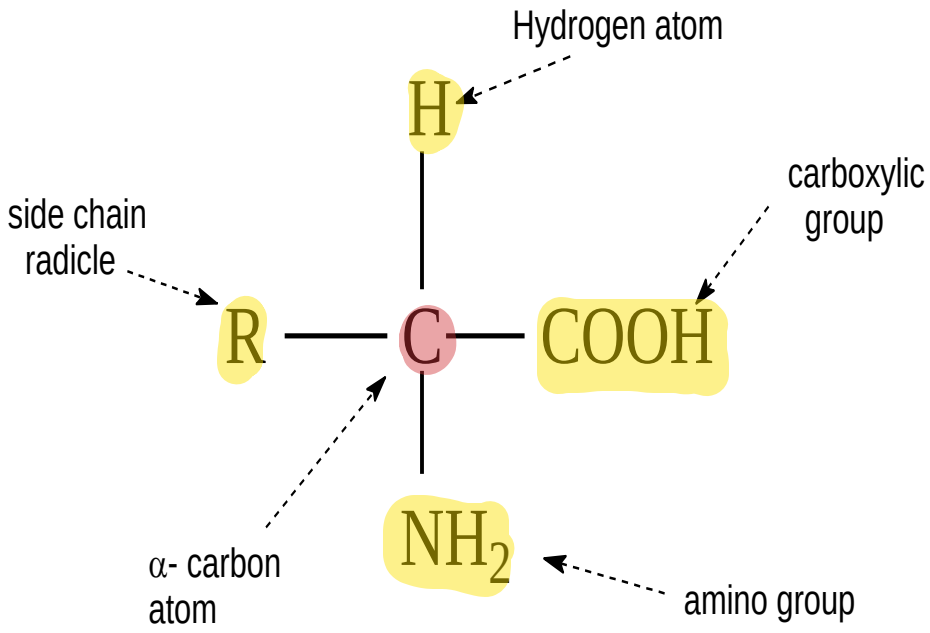
# Protein metabolism

# Proteins

- **Nitrogen** is a characteristic component of proteins forming about ***16%*** of their weight i.e. 100 g of protein contains 16 g of nitrogen.
- Proteins are not stored in body as such
  ← ما بخزن بروتينات بالجسم
- Amino acids are degraded by deamination to ammonia and α-ketoacid
  ← بنزع الأمين
- Ammonia is used to produce urea and excreted in urine → just in liver
- α-ketoacid can be metabolized to $CO_2$ and water, glucose, fatty acid or ketone bodies

- L-a-Amino acids are the structural or the building units of proteins

- The common amino acids have the general structure depicted in the following figure:




**Representation of α Amino Acid**

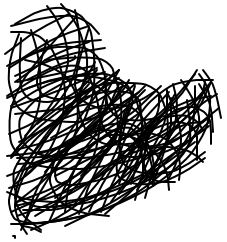
# Abbreviations for the 20 Amino Acids

| Amino Acid | Abbreviation | | Amino Acid | Abbreviation | |
|---|---|---|---|---|---|
| | Three letter | One letter | | Three letter | One letter |
| Alanine | ***Ala*** | **A** | Leucine | ***Leu*** | **L** |
| Arginine | ***Arg*** | **R** | Lysine | ***Lys*** | **K** |
| Asparagine | ***Asn*** | **N** | Methionine | ***Met*** | **M** |
| Aspartic acid | ***Asp*** | **D** | Phenylalanine | ***Phe*** | **F** |
| Cysteine | ***Cys*** | **C** | Proline | ***Pro*** | **P** |
| Glycine | ***Gly*** | **G** | Serine | ***Ser*** | **S** |
| Glutamine | ***Gln*** | **Q** | Threonine | ***Thr*** | **T** |
| Glutamic acid | ***Glu*** | **E** | Tryptophan | ***Trp*** | **W** |
| Histidine | ***His*** | **H** | Tyrosine | ***Tyr*** | **Y** |
| Isoleucine | ***Ile*** | **I** | Valine | ***Val*** | **V** |

# Metabolic Classification of Amino Acids

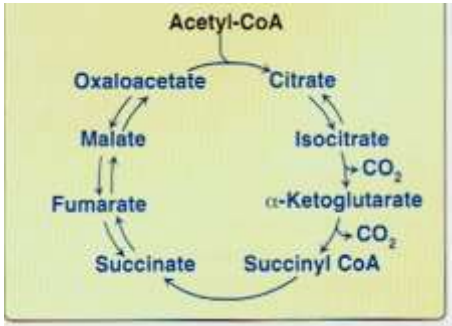
**Glucogenic amino acids:** → convert to glucose
AA that can yield pyruvate, oxaloacetate, α-ketoglutarate Succinyl-CoA, fumarate

**Ketogenic amino acids:** → convert to Ketone body
AA that can form acetyl-coA, acetoacetyl CoA or β-hydroxybutyrate.



| | Glucogenic | Glucogenic and Ketogenic | Ketogenic |
|---|---|---|---|
| Nonessential | Alanine<br>Arginine<br>Asparagine<br>Aspartate<br>Cysteine<br>Glutamate<br>Glutamine<br>Glycine<br>Proline<br>Serine<br>GPS | Tyrosine | |
| Essential | Histidine<br>Methionine<br>Threonine<br>Valine | Isoleucine<br>Phenyl-alanine<br>Tryptophan | Leucine<br>Lysine |

# Glucogenic and ketogenic amino acids




Alanine
Cysteine
Glycine
Serine
Threonine
Tryptophan

Isoleucine
Leucine
Tryptophan

Leucine
Lysine
Phenylalanine
Tryptophan
Tyrosine

Glucose

Phosphoenol-pyruvate

Pyruvate

Acetyl CoA ⇌ Acetoacetyl CoA

Asparagine
Aspartate

Oxaloacetate

Aspartate
Phenylalanine
Tyrosine

Fumarate

Citrate

Isoleucine
Methionine
Threonine
Valine

Succinyl CoA

α-Keto-glutarate

Arginine
Glutamate
Glutamine
Histidine
Proline

# Amino acid metabolism

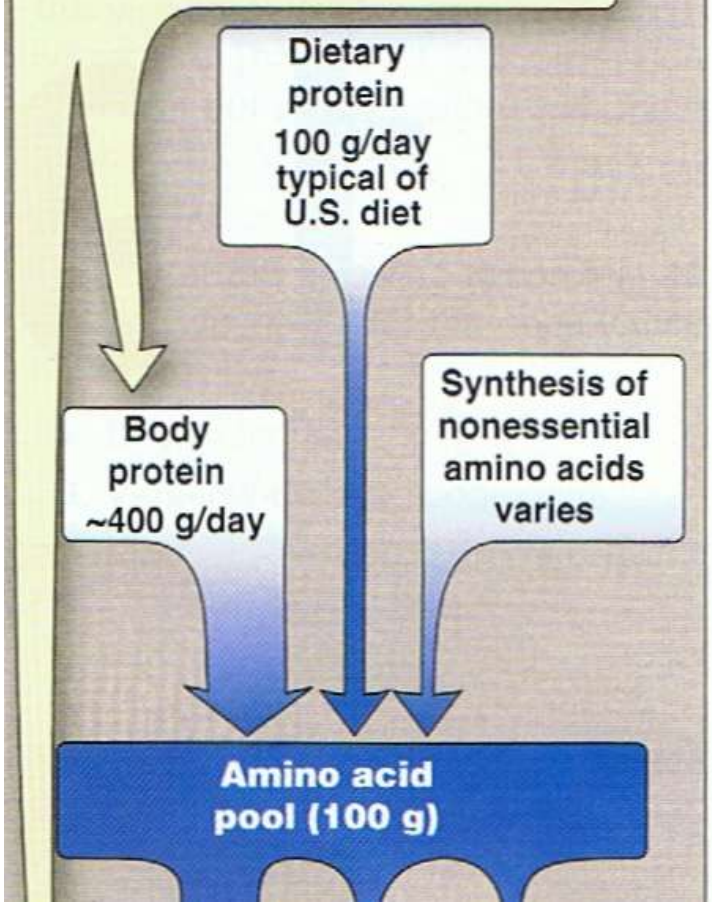
- Amino acid pool: مخزون
  - There is about 12 kg of protein in 70 kg man
  - 75% of aa are used in synthesis of new tissue proteins
  - The remainder is used as precursor for synthesis of many substances → such as neurotransmitter
- Protein turnover: → aa تفكيك البروتينات القديمة والتالفة ب
  - Proteins are constantly degraded and synthesized which is regulated by the concentration of protein in the cell
  - 300-400 g of proteins are hydrolyzed and resynthesized/day
  - Protein turnover varies: short lived (regulatory and misfolded proteins), long-lived (most of tissue proteins) and structurally stable (collagen)

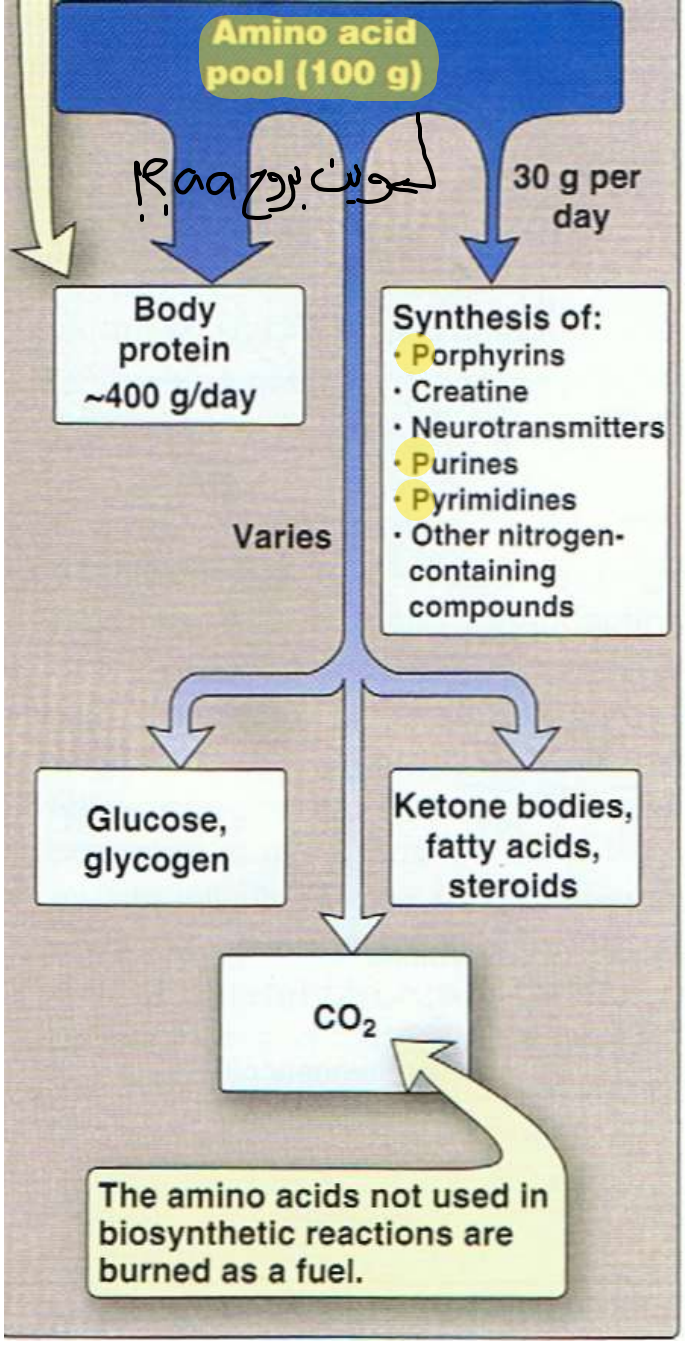
← بروتينات مطوية بشكل خاطئ

## TURNOVER

Protein turnover results from the simultaneous synthesis and degradation of protein molecules. In healthy adults, the total amount of protein in the body remains constant because the rate of protein synthesis is just sufficient to replace the protein that is degraded.

