Amino acid metabolism

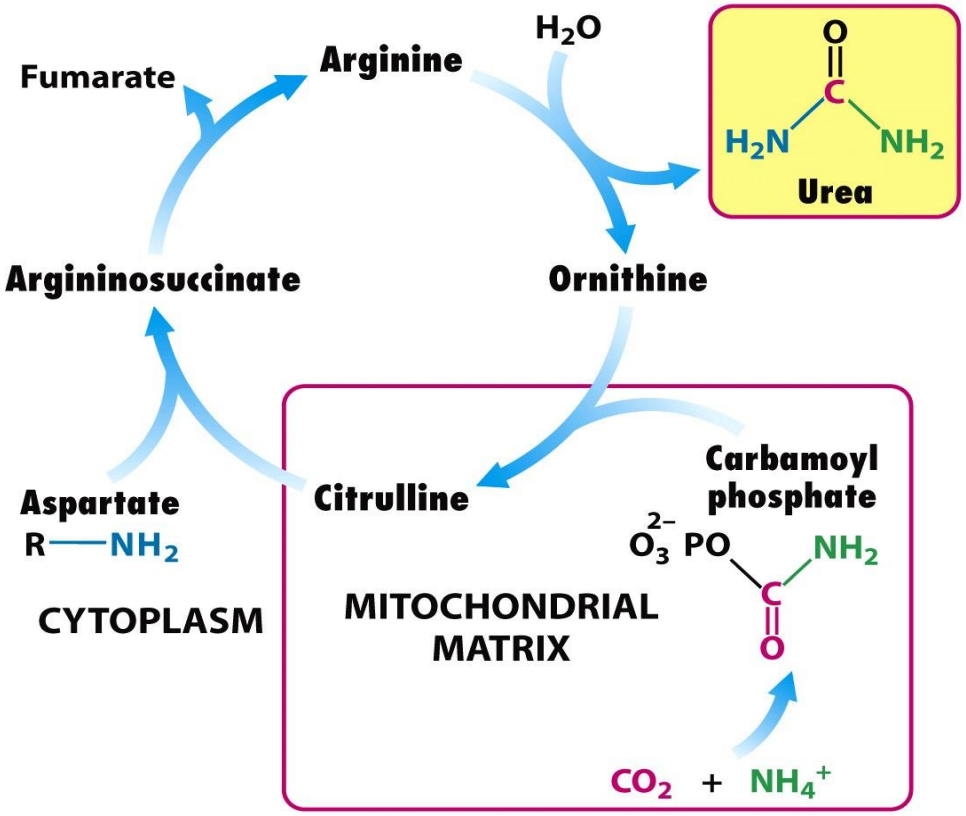


Figure 23-17
Biochemistry, Sixth Edition

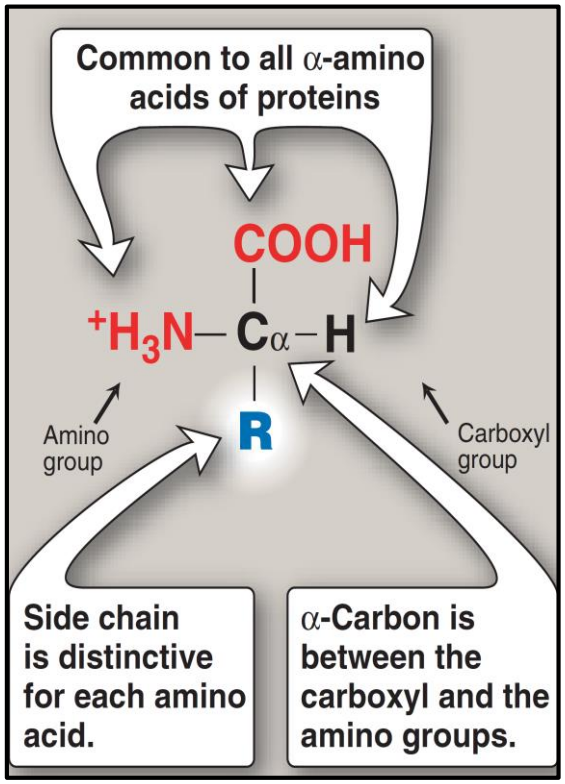
LPG001

Martin Lidell

Lecture outline

- **Amino acids – a short introduction**
- **How do we get access to amino acids?**
- **Biosynthesis of non-essential amino acids**
  - *The origin of the α-amino group and the carbon skeleton*
- **Degradation of amino acids**
  - *What happens with the amino group and the carbon skeleton?*
  - *The urea cycle*
  - *Transport of nitrogen to the liver (alanine/glutamine)*
- **Examples of some defects in amino acid metabolism**

Amino acids



Adapted from Figure 1.1 in Biochemistry 5th ed. / Harvey and Ferrier, Lippincott Williams & Wilkins, 2011

Definition:
An amino acid is a simple organic compound containing both a carboxyl and an amino group

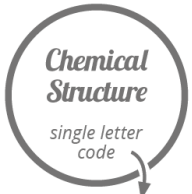
More than 500 different amino acids have been described in nature

Twenty α-amino acids (21 if including selenocysteine) are commonly found in mammalian proteins. These proteinogenic amino acids are the only amino acids that are coded for by DNA

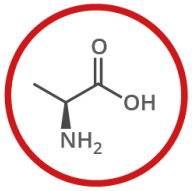
A GUIDE TO THE TWENTY COMMON AMINO ACIDS

AMINO ACIDS ARE THE BUILDING BLOCKS OF PROTEINS IN LIVING ORGANISMS. THERE ARE OVER 500 AMINO ACIDS FOUND IN NATURE - HOWEVER, THE HUMAN GENETIC CODE ONLY DIRECTLY ENCODES 20. 'ESSENTIAL' AMINO ACIDS MUST BE OBTAINED FROM THE DIET, WHILST NON-ESSENTIAL AMINO ACIDS CAN BE SYNTHESISED IN THE BODY.

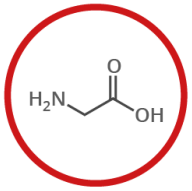
Chart Key: ALIPHATIC · AROMATIC · ACIDIC · BASIC · HYDROXYLIC · SULFUR-CONTAINING · AMIDIC · NON-ESSENTIAL · ESSENTIAL



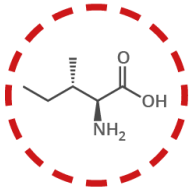
NAME (A)
three letter code
DNA codons



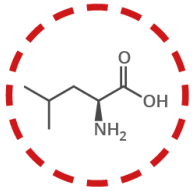
ALANINE (A)
Ala
GCT, GCC, GCA, GCG



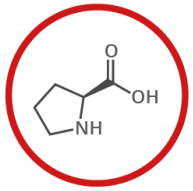
GLYCINE (G)
Gly
GGT, GGC, GGA, GGG



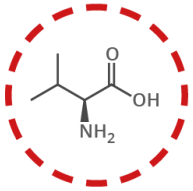
ISOLEUCINE (I)
Ile
ATT, ATC, ATA



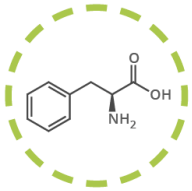
LEUCINE (L)
Leu
CTT, CTC, CTA, CTG, TTA, TTG



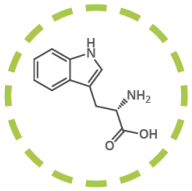
PROLINE (P)
Pro
CCT, CCC, CCA, CCG



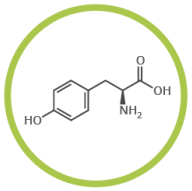
VALINE (V)
Val
GTT, GTC, GTA, GTG



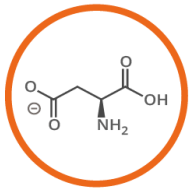
PHENYLALANINE (F)
Phe
TTT, TTC



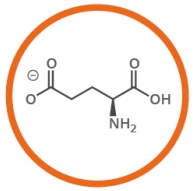
TRYPTOPHAN (W)
Trp
TGG



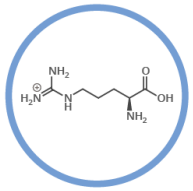
TYROSINE (Y)
Tyr
TAT, TAC



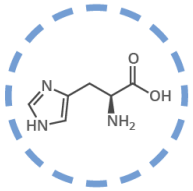
ASPARTIC ACID (D)
Asp
GAT, GAC



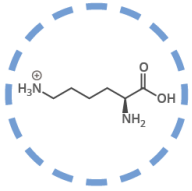
GLUTAMIC ACID (E)
Glu
GAA, GAG



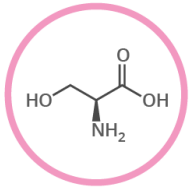
ARGININE (R)
Arg
CGT, CGC, CGA, CGG, AGA, AGG



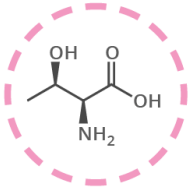
HISTIDINE (H)
His
CAT, CAC



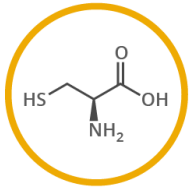
LYSINE (K)
Lys
AAA, AAG



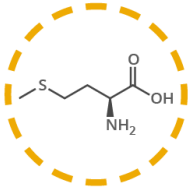
SERINE (S)
Ser
TCT, TCC, TCA, TCG, AGT, AGC



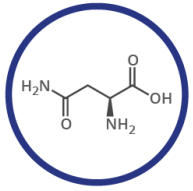
THREONINE (T)
Thr
ACT, ACC, ACA, ACG



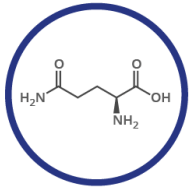
CYSTEINE (C)
Cys
TGT, TGC



METHIONINE (M)
Met
ATG



ASPARAGINE (N)
Asn
AAT, AAC



GLUTAMINE (Q)
Gln
CAA, CAG

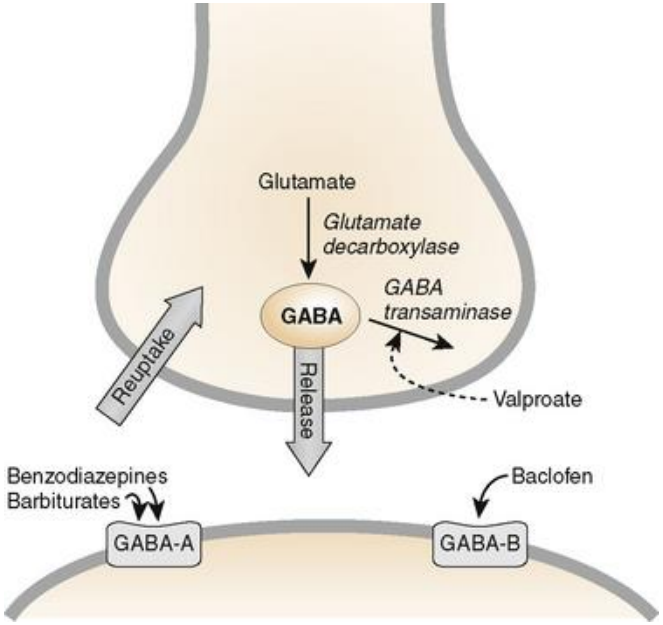
Sahlgrenska akademin

GÖTEBORGS UNIVERSITET

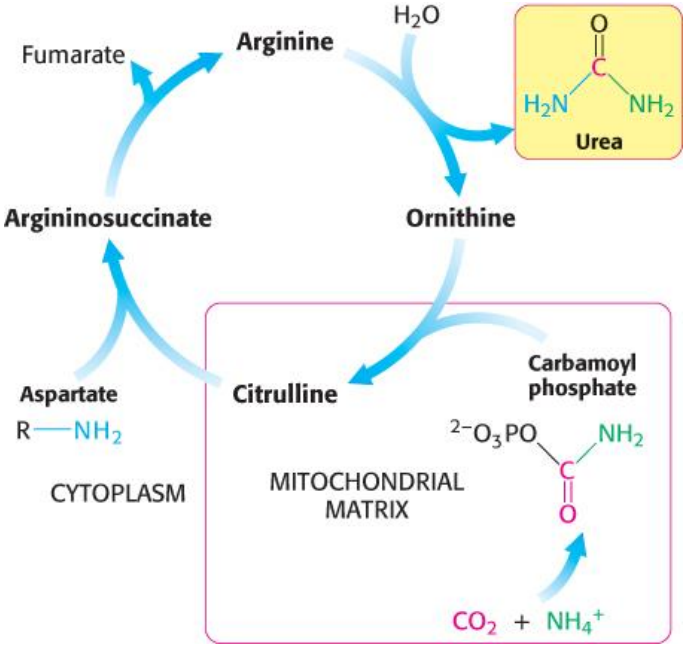
Amino acids

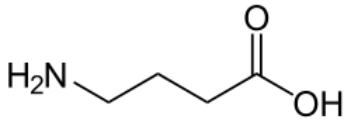
– examples of some important non-proteinogenic amino acids

γ-aminobutyric acid (GABA)
an inhibitory neurotransmitter

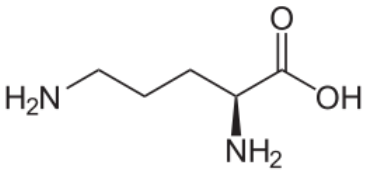


Ornithine and Citrulline
intermediates in the urea cycle

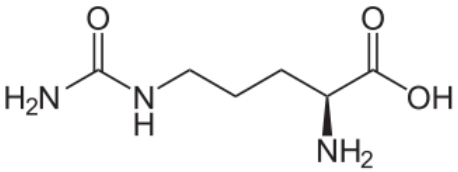




GABA
(γ-amino acid)



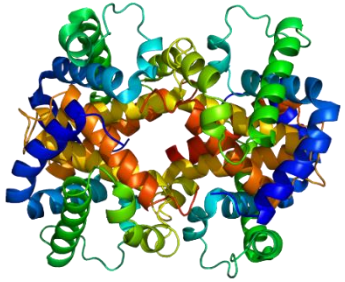
Ornithine
(α-amino acid)



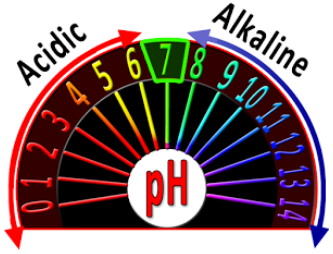
Citrulline
(α-amino acid)

Why are amino acids essential biomolecules?

– some examples

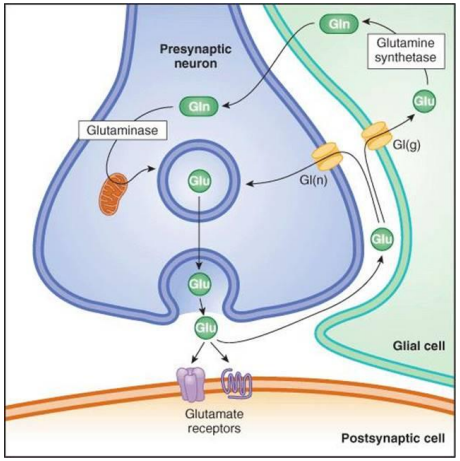


Building blocks in proteins



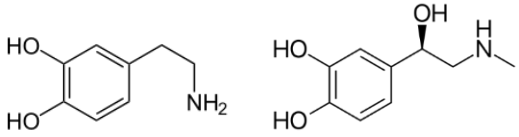
Involved in acid-base homeostasis

(Gln)



Acts as neurotransmitters

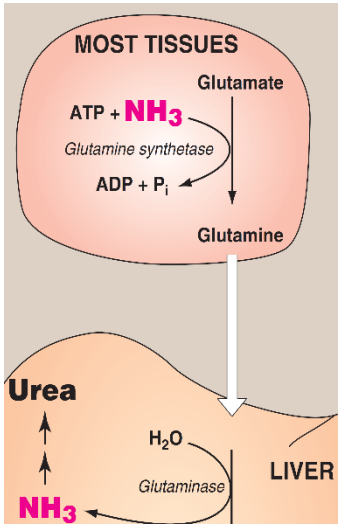
(e.g. Glu and Gly)



Dopamine Epinephrine

Precursors of important biomolecules

(neurotransmitters, hormones, etc. etc.)



