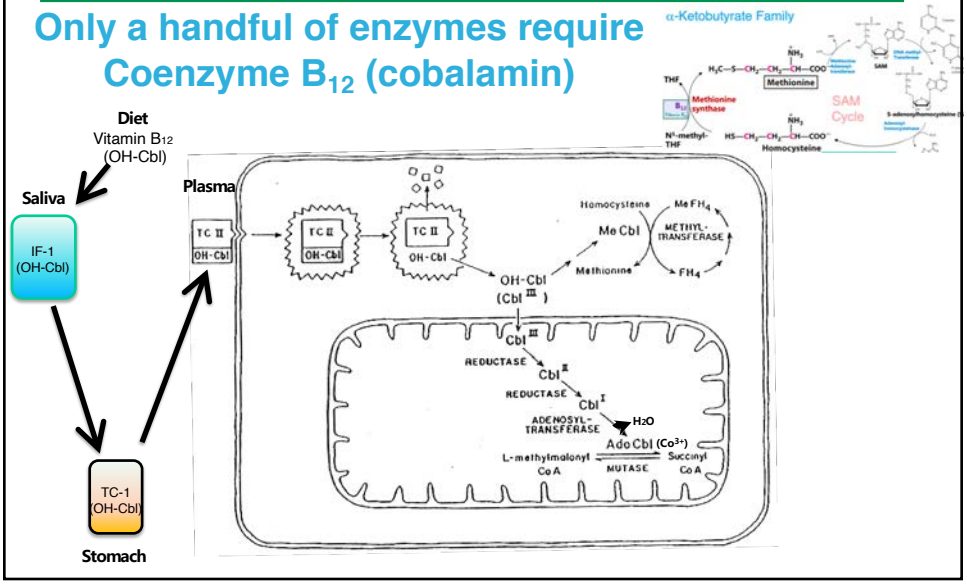


Amino Acid Degradation Meets Fatty Acid Degradation



Amino Acid Degradation Meets Fatty Acid Degradation

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



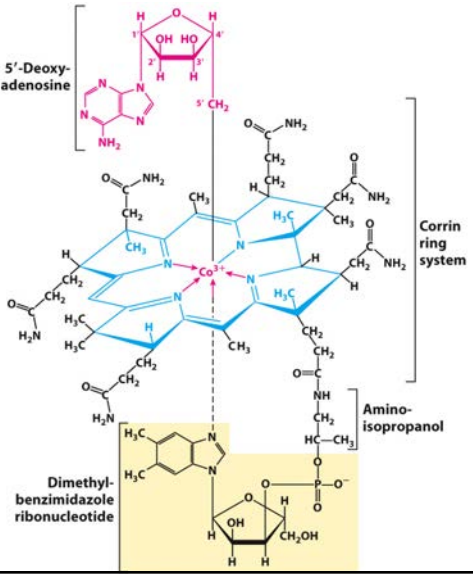
Amino Acid Degradation Meets Fatty Acid Degradation