→ degradation = synthase



# Nitrogen Balance

- **Positive Nitrogen Balance means N2 intake is more than N2 output:**

  لما في حالة بناء أنسجة جديدة

- This exists when intake of N2 exceeds the output. It occurs whenever new tissues are being built up for example:

1- During growth (growing children).
2- Pregnancy.
3- Muscular training. → بناء عضلات
4- Convulsions from different diseases.

# Nitrogen Balance

**B. Negative Nitrogen Balance: $N_2$ Output is more than N2 intake:**

- It occurs in cases of :

  **1- Decreased protein intake:** e.g. starvation, malnutrition and G.I.T. diseases.

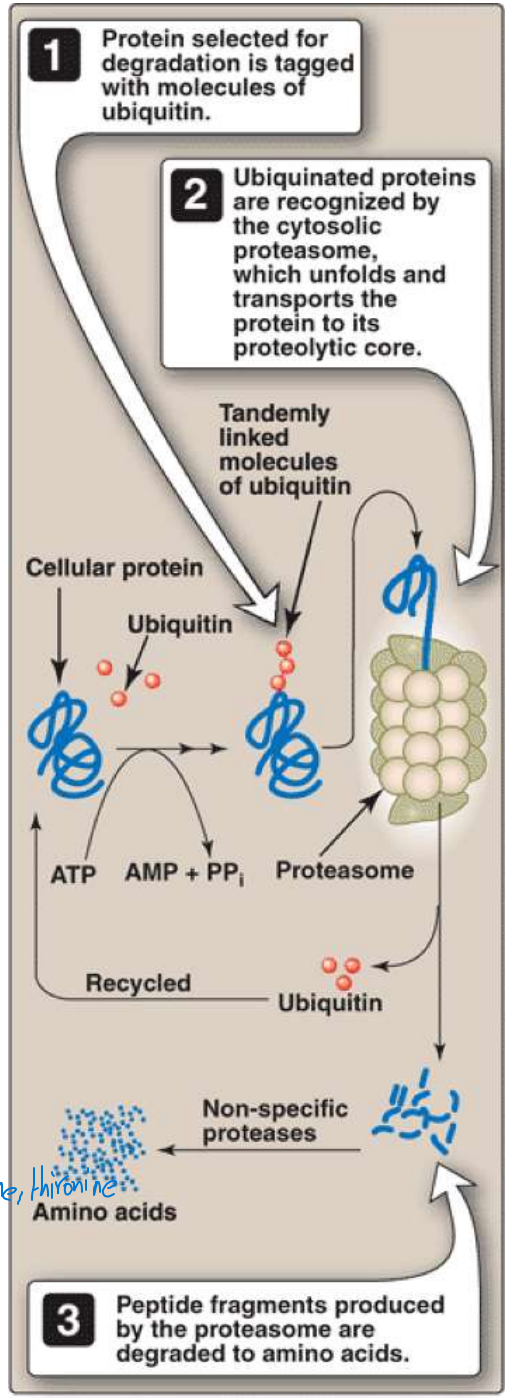
  **2- Increased Loss of proteins:** e.g. in chronic hemorrhage, albuminuria and Lactation on an inadequate protein diet.

  **3- Increased of protein catabolism:** e.g. fever, hyperthyroidism, diabetes mellitus, Cushing syndrome, advanced cancer and post-surgical.

- Prolonged periods of negative nitrogen balance are dangerous and may lead to death.

# Protein metabolism

- Protein degradation occurs by:
  - energy dependent ubiquitin-protesome mechanism (endogenous proteins)
  - non-energy dependent lysosomes (extracellular protein)
- Oxidized or ubiquitin tagged proteins are preferentially degraded
- Certain aa sequences:
  - Serine (S)at N-terminal: long t1/2 (>20 hr)
  - Aspartate (D) at N-terminal: short t1/2 (3 min)
  - Proteins rich in the sequence (PEST) are rapidly degraded → half life short



# Digestion of proteins

→ as injection in blood

- protein is antigenic i.e. able to stimulate an immunologic response. The digestion of protein destroys its antigenicity. So, proteins must be digested into amino acids:

**1) In the stomach :**

**A- gastric acid: denature the protein** → at low ph

**B- Pepsin: is the major proteolytic enzyme in the stomach :**

← هو أول إنزيم يبلش هضم/تحليم البروتين

- Pepsin is produced and secreted by the chief cells of the stomach as the inactive zymogen, pepsinogen, which activated by HCl produced by parietal cells of stomach.
  ↳ increase secretion when eat
- Pepsin catalyzes the cleavage of proteins into smaller polypeptides.

**2) in small intestine:** large polypeptides are further cleaved to oligopeptides and amino acids by a group of pancreatic proteases.

Each of these enzymes has a different specificity (trypsin cleaves only at C-terminal of arginine or lysine).

Activation of zymogens: Enteropeptidase converts the pancreatic trypsinogen to trypsin which starts a cascade of proteolytic activity, because trypsin is the activator of all the pancreatic zymogens

← بيفعل تنشيط لباقي انزيمات pancreas

# Digestion of proteins

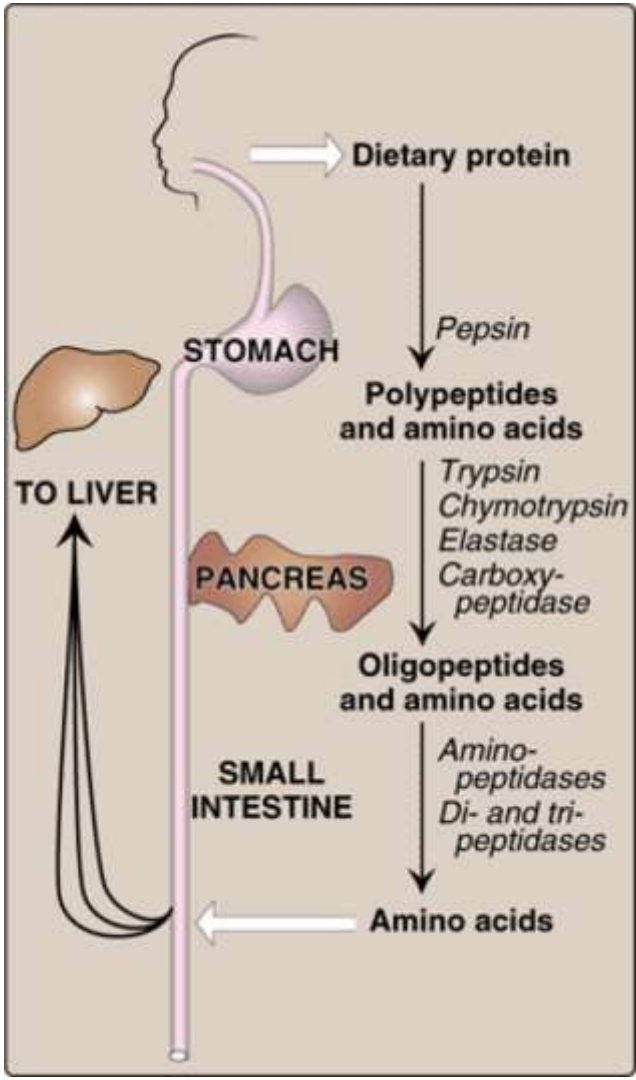
**Abnormalities in protein digestion**:

- In individuals with a deficiency in pancreatic secretion (chronic pancreatitis, cystic fibrosis, or surgical removal of the pancreas), the digestion and absorption of fat and protein is incomplete.
- This results in the abnormal appearance of lipids (Steatorrhea) and undigested protein in the feces.

العلاج بكون عن طريق كبسولة مغلفة/محاطة بخشاء بذوب في الامعاء الدقيقة (ph=7) ← فيها إنزيمات

**Digestion of oligopeptides by enzymes of the small intestine**

- The luminal surface of the intestine contains **aminopeptidase** (an exopeptidase that repeatedly cleaves the N-terminal residue of oligopeptides to produce free amino acids and smaller peptides.



# Absorption of amino acids and dipeptides

→ absorption by carrier

- Free amino acids and dipeptides are taken up by the intestinal epithelial cells. → monopeptide

- the dipeptides are hydrolyzed in the cytosol to amino acids before being released into the portal system (only free amino acids are found in the portal vein)

- The absorption of amino acid is active process that needs energy (ATP).

↳ active transport

# Transport of aa to the cells

- Amino acids are transported to the cells by active transport systems, driven by the hydrolysis of ATP
- At least seven different transport systems are known that have overlapping specificities for different amino acids.
- For example, one transport system is responsible for reabsorption of the amino acids cystine, ornithine, arginine, and lysine in kidney tubules.

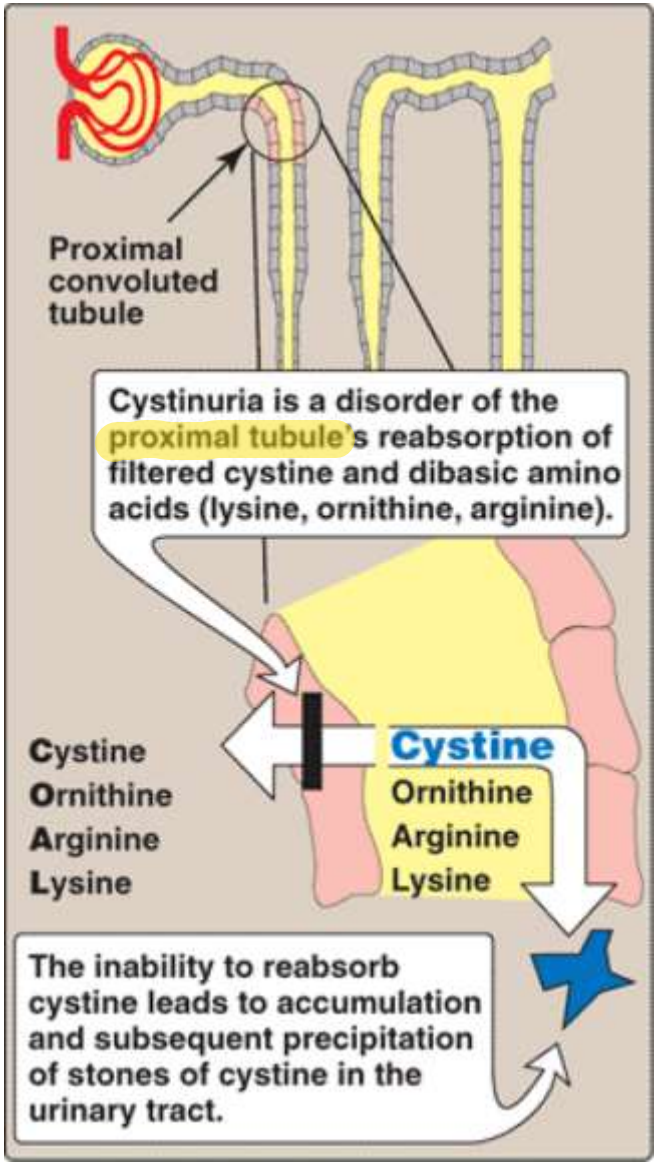
↳ low solubility → accumilation → حصى في الكلى → العلاج شرب ماي كثير

active transport → need ATP

# Cystinuria

- In the inherited disorder **cystinuria**, this carrier system is defective, resulting in the appearance of all four amino acids in the urine.
- Cystinuria is the most common genetic error of amino acid transport.
- The disease expresses itself clinically by the precipitation of cystine to form kidney stones (calculi) that may block the urinary tract.
- Oral hydration is important in treatment for this disorder