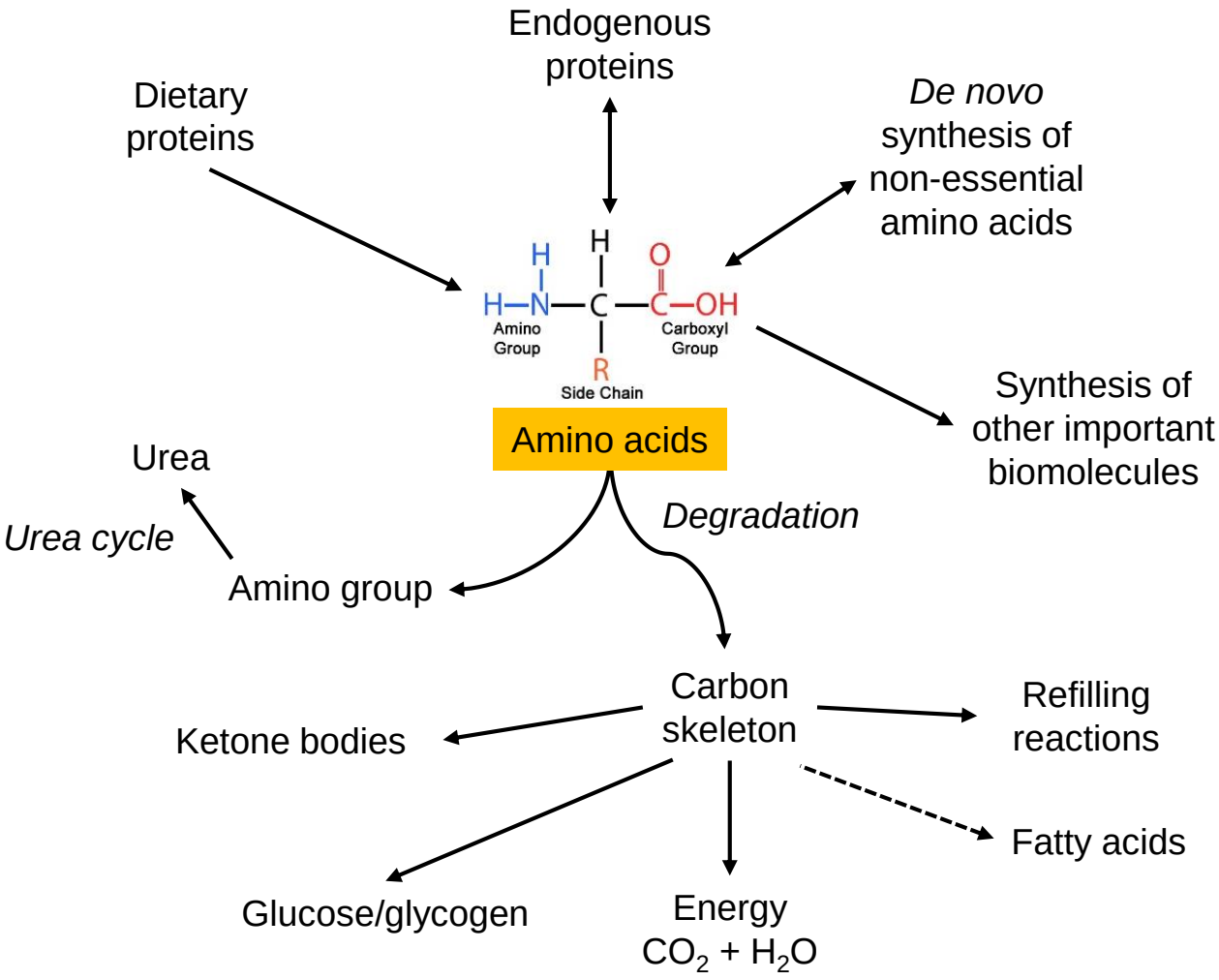
Transport ammonia in a nontoxic form

(Gln and Ala)

Source of energy

"It's amazing what they can do with amino acids these days"

Overview of amino acid metabolism



Digestion of dietary proteins in the gastrointestinal tract

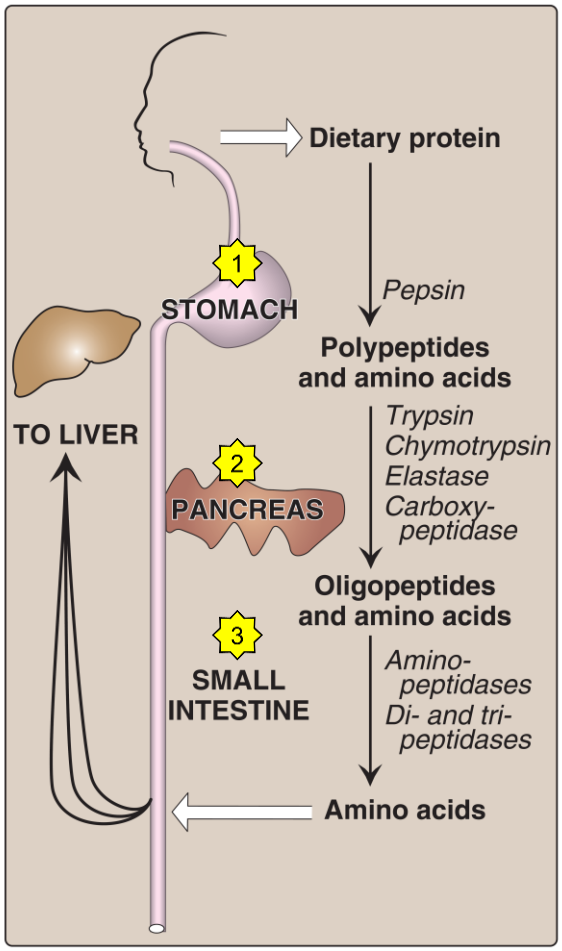


Figure 19.4 in Biochemistry 5th ed. / Harvey and Ferrier
Lippincott Williams & Wilkins, 2011

Amino acids, di- and tripeptides are absorbed by the enterocytes and released as amino acids into the blood

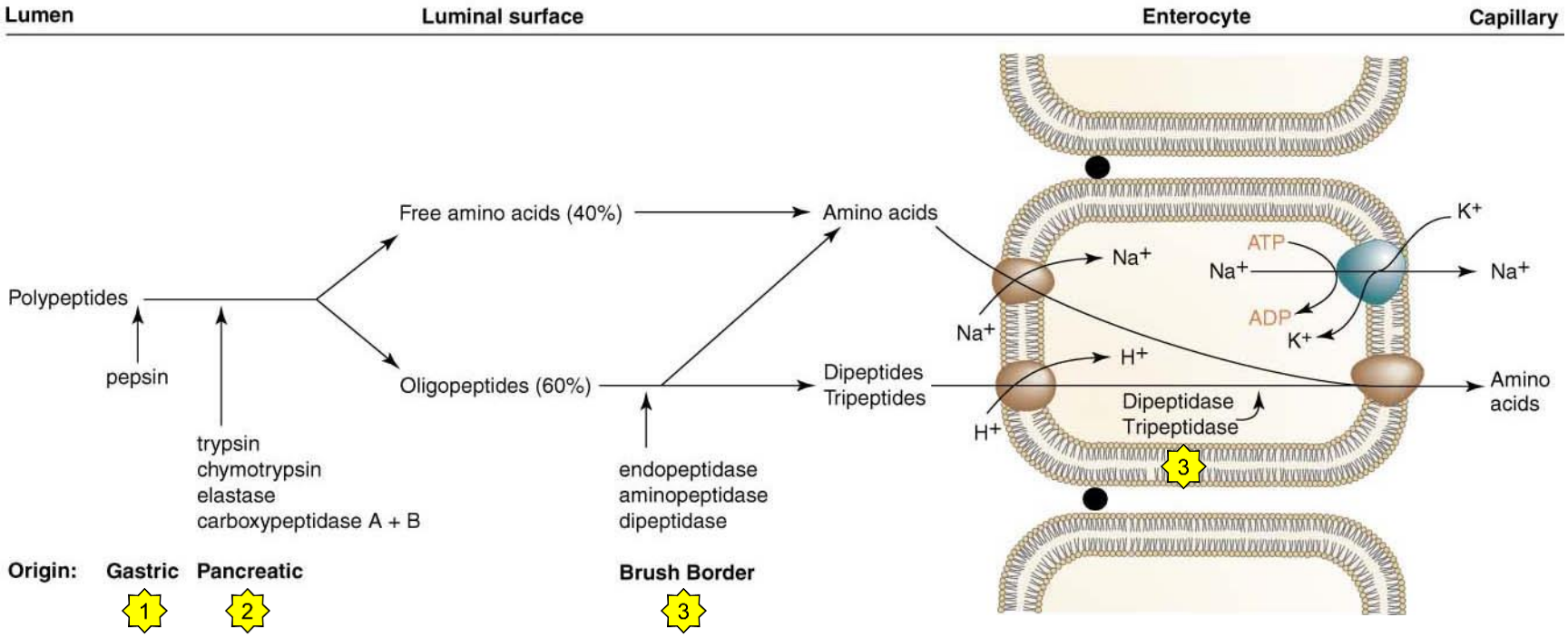


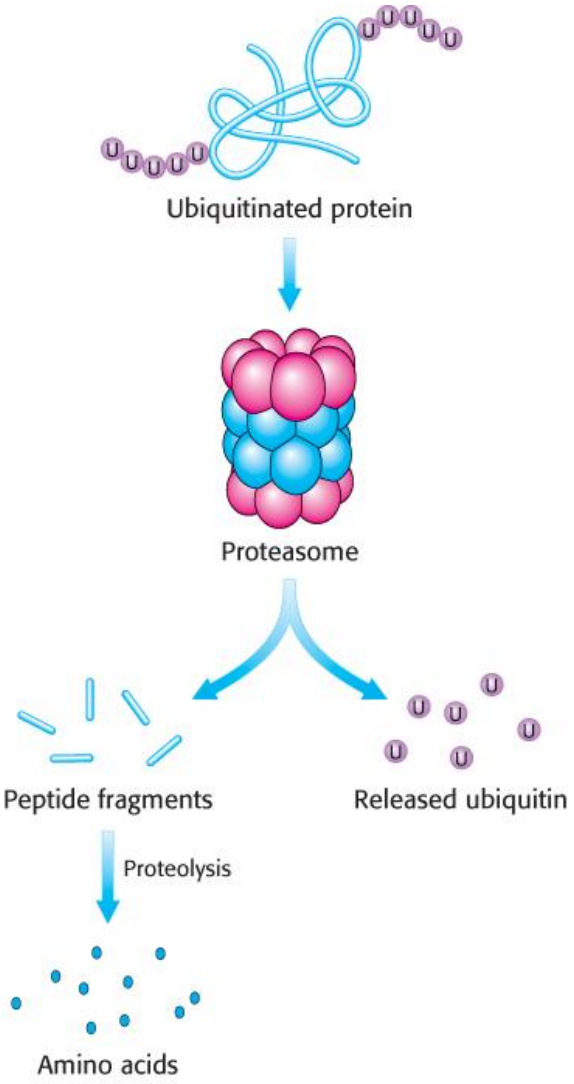
Figure 26.22
Textbook of Biochemistry With Clinical Correlations 6th Ed., John Wiley & Sons, 2006

The absorbed di- and tripeptides are digested by peptidases into free amino acids that are released into the blood

Intracellular degradation of endogenous proteins

– released amino acids can be reused

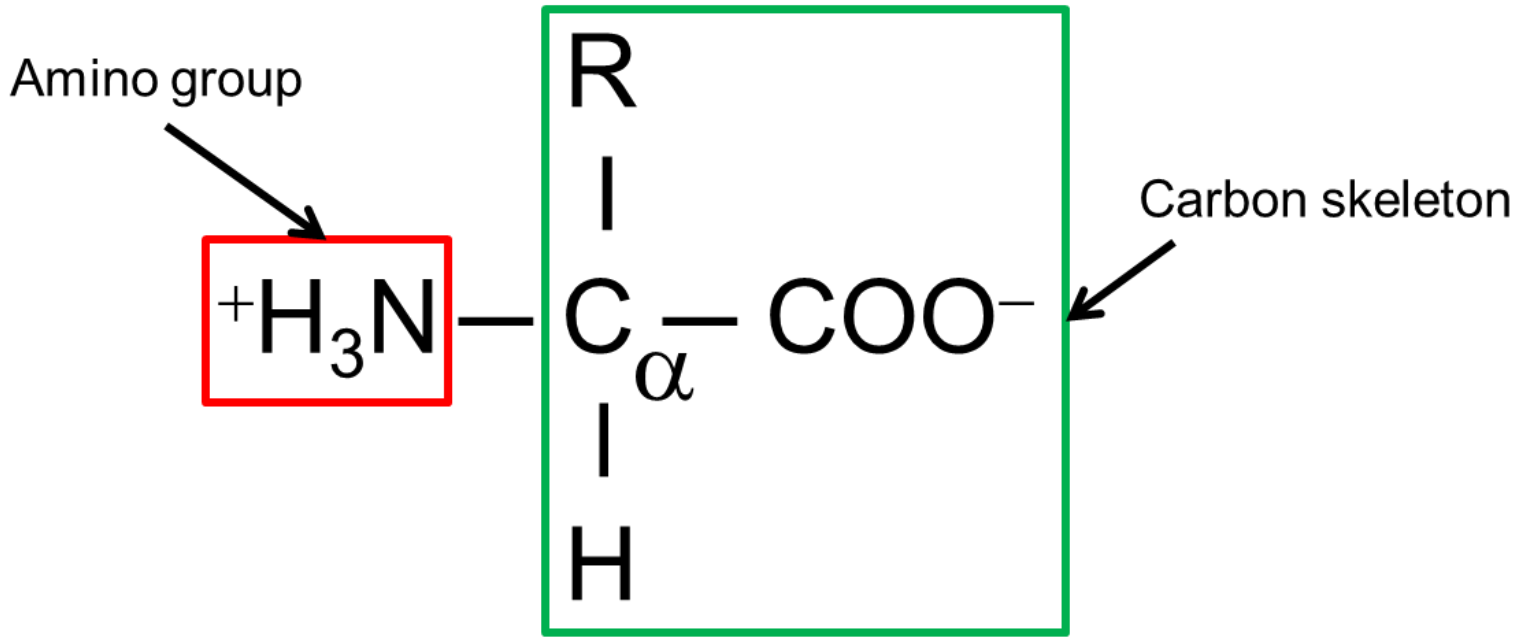
Proteasomal degradation



Adapted from Figure 23.7
Biochemistry, 8th ed, Berg et al.
2015 W.H. Freeman and Company

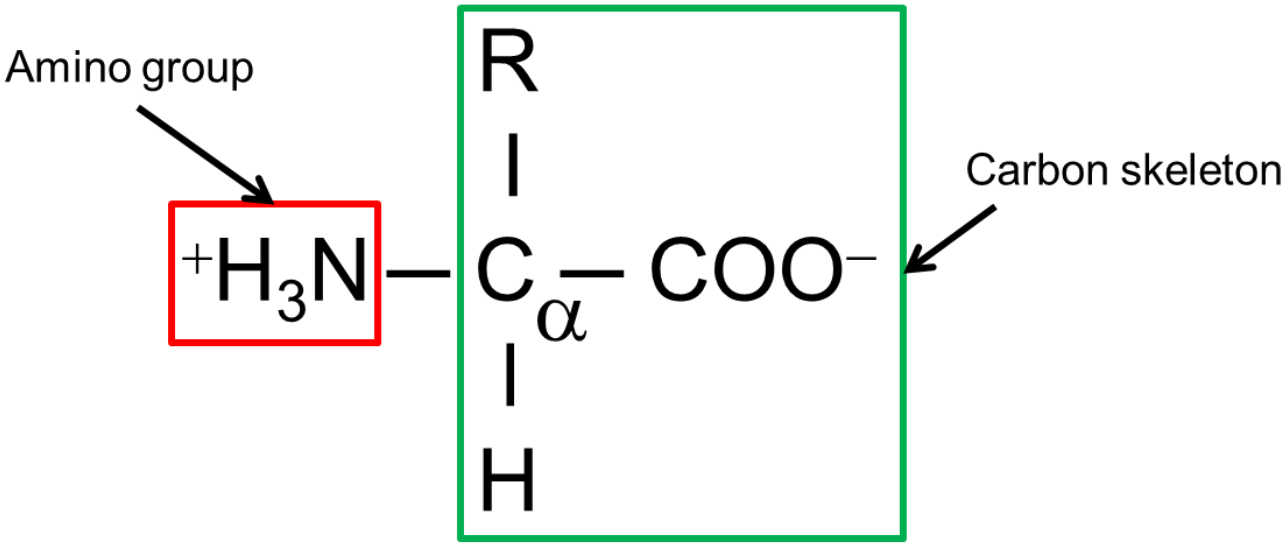
Biosynthesis of amino acids

– the α-amino group and the carbon skeletons

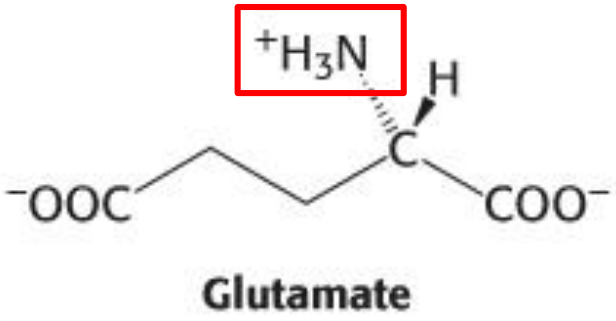


Biosynthesis of amino acids

– the α-amino group



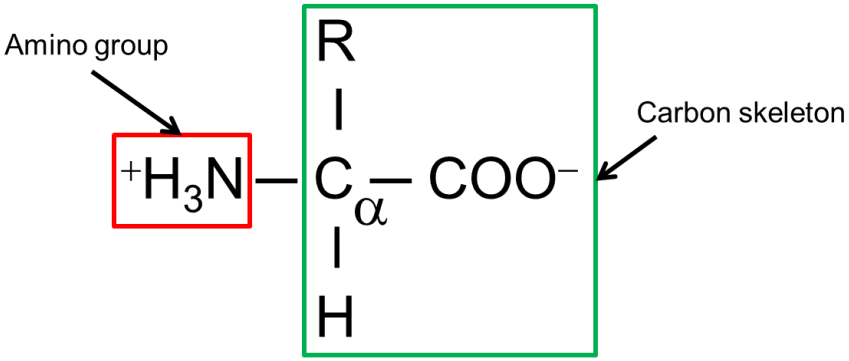
The α-amino group is most often derived from glutamate



