Thus far, you have studied various pathways including, Glycolysis, Gluconeogenesis, synthesis and degradation of fatty acids, Pentose phosphate pathway, glycogen synthesis and degradation, Monosaccharides etc. Now we will study the metabolism of amino acids which contribute significantly to the generation of metabolic energy. carnivores 90% herbivores very little.
Intracellular protein

Dietary protein → Amino acids

Biosynthesis of amino acids, nucleotides, and biological amines

Carbamoyl phosphate

NH₄⁺

Carbon skeletons

α-Keto acids

Aspartate-argininosuccinate shunt of citric acid cycle

Urea cycle

CO₂ + H₂O + ATP

Citric acid cycle

Oxaloacetate

Glucose (synthesized in gluconeogenesis)

Urea (nitrogen excretion product)
Amino acids from ingested protein

Liver

Cellular protein

Amino acids

α-Keto acids

α-Ketoglutarate

Glutamate

Pyruvate

NH₄⁺, urea, or uric acid

Alanine from muscle

Glutamine from muscle and other tissues
Ammonotelic animals: most aquatic vertebrates, such as bony fishes and the larvae of amphibia

Ureotelic animals: many terrestrial vertebrates; also sharks

Uric acid

Uricotelic animals: birds, reptiles
So let's begin metabolism of amino acids in the dietary protein intake and the enzymes involved in degradation. In humans this occurs in the gastrointestinal tract.
30 g of protein/day

Protein denaturation and hydrolysis pH < 2

Secretin into the blood (3) and stimulated the pancreas to release bicarbonate.

Amino acids induce the secretion of cholecystokinin.

Enteropeptidase (6) cleave internal hydrophobic AA convert trypsin which activates Trypsinogen, Chymotrypsinogen, procarboxypepsidase, and proelastase continues what pepsin started in the stomach. Different amino acid specificity.

Further digestion by carbohypeptidase and aminopeptidase (7) absorption and transfer to the liver.

Proenzymes (zymogens) stimulated by cholecystokinin (5) Trypsinogen, chymotrypsinogen, procarboxypepsidase A&B contain (Zn)
Once in the liver amino acids are metabolized through the removal of the amino group and consequent formation of the alpha keto acid. The α-amino keep amino acids safe from oxidation. Once removed the N can be incorporated into other molecules or excreted as urea. N can be used for the synthesis of porphyrins, neurotransmitters, hormones, purines and pyrimidines. The enzymes involved in the removal of the α-amino are called aminotransferases or transaminases.
Pyridoxal phosphate (PLP)
Aldehyde form accepts amino groups

Pyridoxamine phosphate
Aminated form donates to alpha ketoglutarate
Occurs when upper alkene is protonated
Glutamate is transferred to the mitochondria in liver where it releases ammonia.

\[
\text{L-glutamate dehydrogenase} \quad (+\text{ADP}, \quad -\text{GTP})
\]

mutations on the GTP binding site in humans cause hyperinsulinism-hyperammonemia.
Ammonia is toxic to animal tissues (can cause edema in the brain) High levels of Glutamine (osmolarity) low levels of glutamate (- neurotransmitters). and the blood levels are regulated. It is converted to nontoxic forms before exported from extrahepatic tissues. Transported to liver and kidneys. It is transported to the liver in two forms
• Ammonia toxicity, comatose conditions
• cerebral edema (increase brain water content) increase cranial pressure
• speculations centers in ATP depletion
• increase in glutamate dehydrogenase increase ammonia leads to increase glutamine (glutamine synthetase) which acts as an osmotic solute in brain astrocytes leading to swelling. depletion of glutamate and derivative gama aminobutyrate (GABA) are important neurotransmitters so there could also be a depletion of neurotransmitters.
glucose-alanine cycle

Assays for tissue damage ALT (SGPT) and AST (SGOT) after heart attacks creatine kinase (SCK) and liver damage
The image depicts a chemical reaction involving glutamine synthetase. The reaction shows the conversion of L-glutamate to \( \gamma \)-glutamyl phosphate. The reaction is catalyzed by glutamine synthetase, and it involves the consumption of ATP and the release of ADP.