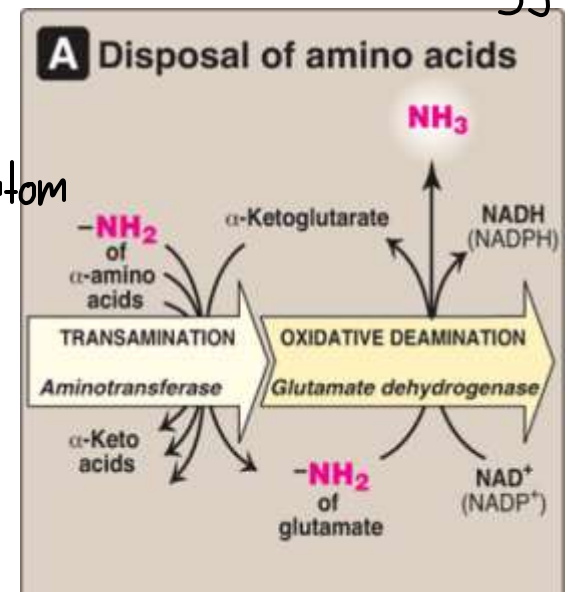
اشرب ماء

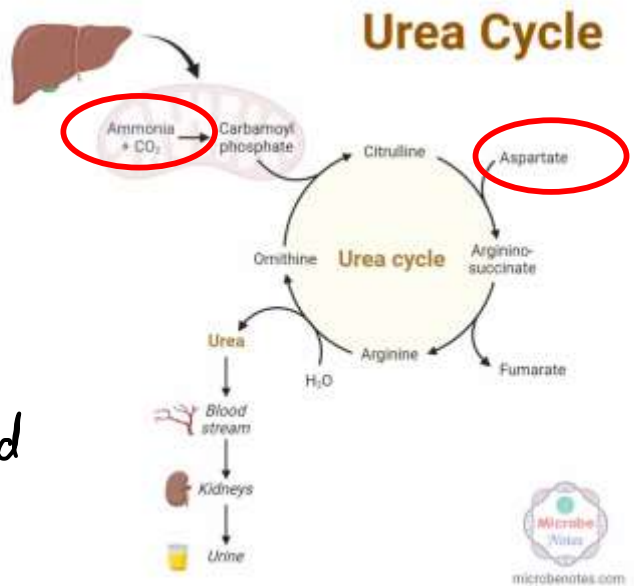


# Metabolism of amino acids → as source of energy

↳ inside the cells

1. Transamination (by aminotransferases) → removal of nitrogen atom from amino acid
2. Oxidative deamination of amino acids → removal of nitrogen from aa ($NH_3$)
3. Transport of ammonia from tissues to the liver and hyperammonimeia
4. Urea cycle. → ammonia convert to urea and excretion in urine



# Transamination and oxidative deamination: removal of nitrogen from aa

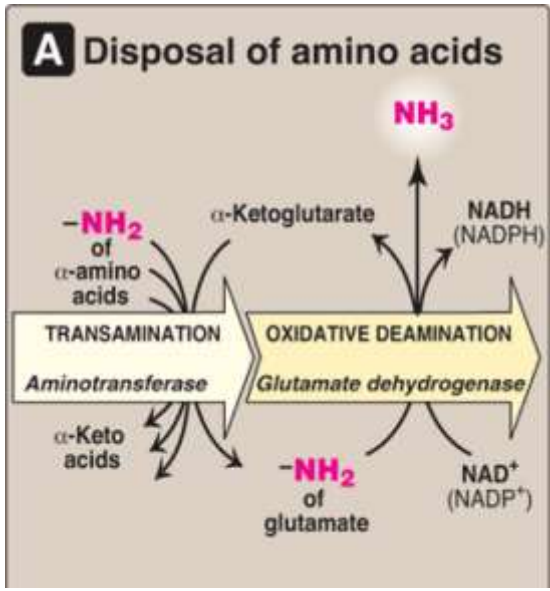
- Removing the α-amino group is essential for producing energy from any amino acid

Urea

- Transamination and oxidative deamination reactions which provide ammonia and aspartate, the two sources of urea nitrogen

- The first step is transfer their α-amino group to α-ketoglutarate to produce an α-ketoacid and glutamate.

- Glutamate produced by transamination can be oxidatively deaminated or used as an amino group donor in the synthesis of nonessential amino acids.



# A) Transamination → in cytosole

- The transfer of amino groups from one carbon skeleton to another is catalyzed by a family of enzymes called **aminotransferases**.
- These enzymes are found in the cytosol of cells throughout the body (especially the liver, kidney, intestine, and muscle).
- All amino acids (except lysine and threonine) participate in transamination at some point in their catabolism.
- Lysine and threonine lose their α-amino groups by deamination

لذ يجن

(Transamination) ← عبارة عن باقي من

# Aminotransferases

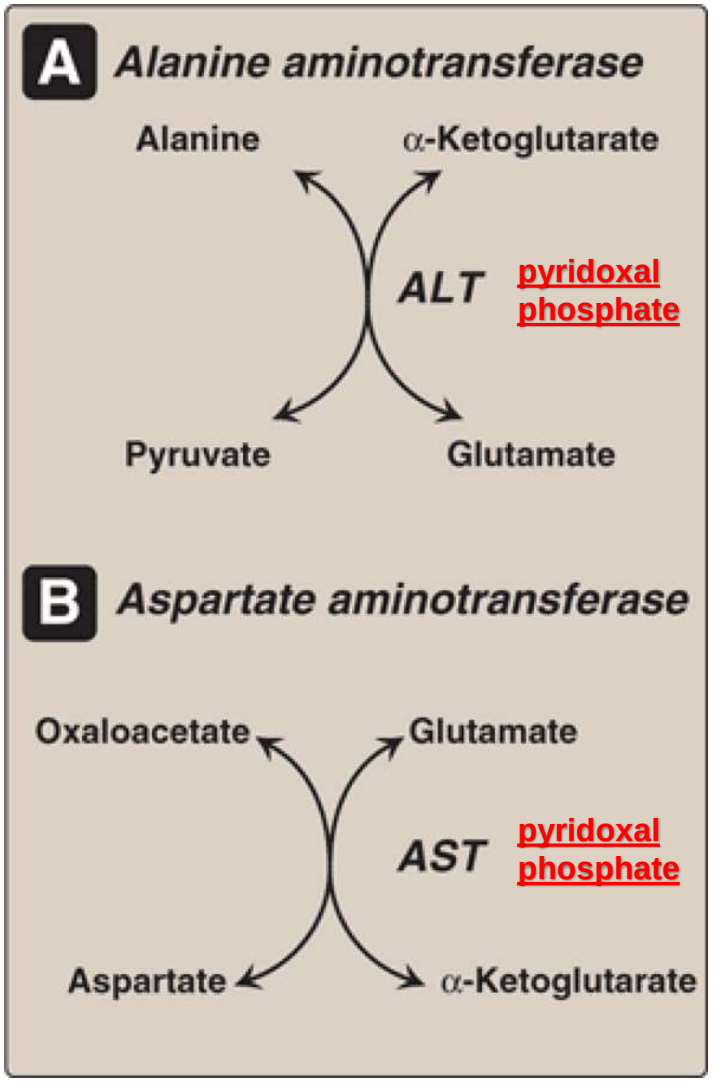
- Each aminotransferase is specific for one or, at most, a few amino group donors and named after that enzyme

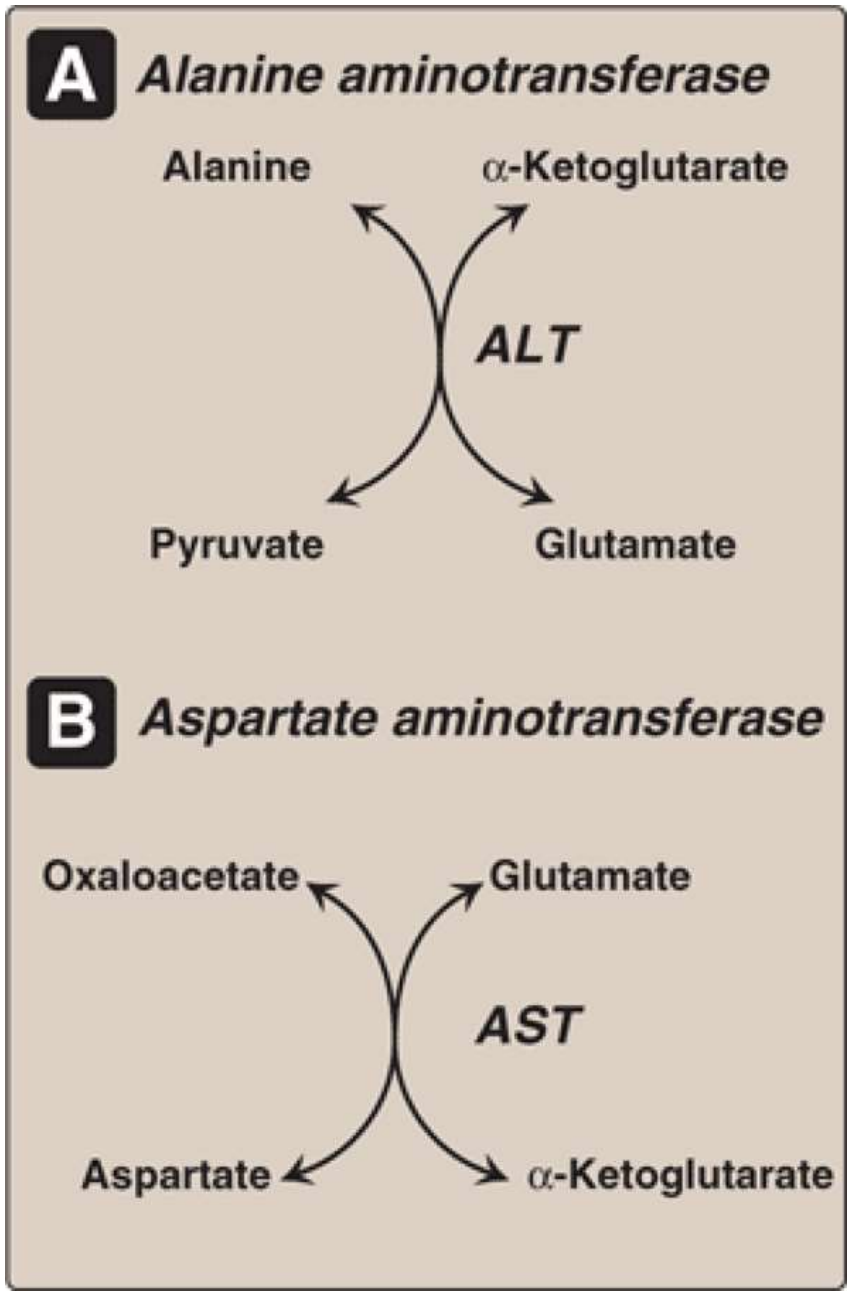
لـ متخصصة لناقل أو تلين والتسمية حسب الأب بجنح الأمين