Complex Cobalt-Containing Compound: Coenzyme B_{12}

Nobel Prize

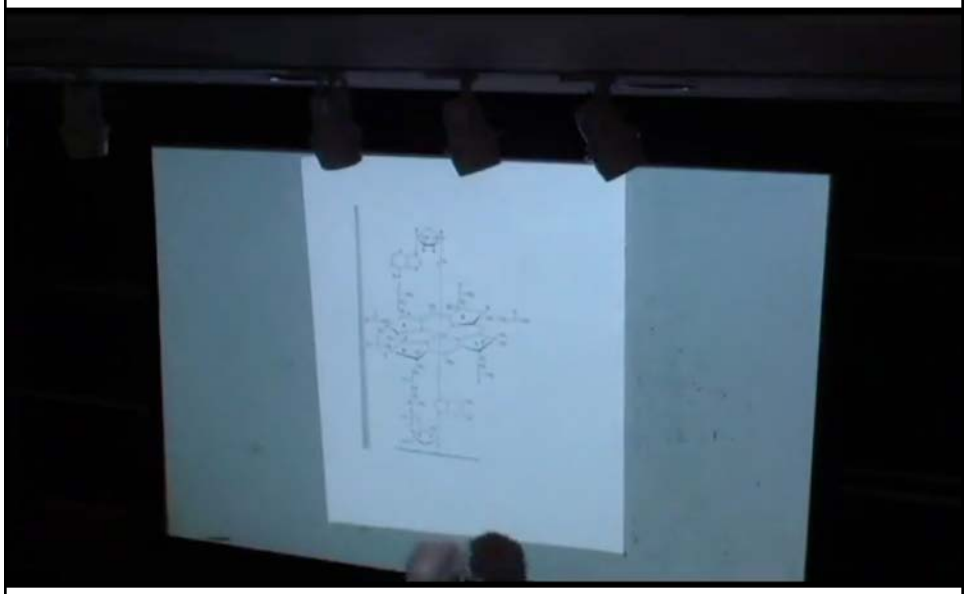
Alexander R. Todd
1957

Dorothy Hodgkin
1964

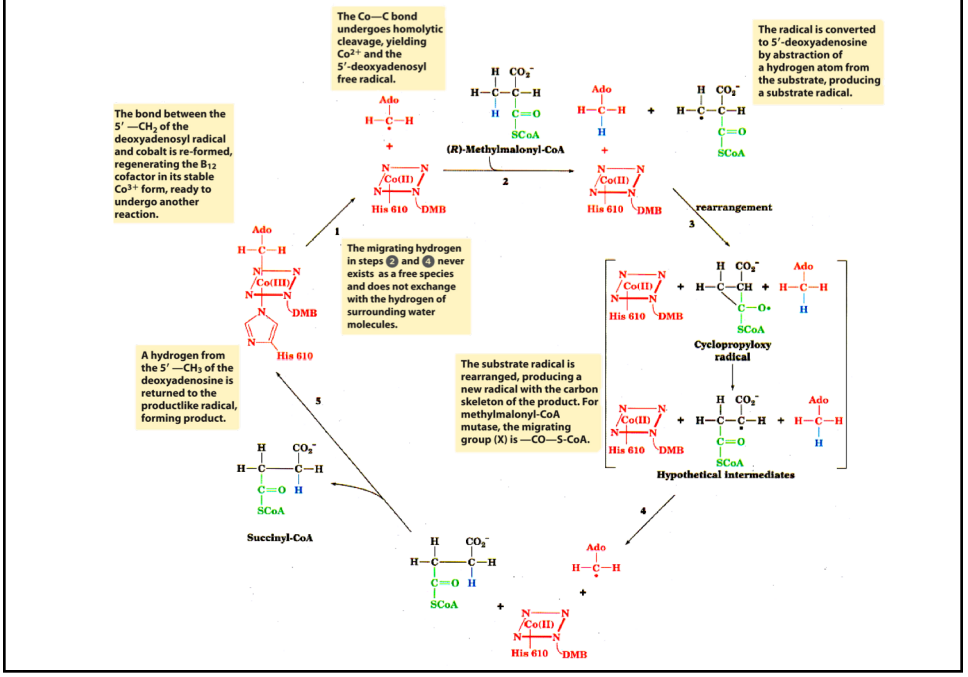