L-Glutamate + ATP → ADP + \( \gamma \)-Glutamyl phosphate + \( \text{NH}_3 \)


\[
\text{O} \quad \text{C} - \text{CH}_2 - \text{CH}_2 - \text{CH} - \text{COO}^- \\
\text{H}_2\text{N} \\
\text{NH}_3 \\
\text{H}_2\text{O} \\
\text{NH}_4^+ \rightarrow \text{Urea} \\
\text{O} \quad \text{C} - \text{CH}_2 - \text{CH}_2 - \text{CH} - \text{COO}^- \\
\text{L-Glutaminase} \\
\text{(liver mitochondria)}
\]

\[\text{L-Glutamine} \rightarrow \text{L-Glutamate}\]
• Nitrogen excretion and the Urea Cycle

• Urea is produced from ammonia in five enzymatic steps (the cycle has 4) it begins inside the mitochondria. Two non-coding amino acids are very important in the cycle. Ornithine and citrulline
Reactions of the Urea cycle

The formation of carbamoyl phosphate (CO2 provides the Carbon for Urea and free ammonia provides one of the nitrogen atoms of urea forming the previous compound Carbamoyl phosphate synthetase 1) uses an ATP. This step requires N-acetylglutamate as activator of the enzyme. Carbamoyl phosphate synthetase 2 does not require the activator and is used in biosynthesis of pyrimidines. Citrulline is then formed from L-Ornithine (2) Ornithine transcarbamoylase). Ornithine is regenerated in each cycle similar to oxaloacetate. The formation of citrulline liberates an inorganic phosphate. Notice that these rxs occur in mitochondria. Arginosuccinate is then synthesized from aspartate in the cytosol as it condenses with citrulline (3) Arginosuccinate synthetase, the amino group of aspartate provides 2nd nitrogen of Urea. Cleavage of arginosuccinate to yield Arginine & fumarate (4) arginosuccinate lyase). Arginine is the precursor of urea, fumarate is hydrated to malate (TCA).
Aspartate-argininosuccinate shunt of citric acid cycle

Urea cycle

Cytosol

Citric acid cycle

Mitochondrial matrix
• Genetic defects in the urea cycle can be life threatening. The absence of urea cycle enzymes result in hyperammononemia or build up of one or more cycle intermediate. Most of the urea cycle steps are irreversible. The only reversible step is by argininosuccinate lyase (argininosuccinase)

• protein -free diet is not a treatment option since many amino acids are essential and needed in the diet.
<table>
<thead>
<tr>
<th>Nonessential</th>
<th>Conditionally essential*</th>
<th>Essential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>Arginine</td>
<td>Histidine</td>
</tr>
<tr>
<td>Asparagine</td>
<td>Cysteine</td>
<td>Isoleucine</td>
</tr>
<tr>
<td>Aspartate</td>
<td>Glutamine</td>
<td>Leucine</td>
</tr>
<tr>
<td>Glutamate</td>
<td>Glycine</td>
<td>Lysine</td>
</tr>
<tr>
<td>Serine</td>
<td>Proline</td>
<td>Methionine</td>
</tr>
<tr>
<td></td>
<td>Tyrosine</td>
<td>Phenylalanine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Threonine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tryptophan</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Valine</td>
</tr>
</tbody>
</table>

*Required to some degree in young, growing animals, and/or sometimes during illness.
• Treatment for urea cycle defects
• aromatic acids benzoate or phenylbutyrate can help lower ammonia levels
• carbamoyl glutamate
deficiency in N-acetylglutamate synthase is treated with the analog shown here. This induces carbamoyl phosphate synthetase 1

