VNIVERSITAT DE VALÈNCIA

LESSON 28: METABOLISM OF AMINO ACIDS (II): MECHANISMS OF DEGRADATION OF AMINO ACIDS AND DESTINATION OF THE CARBON CHAIN OF AMINO ACIDS

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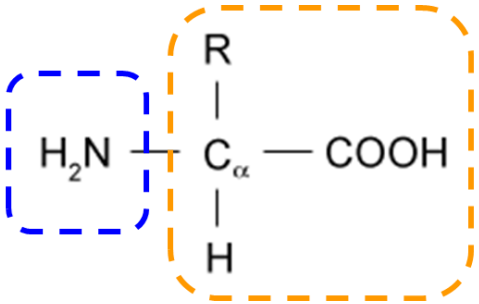
1. CATABOLISM OF AMINO ACIDS: GENERAL MECHANISMS



AMINO ACIDS

PROTEINS

Structural blocks (amino acids)
Plastic or structural function

Protein turnover

Lesson 27

BIOMOLECULES

Prosthetic groups

Neurotransmitters

Biogenic amines

Purines and pyrimidine bases

Lesson 30

DEGRADATION

Amino group loss

NH_3 + Carbon chain

Urea cycle

Lesson 29

Glucose
CO_2
Acetyl-CoA
Ketone bodies

Lesson 28

Amino acids cannot be stored or secreted.
Site of tissue degradation: liver and, occasionally, skeletal muscle.

1. CATABOLISM OF AMINO ACIDS: GENERAL MECHANISMS

Source of amino acids:

- Protein digestion from the diet → Essential amino acids / Non-essential amino acids

Essential	Non-essential
Histidine (His)	Alanine (Ala)
Isoleucine (Ile)	Arginine (Arg)
Leucine (Leu)	Asparagine (Asn)
Lysine (Lys)	Aspartate (Asp)
Methionine (Met)	Cysteine (Cys)
Phenylalanine (Phe)	Glutamate (Glut)
Threonine (Thr)	Glutamine (Gln)
Tryptophan (Trp)	Glycine (Gly)
Valine (Val)	Proline (Pro)
	Serine (Ser)
	Tyrosine (Tyr)

- Intracellular protein degradation due to protein turnover
- Body protein degradation in pathological situations:

  starvation, diabetes mellitus, etc.

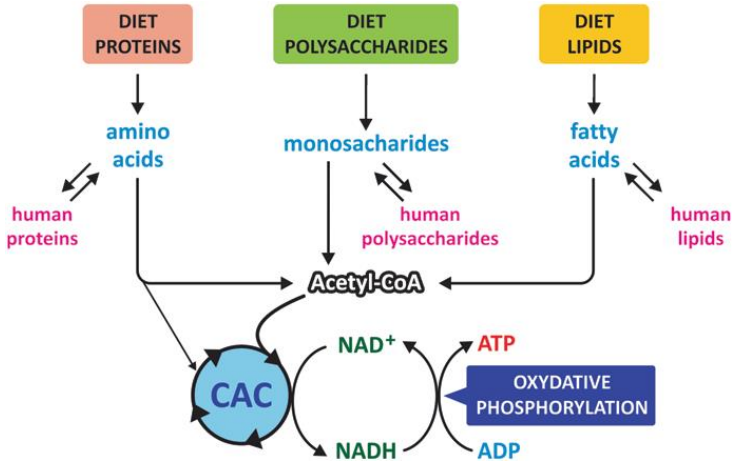
Destination of amino acids:

- Precursor for the synthesis of new proteins and other nitrogen compounds:

  Nucleotides, the heme group, glutathione

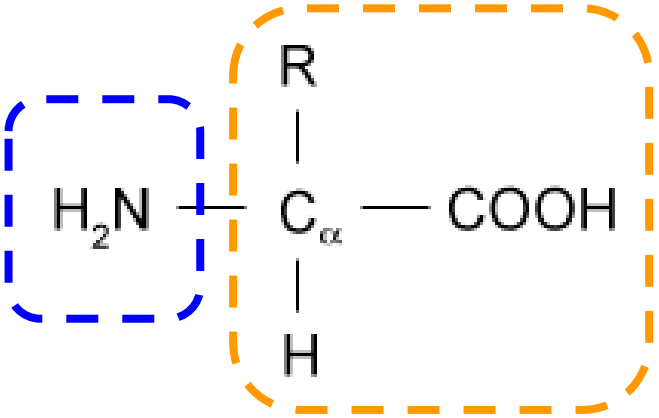
- Surplus is degraded for energetic purposes

  10-15 % of the energy

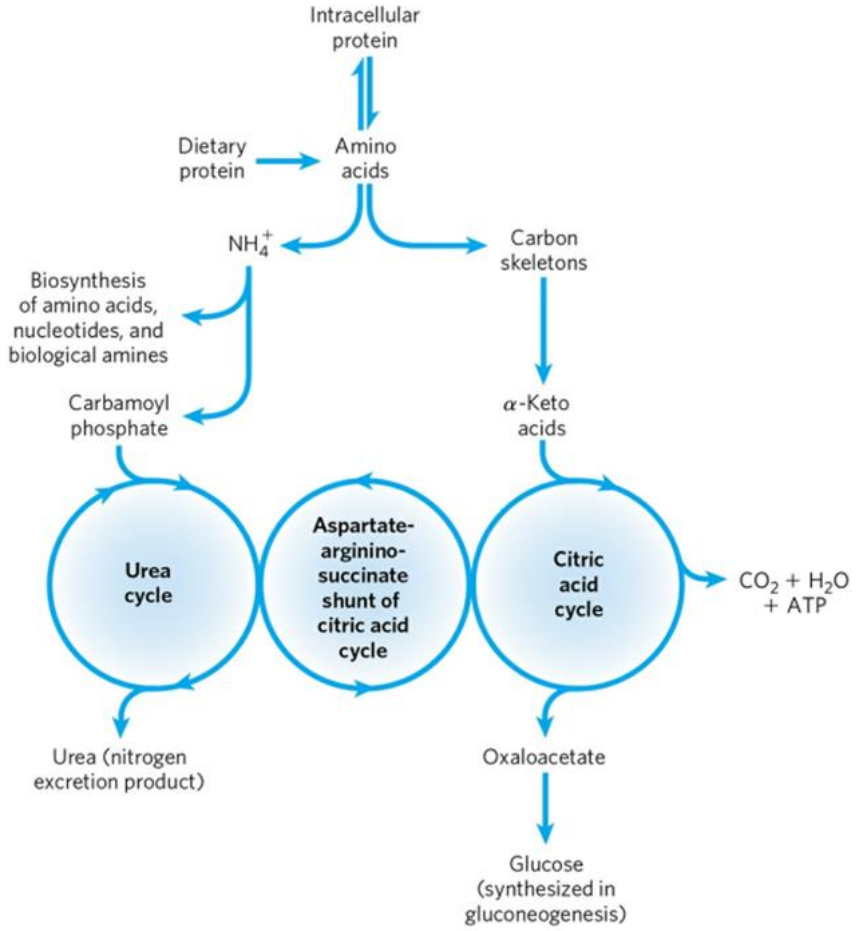


Da Poian *et al.*, 2021

1. CATABOLISM OF AMINO ACIDS: GENERAL MECHANISMS



- Amino acid catabolism comprises 3 steps:
  - Deamination: the ammonia group must be converted into ammonium.
  - Incorporation of ammonia into the urea cycle.
  - Conversion of the carbon chain to common metabolic intermediaries that can be used as a source of energy in other metabolic pathways.