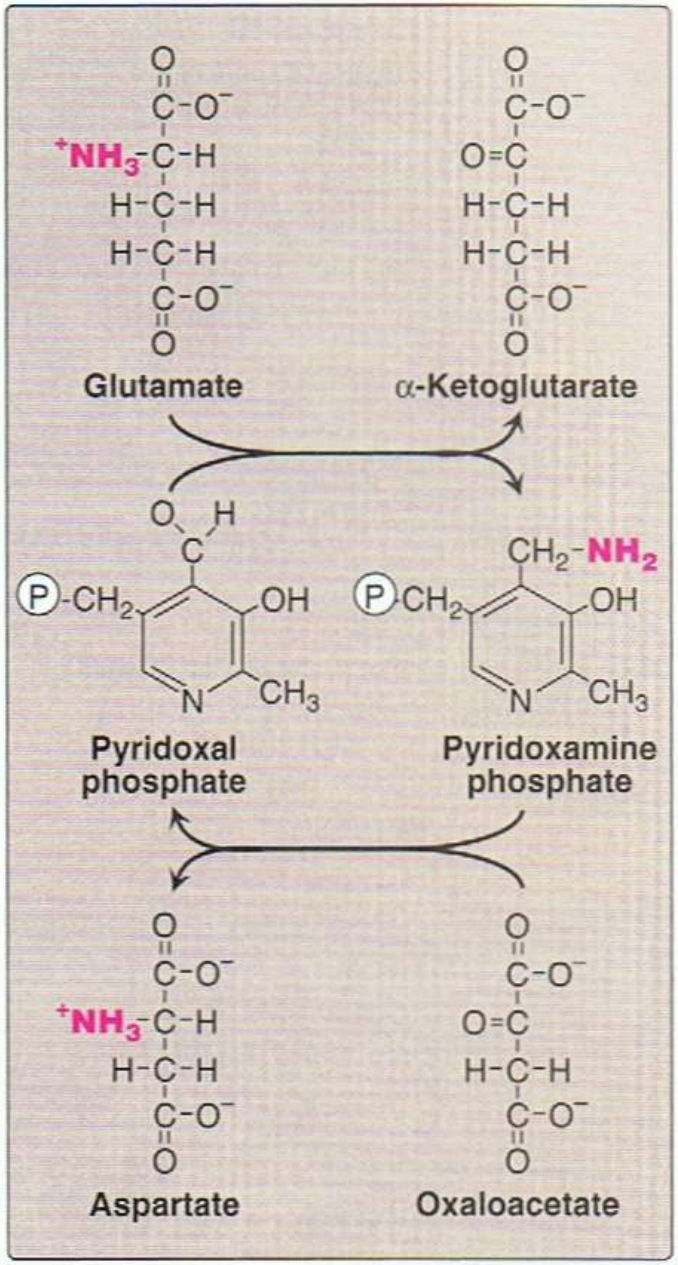
- Alanine aminotransferase (ALT): enzyme catalyzes (reversibly) the transfer of the amino group of alanine to α-ketoglutarate, resulting in the formation of pyruvate and glutamate.

- Aspartate aminotransferase (AST) is During amino acid catabolism, AST transfers amino groups from glutamate to oxaloacetate, forming aspartate, which is used as a source of nitrogen in the urea cycle

- All aminotransferases require the coenzyme **pyridoxal phosphate (vitamin B6)**




A
Alanine aminotransferase
Alanine
α-Ketoglutarate
ALT
Pyruvate
Glutamate
B
Aspartate aminotransferase
Oxaloacetate
Glutamate
AST
Aspartate
α-Ketoglutarate


Glutamate
α-Ketoglutarate
Pyridoxal phosphate
Pyridoxamine phosphate
Aspartate
Oxaloacetate

# Diagnostic value of plasma aminotransferases

- Aminotransferases are normally intracellular enzymes, (low levels in the plasma)

- The presence of elevated plasma levels of aminotransferases indicates damage to cells rich in these enzymes. Two aminotransferases (AST and ALT) are of particular diagnostic value when they are found in the plasma.

a. hepatic disease: Plasma AST and ALT are elevated in nearly all liver diseases, specially in extensive cell necrosis (severe viral hepatitis, toxic injury, and prolonged circulatory collapse).

Elevated serum bilirubin results from hepatocellular damage that decreases the hepatic conjugation and excretion of bilirubin

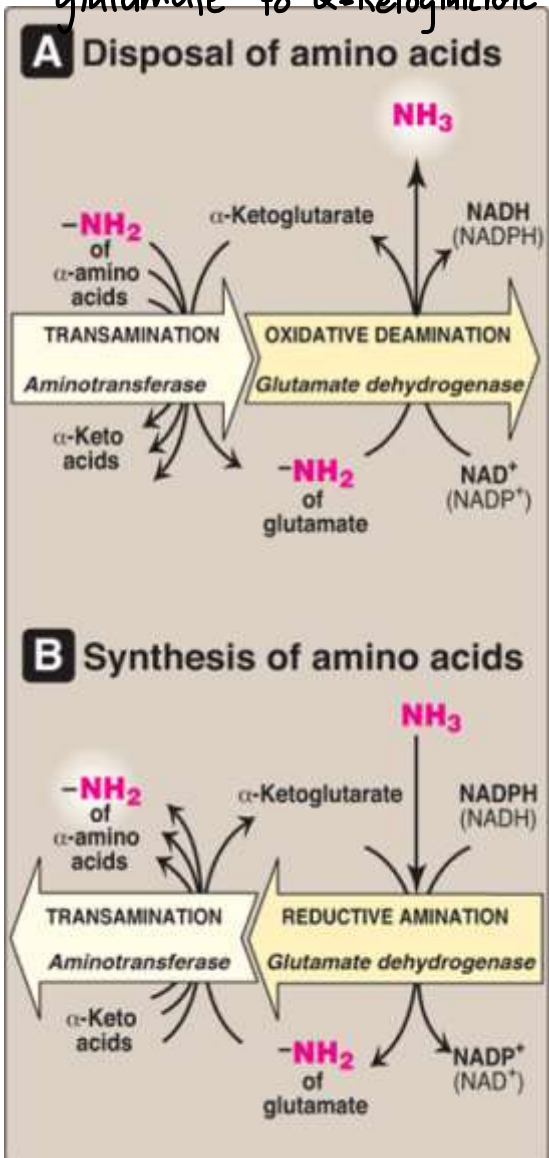
b. Nonhepatic disease: Aminotransferases may be elevated in nonhepatic disease (myocardial infarction and muscle disorders) but those can be clinically distinguished.

# B) Oxidative deamination of amino acids

## Glutamate Dehydrogenase → deamination for glutamate to α-Ketoglutarate

- It is the transfer amino groups from glutamate, oxidative deamination, by glutamate dehydrogenase results in the liberation of the amino group as free ammonia.
- occur primarily in the liver and kidney.
- Glutamate is unique in that it is the only amino acid that undergoes rapid oxidative deamination
- Glutamate dehydrogenase can use either NAD or NADP as a coenzyme. NAD is used primarily in oxidative deamination and NADPH is used in reductive amination

urea cycle just in liver



# Glutamate dehydrogenase

- The direction of the reaction depends on the relative concentrations of glutamate, α-ketoglutarate. and ammonia, and the ratio of oxidized to reduced coenzymes.
- After ingestion of a meal containing protein, glutamate levels in the liver are elevated and enhance amino acid degradation and the formation of ammonia
- The reaction can also be used to synthesize amino acids from the corresponding α-ketoacids
- ATP and GTP are allosteric inhibitors of glutamate dehydrogenase, whereas ADP and GDP are activators of the enzyme.

كل اللي أخذناهم فوق عبارة عن L-amino acid

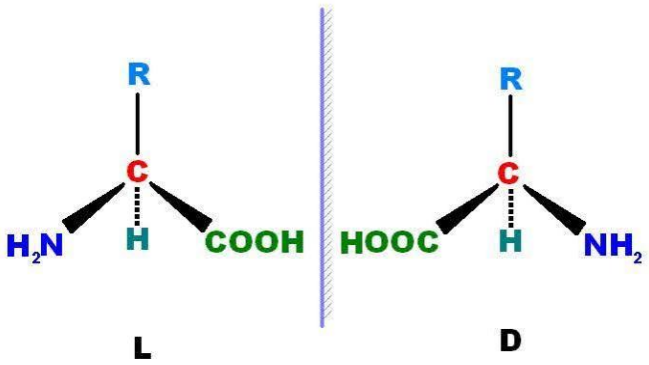
# D-Amino acid oxidase

L→deamination for D-amino acid

- D-Amino acids are present in the diet, and are efficiently metabolized by the liver using D-Amino acid oxidase (FAD-dependent enzyme) that catalyzes the oxidative deamination of these amino acid isomers.

→from deamenation D-amino acid

- The resulting α-ketoacids can enter the general pathways of amino acid metabolism, and be reaminated to L-isomers, or catabalized for energy.



# C) Transport of ammonia from tissues to the liver

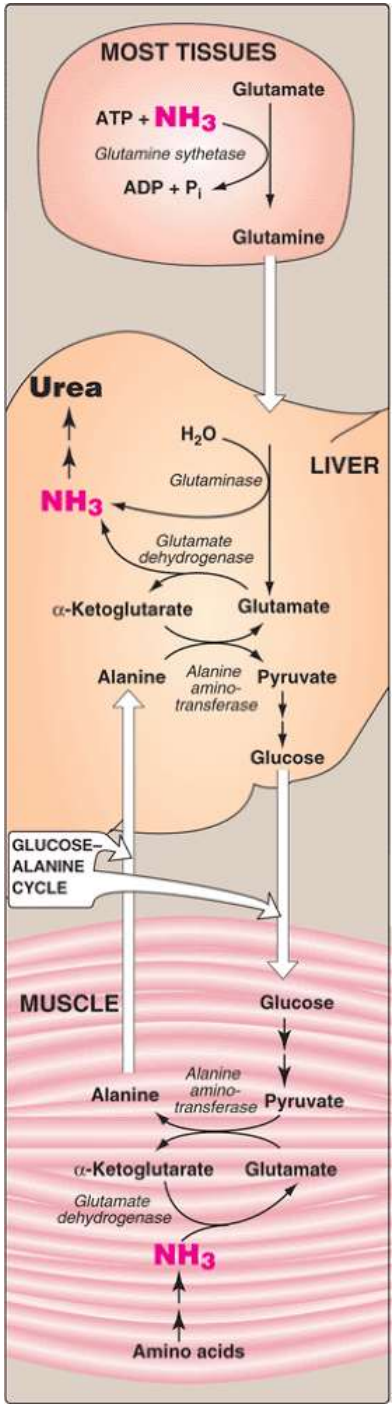
There are two mechanisms:

- found in most tissues, uses glutamine synthetase to combine ammonia with glutamate to form glutamine (a nontoxic transport form of ammonia)

The glutamine is transported in the blood to the liver where is cleaved by glutaminase to produce glutamate and free ammonia

- used primarily by muscle, involves transamination of pyruvate (the end-product of aerobic glycolysis) to form alanine

Alanine is transported by the blood to the liver, where it is converted to pyruvate, again by transamination (pyruvate is used in gluconeogenesis). This pathway called the **glucose-alanine cycle**.



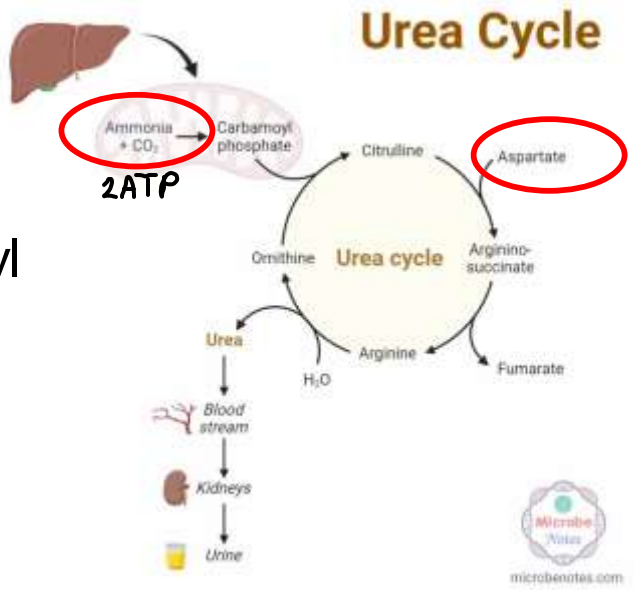
# D) UREA CYCLE → in mitochondria and cytosole

→ $NH_2-\overset{\overset{O}{\|}}{C}-NH_2$

- Urea is the major disposal form of amino groups derived from amino acids (90% of the nitrogen-containing components of urine).