Amino Acid Degradation Meets Fatty Acid Degradation

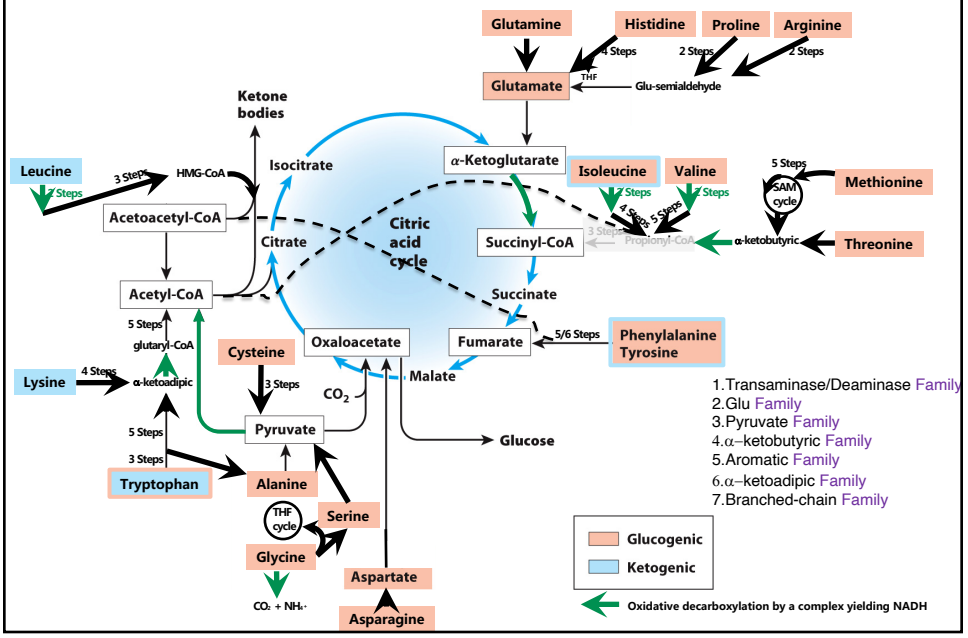
The Vitamin B_{12} Story



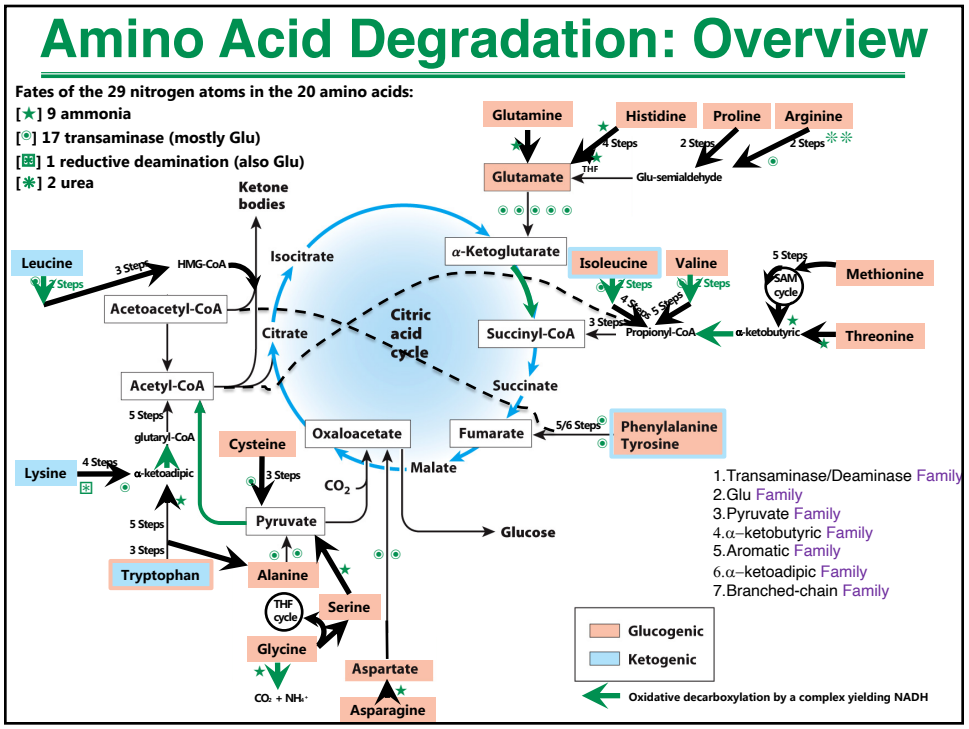
Amino Acid Degradation Meets Fatty Acid Degradation