Glutamate

Biosynthesis of amino acids

– *the carbon skeletons*



Carbon skeletons are derived from

- Glycolysis
- Pentose phosphate pathway
- Citric acid cycle

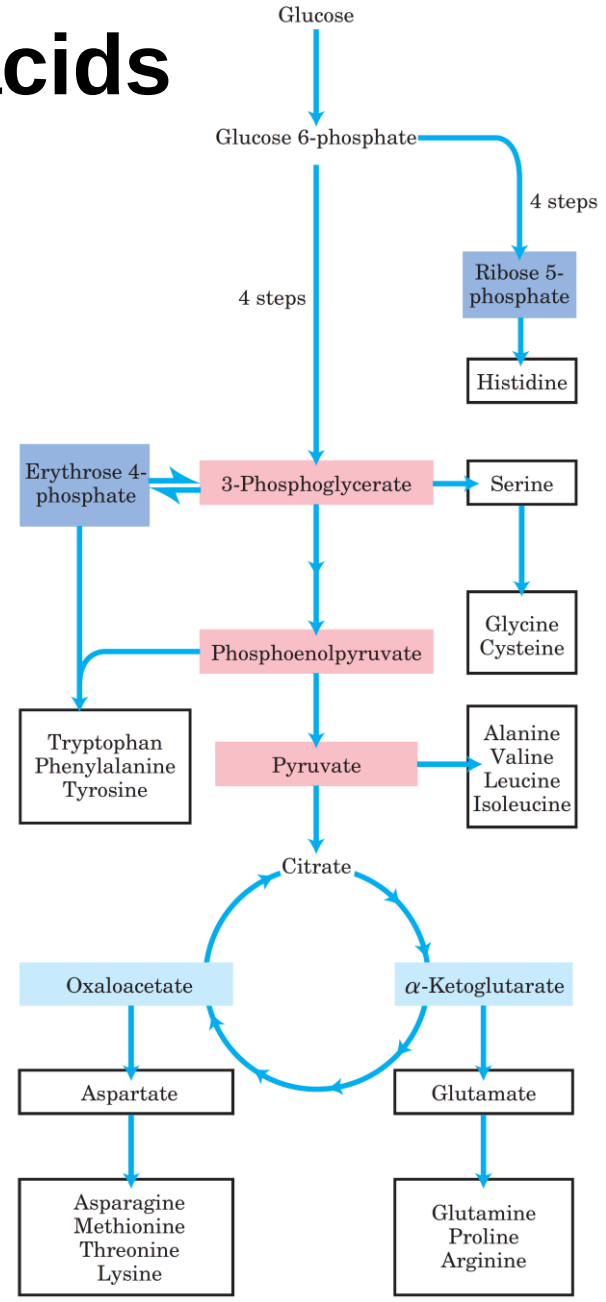
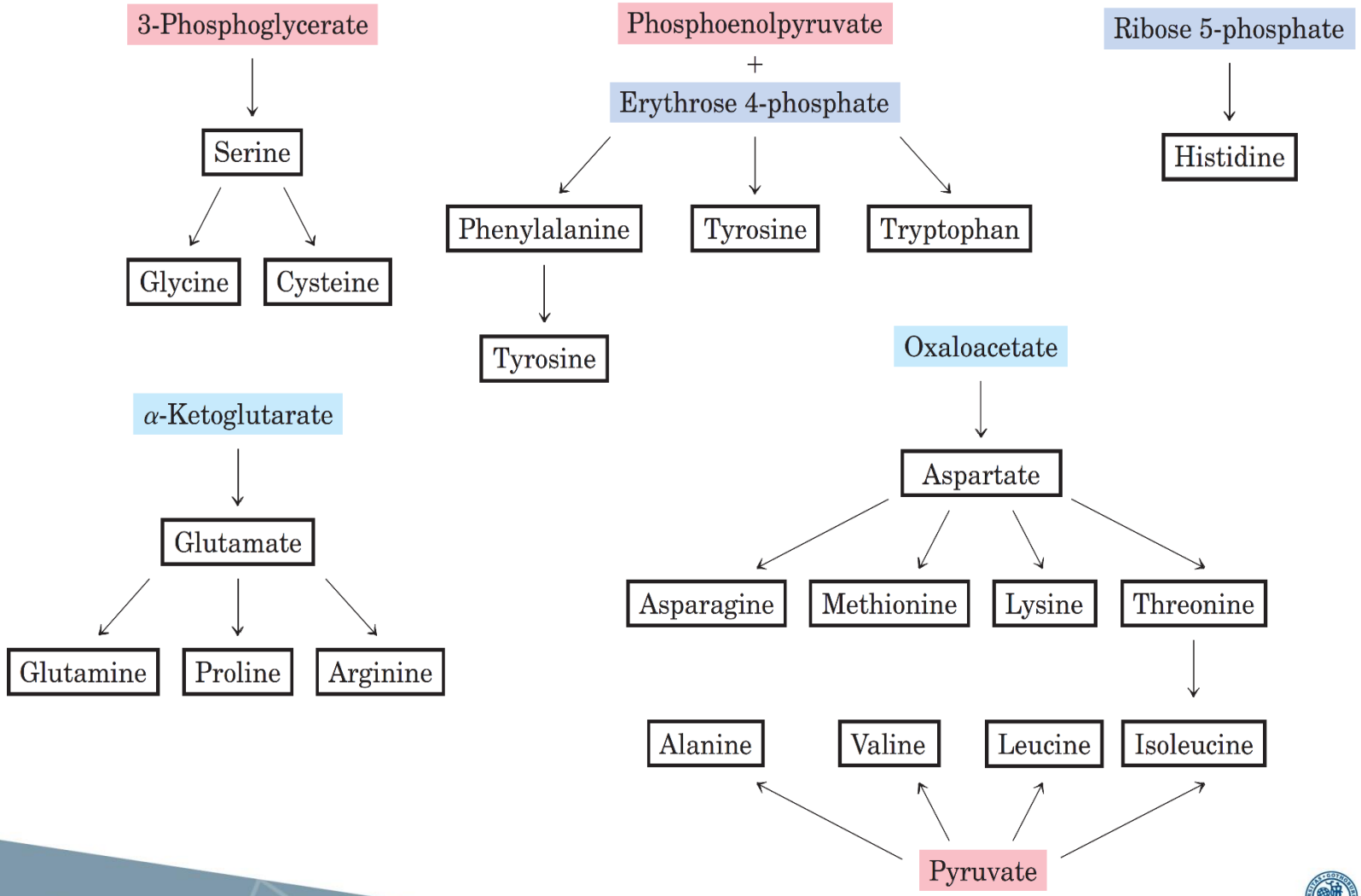


Figure 22-9 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

Most microorganisms can synthesize all of the common proteinogenic amino acids



Biosynthesis of amino acids in humans

– essential and nonessential amino acids

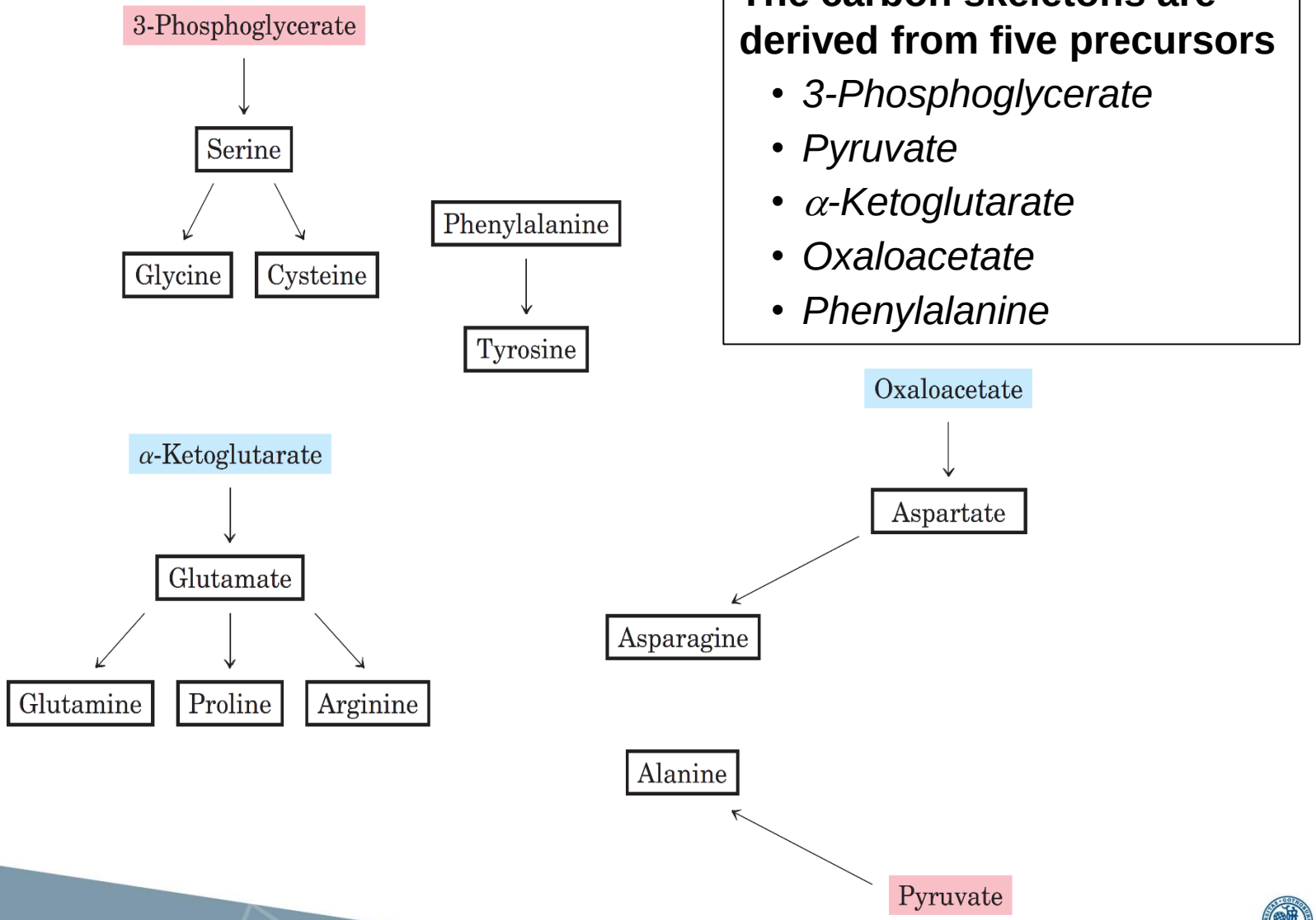
Nonessential	Essential
Alanine	Histidine
Arginine	Isoleucine
Asparagine	Leucine
Aspartate	Lysine
Cysteine	Methionine
Glutamate	Phenylalanine
Glutamine	Threonine
Glycine	Tryptophan
Proline	Valine
Serine	
Tyrosine	

Humans cannot make the essential amino acids; they must be supplied in the diet

Some nonessential amino acids become essential (cannot be synthesized at the required levels) under certain circumstances; they are said to be ”conditionally essential”.

e.g. arginine is nutritionally essential for the fetus and neonate
tyrosine is nutritionally essential in individuals with PKU

Biosynthesis of nonessential amino acids in humans

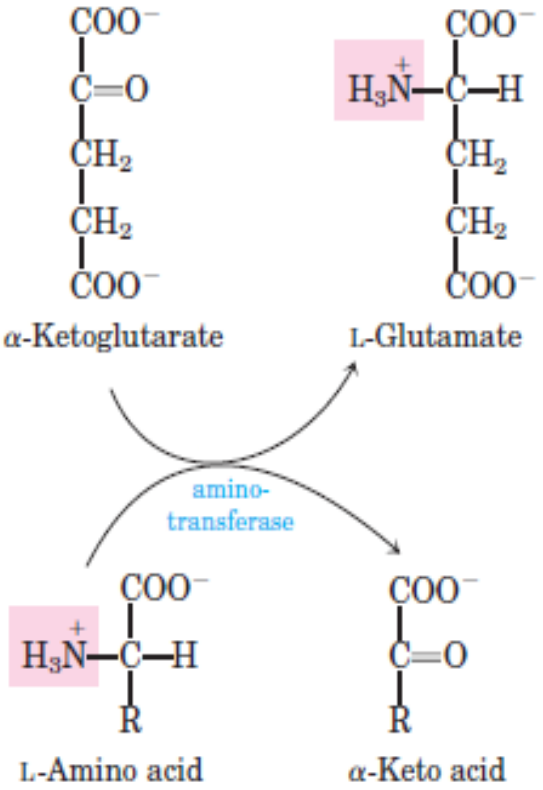


The carbon skeletons are derived from five precursors

- *3-Phosphoglycerate*
- *Pyruvate*
- *α-Ketoglutarate*
- *Oxaloacetate*
- *Phenylalanine*

Formation of glutamate from α-ketoglutarate

Glutamate is primarily formed from α-ketoglutarate in transamination reactions catalyzed by different aminotransferases (transaminases)



Adapted from Figure 18-4 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

Aminotransferases/Transaminases

– enzymes transferring amino groups from α-amino acids to α-keto acids

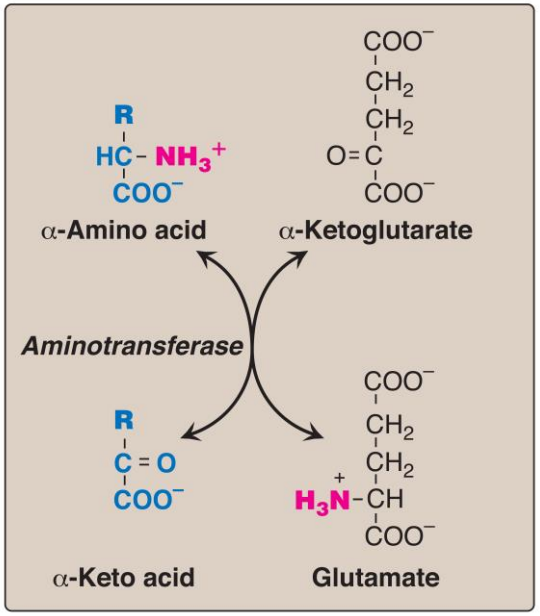
α–amino acid-R1 α–keto acid-R2 α–keto acid-R1 α–amino acid-R2

Adapted from Biochemistry, 8th ed,
Berg et al. 2015 W.H. Freeman and Company

Transfer of an amino group from an α–amino acid to an α–keto acid, generating a new α–keto acid and a new α–amino acid.

IMPORTANT!
The reactions are reversible

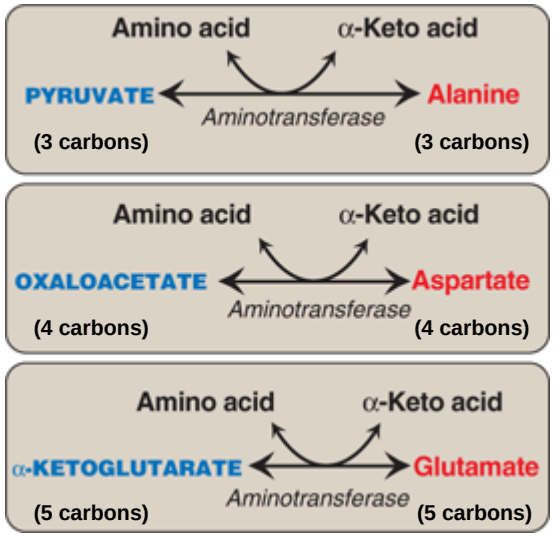
The enzymes play an essential role in both synthesis and degradation of amino acids

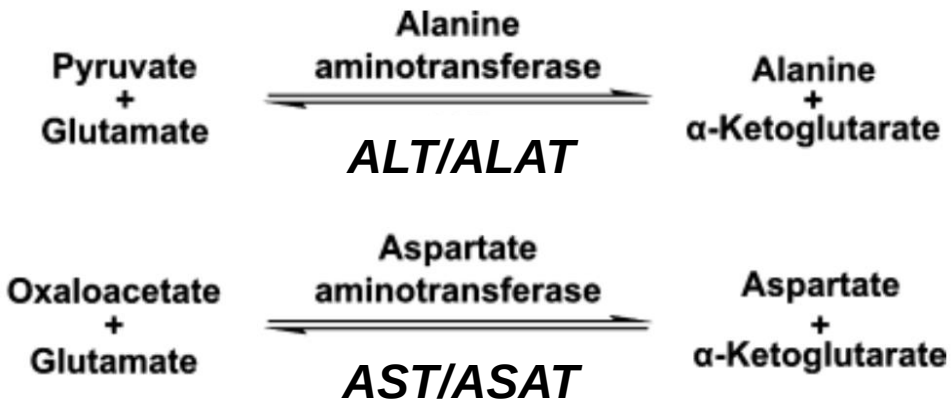


α-Ketoglutarate/Glutamate is the most common amino group acceptor/amino group donor pair.

Figure 19.7 in Biochemistry 5th ed. / Harvey and Ferrier Lippincott Williams & Wilkins, 2011

ALT and AST – two important aminotransferases





Amino acids:
Alanine, Aspartate, Glutamate

α-Keto acids:
Pyruvate, Oxaloacetate, α-ketoglutarate

Aminotransferases as indicators of tissue damage

- Aminotransferases are normally intracellular enzymes
- Elevated plasma levels of aminotransferases indicate damage of cells rich in these enzymes (enzymes leak out into the blood from damaged cells)
- Plasma levels of AST and ALT are elevated in nearly all liver diseases

  (e.g. viral hepatitis, long-term excessive alcohol consumption, toxic injury from drugs such as paracetamol)

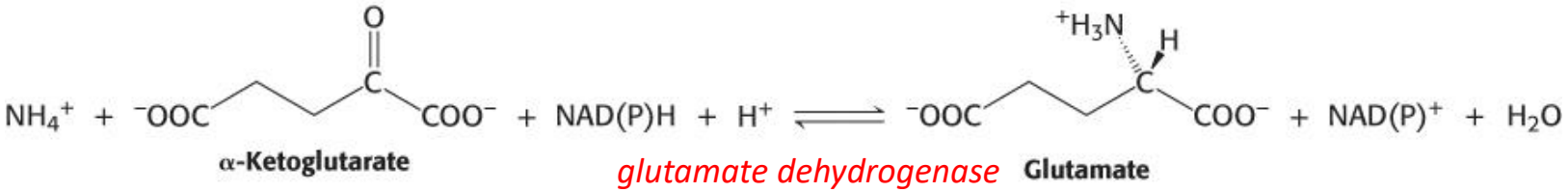
- Alanine aminotransferase (ALT) is present primarily in the liver (but also at lower levels in other tissues such as skeletal muscle)

  Serum elevations of ALT are rarely observed in conditions other than liver disease

- Aspartate aminotransferase (AST) is found in high concentrations in liver, heart, skeletal muscle, and kidney

  High levels of AST can be found in cases such as myocardial infarction, acute liver cell damage, viral hepatitis etc..

