Amino Acid Degradation and Nitrogen Metabolism

Chapter 30, Stryer Short Course

Overview

- Amino Acid Catabolism
  - Nitrogen removal
  - Urea Cycle
  - Metabolism of carbon backbone

Amino acid catabolism

- Amino acids from diet or protein turnover
- Salvaged for use in proteins or catabolized

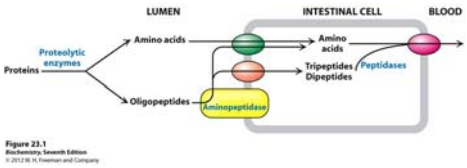
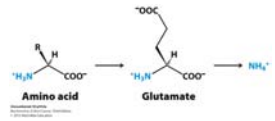


Figure 23.1
Biochemistry, Seventh Edition
© 2012 W. H. Freeman and Company

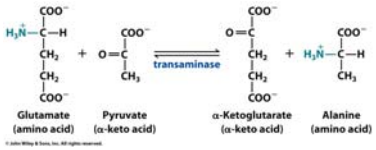
Removal of Nitrogen

- First step in amino acid catabolism
- Process
  - Transamination to glutamate
  - Ammonia released in liver

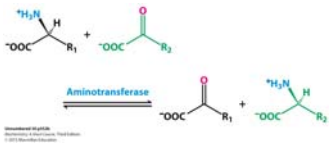


Transamination

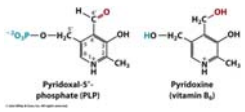
- Transfers nitrogen from other amino acids into glutamate
- Near equilibrium reaction
- Either nitrogen removal or assimilation

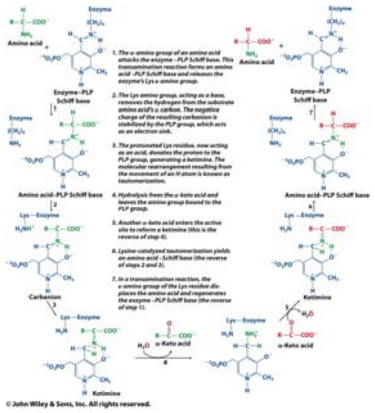


Transamination Mechanism



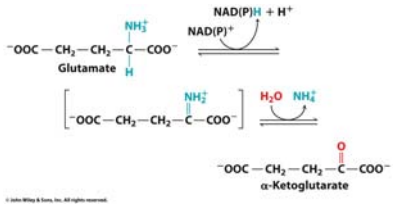
- Not oxidation or reduction
- Requires PLP cofactor





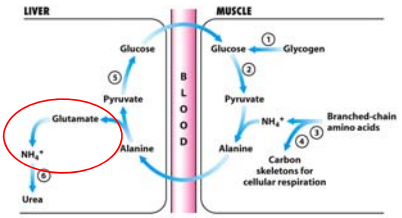
Glutamate Dehydrogenase

- Reversible reaction
- Releases nitrogen from transamination in the form of ammonia in liver mitochondria



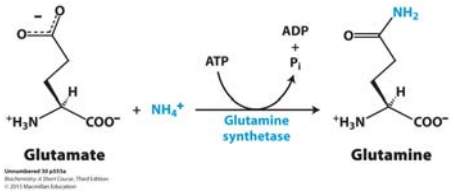
Ammonia Processing in Muscle

- The alanine-glucose cycle
- Then glutamate releases ammonia in the liver



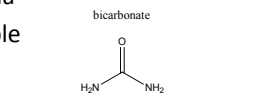
Sequestering free ammonia

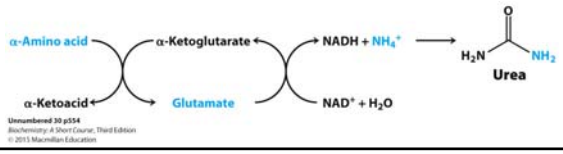
- Most tissues have some free ammonia released
- glutamine synthetase "mops up"
  - glutamine sent through blood to liver
  - Deaminated in liver to give glutamic acid and ammonia
    - glutaminase