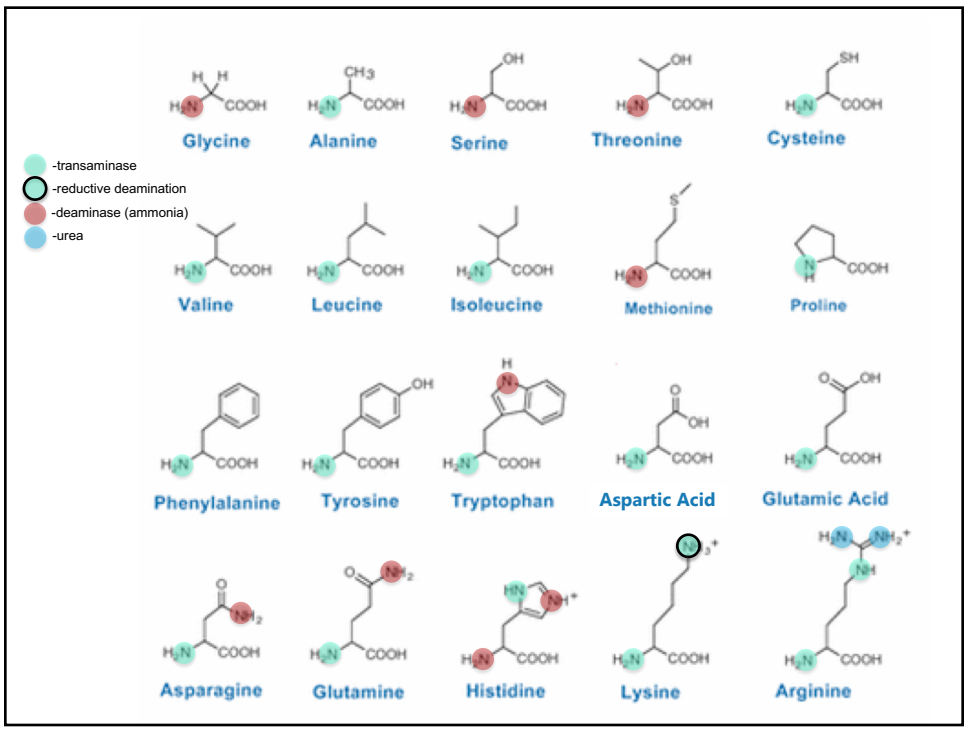


Amino Acid Degradation: Overview



Amino Acid Degradation: Overview





Amino Acid Degradation: Overview

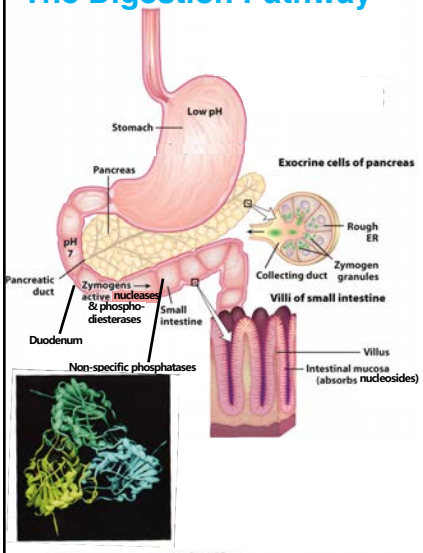
We learned that:

- amino acids from protein are an important energy source in carnivorous animals
- the first step of AA catabolism is often the 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 Gln or directly into carbamoyl phosphate for 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

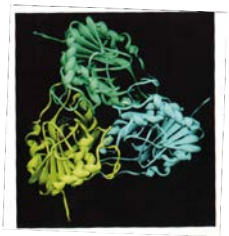


Nucleoside + P_i —(nucleoside phosphorylase)→ base + ribose-1-P

- 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 nucleic acids are degraded to Rib, Rib1P, purines, and pyrimidines.