A second route of synthesis of glutamate from α-ketoglutarate

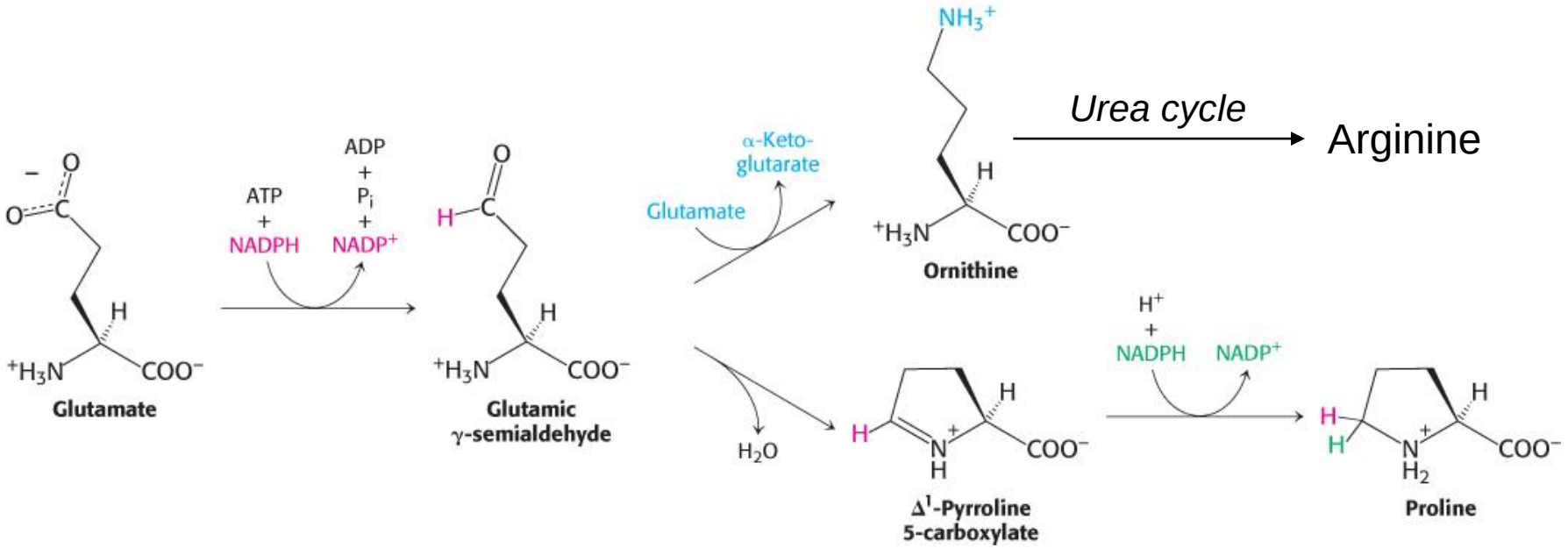


Glutamate dehydrogenase is essentially a liver-specific enzyme (found in the mitochondrial matrix)

Believed to be a minor synthesis route in humans (reverse reaction is normally favoured due to very low intracellular ammonium levels)

Arginine and proline

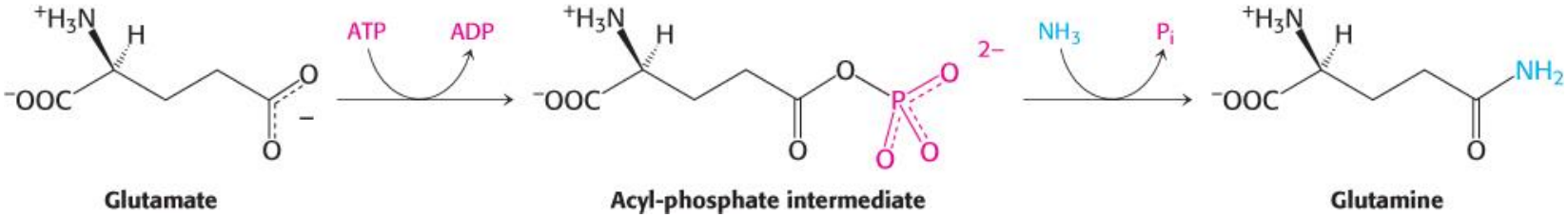
– two amino acids synthesized from glutamate



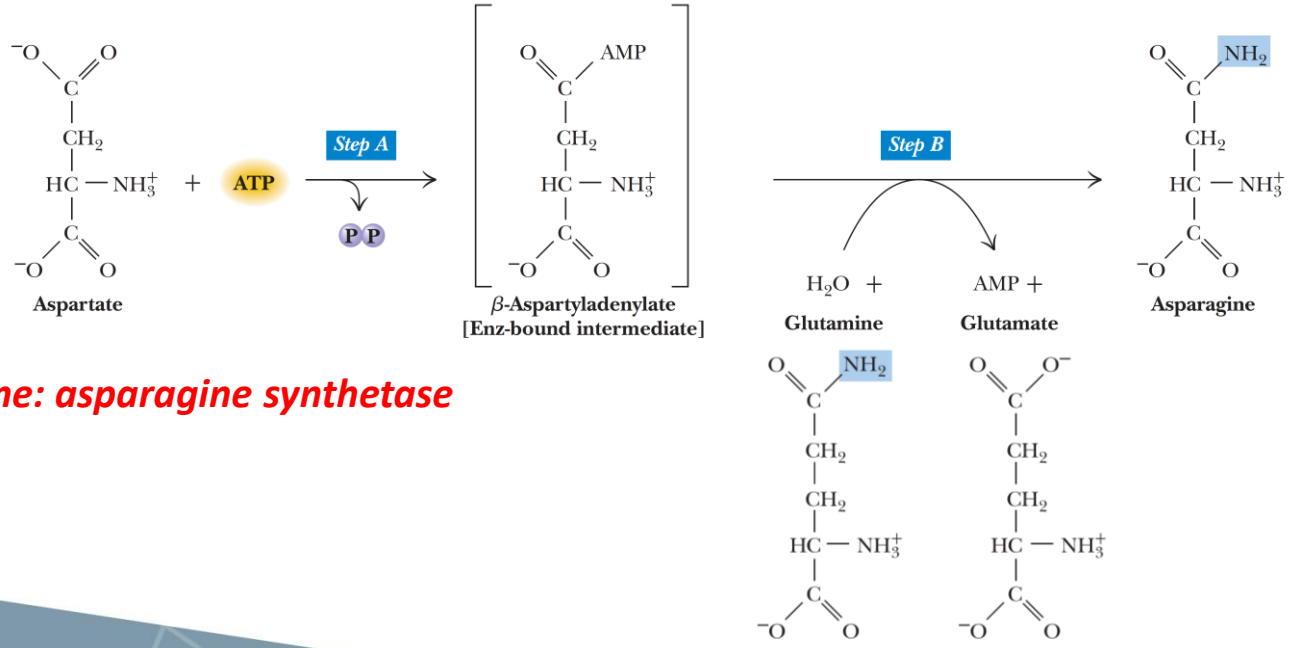
Biochemistry, 8th ed, Berg et al.
2015 W.H. Freeman and Company

Glutamine and asparagine

– formed by amidation reactions



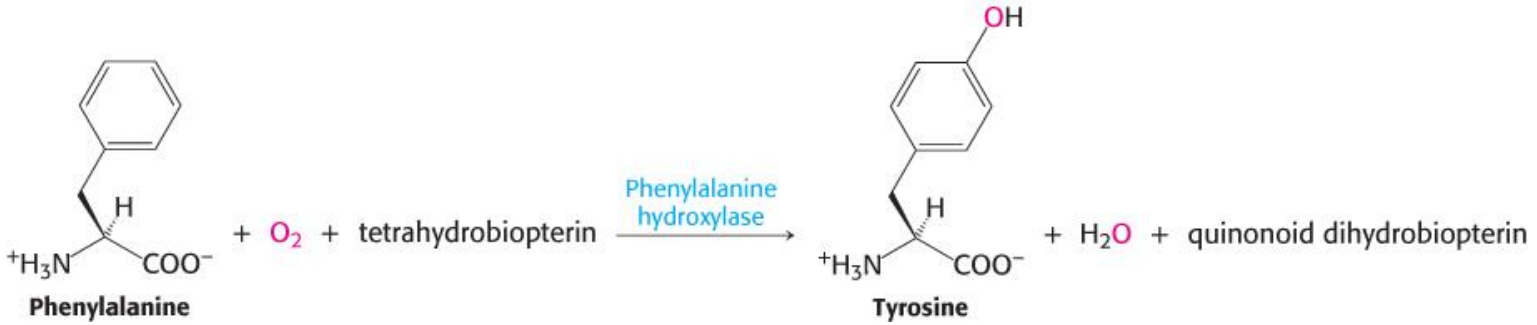
Enzyme: glutamine synthetase

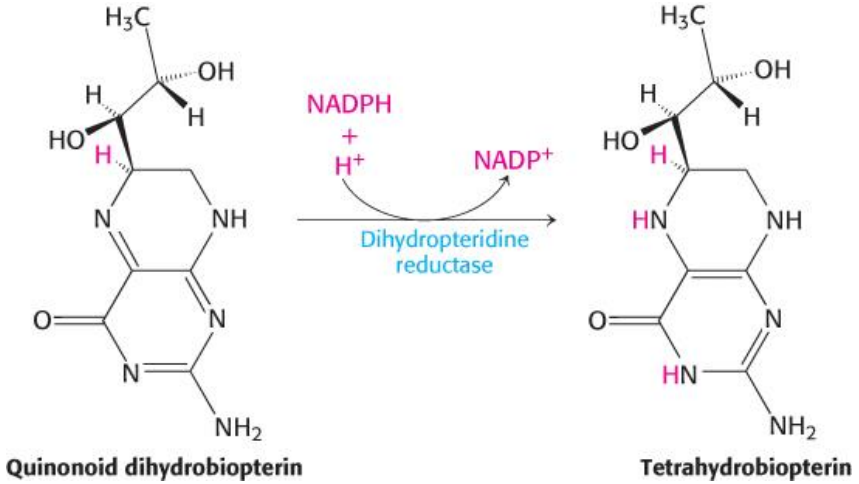


Enzyme: asparagine synthetase

Tyrosine

– *synthesized by hydroxylation of the essential amino acid phenylalanine*

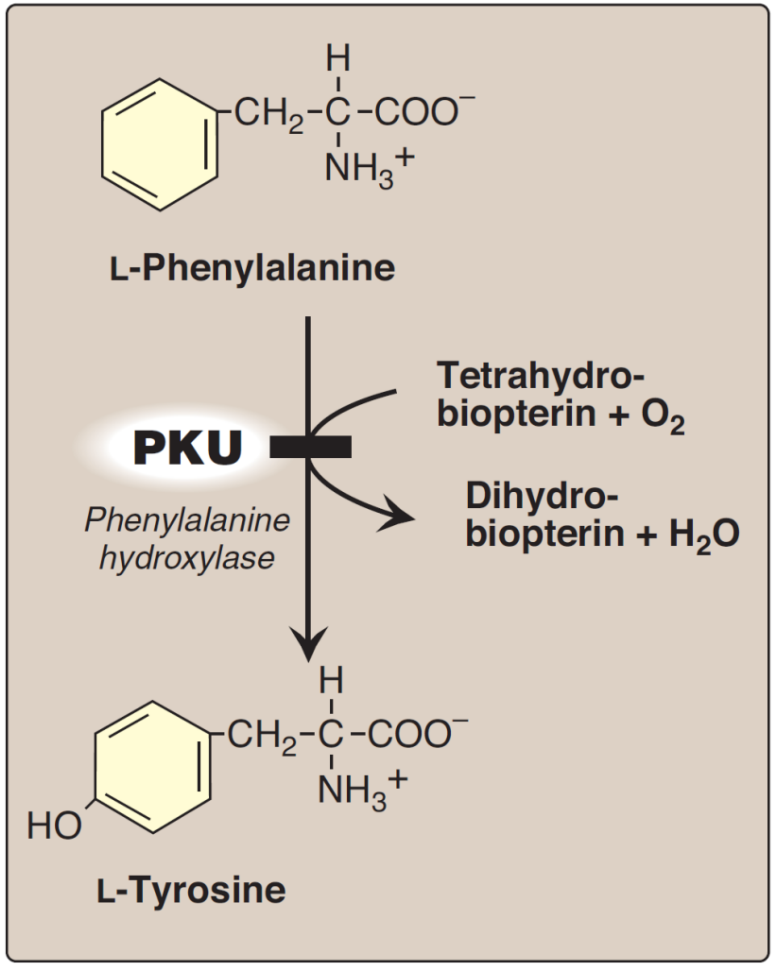


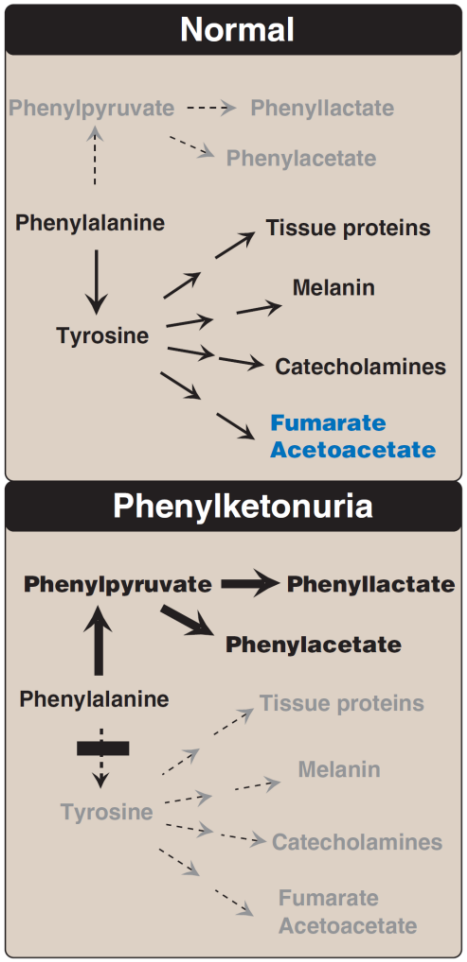


Overall reaction:

Phenylalanine + O_2 + NADPH + H^+ ⟶ Tyrosine + $NADP^+$ + H_2O

Phenylketonuria (PKU)





Biochemistry 5th ed. / Harvey and Ferrier
Lippincott Williams & Wilkins, 2011

Autosomal recessive disorder (defective *PAH* gene)

Hundreds of mutations identified in the *PAH* gene.

Results in an insufficient phenylalanine hydroxylase activity (caused by a defect enzyme and/or a relative deficiency of the enzyme)

Accumulation of:
Phenylalanine, phenylpyruvate, phenyllactate, phenylacetate

Deficiency of:
Tyrosine and its metabolites

Phenylketonuria (PKU)

PKU symptoms (without treatment) can be mild or severe and may include:

- Intellectual disability
- Delayed development
- Neurological problems that may include seizures
- Musty odor in breath, skin or urine (due to high levels of phenylalanine in the body)
- Fair skin and blue eyes (lack of the pigment melanin)
- etc.

Treatment:

Dietary restriction; reduced ingestion of protein. Supplement with amino acid mix (no Phe); tyrosine is now an essential amino acid. Sapropterin (synthetic tetrahydrobiopterin) may help some individuals.

Very good prognosis if the disease is diagnosed, and treatment initiated during the first weeks after birth.

About seven children with PKU is born in Sweden every year

”PKU-provet”
– *nyföddhetsscreening sedan 1965*

Blodprov tas så snart som möjligt efter 48 timmars ålder

Syfte med nyföddhetsscreening:
att hitta barn med någon av ett antal ovanliga men allvarliga medfödda sjukdomar som går att behandla och där en tidig diagnos är viktig för prognosen.

”PKU-provet”

– idag ingår 25 sjukdomar i denna screening

- **Endokrina sjukdomar (2 sjukdomar)**

  Medfödd sköldkörtelhormonbrist (hypotyreos), Medfödd binjurebarkhyperplasi (brist av binjurebarkhormoner)

- **Fel i nedbrytningen eller metabolismen av fettsyror (3 sjukdomar)**

  MCAD-brist, LCHAD-brist och andra defekter i det trifunktionella proteinet, VLCAD-brist

- **Fel i karnitinsystemet (4 sjukdomar)**

  Fel i karnitincykelns beståndsdelar (CPT I, CACT, CPT II), Primär karnitinbrist

- **Organiska acidurier (6 sjukdomar)**

  Isovaleriansyrauri, Propionsyrauri, Metylmalonsyrauri, Glutarsyrauri typ 1, Multipel acyl-CoA dehydrogenasbrist, Betaketotiolasbrist