Role of Liver Mitochondia

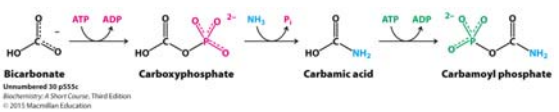
- Sequester toxic ammonia
- Make less toxic, execrable form
- Urea Cycle



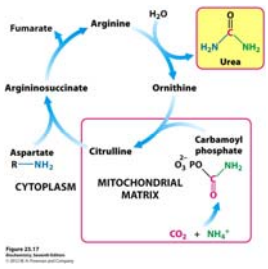


Carbamoyl phosphate

- Cost of 2 ATP
  - Phosphate leaving group
- Activation of ammonia for
  - Excretion
  - biosynthesis



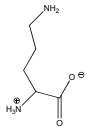
Urea Cycle



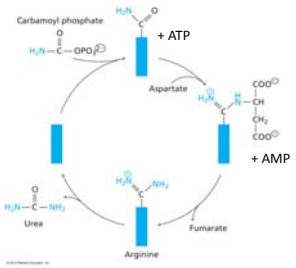
- Compartmentalization
- Write the net reaction of this cycle starting from carbamoyl phosphate

Chemistry of Urea Cycle

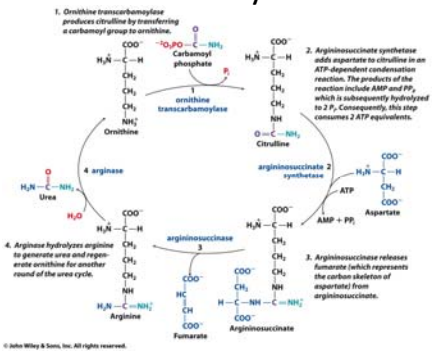
- Catalytic ornithine



- Fumarate
- Urea = 4 ATP

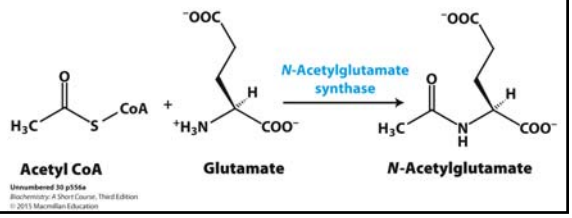


Urea Cycle



Urea Cycle Regulation

- Carbamoyl phosphate synthetase
- Amino acid catabolism boosts acetyl CoA and glutamate levels
- Produces activator

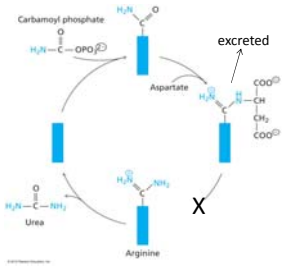


Problem

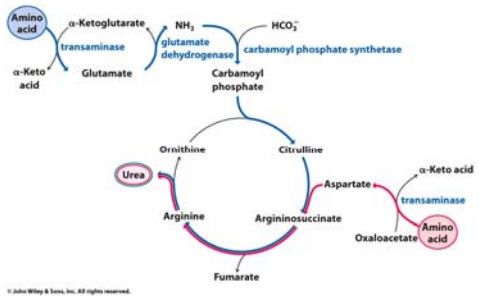
- An inborn error of metabolism causes a deficiency of arginosuccinase and results in *hyperammonemia*. How could the diet be changed to aid in ammonia secretion? (Argininosuccinate can be excreted.)