Carbamoyl glutamate
Pathways of amino acid degradation will concentrate on nonessential amino acids.
• Several cofactors in enzymes involved in catabolism of amino acids
• transaminations (PLP)
• one carbon transfer (biotin, tetrahydrofolate($H_4$ folate) S-adenosylmethionine
most oxidize Carbon

Biotin

6-methylpterin

p-aminobenzoate

glutamate

Tetrahydrofolate (H₄ folate) intermediate

S-Adenosylmethionine (adoMet) methyl groups

methionine

valerate
6 amino acids degraded to Pyruvate (ASCG2T)

- alanine
- glycine
- serine
- cysteine
- tryptophan
- threonine
crystals of Calcium oxalate
75% of kidney stones

defects in this enzyme causes nonketotic hyperglycemia. Elevated serum levels of Glycine leading to mental deficiencies and death in childhood. Glycine is an inhibitory neurotransmitter
Amino acids that form pyruvate

- Alanine loses its amino group by transamination to form pyruvate.
Serine can be converted to glycine and $\text{N}^5,\text{N}^{10}$-methylene tetrahydrofolate. Serine can also be converted to pyruvate by serine dehydratase.

Glycine can either be converted to serine by addition of a methylene group from $\text{N}^5,\text{N}^{10}$-methylene tetrahydrofolate acid, or oxidized to $\text{CO}_2$ and $\text{NH}_4^+$
• Seven amino acids degraded to acetyl CoA
  IP2L3T
• tryptophan, lysine, phenylalanine, tyrosine, leucine isoleucine and threonine.
most complex
• Five amino acids converted to alpha ketoglutarate GGAHP
• glutamate, glutamine, arginine, histidine and Proline
• Four amino acids converted to succinyl CoA. (IMTV)
• isoleucine, methionine, threonine and Valine
donates its methyl group through S-adenosylmethionine

Homocystinuria →

Cystathionuria

Maple syrup disease

lack of this enzyme causes methylmalonic acidemia critical since 4 amino acids metabolize through here
Asparaginase catalyzes the reaction between asparagine and water to produce aspartate and ammonium. Aspartate aminotransferase then transfers an ammonium group from aspartate to \( \alpha \)-ketoglutarate, producing glutamate and oxaloacetate.
abnormal development of the brain, mental retardation and death in infants. Needs rigid diet
• Human genetic disorders affecting amino acid catabolism
Metabolic defects in amino acid metabolism

Caused by mutant genes resulting in abnormal proteins, total lost or partial deficiency (more often). Can result in mental retardation or developmental abnormalities. As much as fifty disorders have been described but are rare (why?) 1:250,000 however, we expect this number to increase (why?). These are some of the most commonly encountered diseases with the incidences in most populations. Phenylketonuria, maple syrup urine disease, albinism, homocystinuria and alkaptonuria.