- **Fel i ureacykeln (3 sjukdomar)**

  Citrullinemi, Argininosuccinatlyasbrist, Arginasbrist

- **Andra fel i omsättningen av aminosyror (4 sjukdomar)**

  Fenylketonuri, Maple syrup urine disease, Tyrosinemi typ 1, Homocystinuri

- **Andra medfödda ämnesomsättningsjukdomar (2 sjukdomar)**

  Biotinidasbrist, Galaktosemi

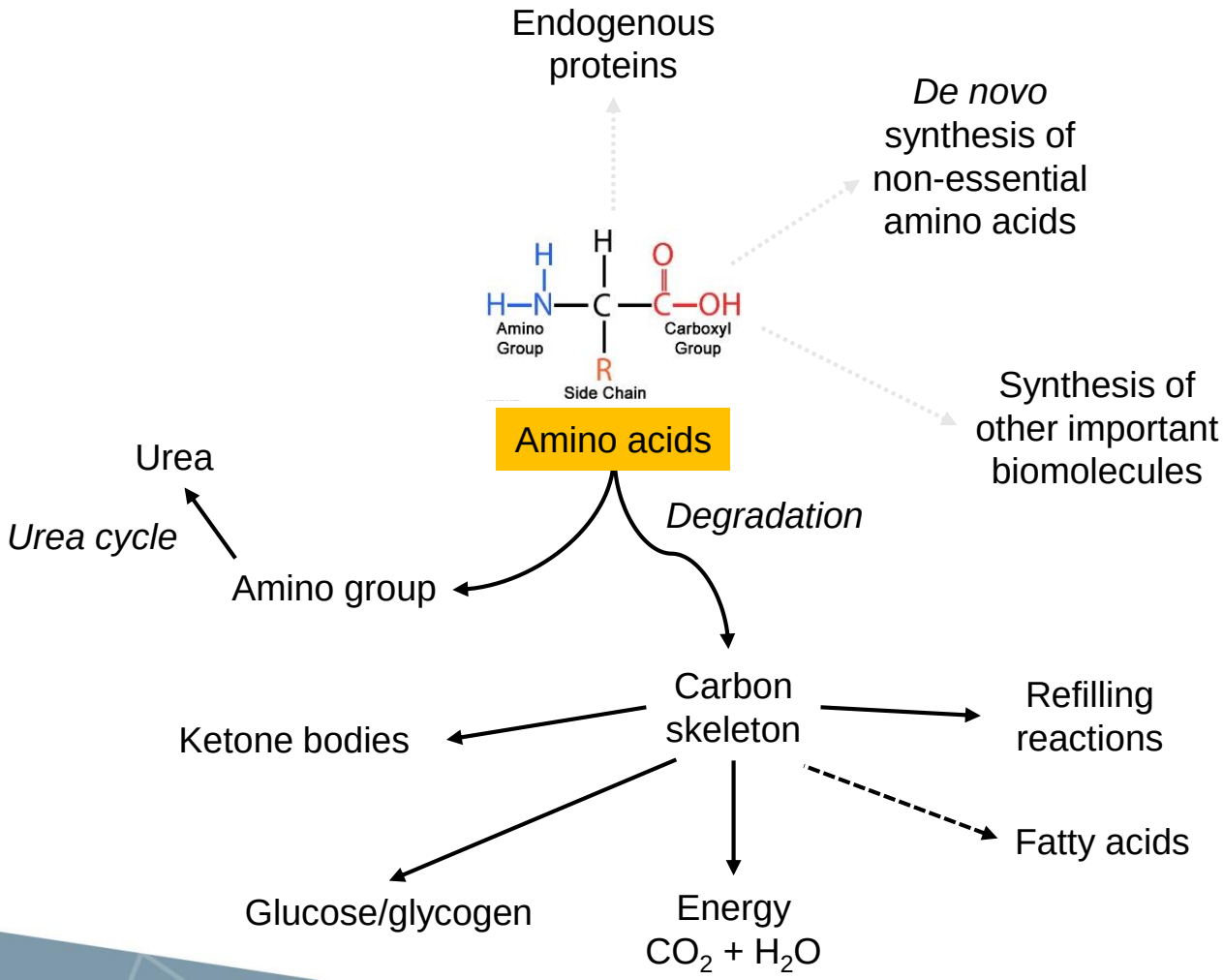
- **Svår kombinerad immunbrist (SCID)**

Summary of part 1

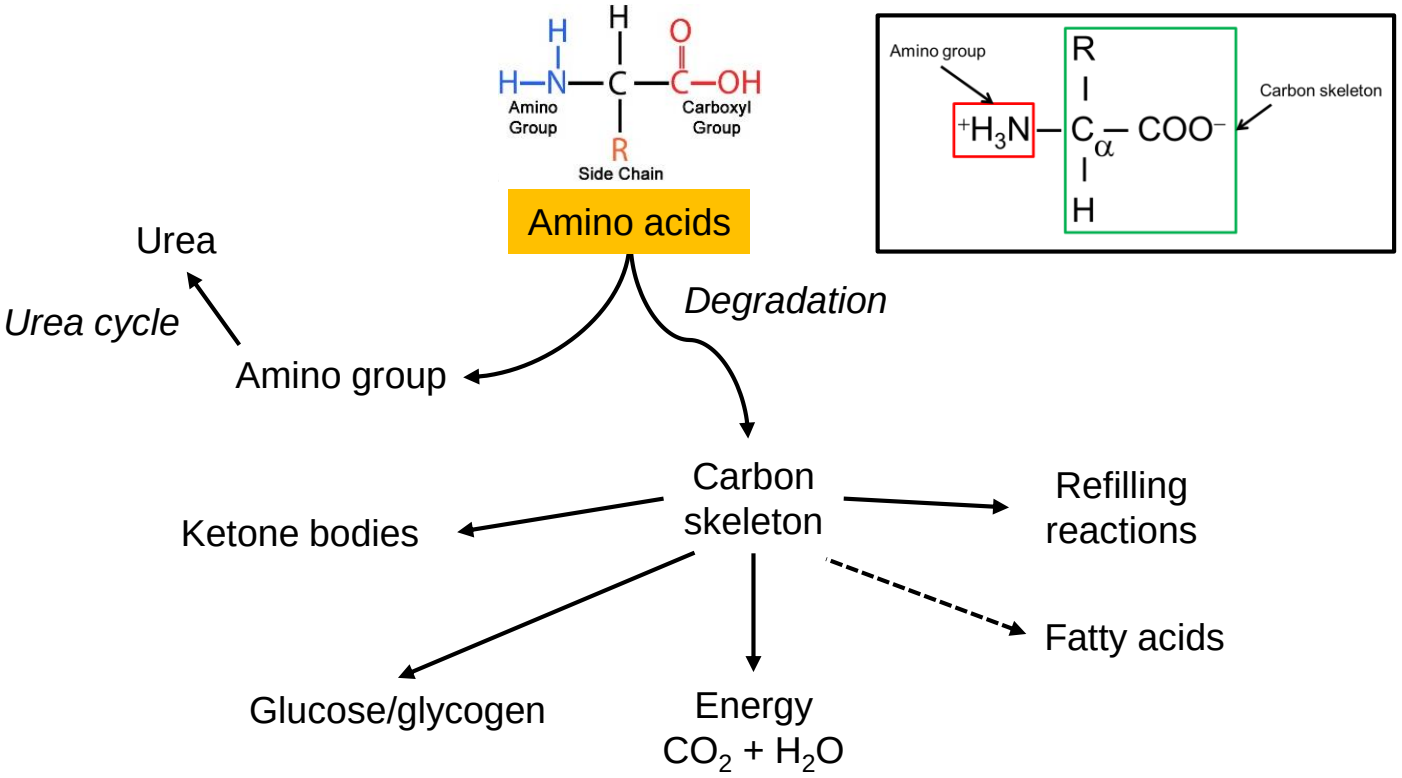
- Amino acids are important as building blocks, signaling molecules, energy source etc
- We get access to amino acids from dietary proteins, degraded endogenous proteins and *de novo* biosynthesis
- Essential amino acids must be supplied in the diet
- Humans can synthesize the eleven nonessential amino acids
  - α-amino group derived from glutamate
  - Carbon skeletons derived from five precursors
- Aminotransferases (transaminanses) are essential enzymes for both synthesis and degradation of amino acids
- Phenylketonuria (PKU); an inborn error in tyrosine biosynthesis/phenylalanine degradation

Excess amino acids cannot be stored

– amino acids not needed as building blocks are degraded to compounds able to enter the metabolic mainstream



How are amino acids degraded?

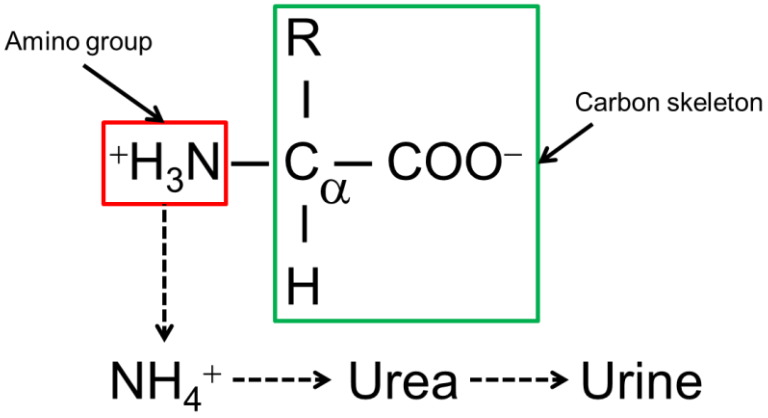


- Removal of the α-amino group
- Metabolism of the carbon skeleton into pyruvate, one of several citric acid cycle intermediates, acetyl-CoA, or acetoacetyl-CoA
- The major site of amino acid degradation is the liver. Skeletal muscle readily degrade branched-chain amino acids (source of fuel)

How are amino acids degraded?

Two steps:

- Removal of the α-amino group
- Metabolism of the carbon skeleton



Challenge for the body: Handling the amino group (and nitrogen-containing side chains), as degradation involves generation of toxic ammonia (ammonium at physiologic pH)

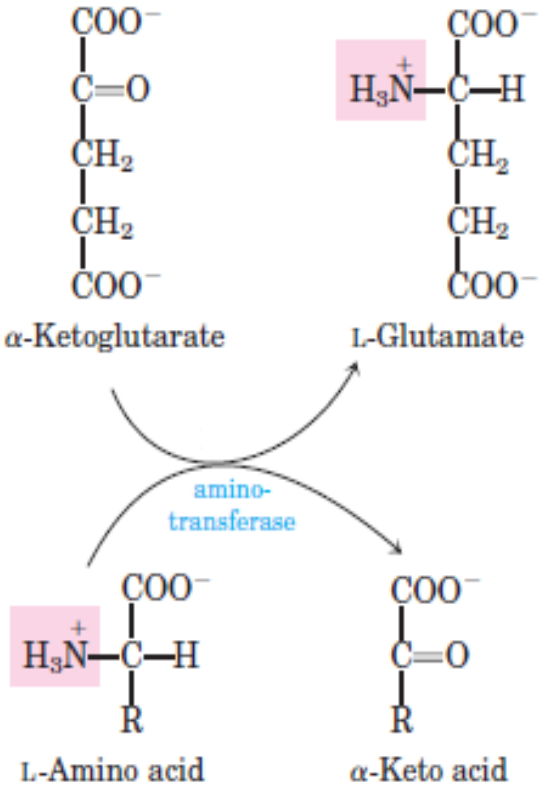
Solution: Most amino acid degadation occurs in the liver that can transform toxic ammonia to non-toxic urea in the urea cycle. Ammonia generated in other tissues is transported to the liver in non-toxic transport forms (glutamine/alanine)

Glutamate is most often an intermediate on the way towards urea

General catabolic process	Amino acid	Nitrogen end product
Amino acids that are converted to other amino acids	Arginine	glutamate
	Asparagine	aspartate
	Glutamine	glutamate
	Histidine	glutamate
	Phenylalanine	tyrosine
	Proline	glutamate
	Serine	glycine
A specific pathway for each amino acid	Glycine	ammonia
	Lysine	glutamate
	Methionine	ammonia
	Serine	ammonia
	Threonine	ammonia
	Tryptophan	ammonia
Transamination/deamination	Alanine	glutamate
	Aspartate	glutamate
	Isoleucine[a]	glutamate
	Leucine[a]	glutamate
	Valine[a]	glutamate
	Ornithine[a]	glutamate
	Tyrosine[a]	glutamate

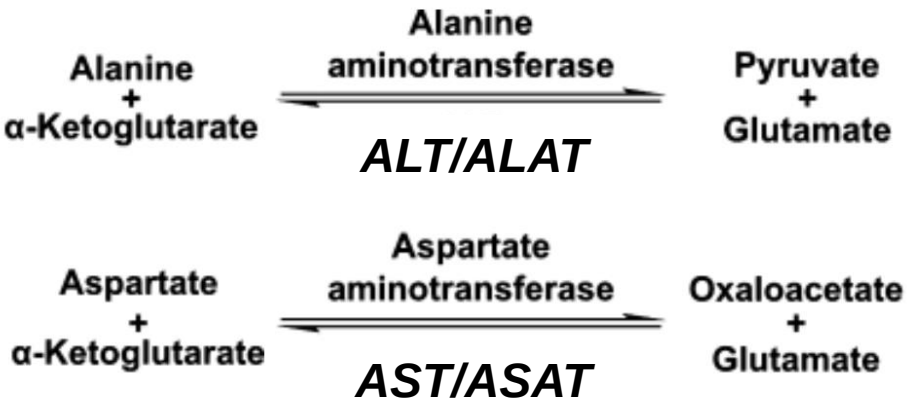
Adapted from Table 8.9
Functional Biochemistry in Health and Disease, Newsholme and Leech, John Wiley & Sons, 2011

The α-amino group of many amino acids is transferred to α-ketoglutarate to form glutamate

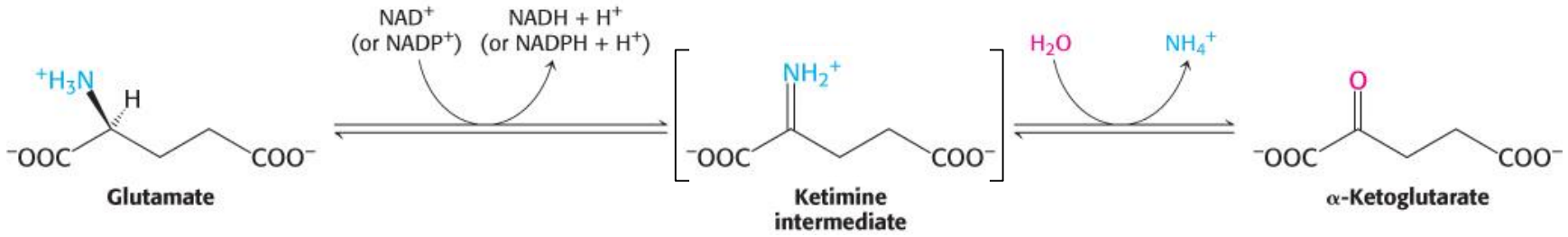


Adapted from Figure 18-4 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

Examples:



The amino group of glutamate is converted into ammonium by oxidative deamination



Forward reaction favoured due to very low intracellular NH_4^+ levels (NH_4^+ consumed by urea cycle)

Catalyzed by glutamate dehydrogenase

(essentially a liver-specific enzyme present in the mitochondrial matrix)

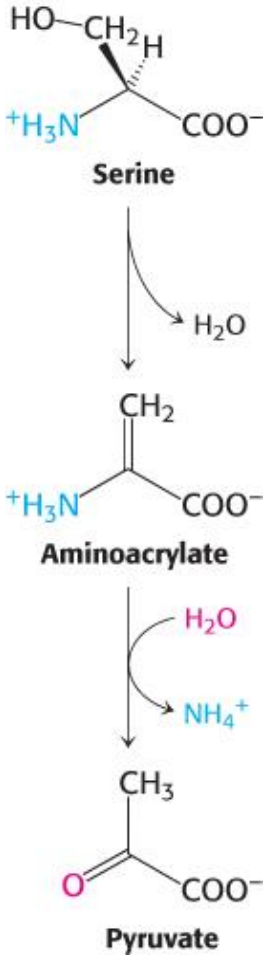
$$\alpha\text{-Amino acid} + NAD^+ + H_2O \rightleftharpoons \alpha\text{-ketoacid} + NH_4^+ + NADH + H^+$$
$$(\text{or } NADP^+) \qquad\qquad (\text{or NADPH})$$

Adapted from Biochemistry, 8th ed, Berg et al. 2015 W.H. Freeman and Company

Serine and threonine can be directly deaminated by dehydratases

The enzymes are called dehydratases because dehydration precedes deamination

No need for transamination



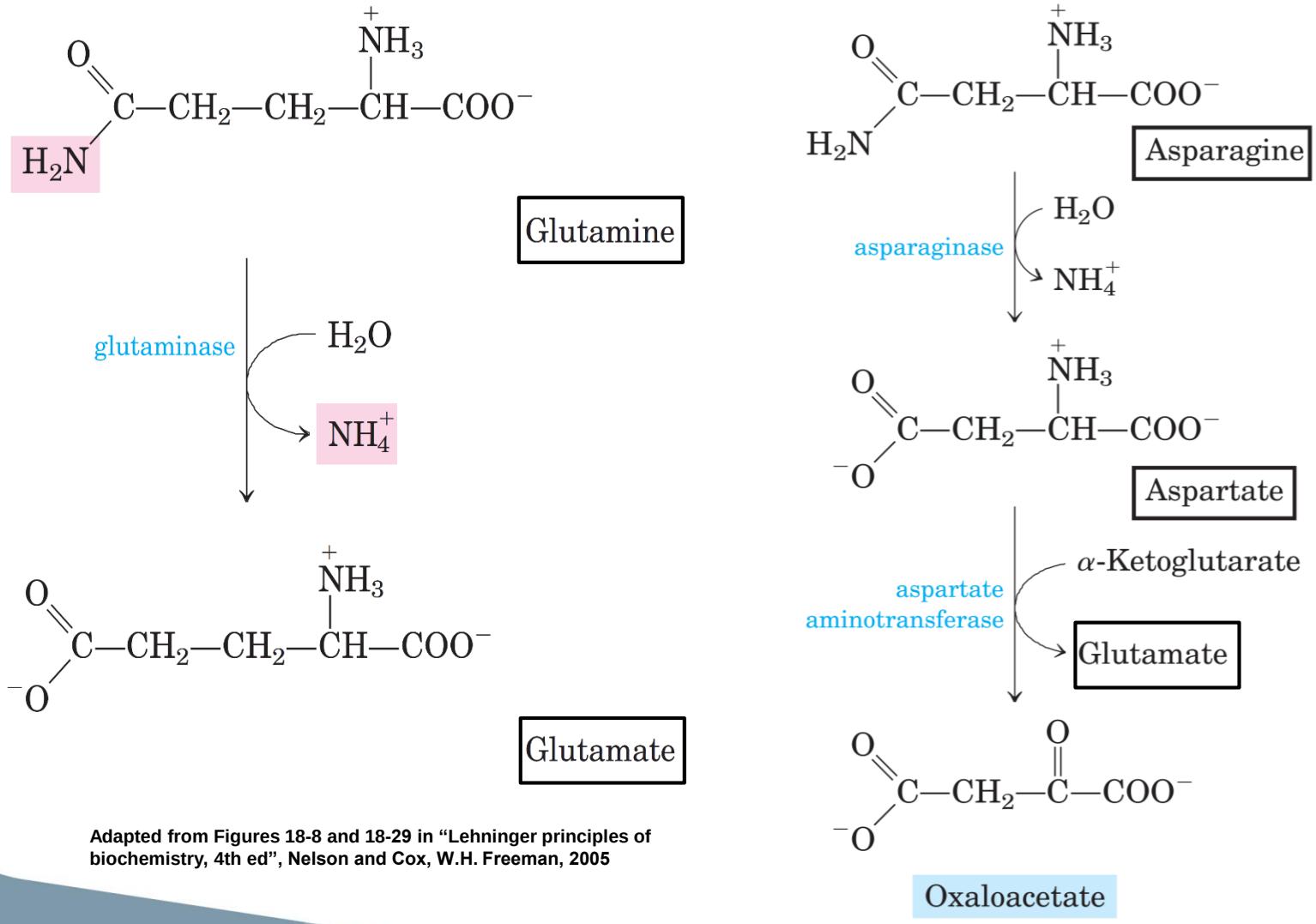
Serine —(*Serine dehydratase*)→ **Pyruvate + NH_4^+**

Threonine —(*Threonine dehydratase*)→ **α-ketobutyrate + NH_4^+**

Adapted from Biochemistry, 8th ed,
Berg et al. 2015 W.H. Freeman and Company

The side-chain nitrogen of glutamine and asparagine

– generation of ammonia and glutamate



Adapted from Figures 18-8 and 18-29 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

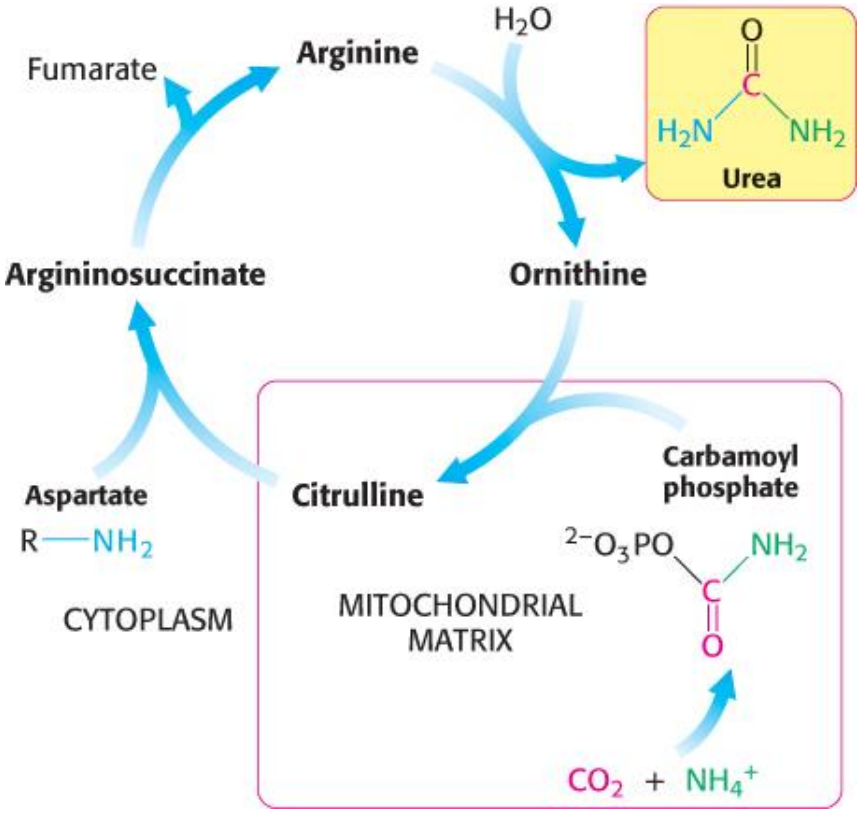
Ammonia is toxic to the central nervous system