- One nitrogen of the urea molecule is supplied by free NH3, and the other nitrogen by aspartate, the carbon and oxygen of urea are derived from CO2. → from metabolism process

- Urea is produced by the liver, and then is transported in the blood to the kidneys for excretion in the urine. by Kidney




- Reactions of the cycle:

1. Formation of carbamoyl phosphate by carbamoyl phosphate synthetase I which requires 2 ATP. N-acetylglutamate is required as allosteric activator

# UREA CYCLE

ما بدخلوا بتصنيع البروتينات

2. Formation of citrulline: (Ornithine and citrulline) are basic amino acids that participate in the urea cycle (But not into cellular proteins, no codons). citrulline is transported to the cytosol. → just in urea cycle

→ = N with aspartate

3. Citrulline condenses with aspartate to form argininosuccinate. The α-amino group of aspartate provides the second nitrogen that is ultimately incorporated into urea, which is driven by the cleavage of ATP to AMP and pyrophosphate (PPi).

→ by lyase enzyme

4. Argininosuccinate is cleaved to yield arginine and fumarate. The arginine formed by this reaction serves as the immediate precursor of urea. Fumarate can reenter the TCA cycle

→ just in liver

5. Cleavage of arginine to ornithine and urea by **arginase**

occurs almost exclusively in the liver, whereas other tissues (kidney), can synthesize arginine by these reactions

# UREA CYCLE

6. Fate of urea: Urea diffuses from the liver, and is transported in the blood to the kidneys, where it is filtered and excreted in the urine.

A portion of the urea diffuses from the blood into the intestine, and is cleaved to CO2 and NH3 by bacterial urease. This ammonia is partly lost in the feces and is partly reabsorbed into the blood.

In patients with kidney failure, plasma urea levels are elevated (hyperammonemia), promoting a greater transfer of urea from blood into the gut.

Oral administration of **neomycin** reduces the number of intestinal bacteria responsible for this $NH_3$ production.

# Overall stoichiometry of the urea cycle

Aspartate + $NH_3$ + $CO_2$ + 3ATP ⟶ Urea + fumarate + 2ADP + AMP + 2 Pi +PPi + 3 $H_2O$

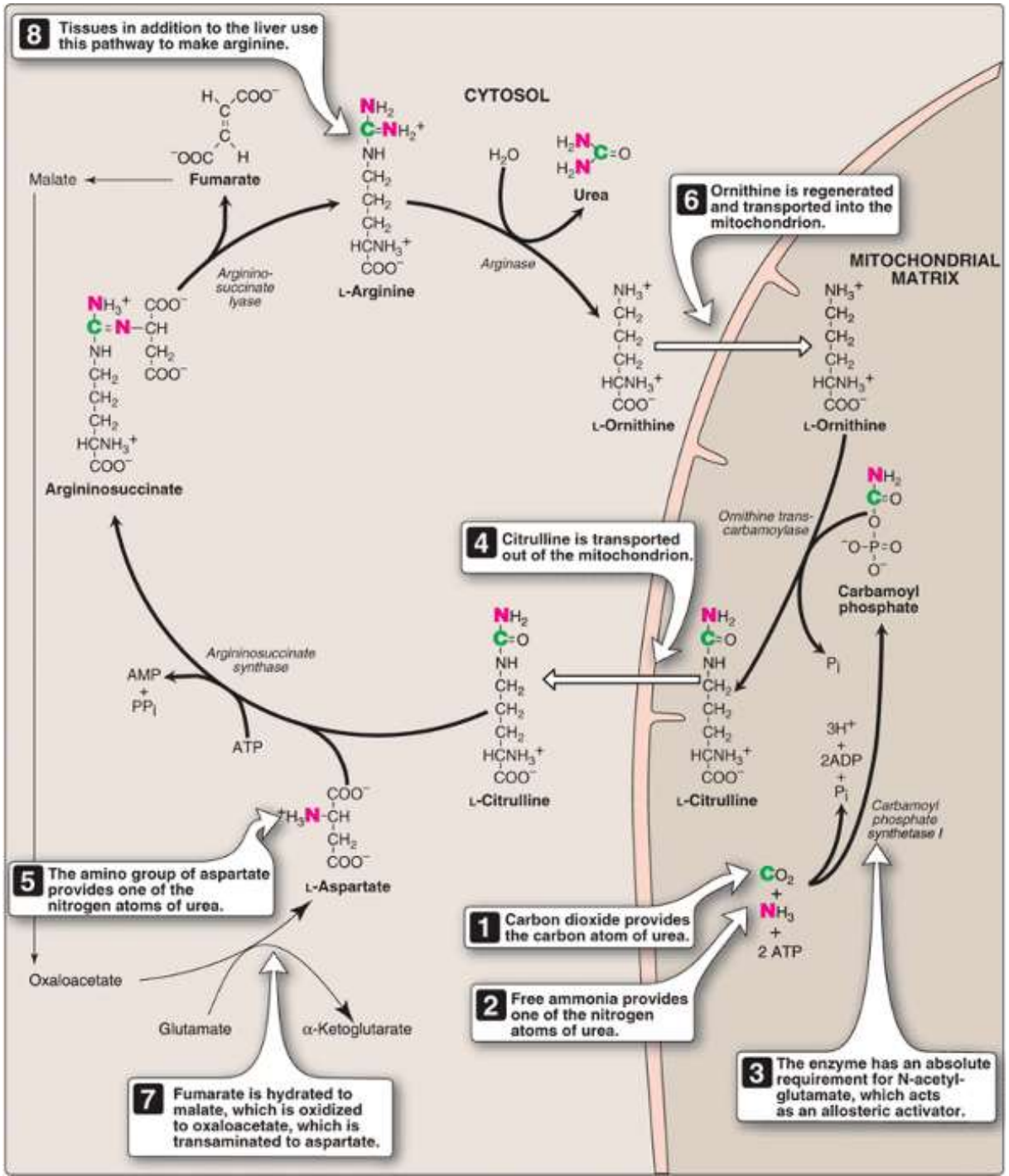
↳ ammonia ↳ metabolism

- the synthesis of urea is irreversible, with a large, negative ΔG.

لا تلقائية

**Regulation of the urea cycle**

- N-Acetylglutamate is an essential activator for carbamoyl phosphate synthetase I (the rate-limiting step in the urea cycle) (synthesized from acetyl CoA and glutamate using arginine as an activator).
- the intrahepatic concentration of N-acetylglutamate increases after ingestion of a protein-rich meal, which provides both the substrate (glutamate) and the regulator of N-acetylglutamate synthesis.
- This leads to an increased rate of urea synthesis.

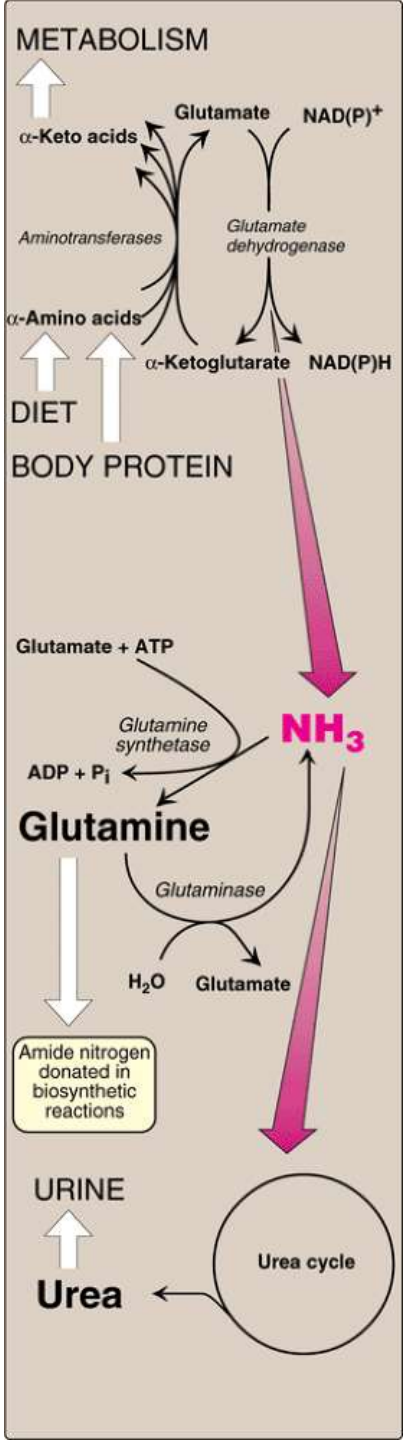

8 Tissues in addition to the liver use this pathway to make arginine.
CYTOSOL
MITOCHONDRIAL MATRIX
Fumarate
Malate
Argininosuccinate lyase
L-Arginine
Arginase
Urea
6 Ornithine is regenerated and transported into the mitochondrion.
L-Ornithine
L-Ornithine
Argininosuccinate
Ornithine transcarbamoylase
Carbamoyl phosphate
4 Citrulline is transported out of the mitochondrion.
Argininosuccinate synthase
AMP + PPi
ATP
L-Citrulline
L-Citrulline
Pi
3H+ + 2ADP + Pi
Carbamoyl phosphate synthetase I
L-Aspartate
5 The amino group of aspartate provides one of the nitrogen atoms of urea.
CO2 + NH3 + 2 ATP
1 Carbon dioxide provides the carbon atom of urea.
2 Free ammonia provides one of the nitrogen atoms of urea.
3 The enzyme has an absolute requirement for N-acetylglutamate, which acts as an allosteric activator.
Oxaloacetate
Glutamate
α-Ketoglutarate
7 Fumarate is hydrated to malate, which is oxidized to oxaloacetate, which is transaminated to aspartate.

# Metabolism of ammonia

- Slight increase in the concentration of urea in blood leads to hyperammonemia which is toxic to the CNS

- Sources of ammonia:
  - From amino acids: mainly in liver by the aminotransferase and glutamate dehydrogenase reactions
  - From glutamine: The kidneys form ammonia from glutamine by the action of renal glutaminase. Ammonia is also obtained from the hydrolysis of glutamine by intestinal glutaminase.
  - From bacterial action in the intestine: Ammonia is formed from urea by the action of bacterial urease in the lumen of the intestine.
  - From amines: Amines obtained from the diet, and monoamines that serve as hormones or neurotransmitters
  - From the catabolism of purines and pyrimidines

↳ uric acid ↳ ammonia



# Transport of ammonia in circulation

بالدم حا بنتقل إلا أشياء ما إلها لازمة زي جلوتامين، ألانين ويوريا

- As **urea**: the most disposal form of ammonia which moves from liver to the kidney

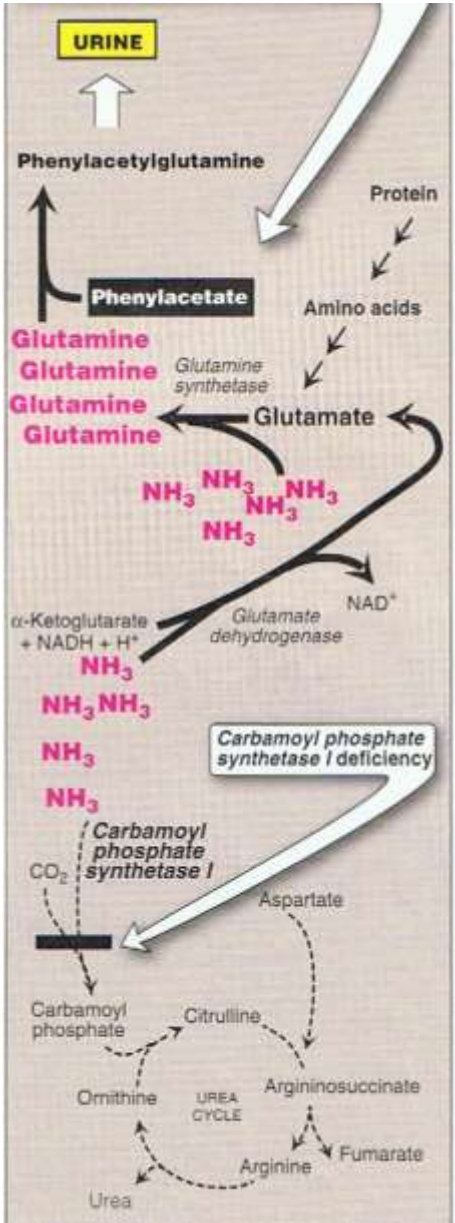
- As **Glutamine**:
  - Occurs primarily in the muscle and liver and nervous system.
  - Circulating glutamine is removed by the kidneys and deaminated by glutaminase.