Nucleotide Degradation: Overview

Fate of Nucleic Acids:



Purine Nucleoside Phosphorylase

nucleases

Nucleotides

phosphatases/ nucleotidases → P_i

Nucleosides

P_i → αD-Rib 1-P & αD-dRib 1-P

Bases

Purine & Pyrimidine Salvage Pathway

Oxidation

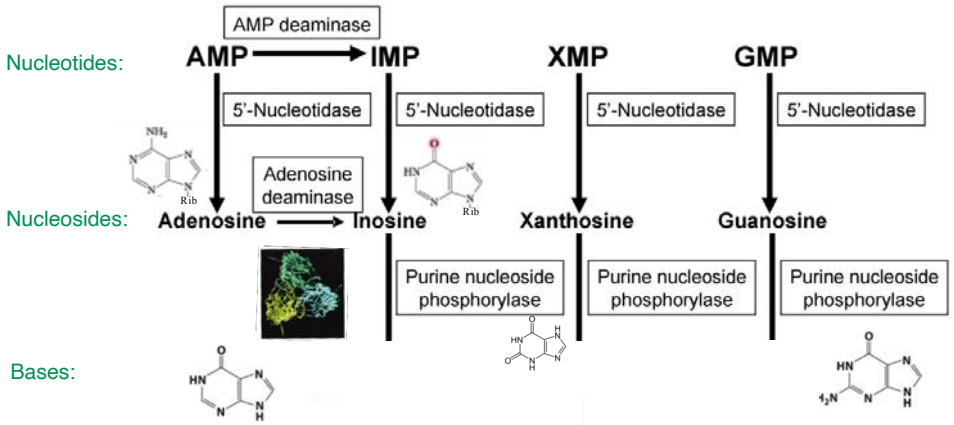
Once broken down to the nitrogenous bases they are either:

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)

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

Nucleotide Degradation

Catabolism of Purines

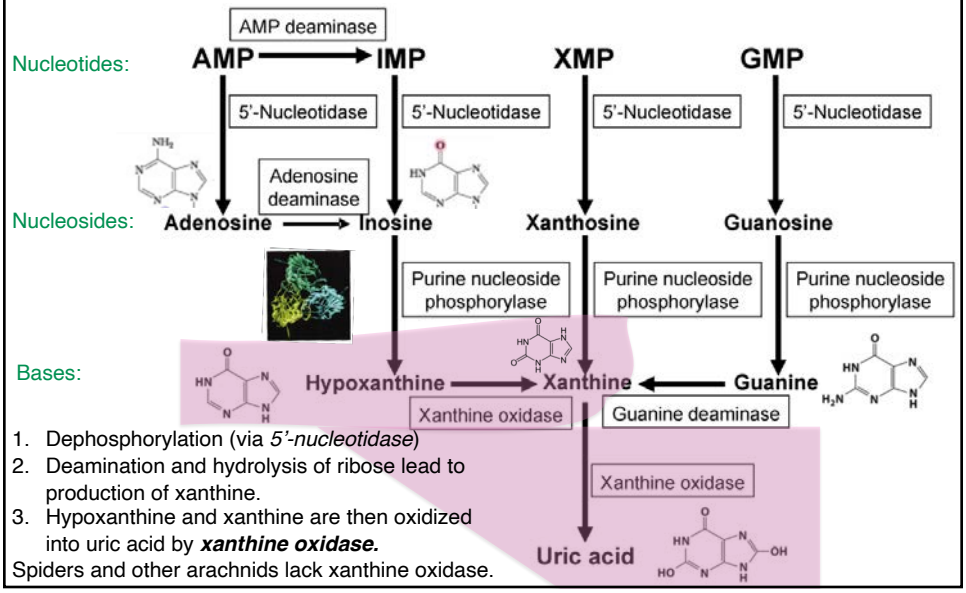


1. Dephosphorylation (via *5'-nucleotidase*)
2. Deamination and hydrolysis of ribose lead to production of hypoxanthine and xanthine.
3. Hypoxanthine and xanthine are then oxidized into uric acid by ***xanthine oxidase.***

Spiders and other arachnids lack xanthine oxidase.