The level of ammonia in the blood must be kept very low
(even slightly elevated concentrations are toxic to the CNS)

Solution:
Transform ammonia into non-toxic urea that can be excreted in the urine

Occurs in the **Urea cycle**

The Urea cycle is active only in the **liver**



The urea cycle

- transforms toxic ammonia into non-toxic urea

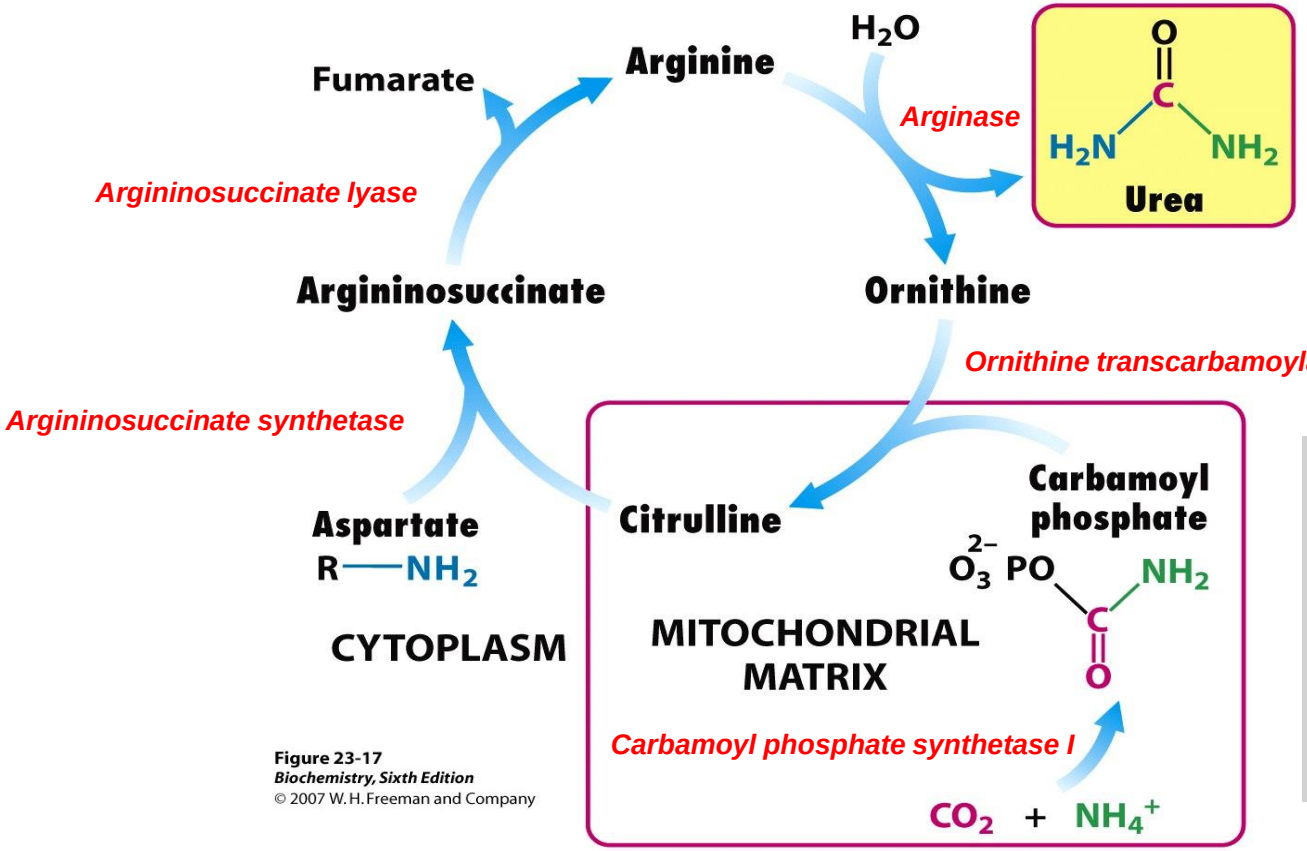


Figure 23-17
Biochemistry, Sixth Edition

UREA contains **2 amino groups:** one from free NH_4^+, and one from **aspartate**.

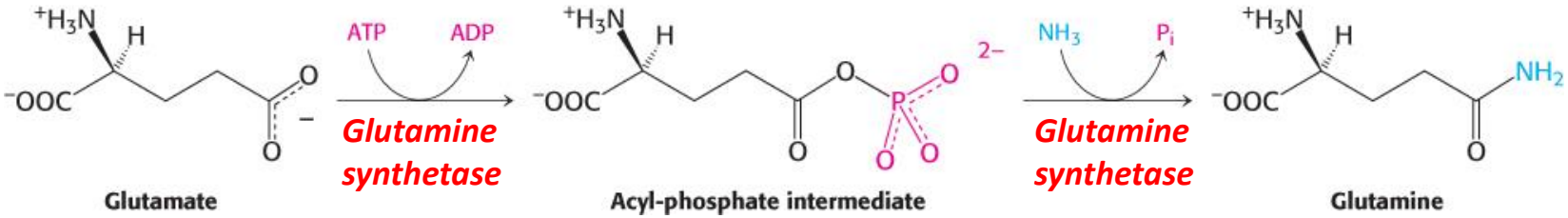
The carbon atom comes from HCO_3^-, (hydrated form of CO_2).

Defects in the urea cycle leads to elevated ammonia levels (hyperammonemia)

High concentrations of ammonia are highly toxic; in particular as it affects the function of the central nervous system

Why is ammonia toxic to the central nervous system?

Still not fully understood, but it is associated with brain swelling (edema)



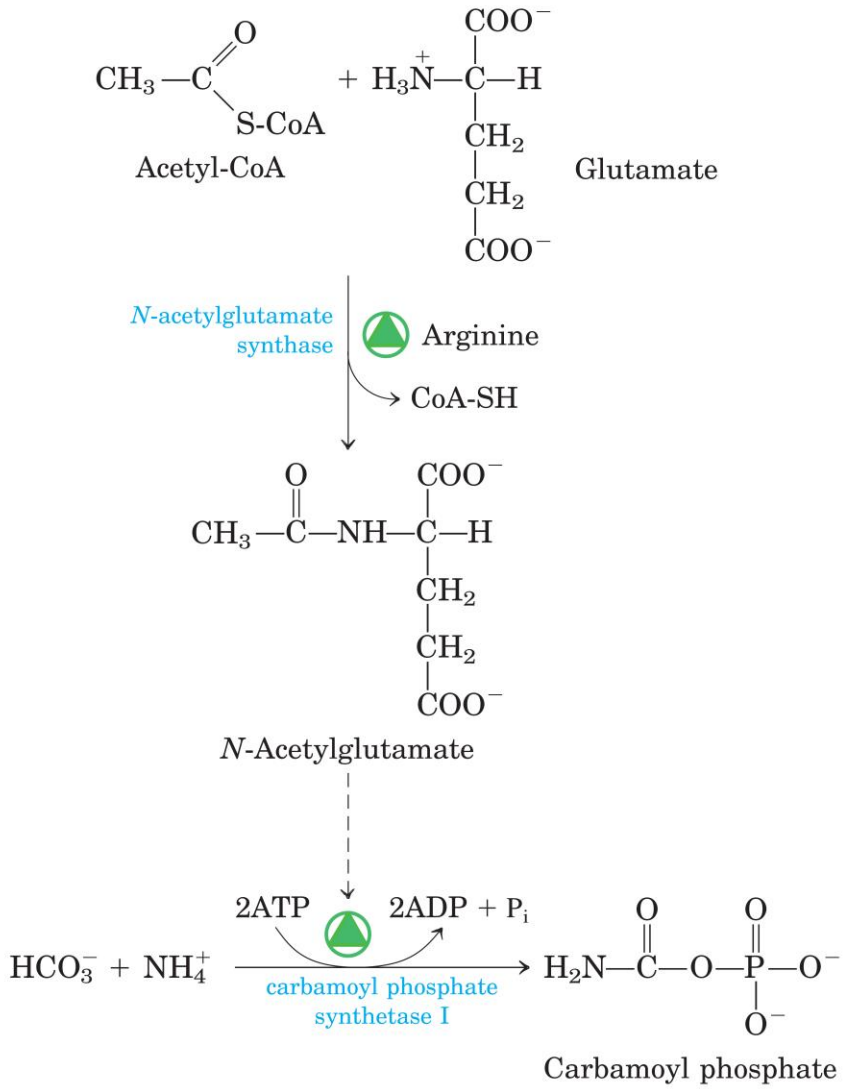
Theory:
High levels of ammonia drives formation of glutamine in astrocytes (express high levels of the enzyme glutamine synthetase).
Glutamine is osmotically active; attracts water into the cells leading to astrocytic swelling and brain edema, hampering brain function

Allosteric regulation of carbamoyl phosphate synthetase I

– regulation of flux through the urea cycle

N-acetylglutamate is an activator of carbamoyl phosphate synthetase I, and thereby the urea cycle.

High levels of glutamate and arginine (reflecting high levels of circulating amino acids) induce synthesis of the activator.



Defekter i ureacykeln

- Exempel: Argininosuccinatlyasbrist

Nedärvs autosomalt recessivt (mutationer *ASL* genen); 1-2 fall per 100 000 nyfödda

Symtom utan behandling:
Vid svår ASL brist visar sig symtom på ammoniakförgiftning redan under de första levnadsdagarna. Vanliga symtom är oregelbunden och ökad andning, muskelslapphet, kräkningar, alkalos, svullen hjärna, kramper, sviktande livsfunktioner

Sjukdomen kan också visa sig senare i livet och ha ett lindrigare förlopp, med antingen akuta eller kroniska symtom.

Behandlingsmål
Huvudmålet med behandlingen är att hålla ammoniaknivån i blodet på säkra nivåer
Faktorer som infektioner eller plötsligt ökat proteinintag kan stegra ammoniaknivån i blodet

Akutbehandling
Högglukoshaltig energidryck, glukosdropp, läkemedel som ökar utsöndringen av kvävehaltiga ämnen, dialys

Långtidsbehandling
Diet med reducerat intag av protein, läkemedel som ökar utsöndringen av kvävehaltiga ämnen.
Levertransplantation utförs som behandling vid störning i ureacykeln då konventionella behandlingar inte haft effekt.

Drug treatment of argininosuccinate lyase deficiency
– *arginine and phenylbutyrate*

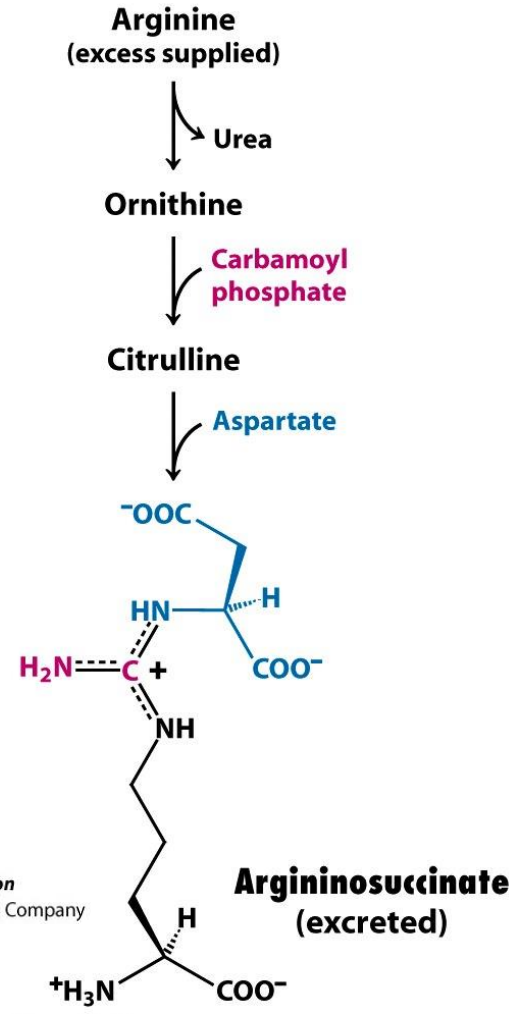
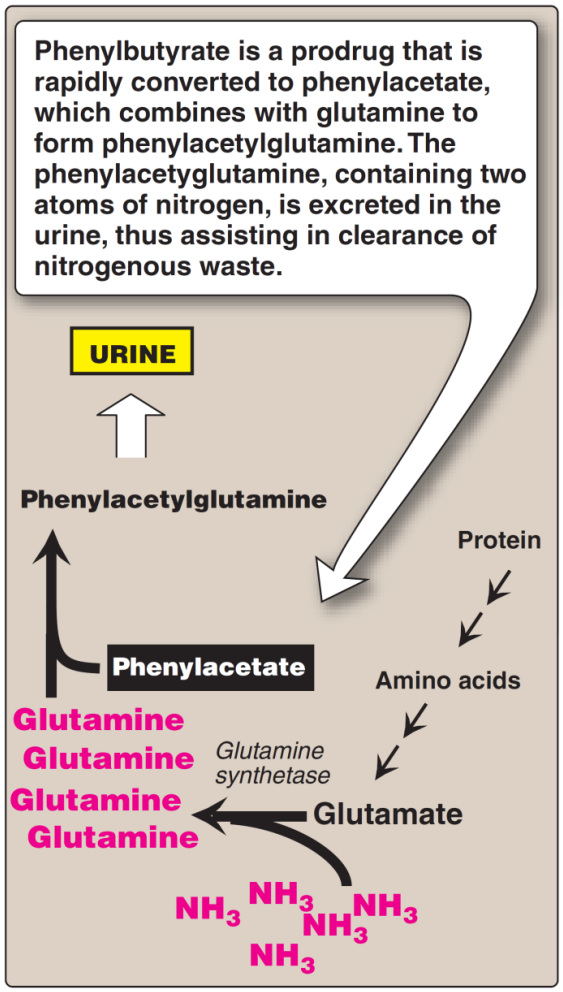


Figure 23-20
Biochemistry, Sixth Edition



Biochemistry 5th ed. / Harvey and Ferrier
Lippincott Williams & Wilkins, 2011

Extrahepatic tissues transport nitrogen to the liver for conversion to urea

- Degradation of amino acids occurs primarily in the liver but other tissues (extrahepatic tissues) can also degrade amino acids

  e.g. skeletal muscle uses branched-chain amino acids as a source of fuel during prolonged exercise and fasting.

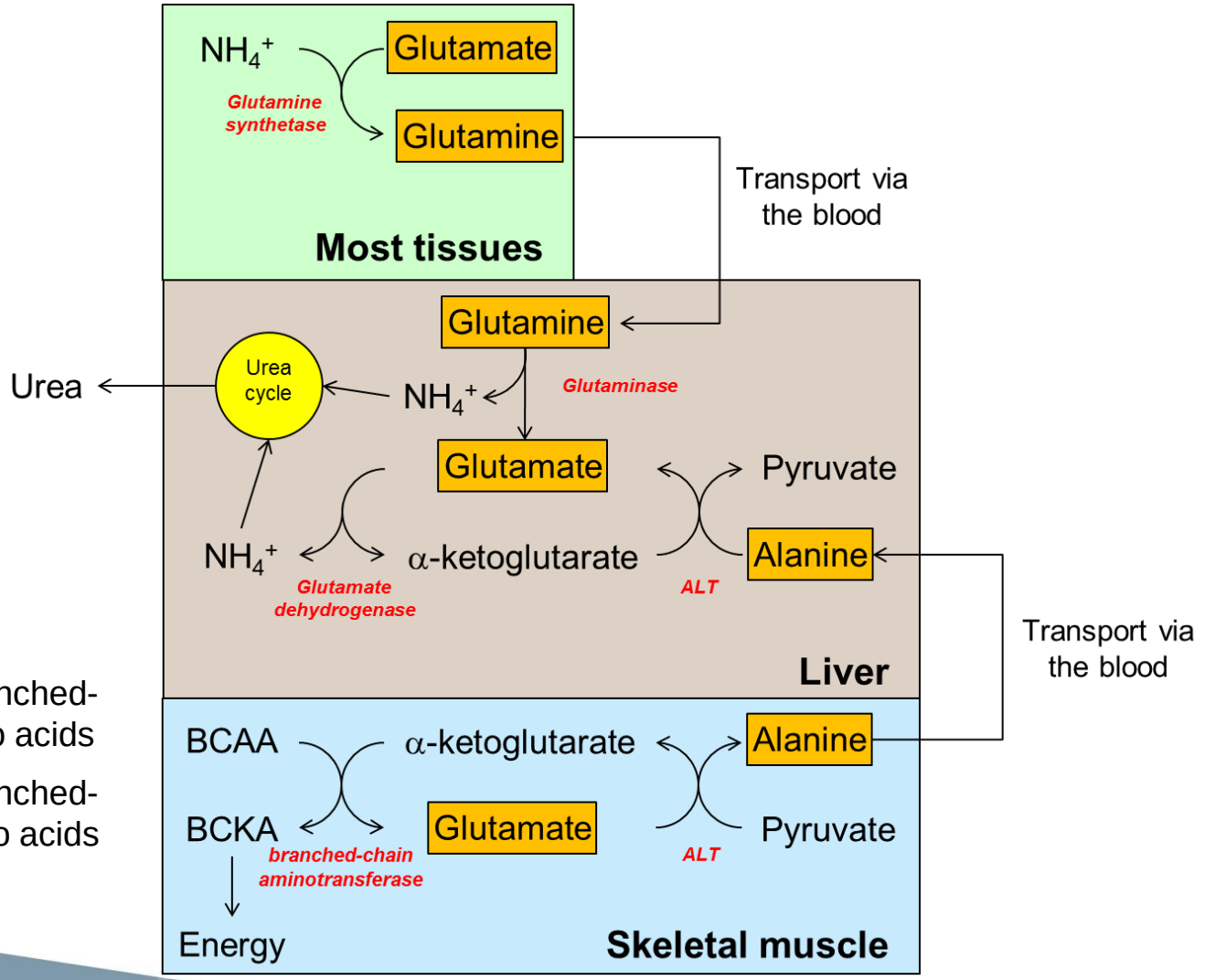
- Extrahepatic tissues lack the enzymes of the urea cycle

- Nitrogen must be released in a non-toxic form that can be transported to, and absorbed by, the liver

- Nitrogen is transported from extrahepatic tissues to the liver in two principal forms; glutamine and alanine