Solving Metabolic Problems

- Arginosuccinase deficiency
- Low protein diet
  - Minimize ammonium
- High arginine diet
  - Provide carrier



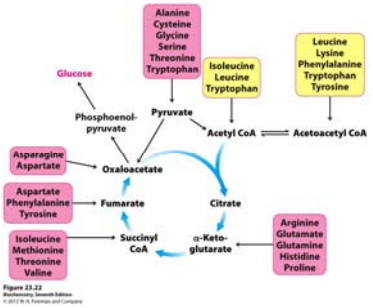
Nitrogen Flow Overview



Summary: Main Players

- Glutamate: in liver, receives nitrogen from AA, then ammonia is released in liver mitochondria
- Glutamine: ammonia transport; biosynthesis
- Alanine: ammonia transport
- Aspartate: nitrogen donor to urea
- Arginine: urea cycle

Degradation of Carbon Backbone



Glucogenic vs. Ketogenic

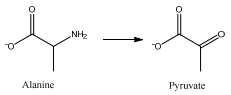
- Glucogenic
  - Pyruvate
  - Oxaloacetate
  - α-ketoglutarate
  - Succinyl CoA
  - Fumarate
- Ketogenic
  - Acetyl CoA
  - Acetoacetatyl CoA

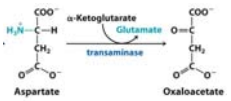
TABLE 18-2 Catabolic Fates of Amino Acids

Glucogenic	Both Glucogenic and Ketogenic	Ketogenic
Alanine	Isoleucine	Leucine
Arginine	Phenylalanine	Lysine
Asparagine	Threonine	
Aspartate	Tryptophan	
Cysteine	Tyrosine	
Glutamate		
Glutamine		
Glycine		
Histidine		
Methionine		
Proline		
Serine		
Valine		

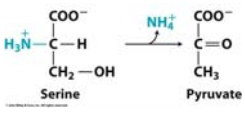
Transamination

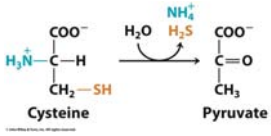
- Some transaminations lead from amino acid to intermediate in one step
- Examples:



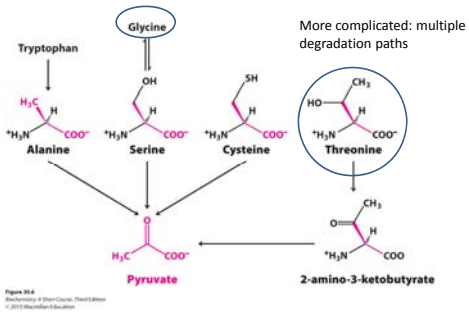


1. Pyruvate Family: 3-carbon AA



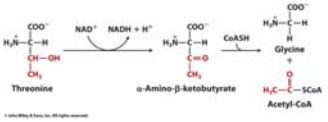


Pyruvate Family

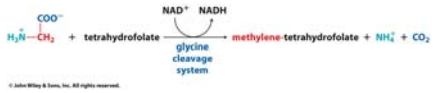


More complicated: multiple degradation paths

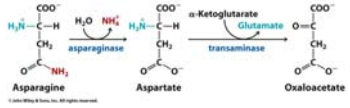
- Thr: Glucogenic and Ketogenic



- Gly—major source of methylene-THF (Ch. 31)

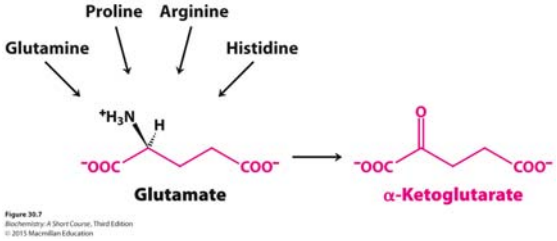


2. Oxaloacetate Family: 4 Carbon AA



3. a-Ketoglutarate Family

- 25% of dietary intake
- "5" carbon amino acids



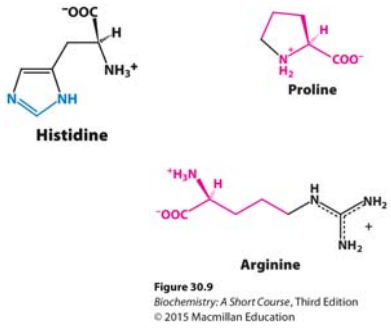
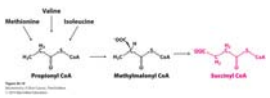