General description of amino acid catabolism in mammals. Amino groups and carbon chains take separate but interconnected routes.

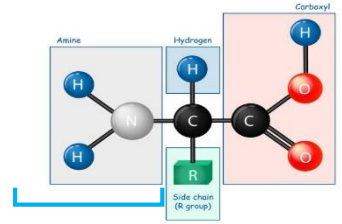
STEPS IN THE CATABOLISM OF AMINO ACIDS:

Catabolism requires:

1) **the elimination and metabolism of the N of the amino acids that is finally excreted by urine and faeces, and**
2) **the metabolism of the carbon chain that is reused.**

First phase:
Elimination of α-amino groups: transamination and subsequent oxidative deamination.

Second phase:
α-ketoacids (carbon chain) are converted into common intermediates of energy-producing pathways (intermediates of the Krebs cycle and gluconeogenesis).

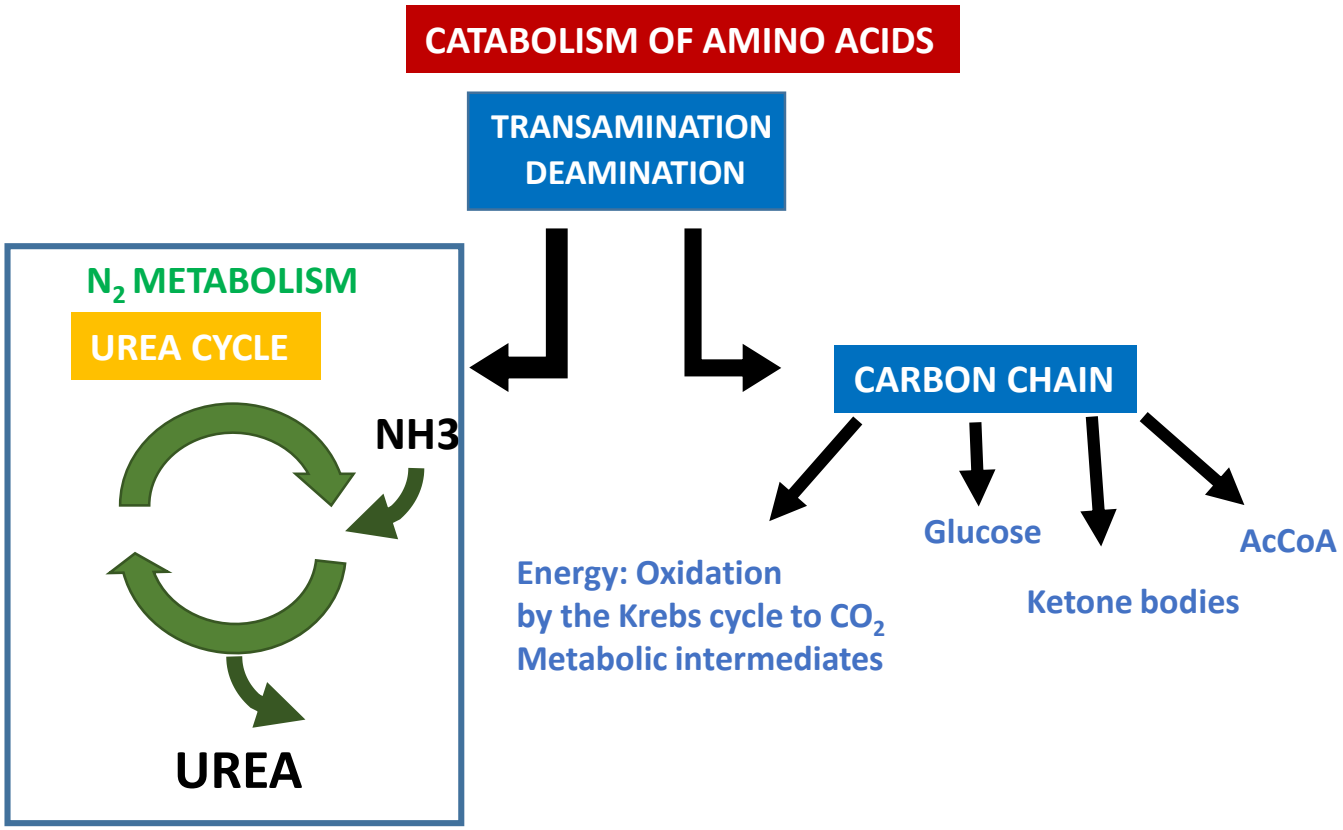


Amino acids → NH_3 + α-ketoacids

NH_3: Urine and synthesis of urea (mostly, the urea cycle)

α-ketoacids: metabolic intermediates

1. CATABOLISM OF AMINO ACIDS: GENERAL MECHANISMS



Although body proteins represent a significant proportion of potential energy reserves, under normal circumstances they are not used for energy production.