Nucleotide Degradation

Catabolism of Purines

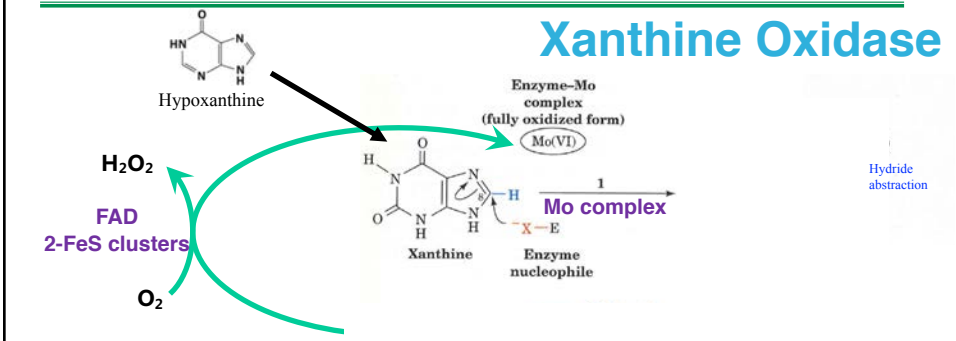


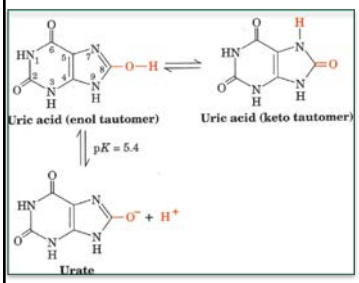
1. Dephosphorylation (via *5'-nucleotidase*)
2. Deamination and hydrolysis of ribose lead to production of xanthine.
3. Hypoxanthine and xanthine are then oxidized into uric acid by ***xanthine oxidase.***

Spiders and other arachnids lack xanthine oxidase.