Hyperammonemia → defect in urea cycle

- when the liver function is compromised, due either to genetic defects of the urea cycle, or liver disease, blood levels can rise above 1000 µmol/L. → renal failure
- hyperammonemia is a medical emergency, because ammonia has a direct neurotoxic effect on the CNS (tremors, slurring of speech, somnolence, vomiting, cerebral edema, and blurring of vision). → نوم كتير
- At high concentrations, ammonia can cause coma and death.

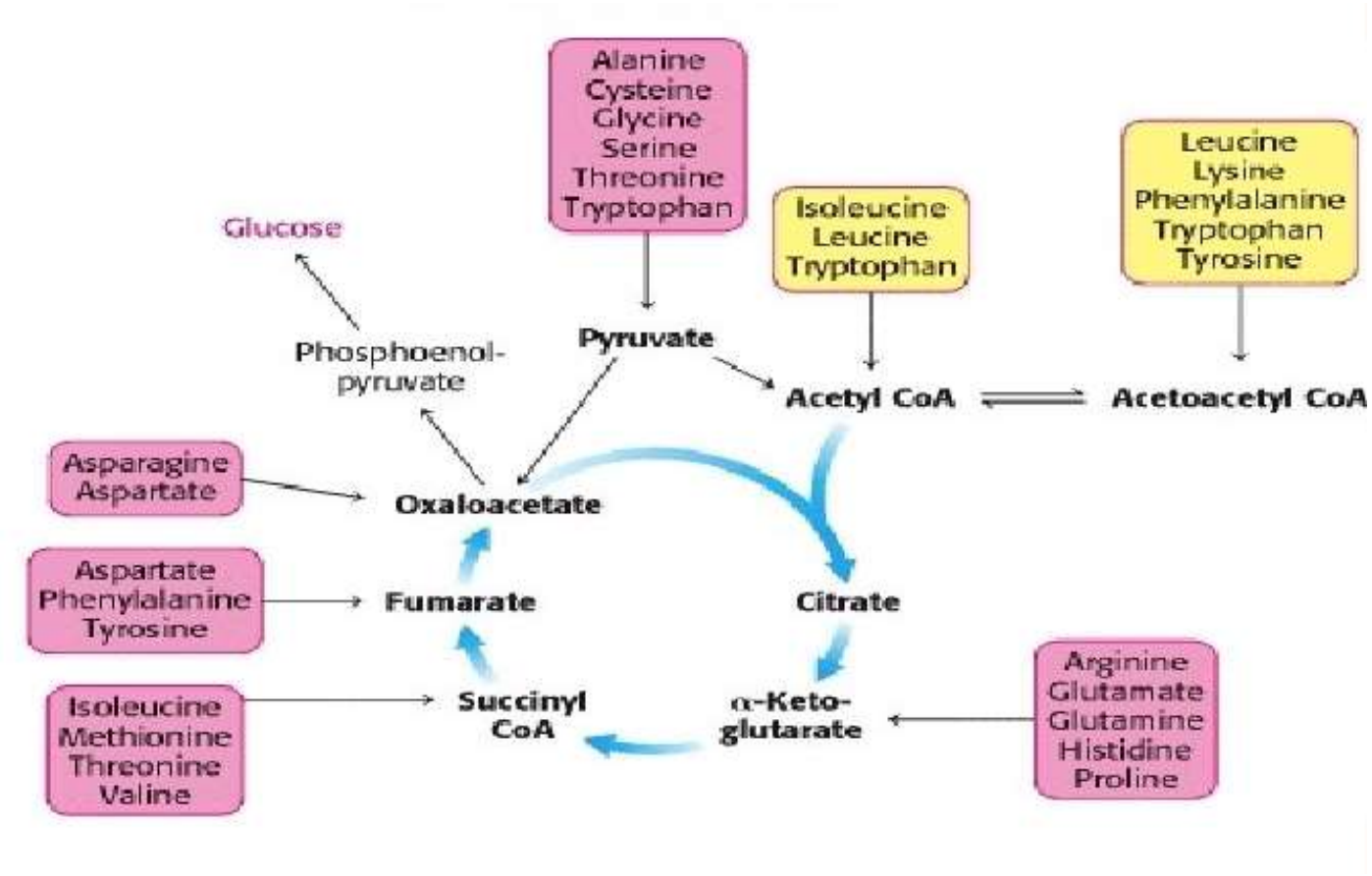
# Hyperammonemia

- **Acquired hyperammonemia**: It may be due to viral hepatitis, ischemia, or hepatotoxins. Cirrhosis of the liver caused by alcoholism, hepatitis, or biliary obstruction may result in formation of collateral circulation around the liver.
- **Hereditary hyperammonemia**: Genetic deficiencies of each of the five enzymes of the urea cycle had an overall prevalence estimated to be 1 in 30,000 live births.
  - Ornithine transcarbamoylase deficiency, which is X-linked, is the most common of these disorders, affecting males predominantly
  - All of the other urea cycle disorders follow an autosomal recessive inheritance pattern. The failure to synthesize urea leads to hyperammonemia during the first weeks following birth leading to mental retardation
  - Treatment includes:
    - limiting protein in the diet
    - administering compounds that bind covalently to amino acids, producing nitrogen-containing molecules that are excreted in the urine (phenylbutyrate given orally is converted to phenylacetate)



# Amino acid are catabolized to form:

1. oxaloacetate
2. α-ketoglutarate
3. pyruvate
5. fumarate
6. succinyl-CoA
7. acetyl-CoA and acetoacetyl CoA.



# Catabolism of the carbon skeleton

## 1. Amino acids that form oxaloacetate

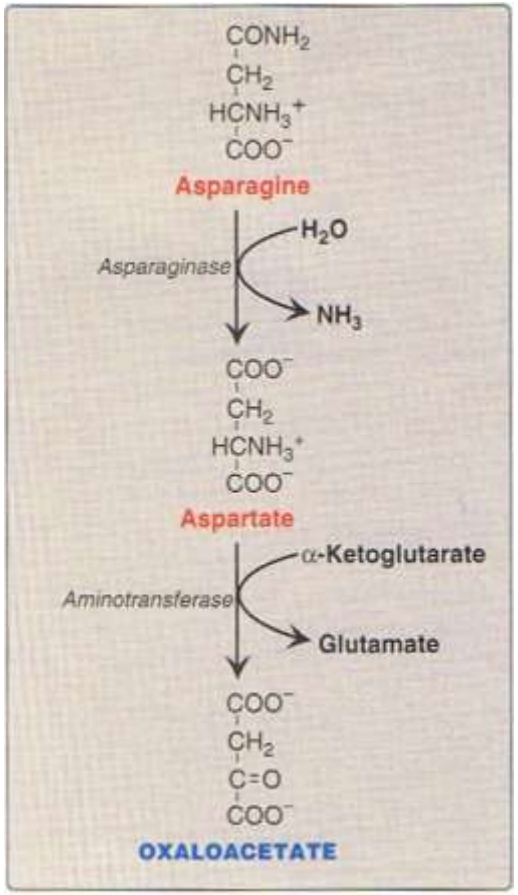
تدخل في حلقة كربس ←

glucose produce ← gluconeogenisis

- Asparagine is hydrolyzed by asparaginase, liberating ammonia and aspartate
- Aspartate loses its amino group by transamination to form oxaloacetate
- Some rapidly dividing leukemic cells are unable to synthesize sufficient asparagine to support their growth. This makes asparagine an essential amino acid for these leukemia cells.

خلايا سرطانية ←

- Asparaginase can be administered systemically to treat leukemic patients. Asparaginase degrade asparagine which help in the growth of leukemia tumors.

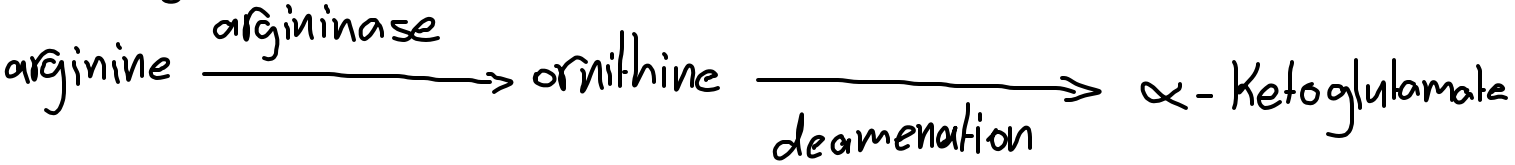


# 2. Amino acids that form α-ketoglutarate

1. **Glutamine** is converted to glutamate and ammonia by the enzyme glutaminase. Glutamate is converted to α-ketoglutarate by transamination, or through oxidative deamination by glutamate dehydrogenase.

2. **Proline** is oxidized to glutamate. Glutamate is transaminated or oxidatively deaminated to form α-ketoglutarate.

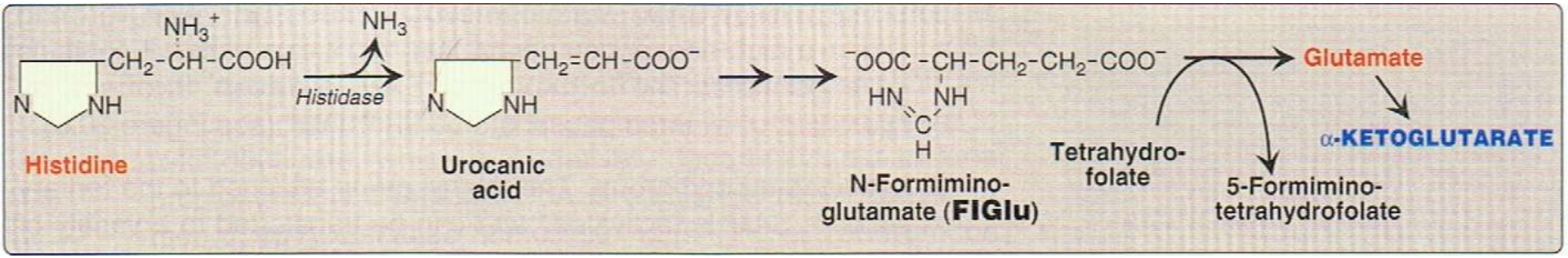
3. **Arginine** is cleaved by arginase (→ in liver) to produce ornithine (occurs primarily in the liver). Ornithine is subsequently converted to α-ketoglutarate.