Glutamine and alanine

– nitrogen transport to the liver from extrahepatic tissues

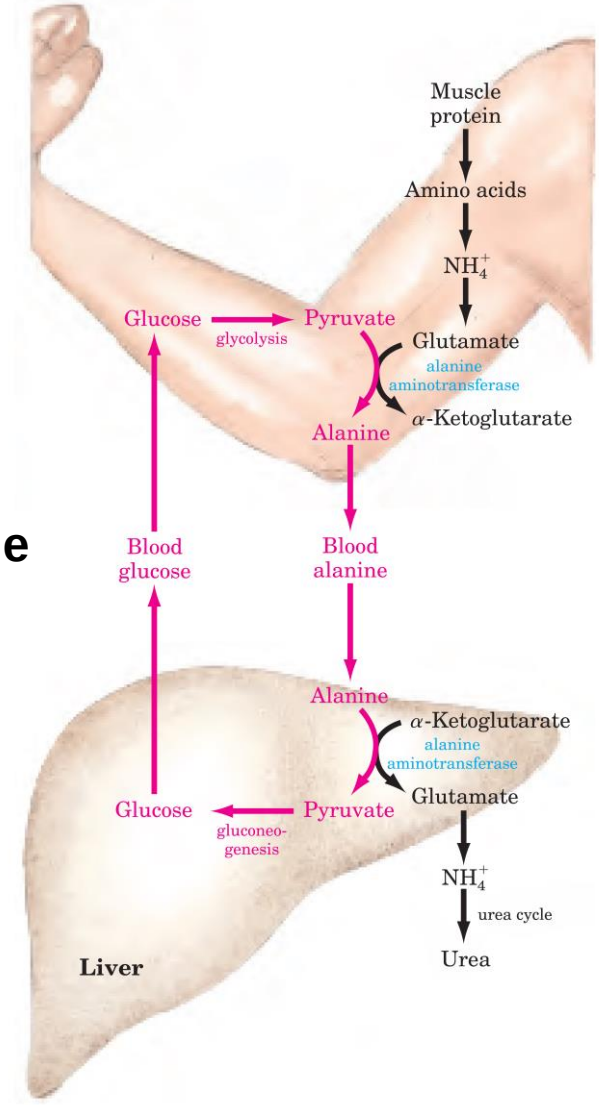


BCAA= branched-chain amino acids

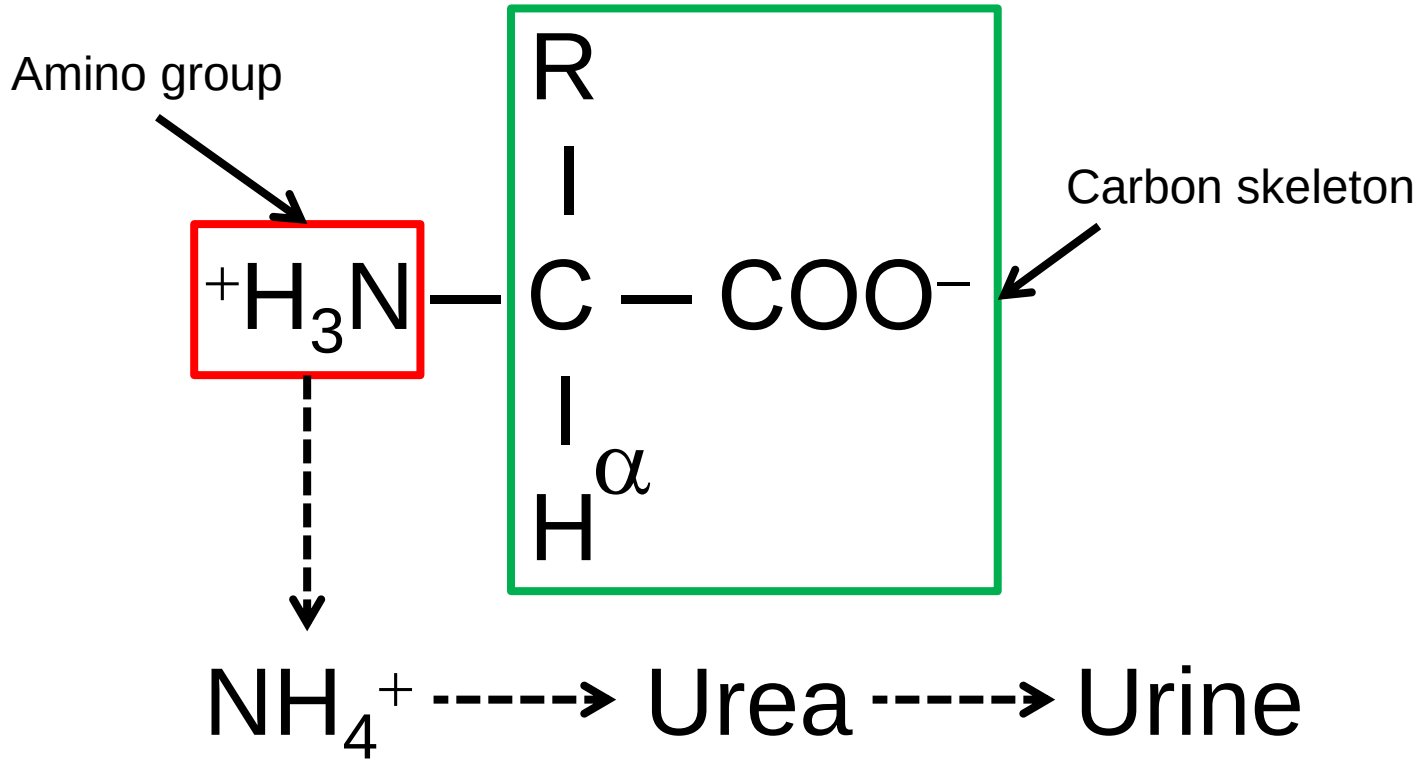
BCKA= branched-chain α-keto acids

Alanine transports ammonia from skeletal muscles to the liver

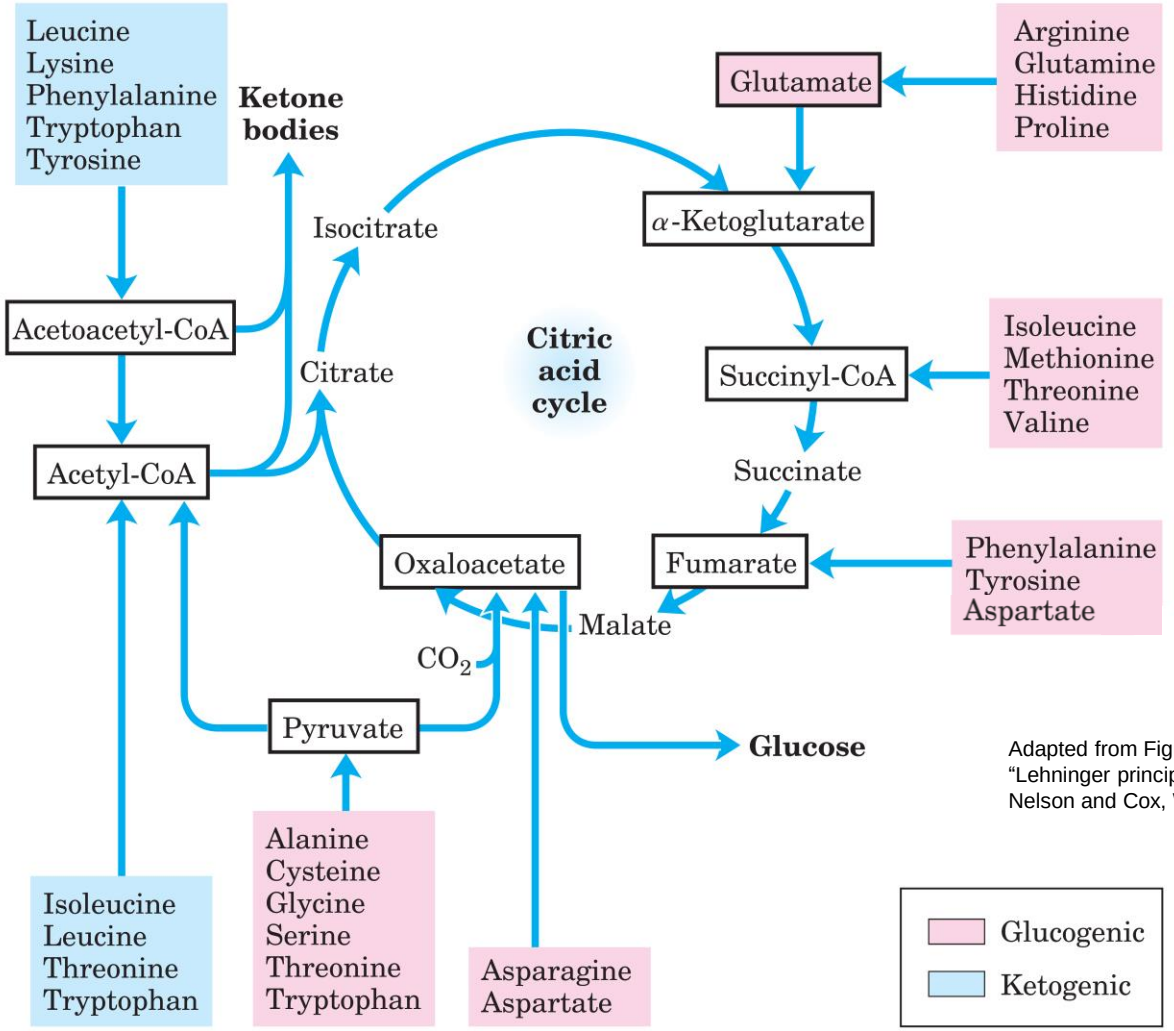
The glucose-alanine cycle



Where do the carbon skeletons of the different amino acids end up?



The carbon skeletons of amino acids ends up in only seven molecules



Adapted from Figure 18-15 in
"Lehninger principles of biochemistry, 4th ed",
Nelson and Cox, W.H. Freeman, 2005

The citric acid cycle

– a source for building blocks

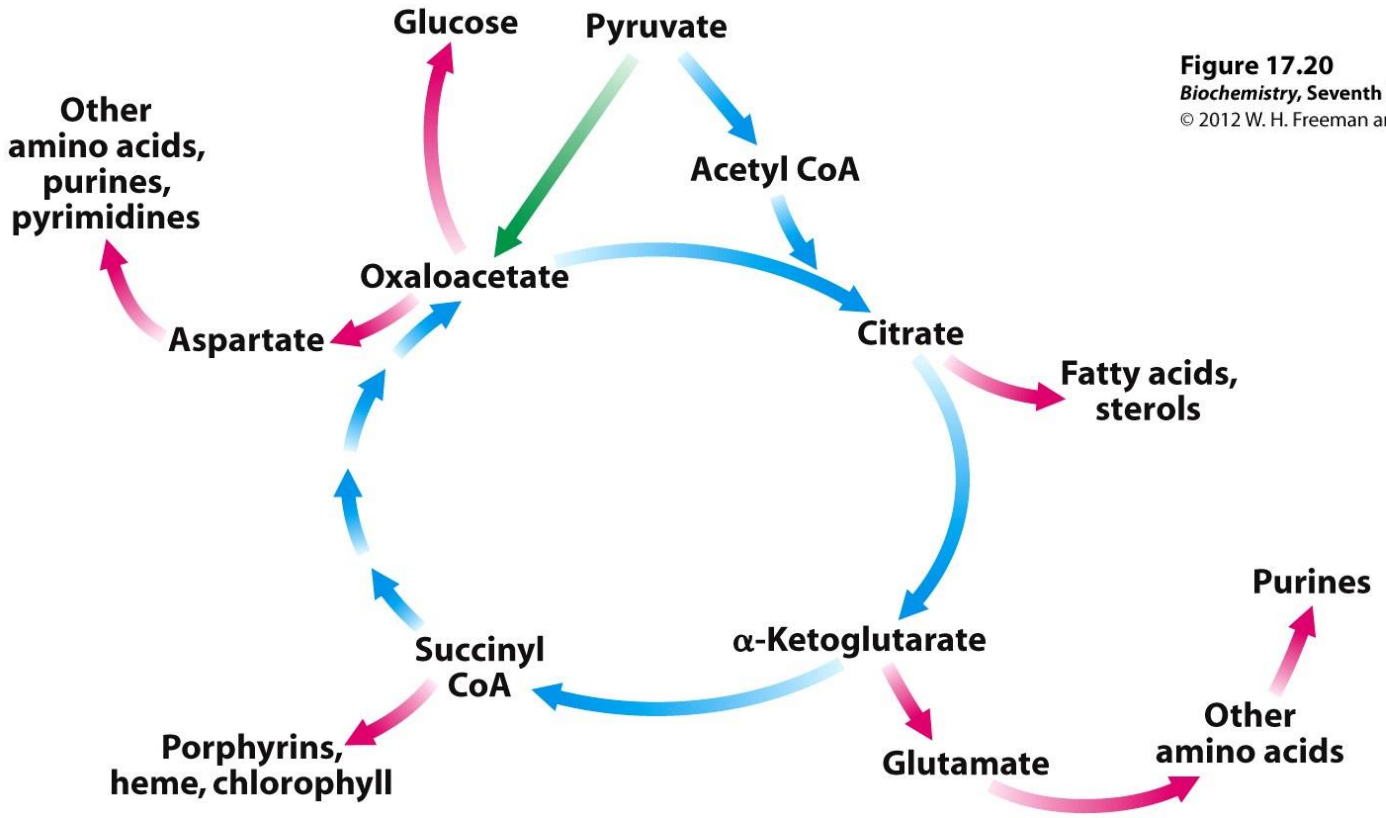


Figure 17.20
Biochemistry, Seventh Edition

The cycle must be refilled with its constituents to retain its full function!

Refilling the citric acid cycle

– pyruvate and the carbon skeletons of amino acids are important

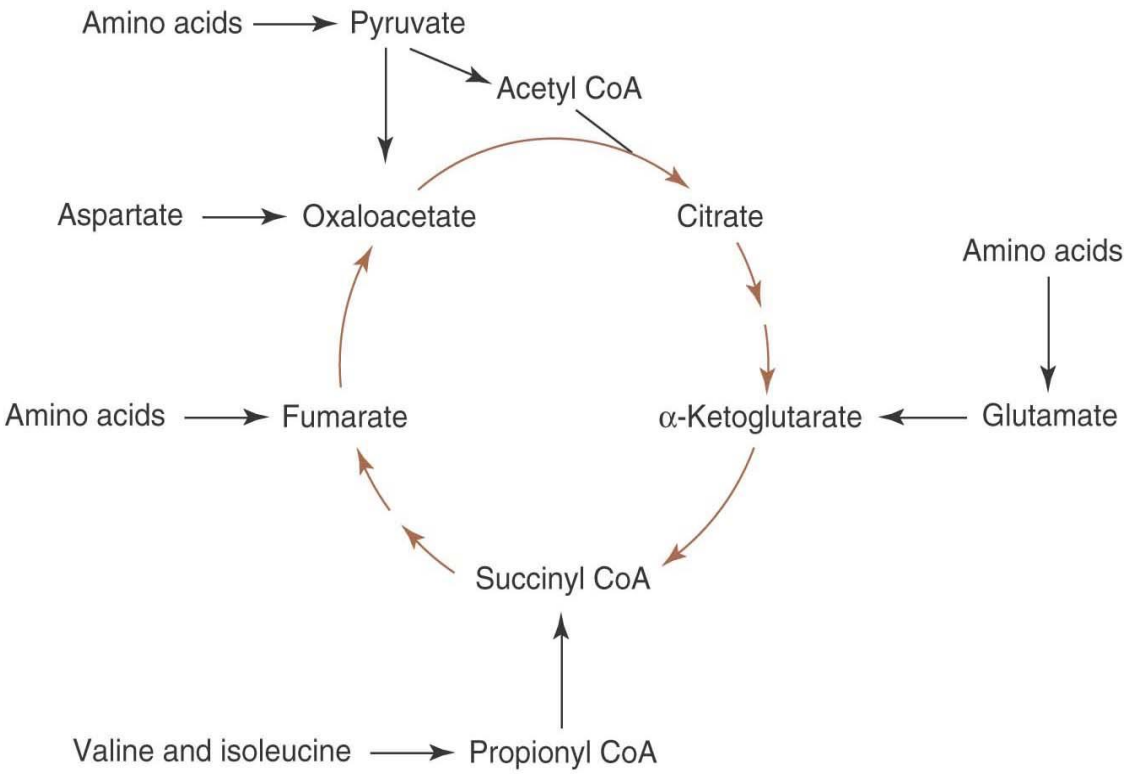


Figure 14.24. Anaplerotic reactions replenish intermediates of the TCA cycle.