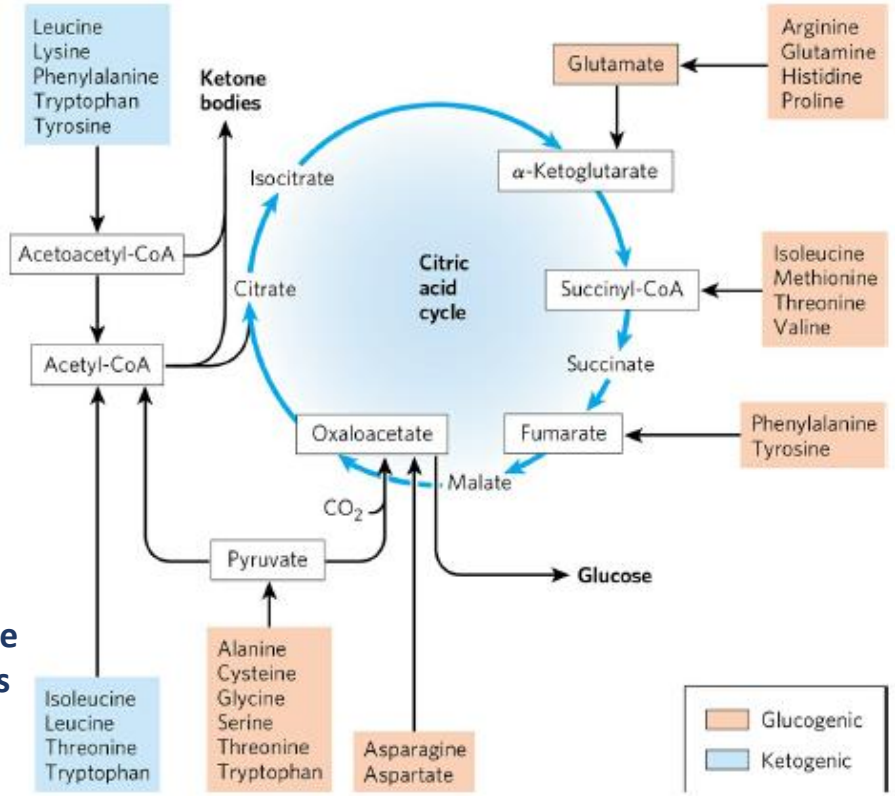
In an extended fast, however, muscle protein is degraded to amino acids for the synthesis of essential proteins and to ketoacids for gluconeogenesis in order to maintain blood glucose concentration and provide metabolites for energy production. This accounts for the loss of muscle mass during fasting.

In addition to its role as an important source of carbon skeletons for oxidative metabolism and energy production, dietary protein must provide adequate amounts of those amino acids that we cannot make to support normal protein synthesis (essential and conditionally essential amino acids)

1.1 CARBON CHAIN DESTINATION

Amino acid catabolism

Amino acid catabolism normally accounts for only 10% to 15% of the human body's energy production; these pathways are not nearly as active as glycolysis and fatty acid oxidation. Flux through these catabolic routes also varies greatly, depending on the balance between requirements for biosynthetic processes and the availability of a particular amino acid.



Amino acids are grouped according to their major degradative end product. Some amino acids are listed more than once because different parts of their carbon skeletons are degraded to different end products.

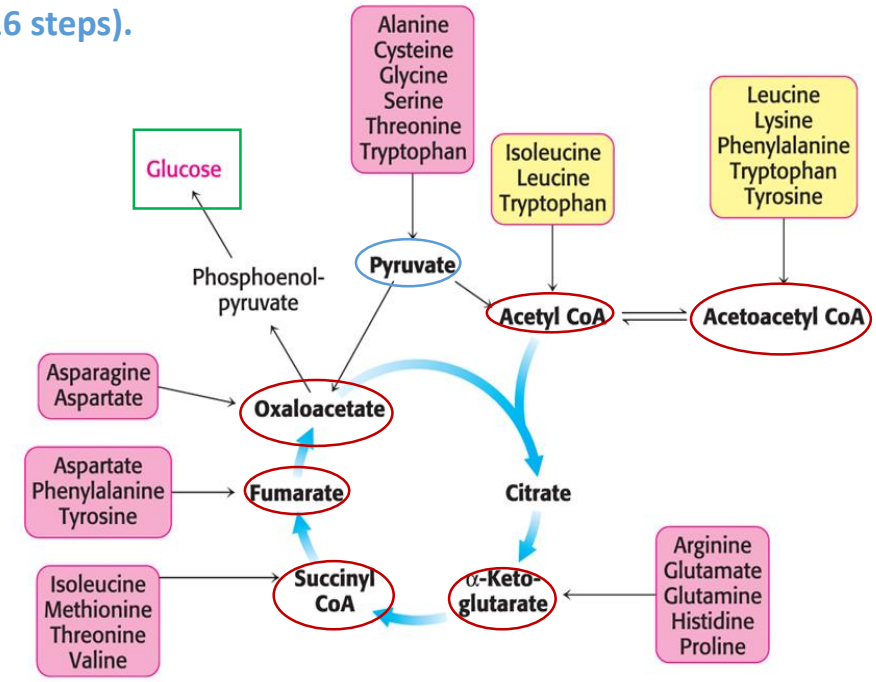
Lehninger

Depending on their degradative end product, some amino acids can be converted to ketone bodies, some to glucose, and some to both. Amino acid degradation is therefore integrated into intermediary metabolism and can be critical to survival under conditions in which amino acids are a significant source of metabolic energy.

1.1 CARBON CHAIN DESTINATION

There are 20 degradation pathways for the carbon chain of the 20 amino acids.

- These range from very simple (1 step) to very complex (16 steps).
- They all converge in 7 different metabolites, all of which enter the citric acid cycle
  - Acetyl-CoA
  - Acetoacetyl CoA
  - α-Ketoglutarate
  - Succinyl CoA
  - Fumarate
  - Oxaloacetate



- From here the carbon skeletons are diverted to:
  - Gluconeogenesis or ketogenesis
  - Complete oxidation to CO_2 and H_2O

Depending on their degradative end product, some amino acids can be converted to ketone bodies (ketogenic), some to glucose (glucogenic), and some to both. Amino acid degradation is therefore integrated into intermediary metabolism and can be critical to survival under conditions in which amino acids are a significant source of metabolic energy.

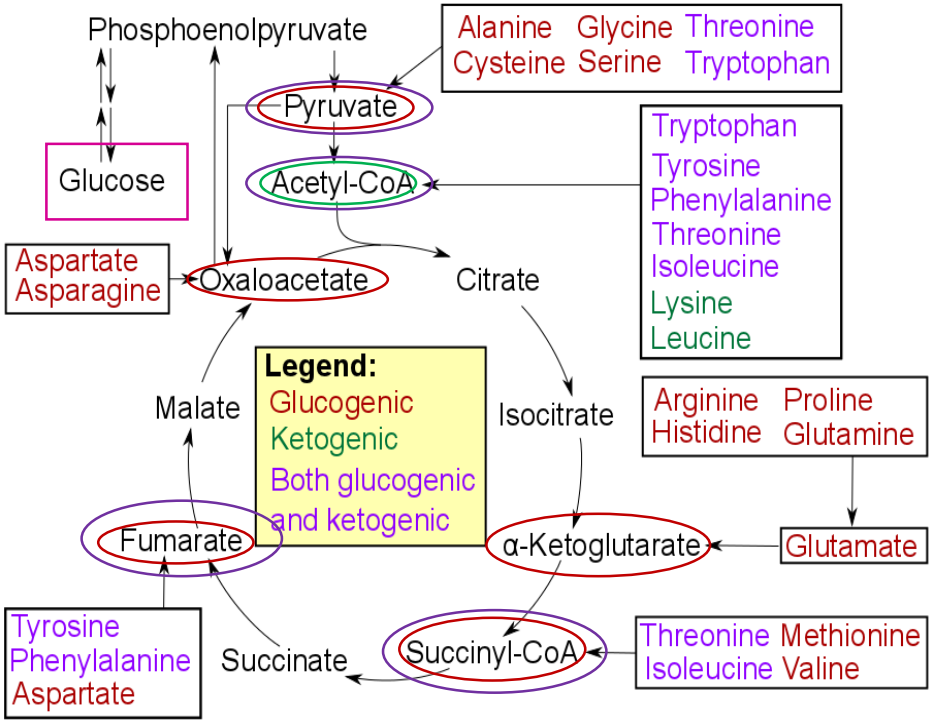
Some amino acids are listed more than once because different parts of their carbon skeletons are degraded to different end products.