Nucleotide Degradation

Xanthine Oxidase

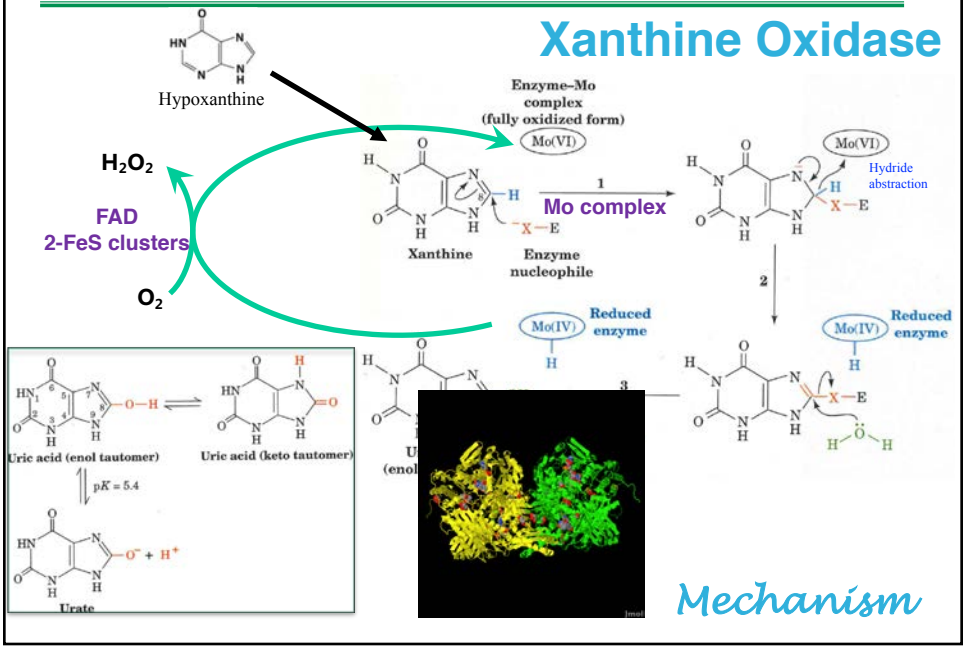




Mechanism

Nucleotide Degradation

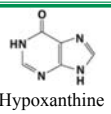
Xanthine Oxidase



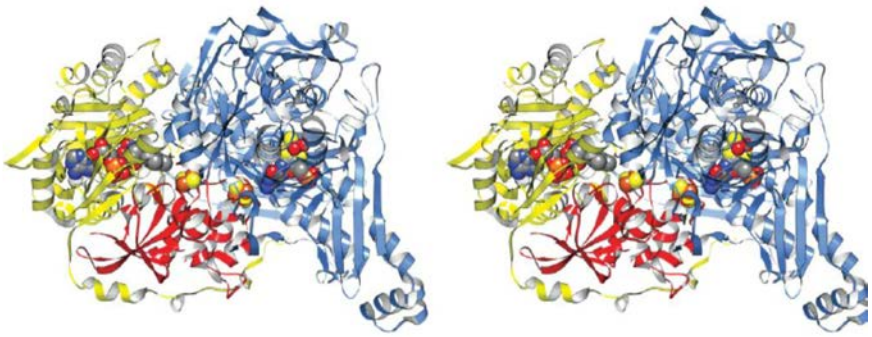
Mechanism

Nucleotide Degradation

Xanthine Oxidase

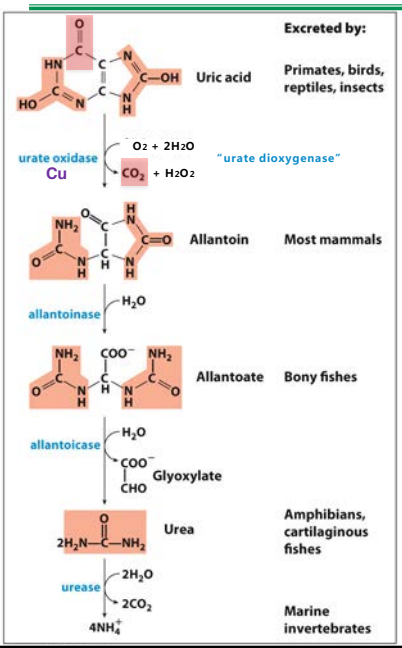


Hypoxanthine



Structure

Nucleotide Degradation

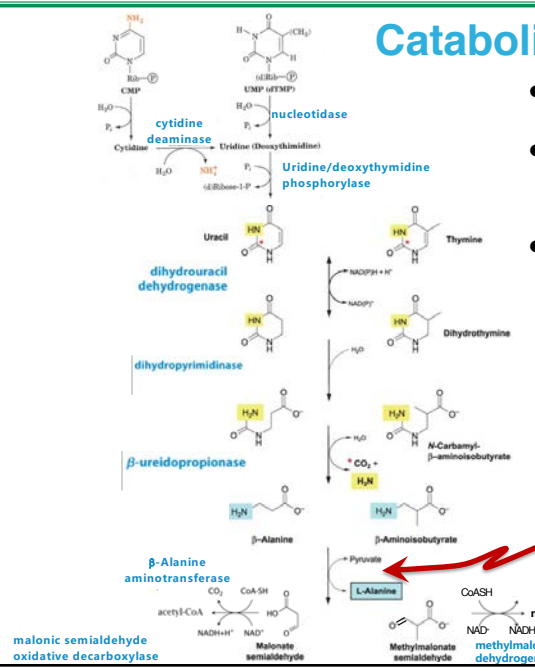


- Degree of further oxidation of uric acid is organism dependent.
- Birds and insects don't excrete amino-acid nitrogen as urea, but as uric acid to conserve water.