Figure 20.13
Incidence of inherited diseases of amino acid metabolism. [Note: Cystinuria is the most common genetic error of amino acid transport.]
<table>
<thead>
<tr>
<th>Medical condition</th>
<th>Approximate incidence (per 100,000 births)</th>
<th>Defective process</th>
<th>Defective enzyme</th>
<th>Symptoms and effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albinism</td>
<td>&lt;3</td>
<td>Melanin synthesis from tyrosine</td>
<td>Tyrosine 3-monoxygenase (tyrosinase)</td>
<td>Lack of pigmentation: white hair, pink skin</td>
</tr>
<tr>
<td>Alkaptonuria</td>
<td>&lt;0.4</td>
<td>Tyrosine degradation</td>
<td>Homogentisate 1,2-dioxygenase</td>
<td>Dark pigment in urine; late-developing arthritis</td>
</tr>
<tr>
<td>Argininemia</td>
<td>&lt;0.5</td>
<td>Urea synthesis</td>
<td>Arginase</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Argininosuccinic acidemia</td>
<td>&lt;1.5</td>
<td>Urea synthesis</td>
<td>Argininosuccinase</td>
<td>Vomiting; convulsions</td>
</tr>
<tr>
<td>Carbamoyl phosphate synthetase I deficiency</td>
<td>&lt;0.5</td>
<td>Urea synthesis</td>
<td>Carbamoyl phosphate synthetase I</td>
<td>Lethargy; convulsions; early death</td>
</tr>
<tr>
<td>Homocystinuria</td>
<td>&lt;0.5</td>
<td>Methionine degradation</td>
<td>Cystathionine β-synthase</td>
<td>Faulty bone development; mental retardation</td>
</tr>
<tr>
<td>Maple syrup urine disease (branched-chain ketoaciduria)</td>
<td>&lt;0.4</td>
<td>Isoleucine, leucine, and valine degradation</td>
<td>Branched-chain α-ketoadipic dehydrogenase complex</td>
<td>Vomiting; convulsions; mental retardation; early death</td>
</tr>
<tr>
<td>Methylmalonic acidemia</td>
<td>&lt;0.5</td>
<td>Conversion of propionyl-CoA to succinyl-CoA</td>
<td>Methylmalonyl-CoA mutase</td>
<td>Vomiting; convulsions; mental retardation; early death</td>
</tr>
<tr>
<td>Phenylketonuria</td>
<td>&lt;8</td>
<td>Conversion of phenylalanine to tyrosine</td>
<td>Phenylalanine hydroxylase</td>
<td>Neonatal vomiting; mental retardation</td>
</tr>
</tbody>
</table>
PKU (phenylketonuria) causes mental retardation due to the lack of phenylalanine hydroxylase. Phenylalanine cannot be converted to tyrosine, leading to an accumulation of phenylalanine and the production of phenylpyruvate.
oxidation turns the urine black

prone to develop a form of arthritis

\[ \text{Homогентисат} \]

\[ \text{Alkaptonuria} \]

\[ \text{Maleylacetoacetate} \]
Phenylketonuria (PKU)

- Caused by a deficiency in phenylalanine hydroxylase 1:11,000.
- Hyperphenylalaninemia deficiency in enzymes involved in synthesis of the coenzyme tetrahydrobiopterin BH$_4$
Hyperphenylalaninemia

- Dihydrobiopterin (BH$_4$) synthetase
- Dihydrobiopterin (BH$_4$) reductase
- They are very important in synthesis of neurotransmitters, serotonin and catecolamines, dietary restriction of phenylalanine does not reverse CNS effects replacement therapy with BH$_4$ and 5-hydroxytryptophan and DOPA (sueño?)

---

**Figure 20.16**

Biosynthetic reactions involving amino acids and tetrahydrobiopterin.
Characteristics of PKU

- Elevated phenylalanine (tissue, plasma, and urine. Phenylpyruvate, Phenyllactate and Phenylacetate also elevated when normally not. Musty (hongo) odor urine.
- Mental retardation failure to walk or talk, seizures, hyperactivity, tremor, microcephaly, failure to grow. IQ below 50.

- Hypopigmentation deficiency in pigmentation (fair hair, light skin and blue eyes) due to hydroxylation of Tyrosine to melanin which is inhibited by high levels of phenylalanine.
Intellectual ability in untreated PKU patients of different ages.

- Maternal PKU syndrome causes microcephaly, mental retardation and congenital heart abnormalities.
- 40 different mutations of the gene phenylalanine hydroxylase 6-10 are causes of PKU.
- Feeding synthetic amino acid preparations low in phenylalanine, with natural foods fruits, vegetables & certain cereals.

Treatment must start within 7-10 days of life to prevent retardation.
Changes in IQ scores after discontinuation of low-phenylalanine diet in patients with PKU

- Life long restriction of dietary phenylalanine is recommended
- Maple syrup urine disease (MSUD) recessive disorder deficiency in the branched-chain \( \alpha \)-ketoacid dehydrogenase enzyme that decarboxylates leucine, isoleucine and valine these amino acids and their \( \alpha \)-ketoacids accumulate in blood with toxic effects that interferes with brain function. Feeding problems, vomiting, dehydration, severe metabolic acidosis and maple syrup odor. Mental retardation, physical disability and death.