1.1 CARBON CHAIN DESTINATION

Depending on their degradative end product, amino acids can be classified as:

- **Glucogenic (Glycogenic):** amino acids whose metabolism produces pyruvate or one of the intermediaries of the citric acid cycle. Under certain conditions they can generate glucose by gluconeogenesis.
- **Ketogenic:** amino acids that can be degraded directly into Acetyl-CoA (and/or Acetoacetyl-CoA), which is the precursor of ketone bodies.
- **Both:** amino acids can be degraded to both kinds of precursors depending on conditions or needs.

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



Five amino acids are **both** glucogenic and ketogenic. The amino acids that degrade to **pyruvate**, **succinyl CoA** and **fumarate** are also potentially ketogenic.

Only two amino acids, **leucine** and **lysine**, are exclusively **ketogenic**.

1.1 CARBON CHAIN DESTINATION

All or part of the carbon skeletons of seven amino acids are ultimately broken down into acetyl-CoA.

Five amino acids are converted into α-ketoglutarate

Arginine Proline Histidine Glutamine → Glutamate

Tryptophan Tyrosine Phenylalanine Threonine Isoleucine Lysine Leucine

Four are converted into succinyl-CoA

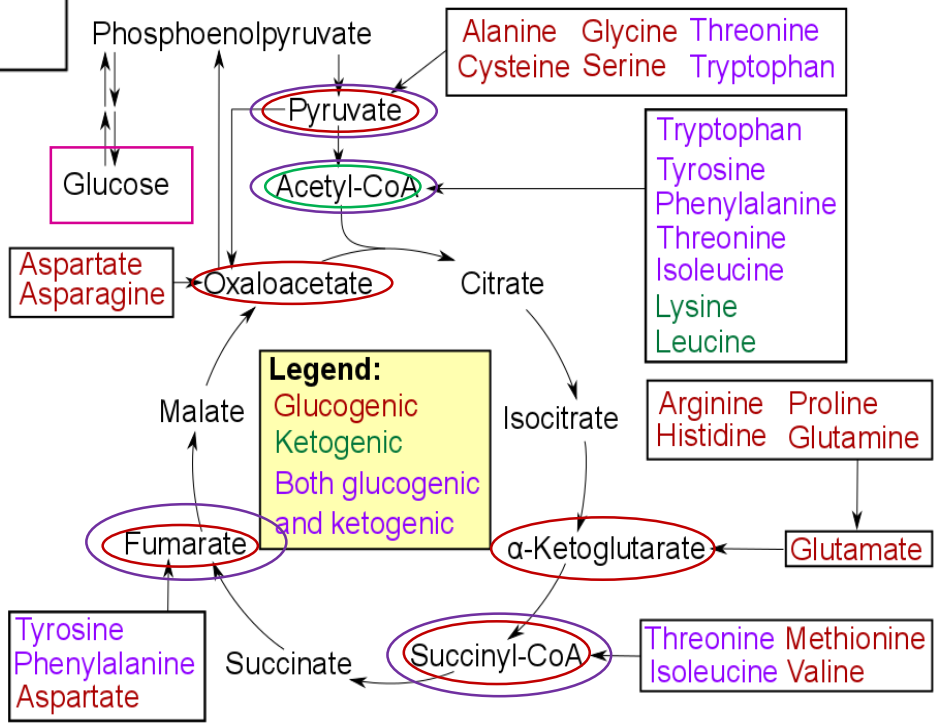
Threonine Methionine Isoleucine Valine

Two are converted into oxaloacetate.

Aspartate Asparagine

All or parts of six amino acids are converted into pyruvate, which can be converted into either acetyl-CoA or oxaloacetate.

Alanine Glycine Threonine Cysteine Serine Tryptophan

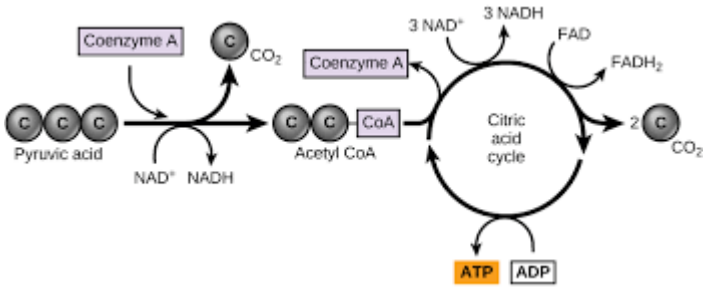


Some amino acids appear more than once. This reflects different fates for different parts of their carbon skeletons.

These transformations take place in the liver, except for the branched-chain amino acids (BCAA) (Isoleucine, Leucine and Valine), which are metabolized in the muscle.

1.1 CARBON CHAIN DESTINATION

- If amino acids are to be used as a respiratory fuel, their carbon skeletons must be converted into acetyl CoA, which must then enter the Krebs cycle for oxidation, thus producing ATP.

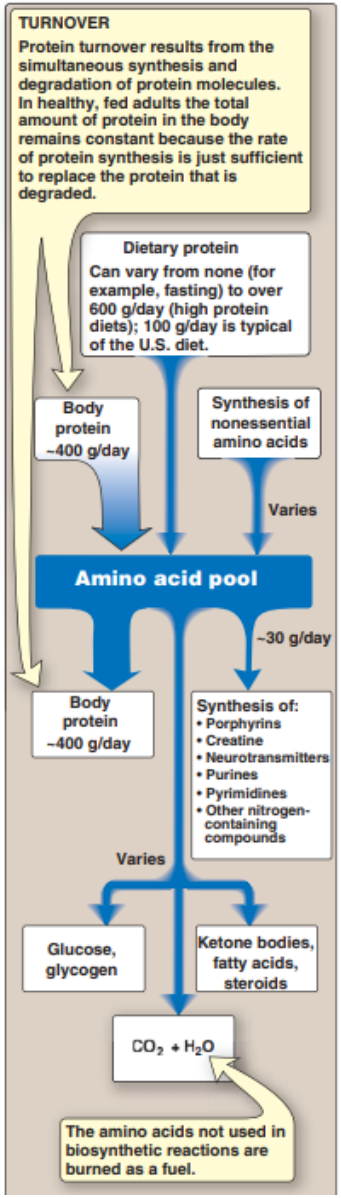


- For complete oxidation, amino acids must be converted into acetyl CoA to finally obtain energy.