Figure 30.9
Biochemistry: A Short Course, Third Edition
© 2015 Macmillan Education

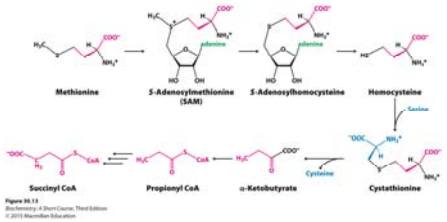
4. Succinyl CoA Family

- Don't need to memorize these
- Need of vitamin B12
- Glucogenic—what is the pathway?



Methionine

- Production of SAM
- Activated carbon carrier

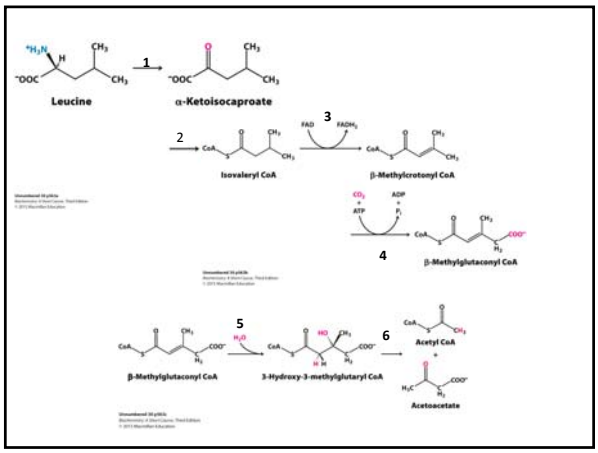


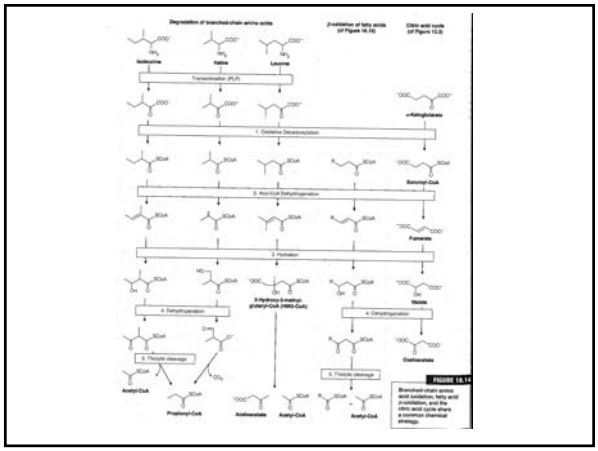
Branched Amino Acids

- Major energy source in muscle
- Steps of degradation
  - Transamination
  - Oxidative decarboxylation (Pyruvate DH)
  - Beta oxidation
- Valine: succinyl CoA
- Isoleucine: succinyl CoA and acetylCoA
- Leucine: acetyl CoA and ketone body

Problem

- Leucine is degraded to acetyl CoA and acetoacetate by a pathway whose first two steps are transamination and oxidative decarboxylation. The third step is the same as the first step of fatty acid oxidation. The fourth step involves an ATP-dependent carboxylation, the fifth step is a hydration, and the last step is a cleavage reaction to give products. Draw the intermediates of leucine degradation.





Aromatic Amino Acids

- Complicated mono- and dioxygenases

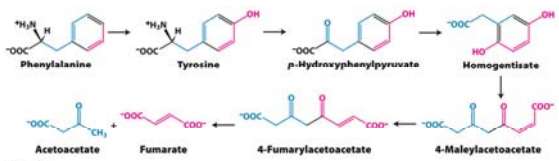


Figure 30.11
Biochemistry: A Short Course, Third Edition
© 2015 Macmillan Education

Inborn Errors of Metabolism