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

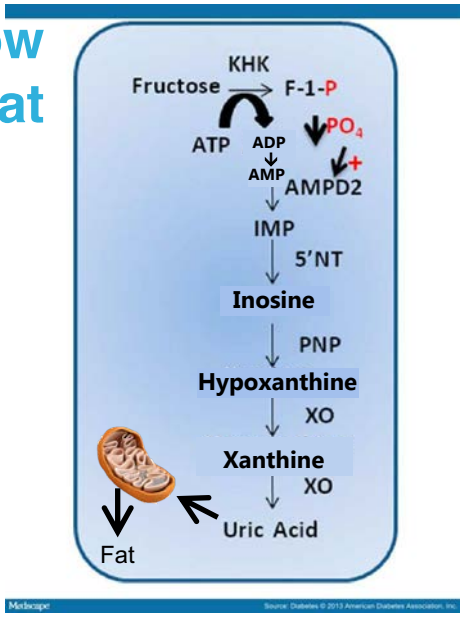
Val

Like reaction putting CoA on isobutryl-semialdehyde in Val degradation

Nucleotide Degradation

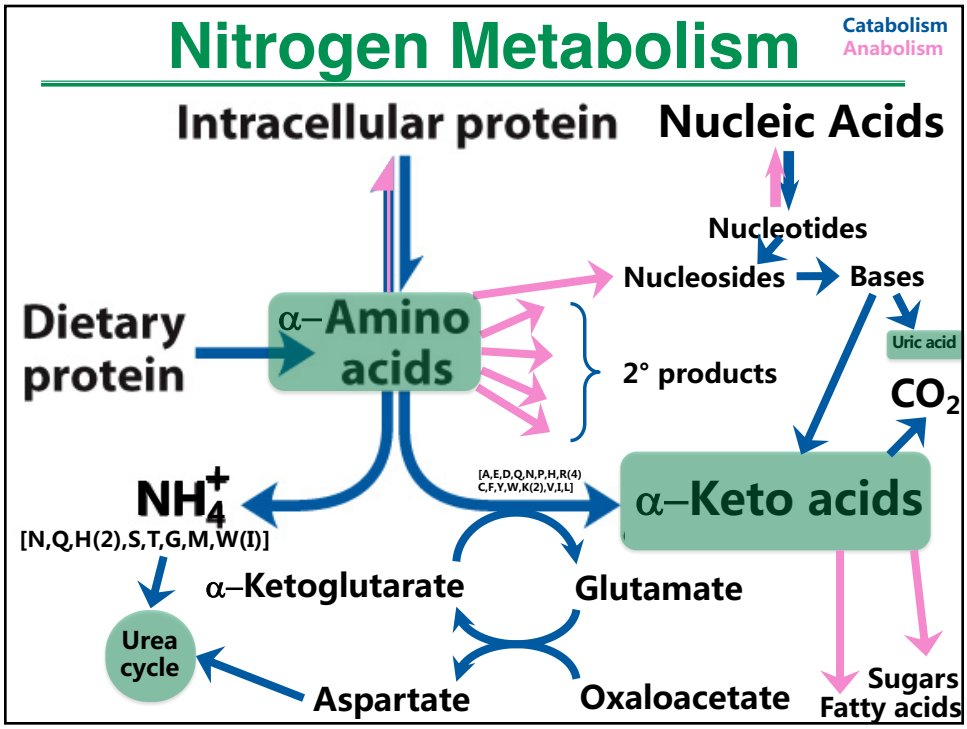
Hyperuricemia: how sugar "becomes" fat

- 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

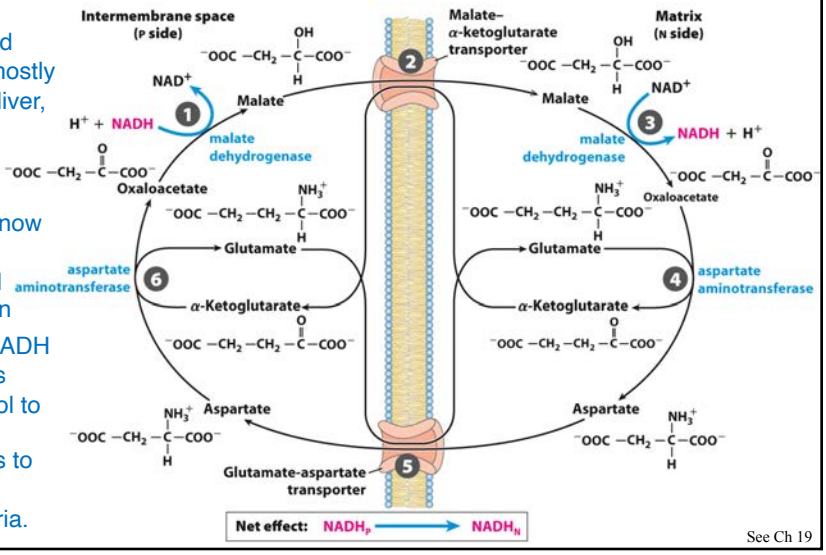


Oxidative Phosphorylation

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