- The simple entry of the carbon skeletons into the Krebs cycle as dicarboxylic acids (α-ketoglutarate, succinate, fumarate or oxaloacetate) does not ensure their complete oxidation for energy metabolism.

2. GENERAL OVERVIEW OF THE METABOLISM OF AMINO ACIDS

ORIGIN AND DESTINATION OF AMINO ACIDS



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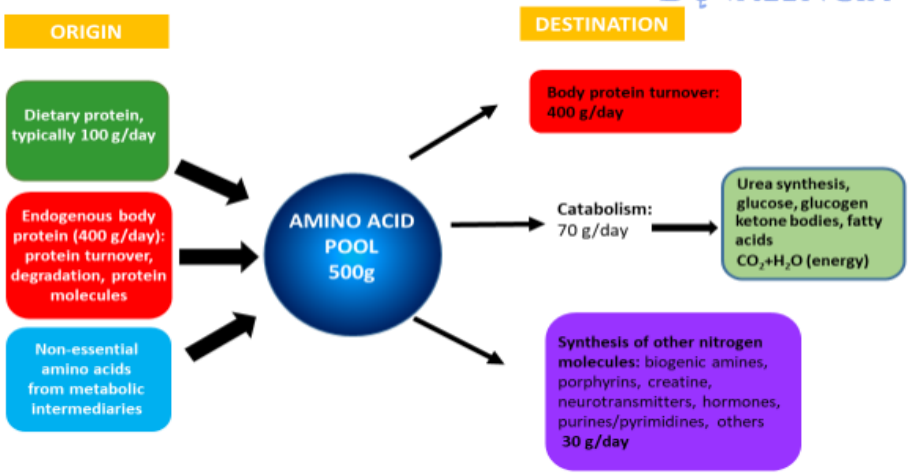
ORIGIN AND DESTINATION OF AMINO ACIDS



Proteins are degraded to amino acids

Dietary protein is digested in the intestine thanks to activated zymogens, exopeptidases and endopeptidases to produce amino acids that are absorbed in enterocytes and transported throughout the body.
Essential amino acids can only be incorporated through diet.

Protein turnover is tightly regulated

The turnover of cellular proteins is a regulated process that requires complex enzyme systems.
Cellular proteins are degraded at widely variable rates, ranging from minutes to the life of the organism.
In the main, proteins to be degraded are conjugated with ubiquitin, a small conserved protein, in a reaction driven by ATP hydrolysis. The ubiquitin-conjugating system is made up of three distinct enzymes. A large, barrel-shaped complex called the proteasome digests the ubiquitinated proteins. The proteasome also requires ATP hydrolysis to function. The resulting amino acids provide a source of precursors for protein, nucleotide bases, and other nitrogenous compounds.

Amino acid biosynthesis

Non-essential amino acids can be synthesized in our body.
Ten out of 11 amino acids come directly from the glucose carbon chain.
Amino acids can be classified as essential, non-essential or conditionally essential.

Essential	Non-essential
Histidine (His)	Alanine (Ala)
Isoleucine (Ile)	Arginine (Arg)
Leucine (Leu)	Asparagine (Asn)
Lysine (Lys)	Aspartate (Asp)
Methionine (Met)	Cysteine (Cys)
Phenylalanine (Phe)	Glutamate (Glut)
Threonine (Thr)	Glutamine (Gln)
Tryptophan (Trp)	Glycine (Gly)
Valine (Val)	Proline (Pro)
	Serine (Ser)
	Tyrosine (Tyr)

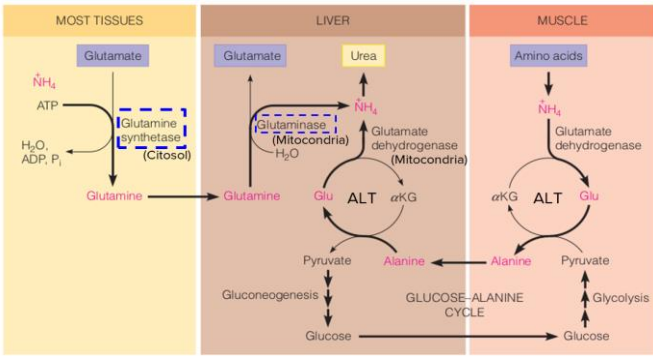
Amino acids as precursor of nitrogen biomolecules

In addition to their role as the building blocks of proteins, amino acids are precursors of many specialized biomolecules, including hormones, coenzymes, nucleotides, alkaloids, cell wall polymers, porphyrins, antibiotics, pigments, and neurotransmitters, e.g. catecholamines (adrenaline/noradrenaline/ dopamine).

2. GENERAL OVERVIEW OF THE METABOLISM OF AMINO ACIDS

CATABOLISM OF AMINO ACIDS

FATE OF AMMONIA AND THE UREA CYCLE



The first step in amino acid degradation is the removal of Nitrogen

The removal of α-amino groups is by transaminases to obtain α-ketoacids.

Most of the α-amino group funnels into α-ketoglutarate to form glutamate, which is then oxidatively deaminated by glutamate dehydrogenase to produce NH_4^+ and α-ketoglutarate.

This reaction takes place in the mitochondria from hepatocytes.

The amino group is transported to the liver from extra-hepatic tissues by glutamine or by alanine (glucose-alanine cycle) when they come from muscle.

Ammonium ion is converted into urea

The first step in the synthesis of urea is the formation of carbamoyl phosphate, which is synthesized from HCO_3^-, NH_3, and two molecules of ATP by carbamoyl phosphate synthetase (CPSI).

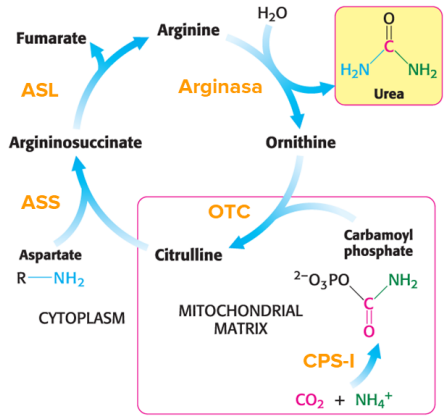
Ornithine is then carbamylated to citrulline by ornithine transcarbamylase (OTC).

These two reactions take place in the mitochondria.