Anaplerotic reactions = refilling reactions

Glucogenic and ketogenic amino acids

Glucogenic amino acids

- Degraded to pyruvate, α-ketoglutarate, succinyl CoA, fumarate, or oxaloacetate
- Can be converted into glucose (gluconeogenesis)

Ketogenic amino acids

- Degraded to acetyl CoA or acetoacetyl CoA
- Can give rise to ketone bodies or fatty acids

  - 13 amino acids are pure glucogenic
  - 5 amino acids are both glucogenic and ketogenic (Phe, Iso, Thr, Trp, Tyr; mnemonic ”PITTT”)
  - Only Lys and Leu are pure ketogenic amino acids

Oxaloacetate is an entry point into metabolism for aspartate and asparagine

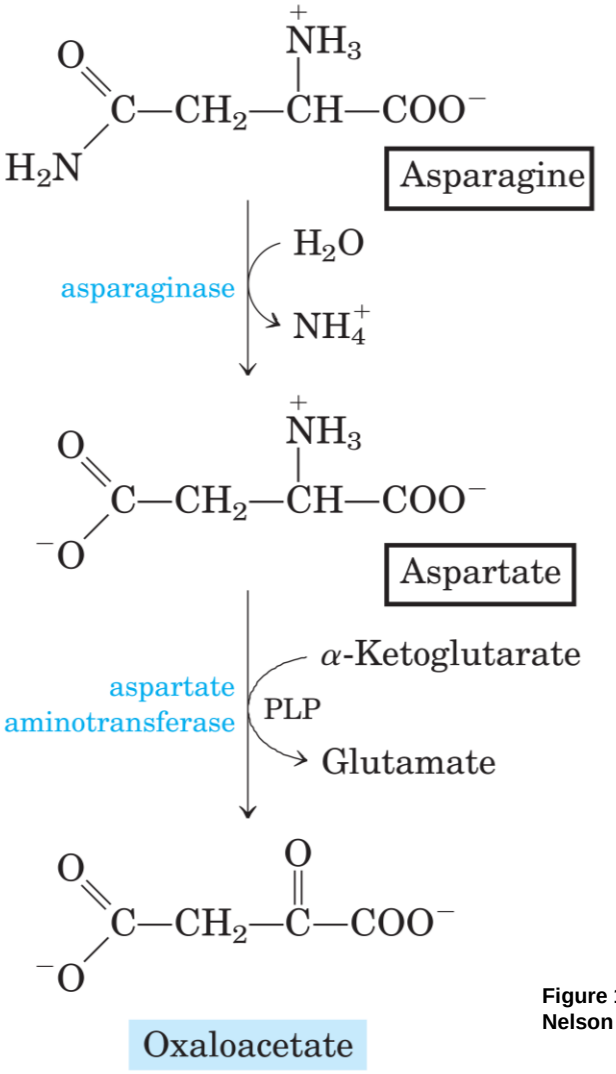
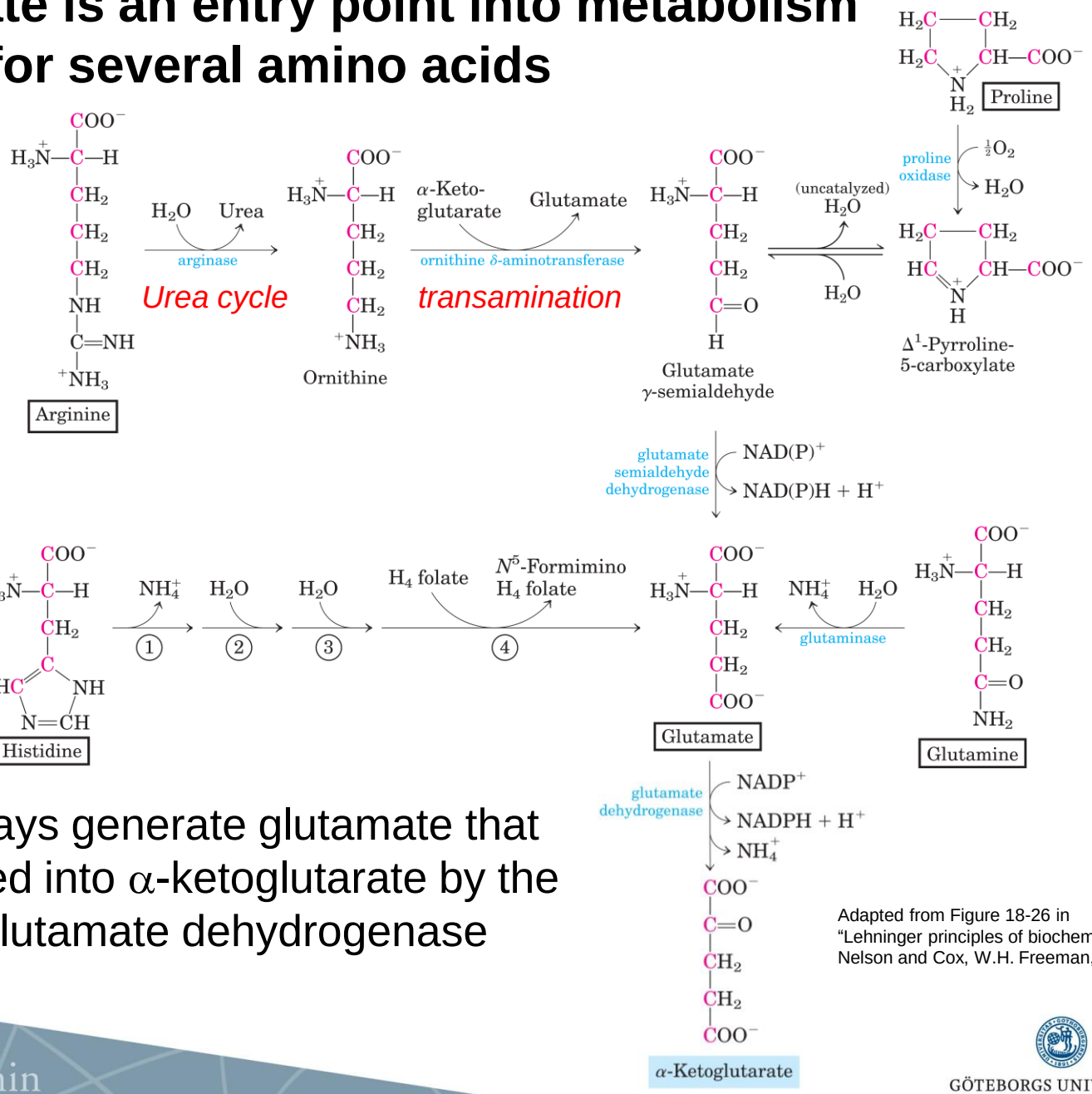


Figure 18-29 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

α-ketoglutarate is an entry point into metabolism for several amino acids



The pathways generate glutamate that is processed into α-ketoglutarate by the action of glutamate dehydrogenase

Adapted from Figure 18-26 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

Degradation pathways that generate acetyl-CoA

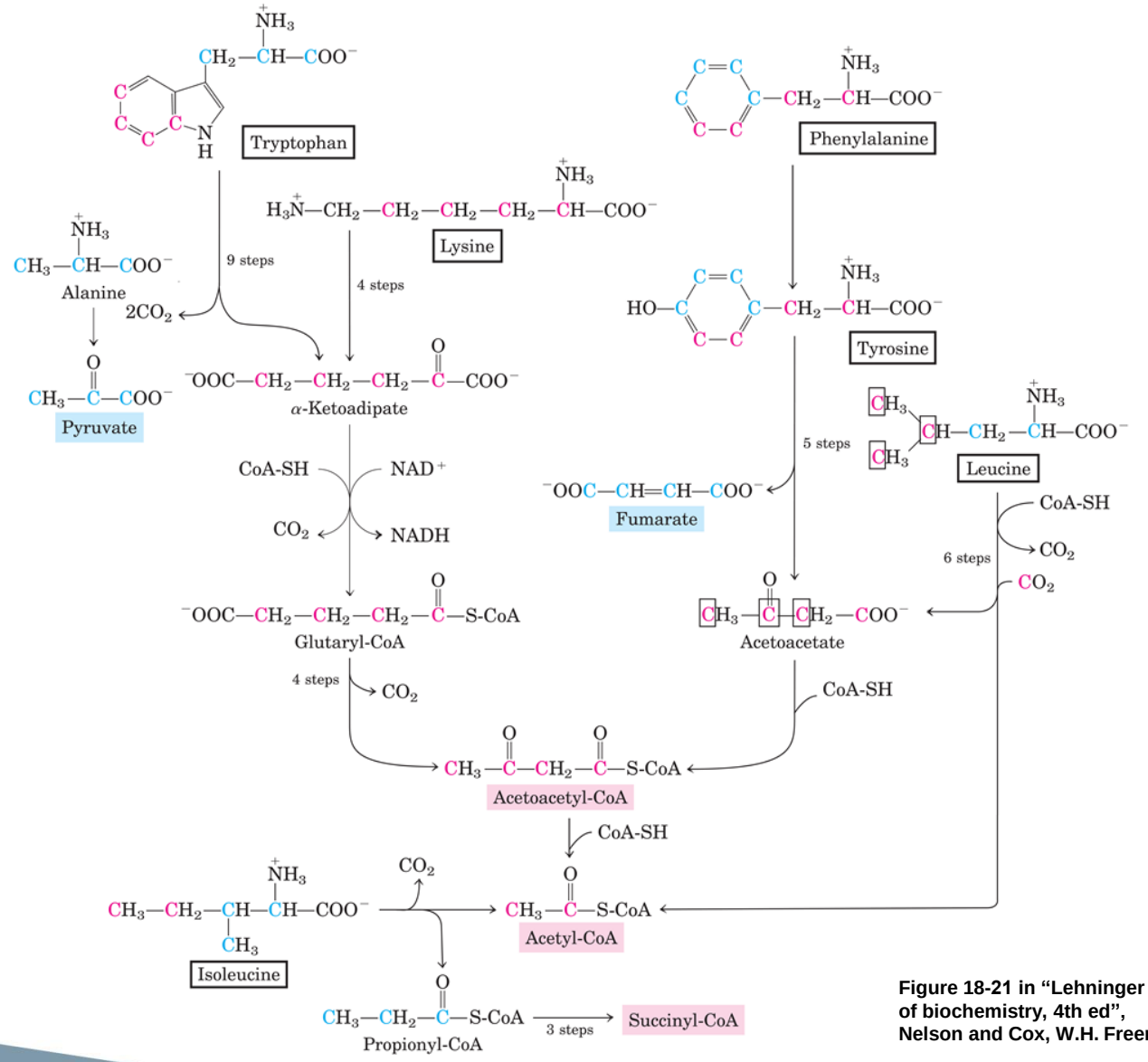
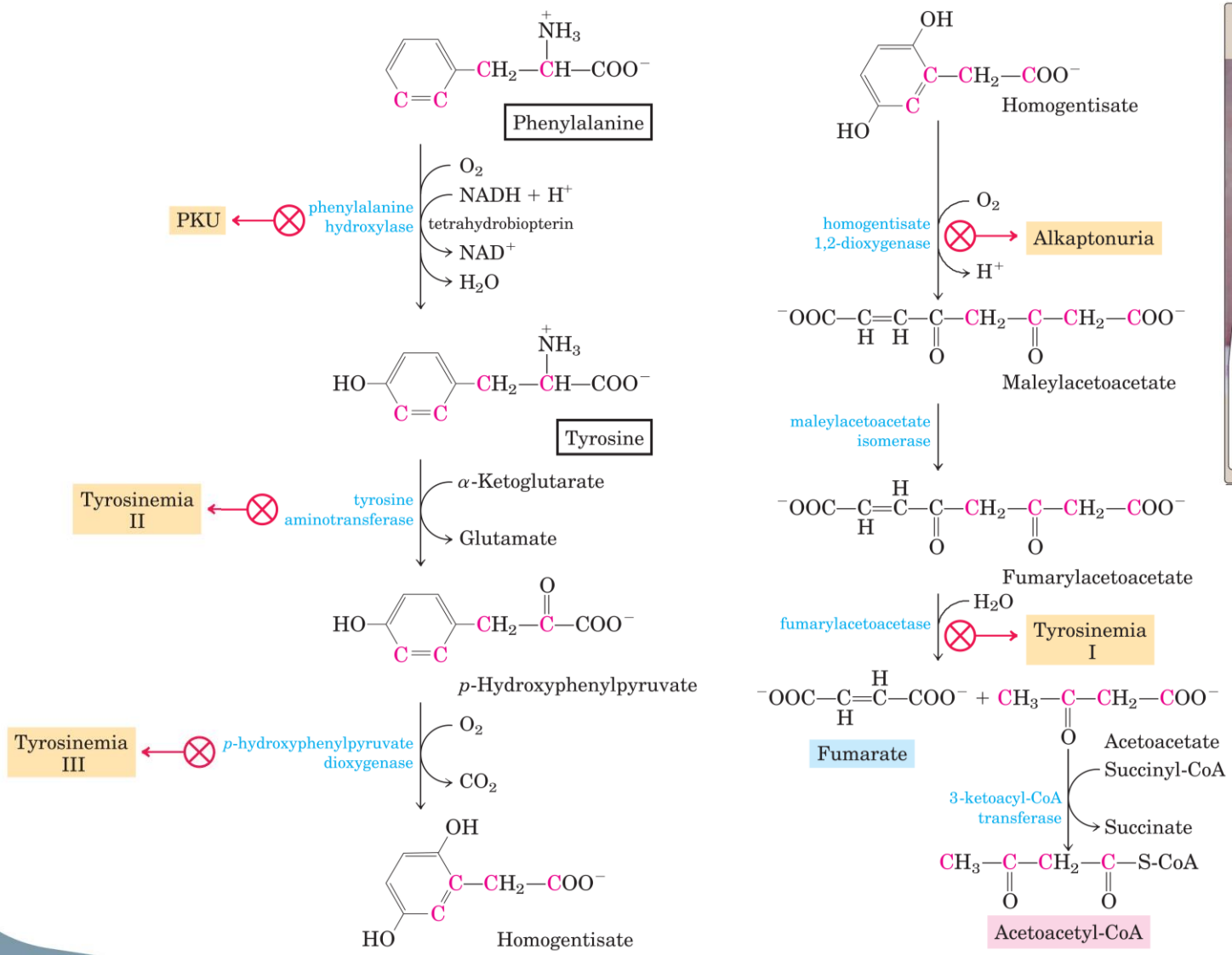


Figure 18-21 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

Degradation of phenylalanine and tyrosine



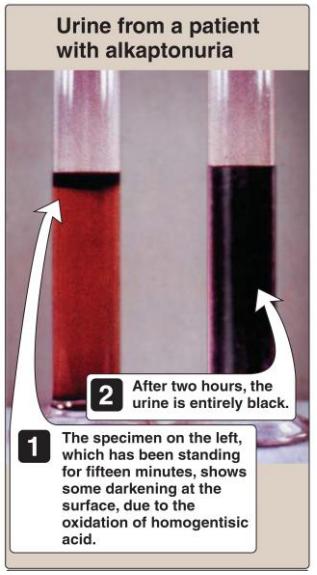


Figure 18-23 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

Degradation of branched-chain amino acids

– takes part primarily in skeletal muscle

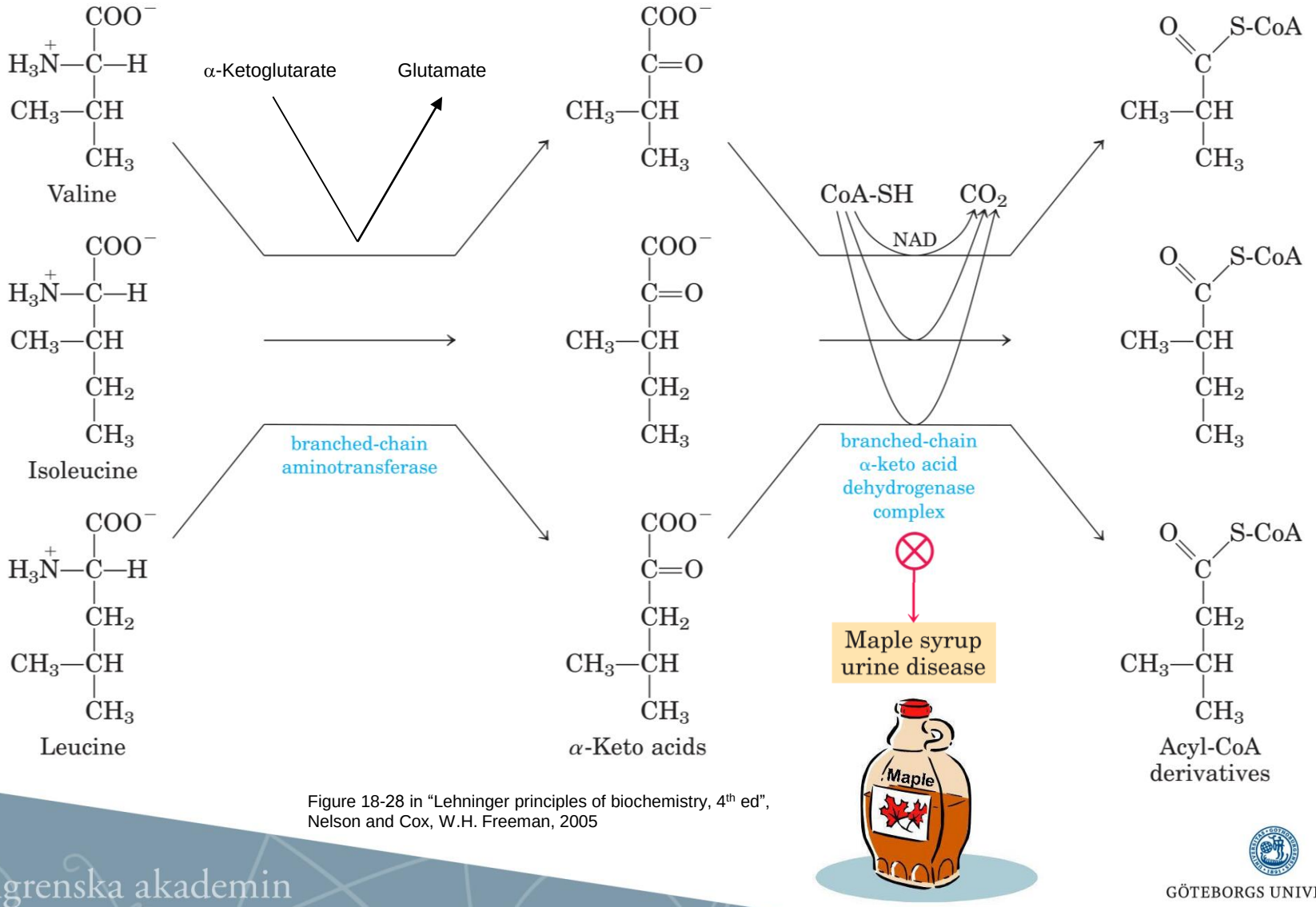


Figure 18-28 in "Lehninger principles of biochemistry, 4th ed", Nelson and Cox, W.H. Freeman, 2005

Maple syrup urine disease (MSUD)

Autosomal recessive disorder

Deficiency of the branched-chain α-keto acid dehydrogenase complex (due to mutations in *BCKDHA, BCKDHB, DBT* or *DLD*)

$\approx$ 2 cases per 100 000 newborns (Sweden). Common in populations such as the Amish.

Accumulation of branched-chain amino acids (Leu, Iso, and Val) and their corresponding α-keto acids in tissues, blood and urine

The disorder gets its name from the sweet odor of affected infants' urine

Symptoms: Poor feeding, vomiting, lack of energy, abnormal movements, and delayed development. If untreated, MSUD can lead to seizures, coma, and death.

Treatment: Protein-restrictive diet (limits the amount of ingested Leu, Iso, and Val) + addition of nutritional formulas providing necessary nutrients (but lacking Leu, Iso and Val). Leu, Iso and Val are added to the diet separately in small amounts.

Summary of part 2

- Degradation of amino acids proceeds through production of ammonia that is toxic, primarily for the brain
- Ammonia is produced by deamination of amino acids, most often of glutamate produced from other amino acids by transamination
- Amino acid degradation occurs primarily in the liver that is the only organ that can produce non-toxic urea from ammonia
- Ammonia produced in extrahepatic tissues needs to be converted to glutamine or alanine for safe transport to the liver
- The carbon skeletons of amino acids can be used for refilling reactions, production of energy-containing molecules (glucose, ketone bodies, fatty acids) or used for energy

Some important enzymes to keep in mind

Alanine aminotransferase

Aspartate aminotransferase

Glutamate dehydrogenase

Glutamine synthetase

Glutaminase

Phenylalanine hydroxylase

Carbamoyl phosphate synthetase I

Amino acid metabolism

Läsanvisningar

Detta föreläsningsmaterial

Biochemistry, 10th ed, Berg et al.
2023 W.H., Macmillian Learning

Kapitel 23: sidorna 701-703 och 708-731
Kapitel 25: sidorna 766-790

Instuderingsfrågor

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