# Amino acids that form α-ketoglutarate

4. **Histidine** is oxidatively deaminated by histidase to urocanic acid. which subsequently forms N-formiminoglutamate (FlGIu). FlGlu donates its formimino group to tetrahydrofolate, leaving glutamate.

- Individuals deficient in folic acid excrete increased amounts of FIGlu in the urine (after ingestion of a large dose of histidine). The FlGIu excretion test has been used in diagnosing a deficiency of folic acid.



# 3. Amino acids that form pyruvate → glucogenic

1. **Alanine** loses its amino group by transamination to form pyruvate

→ عليه هيدروكسي ميثيل → oMet remove

2. **Serine** can be converted to glycine and N5,N10-methylenetetra-hydrofolate. Serine can also be converted to pyruvate by serine dehydratase. → serine $\xrightarrow[-OH^-]{}$ alanine → pyroval-e

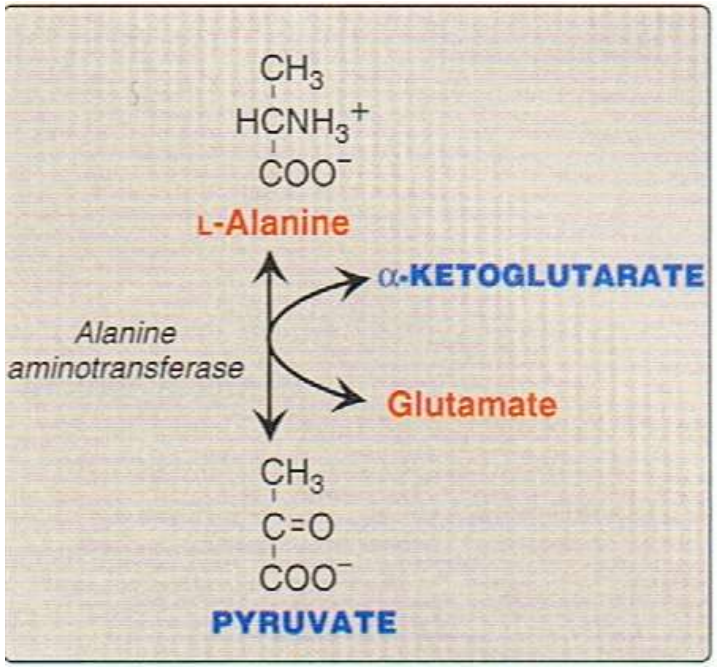
3. **Glycine** can either be converted to serine by addition of a methylene group from N5,N10-methylenetetrahydrofolic acid, or oxidized to $CO_2$ and $NH_4^+$

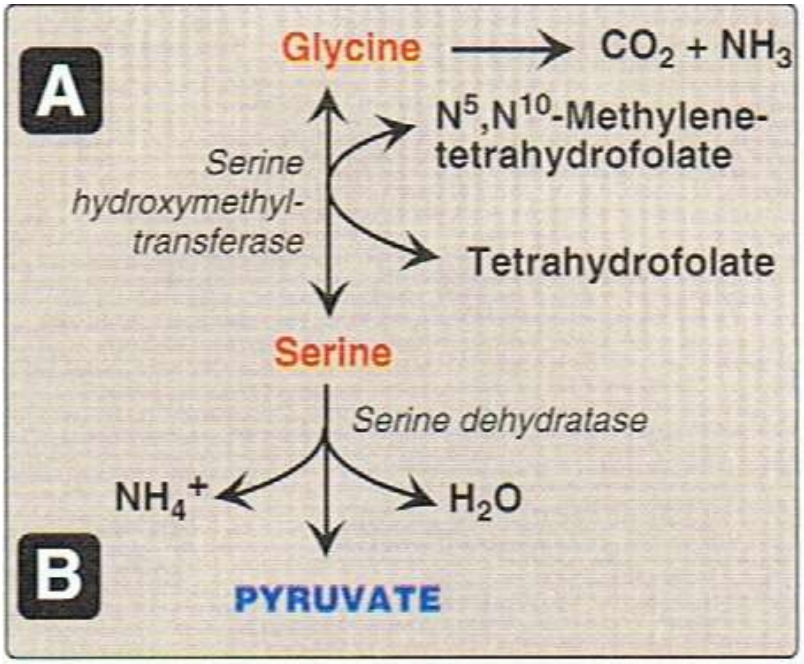
4. **Cystine** is reduced to cysteine, using NADH + H as a reductant. Cysteine undergoes desulfuration to yield pyruvate.

5. **Threonine** is converted to pyruvate or to α-ketobutyrate, which forms succinyl CoA.

glucogenic

# Amino acids that form pyruvate



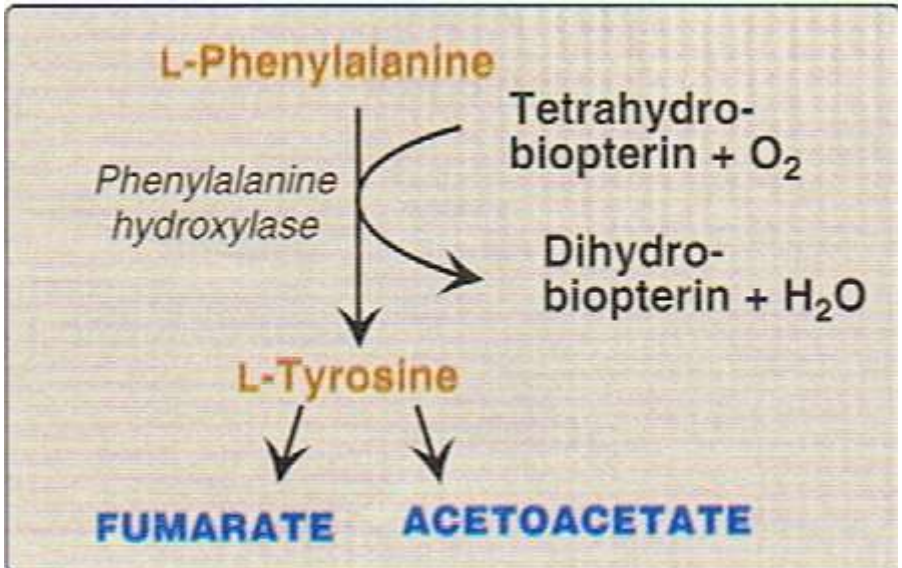
glucogenic and ketogenic

# 4. Amino acids that form fumarate

and acetoacetate

أساسي ← غير أساسي

1. **Phenylalanine and tyrosine:** Hydroxylation of phenylalanine leads to the formation of tyrosine, which is catalyzed by phenylalanine hydroxylase. Thus, the metabolism of phenylalanine and tyrosine merge, leading ultimately to the formation of fumarate and acetoacetate. Phenylalanine and tyrosine are, therefore, both glucogenic and ketogenic.
2. Inherited deficiencies in the enzymes of phenylalanine and tyrosine metabolism lead to the diseases phenylketonuria and alkaptonuria, and the condition of albinism.



glucogenic ←

# 5. Amino acids that form succinyl CoA

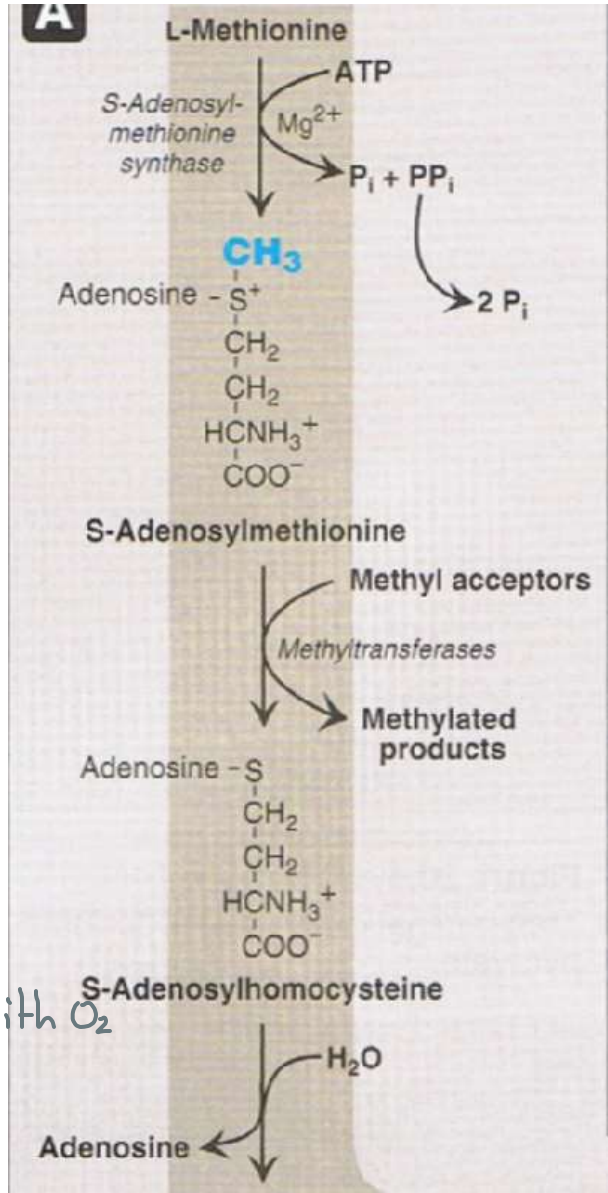
أساسي ←

- **Methionine:** Methionine is one of four amino acids that form succinyl CoA. This sulfur-containing amino acid deserves special attention because it is converted to S-adenosylmethionine (SAM), the major methyl-group donor in one-carbon metabolism

- Methionine is also the source of homocysteine, a metabolite associated with atherosclerotic vascular disease. → angina

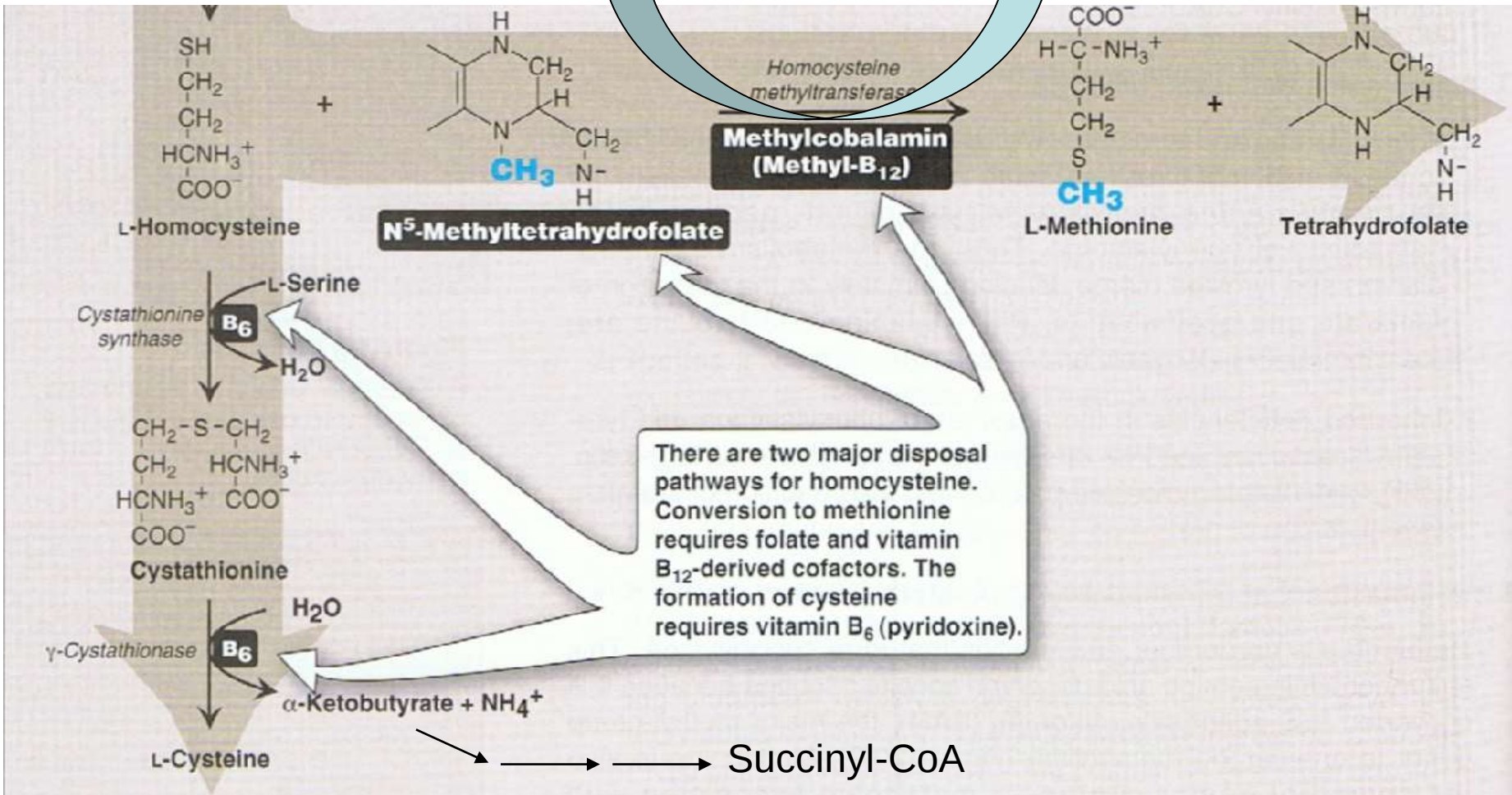
← تتراكم بسبب نقص $B_{12}$ $B_6$ and folate