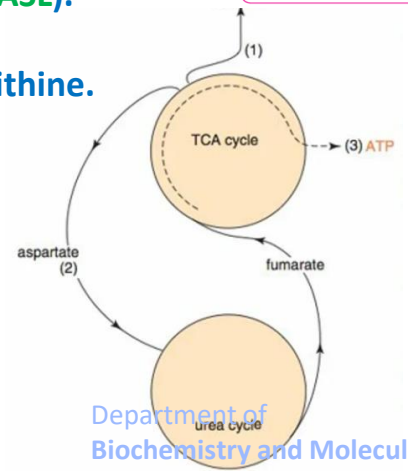
Citrulline leaves the mitochondrion and condenses with aspartate to form argininosuccinate in the cytosol, which is cleaved into arginine and fumarate (ASS, ASL).

The other nitrogen atom of urea comes from aspartate.

Urea is formed by the hydrolysis of arginine (Arginase), which also regenerates ornithine.



Fumarate released in urea cycle **interconnects** with the **Krebs cycle** and can produce glucose (1), aspartate (2) or energy (3).



Urea diffuses to the kidney and is excreted with urine, but in renal failure and other pathological situations, it increases in plasma to produce hyperammonemia.

2. GENERAL OVERVIEW OF THE METABOLISM OF AMINO ACIDS

CATABOLISM OF AMINO ACIDS

DESTINATION OF CARBON CHAINS

Carbon atoms of degraded amino acids emerge as major metabolic intermediates

The carbon atoms of degraded amino acids are converted into pyruvate, acetyl CoA, acetoacetate or an intermediate of the citric acid cycle.

Most amino acids are solely glycogenic, two are solely ketogenic, and five are both ketogenic and glycogenic.

Alanine, serine, cysteine, glycine, threonine, and tryptophan are degraded to pyruvate.

Asparagine and aspartate are converted into oxaloacetate.

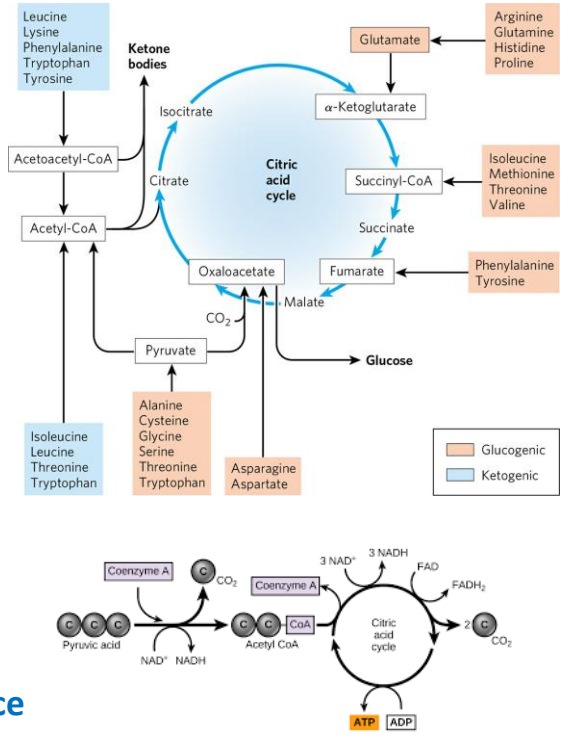
α-Ketoglutarate is the point of entry for glutamate and four amino acids (glutamine, histidine, proline, and arginine) that can be converted into glutamate.

Succinyl-CoA is the point of entry for some carbon atoms of three amino acids (methionine, isoleucine and valine) that are degraded through the intermediate methyl malonyl CoA.

Leucine is degraded to acetoacetate and acetyl-CoA while lysine is degraded only to acetoacetate.

Four carbon atoms of phenylalanine and tyrosine are converted into fumarate, while four emerge in acetoacetate.

These reactions take place in the liver, except for BCAA degradation, which takes place in the muscle. The breakdown of valine and isoleucine is like that of leucine (all three BCAA).



If amino acids are to convert in respiration fuel, their carbon skeletons must convert to acetyl-CoA, which will then enter the Krebs cycle for their complete oxidation, thus producing ATP.

3. IMPLICATIONS IN PATHOLOGICAL PROCESSES

INBORN DISEASES

- Most diseases are related to inborn errors of amino acid metabolism associated with:
- **Amino acid synthesis disruption or degradation**

Errors in amino acid metabolism were the sources of some of the first insights into the correlation between pathology and biochemistry.

Phenylketonuria is the best known of the many hereditary errors of amino acid metabolism. This condition results from the accumulation of high levels of phenylalanine in body fluids. This accumulation leads to mental retardation unless those afflicted are placed on low phenylalanine diets immediately after birth.

- **Urea cycle failure**

People with genetic defects in any enzyme involved in the urea cycle cannot tolerate protein-rich diets. The absence of one urea cycle enzyme can result in hyperammonemia or the buildup of one or more urea cycle intermediates depending on the enzyme that is missing.

- Very low incidence

NON-INBORN DISEASES

- are related mainly with protein turnover mechanisms such as in Parkinson's disease
- are related mainly with ammonia transport, which can be indicative of pathological processes.

Analysis of certain enzyme activities in serum provides information about diagnostic value for different pathological conditions. **Alanine aminotransferase** (**ALT**) and **aspartate aminotransferase** (**AAT**) are important in the diagnosis of heart and liver damage caused by heart attack, drug toxicity or infection.

3. IMPLICATIONS IN PATHOLOGICAL PROCESSES

INBORN DISEASES

Some human genetic disorders affecting amino acid metabolism are:

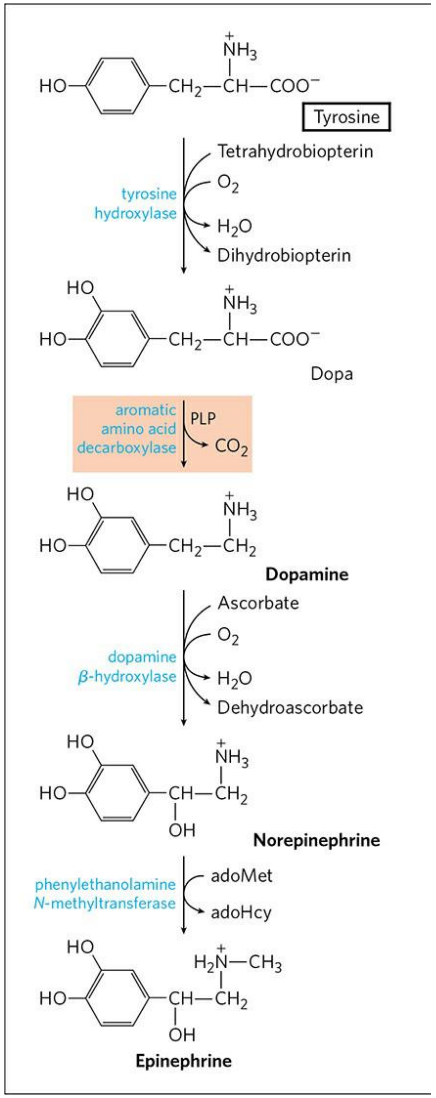
Medical condition	Approximate incidence (per 100,000 births)	Defective process	Defective enzyme
Albinism	<3	Melanin synthesis from tyrosine	Tyrosine 3-monooxygenase
Alkaptonuria	<0.4	Tyrosine	Homogentisate 1,2-dioxygenase degradation
Argininemia	<0.5	Urea synthesis	Arginase
Argininosuccinic acidemia	<1.5	Urea synthesis	Argininosuccinase
Carbamoyl Phosphate deficiency	<0.5	Urea synthesis	CPSI deficiency
Homocystinuria	<0.5	Methionine degradation	Cystathionine *β* synthase
Maple syrup urine disease	<0.4	BCAA degradation	Branched-chain keto acid urine disease dehydrogenase complex
Methylmalonic Acidemia	<0.5	Conversion of propionyl-CoA to succinyl-CoA	Methylmalonyl-CoA mutase
Phenylketonuria	<8	Conversion of phenylalanine to tyrosine	Phenylalanine hydroxylase

3. IMPLICATIONS IN PATHOLOGICAL PROCESSES

INBORN DISEASES

Related to Tyrosine

Phenylalanine can be hydroxylated to tyrosine, which is the precursor of:
(I) the pigment melanin
(II) the thyroid hormones thyroxine (T4) and triiodothyronine (T3)
(III) the catecholamines dopamine, noradrenaline and adrenaline
Any additional phenylalanine or tyrosine surplus to requirements for protein synthesis is oxidized to acetoacetate and fumarate.



Catecholamines

- **Dopamine**, **norepinephrine** (**NE, noradrenaline**) and **epinephrine** (**or adrenaline**) are biologically active amines. They come from **tyrosine** and are biogenic amines.
- **Dopamine** and **norepinephrine** are synthesized in the brain and act as neurotransmitters.
- **Adrenaline** is synthesized from **norepinephrine** in the suprarenal gland and is a hormone.

Functions:

- Catecholamines are vasoconstrictors in some tissues and vasodilators in others.
- They increase cardiac frequency or relax bronchial muscle.
- They stimulate glycogenolysis in muscle and lipolysis in adipose tissue.

3. IMPLICATIONS IN PATHOLOGICAL PROCESSES

INBORN DISEASES

Phenylketonuria (PKU)

-This is the most common inborn error of amino acid metabolism (incidence 1:15,000).
-Genetic defect of **phenylalanine hydroxylase** (phenylalanine monooxigenase). In 3% of cases the disorder is due to impaired synthesis of its coenzyme, tetrahydrobiopterin.

- **Phenylalanine** cannot metabolize to **tyrosine**

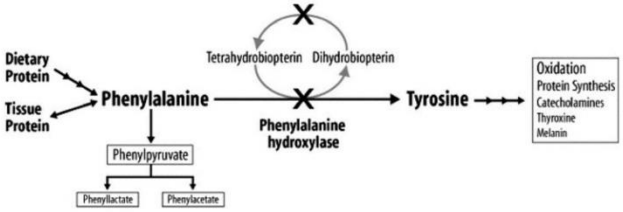
-**Accumulation of phenylalanine** (hyperphenylalaninemia, intellectual disability) and its metabolites: phenylpyruvate, phenyllactate and phenylacetate.

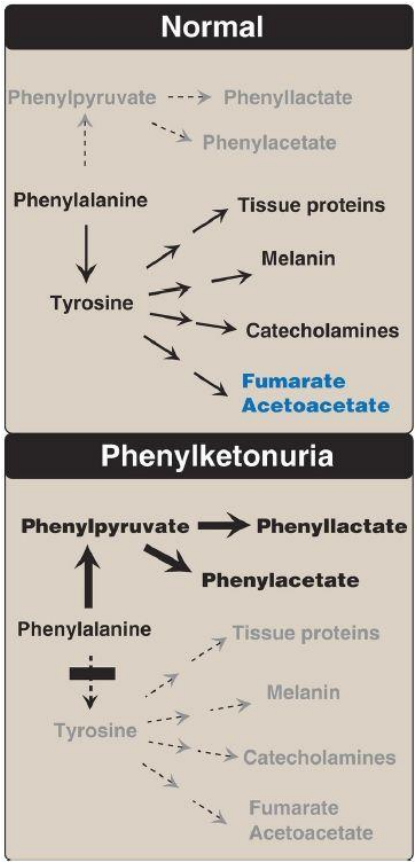
-**Tyrosine deficiency**: a defect in the synthesis of **catecholamines** (e.g. dopamine, adrenaline, noradrenaline and melanin)

-**Symptomatology**:
- Delayed mental development, low IQ
- Characteristic smell in the urine
- Early diagnosis (heel test)

-**Treatment**:
- **Restriction** of phenylalanine in the diet and supplements with tyrosine
- Phenylalanine ammonium lyase (oral/injection)

Phenylketonuria (PKU)





Harvey and Ferrier

3. IMPLICATIONS IN PATHOLOGICAL PROCESSES

INBORN DISEASES

Related to Tyrosine

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(II) the thyroid hormones thyroxine (T4) and triiodothyronine (T3).
(III) the catecholamines dopamine, noradrenaline and adrenaline.
Any additional phenylalanine or tyrosine surplus to requirement for protein synthesis is oxidized to acetoacetate and fumarate.

Albinism

Tyrosine is metabolized by tyrosinase in melanocytes to form the pigment melanin.
A deficiency of tyrosinase results in albinism.

Type-I tyrosinemia

Type-I Tyrosinemia is an autosomal recessive disease caused by a deficiency in fumarylacetoacetate hydrolase (FAH), the terminal enzyme of tyrosine metabolism.
This leads to the accumulation of toxic intermediates, particularly fumarylacetoacetate, which is an inhibitor of porphobilinogen synthase, which produces a characteristic cabbage odour in the urine.
The treatment of type-I tyrosinemia has been revolutionized by the use of NTBC.
Restriction of dietary phenylalanine and tyrosine is also necessary.

INBORN DISEASES

Related to Tyrosine

Alkaptonuria

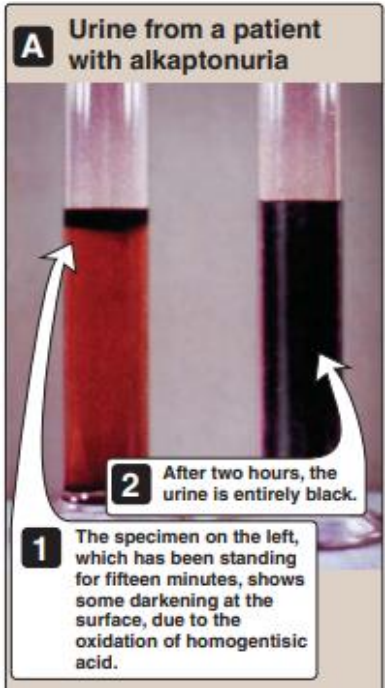
Alkaptonuria is a rare organic aciduria consisting of a lack of homogentisic acid oxidase (homogentisate 1,2-dioxygenase), which causes the accumulation of homogentisic acid (HA), an intermediate in the degradative pathway of tyrosine. This autosomal recessive condition provokes HA accumulation and is excreted in the urine where, under alkaline conditions, it can undergo oxidation and polymerization to form the black pigment alkapton.

Characteristic symptoms:

- **Homogentisic aciduria (urine contains high levels of HA, which oxidizes to a dark pigment when left to stand).**
- **The early onset of arthritis in the large joints.**
- **The deposit of a black pigment (ochronosis) in cartilage and collagenous tissue.**

Dark spots on nappies (diapers) may indicate disease in the infant but usually no symptoms are present until roughly 40 years of age.

Diets low in phenylalanine and tyrosine reduce HA levels. Although alkaptonuria is not fatal, associated arthritis can lead to severe disability.



Harvey and Ferrier

INBORN DISEASES

Maple syrup urine disease (EOOJA)

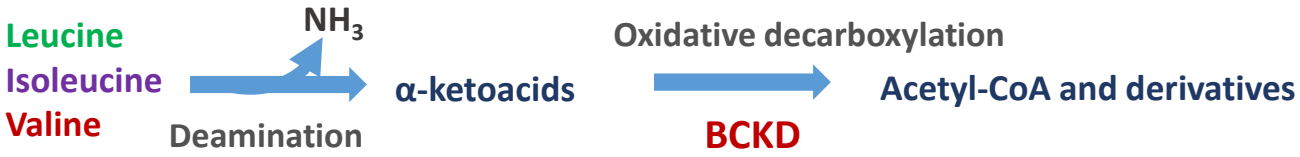
-Branched-chain amino acids (BCAA) are not degraded in the liver.

-This disease is caused by partial or total defect of the enzymatic complex BCKD (branched-chain α-ketoacid dehydrogenase).

-The mitochondrial enzymatic complex that oxidatively decarboxylates the branched-chain amino acids leucine, isoleucine and valine does not work properly.

-These BCAA and α-ketoacids get accumulated: brain toxicity, ketoacidosis, change in muscle tone, coma and sometimes death (due to leucine accumulation).

-In urine these compounds smell like maple syrup (due to isoleucine and α-ketoacids accumulation), hence the name of this condition.



Maple syrup urine disease

INBORN DISEASES

People with genetic defects in any enzyme involved in the urea cycle cannot tolerate protein-rich diets.

The absence of one urea cycle enzyme can result in hyperammonemia or the buildup of one or more urea cycle intermediates depending on the enzyme that is missing.

Since most urea cycle steps are irreversible, the absent enzyme activity can often be identified by determining which cycle intermediate is present at elevated concentration in the blood and/or urine.

Although the breakdown of amino acids can have serious health consequences in individuals with urea cycle deficiencies, a protein-free diet is not a treatment option. Humans are unable to synthesize half of the 20 common amino acids, so these essential amino acids must be provided by the diet.

Genetic defects in the urea cycle can be life-threatening

TABLE 18-1 Nonessential and Essential Amino Acids for Humans and the Albino Rat

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

[a] Required to some degree in young, growing animals and/or sometim during illness.

Lehninger

3. IMPLICATIONS IN PATHOLOGICAL PROCESSES

INBORN DISEASES

Some of the most common individual disorders are:

- **N-Acetylglutamate synthetase (NAGS) deficiency**
- **Carbamoyl phosphate synthetase (CPS) deficiency**
- **Ornithine transcarbamoylase (OTC) deficiency**
- **Citrullinemia type-I (deficiency of argininosuccinic acid synthetase)**
- **Argininosuccinic aciduria (deficiency of argininosuccinic acid lyase)**
- **Argininemia (deficiency of arginase)**
- **Hyperornithinemoa, hyperammonemia, homocitrullinaria (HHH) syndrome (deficiency of the mitochondrial ornithine transporter)**

All urea cycle defects, except OTC deficiency, are inherited in an autosomal recessive manner. OTC deficiency is inherited as an X-linked recessive disorder. Affected boys therefore develop severe hyperammonemia, which often leads to early death. In heterozygous girls, the condition can vary from being undetectable to a severity equal to that in boys. Most urea cycle disorders are associated with hyperammonemia. However, argininemia and some forms of argininosuccinic aciduria do not present with elevated ammonia.

NON-INBORN DISEASES

Parkinson's disease

This disease, which usually develops from age 60 onwards, is caused by the destruction of the brain region known as *substantia nigra*, which produces the neurotransmitter dopamine.
In this process, the lysosome-dependent autophagy degradation pathway (protein turnover) is one of those dysregulated.
The symptoms of Parkinson's disease include shakes, muscular rigidity and akinesia.
Treatment: dopamine precursor L-DOPA decarboxylase Inhibitor.

Pheochromocytoma

This rare condition is usually caused by a tumour in the adrenal medulla, which produces excessive amounts of the catecholamines adrenaline and noradrenaline. If the tumour releases a surge of catecholamines, patients suffer a hypertensive attack associated with severe headaches, sweating, palpitations, anxiety, glucosuria and, if adrenaline predominates, tachycardia.
The tumour can be surgically removed after the administration of adrenergic blockers.

Neuroblastoma

This rare tumour usually presents in children under 5 years of age and 70% have metastatic disease at diagnosis.
Urine diagnosis.

Dopamine and mental illness

The "Dopamine Hypothesis" for schizophrenia postulates increased brain dopaminergic activity. Although several research approaches suggest an association between psychosis and altered dopaminergic transmissions, the evidence is not conclusive. The *COMT* gene is receiving special attention as a candidate risk factor for schizophrenia.

NON-INBORN DISEASES

Analysis of certain enzyme activities in serum provides information on diagnostic value for different pathological conditions.

Alanine aminotransferase (ALT, also called glutamate-pyruvate transaminase, GPT) and aspartate aminotransferase (AAT, also called glutamate-oxaloacetate transaminase, GOT) are important in the diagnosis of heart and liver damage caused by heart attack, drug toxicity or infection.