→ RBCs large and small amount → hemoglobin ↓ bind with $O_2$ → effort state → heart failure



Methyl-malonyl-CoA

Succinyl-CoA




Succinyl-CoA

# Amino acids that form succinyl CoA

Degradation of valine, isoleucine, and threonine also results in the production of succinyl CoA- a TCA cycle intermediate and glucogenic compound.

1. Valine and isoleucine are branched-chain amino acids that yield succinyl CoA.

2. Threonine is dehydrated to a-ketobutyrate, which is converted to propionyl CoA, the precursor of succinyl CoA

3. Threonine can also be converted to pyruvate.

# 6. Amino acids that form acetyl CoA or acetoacetyl CoA

- Leucine, isoleucine, lysine, and Tryptophan form acetyl CoA or acetoacetyl CoA directly, without pyruvate serving as an intermediate (through the pyruvate dehydrogenase reaction.
- there are a total of six ketogenic amino acids.

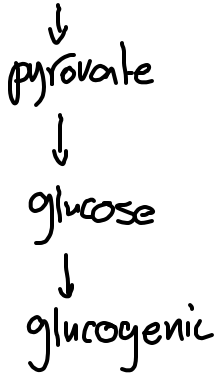
1. **Leucine** is exclusively ketogenic in its catabolism, forming acetyl CoA and acetoacetate. Like other branched-chain amino acids, isoleucine and valine.

2. **Isoleucine:** is both ketogenic and glucogenic, because its metabolism yields acetyl CoA and propionyl CoA. The first three steps in the metabolism of isoleucine are virtually identical to the initial steps in the degradation of the other branched-chain amino acids. valine and leucine.

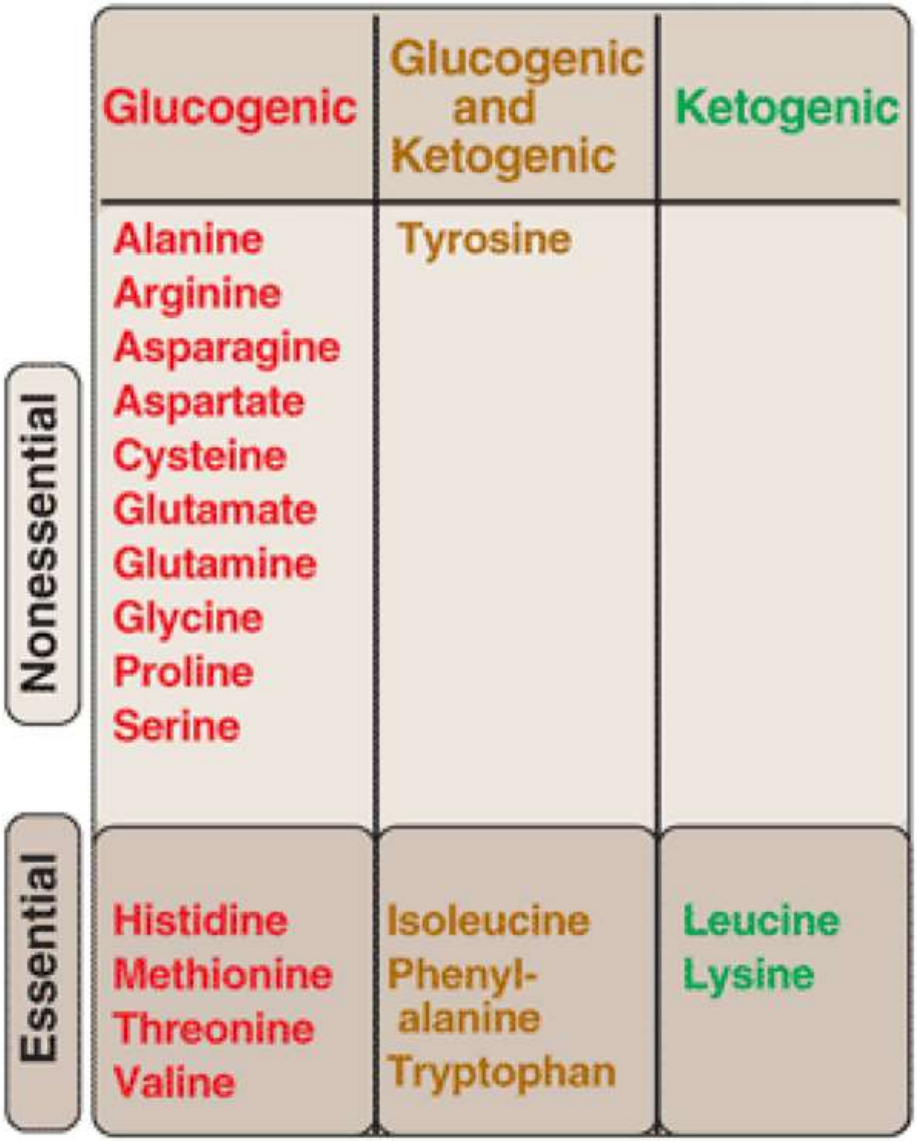
# Amino acids that form acetyl CoA or acetoacetyl CoA

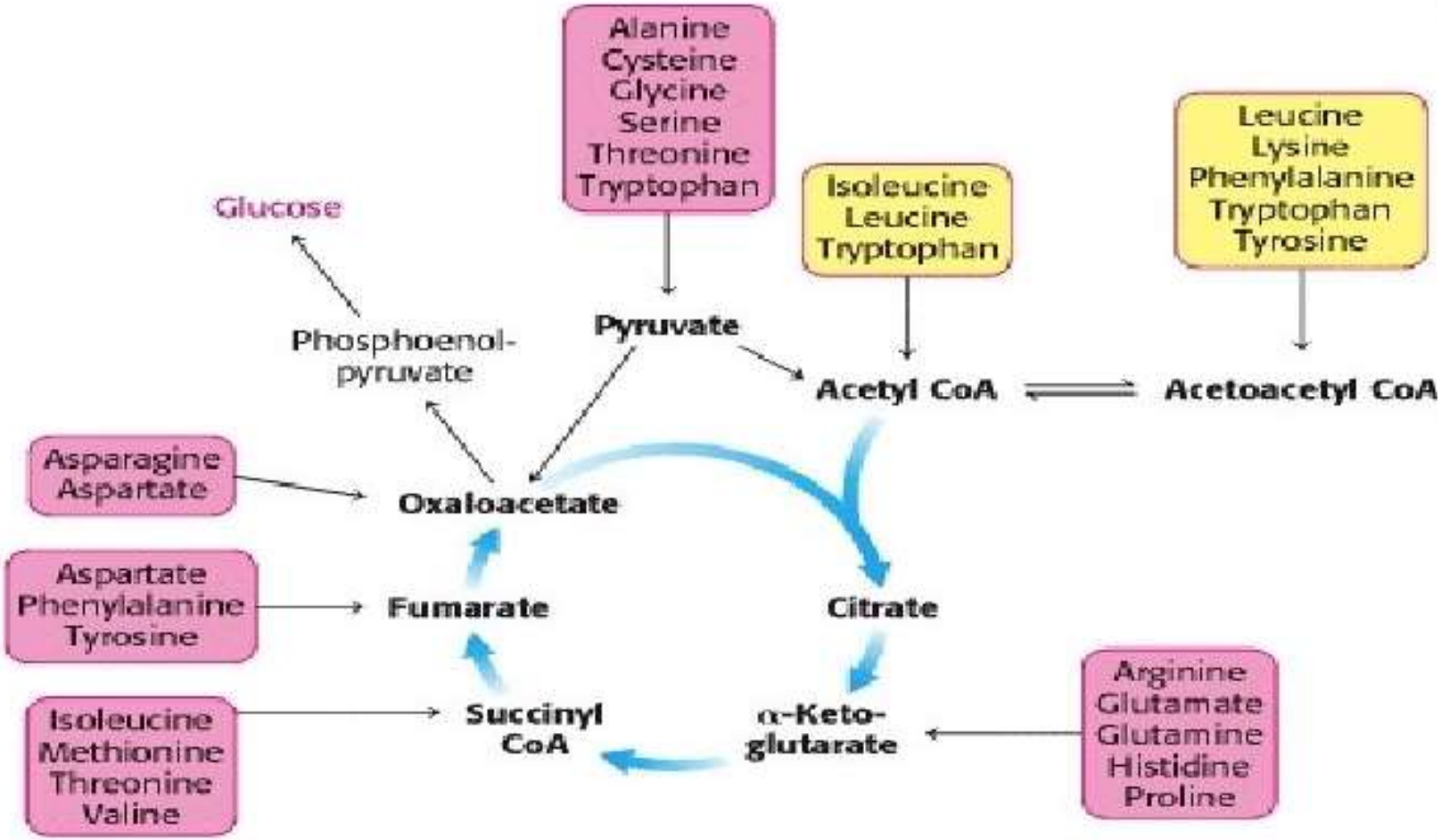
* **3. Lysine**, an exclusively ketogenic amino acid, is unusual in that neither of its amino groups undergoes transamination as the first step in catabolism. Lysine is ultimately converted to acetoacetyl CoA.

4. **Tryptophan** is both glucogenic and ketogenic because its metabolism yields alanine and acetoacetyl CoA.



# Metabolic Classification of Amino Acids




Alanine
Cysteine
Glycine
Serine
Threonine
Tryptophan
Isoleucine
Leucine
Tryptophan
Leucine
Lysine
Phenylalanine
Tryptophan
Tyrosine
Glucose
Phosphoenol-
pyruvate
Pyruvate
Acetyl CoA
Acetoacetyl CoA
Asparagine
Aspartate
Oxaloacetate
Aspartate
Phenylalanine
Tyrosine
Fumarate
Citrate
Isoleucine
Methionine
Threonine
Valine
Succinyl
CoA
α-Keto-
glutarate
Arginine
Glutamate
Glutamine
Histidine
Proline