Synthetic formula with limited amounts of leucine, isoleucine and valine.

Figure 20.19
Changes in IQ scores after discontinuation of low-phenylalanine diet in patients with phenylketonuria.
Alkaptonuria

• Rare metabolic disease involving the deficiency in homogentisic acid oxidase, resulting in accumulation of homogentisic acid (degradative pathway of tyrosine)

Symptoms

• Homogentisic aciduria (high levels of this acid in urine gives it a dark color upon standing (Fig. A))

• Large joint arthritis

• Pigmentation of cartilage (Fig. B) asymptomatic until age of forty

• Diets low in protein recommended although no treatment as such
Albinism

A group of conditions with a defect of in tyrosine metabolism in a deficiency in the production of melanin. This suggest that melanin production depends on this pathway and other pathways are not available. Autosomal recessive, autosomal dominant and X-linked. Photophobia, they sunburn easily and do not tan.
Homocystinuria

- Disorder involving defects in the metabolism of homocysteine (autosomal recessive) High plasma and urinary levels of this amino acid and methionine and low levels of cysteine. Common cause is the defect of cystathionine synthase which converts homocysteine to cystathionine. Homozygous show ectopia lentis (displacement of the lens) skeletal abnormalities, premature arterial disease, osteoporosis and mental retardation. Patients could or not be responsive to vitamin B₆ (cofactor).

TREATMENT: restriction of methionine intake and supplement with vitamins B₆ and B₁₂ and folate.
Good review slide for metabolism of amino acids and diseases caused by enzyme deficiency. Notice glucogenic and ketogenic amino acids and metabolites of each amino acid.
Summary

Amino acids that yield Pyruvate or intermediates in the TCA cycle are called glycogenic. They can give rise to glycogen or glucose in the liver and glycogen in muscle. Amino acids that whose catabolism yield acetyl CoA, acetoacetyl CoA are termed ketogenic (Tyrosine, phenylalanine, tryptophan isoleucine are both ketogenic and glucogenic) Leucine and lysine are ketogenic. Non-essential AA can be synthesized from metabolic intermediates or carbon skeletons of essential AA. Alanine, aspartate, glutamate, glutamine, asparagine, proline, cysteine, serine, glycine, and tyrosine.

Essential AA in diet methionine, phenylalanine.

Metabolic diseases

PKU (-) phenylalanine hydroxylase,
Hyperphenylalanine (-) BH$_4$ Synthetase or reductase coenzyme of PH tetrahydrobiopterin. Untreated patients of PKU suffer mental retardation failure to walk or talk, seizure, hyperactivity, tremor etc. Tyrosine becomes essential under this condition.

(MSUD) (-) branched chain $\alpha$-ketoacid dehydrogenase
• Biosynthesis of amino acids (non-essential)
• most N2 is bound to amino acids and nucleotides
• pathways of amino acid synthesis and nucleotides are intertwined with common intermediates. Amino acids are incorporated into the structures of pyrimidines and purines and the purine ring is incorporated into an amino acid Histidine.
The nitrogen cycle involves the following processes:

- **Nitrate (NO₃⁻)**
  - Nitrification by soil bacteria (e.g., *Nitrobacter*).
  - Denitrification.

- **Nitrite (NO₂⁻)**
  - Nitrification by soil bacteria (e.g., *Nitrosomonas*).

- **Ammonia (NH₄⁺)**
  - Nitrogen fixation by some bacteria (e.g., *Klebsiella*, *Azotobacter*, *Rhizobium*).
  - Reduction by some anaerobic bacteria, most plants.
  - Synthesis in plants and microorganisms.
  - Degradation by animals and microorganisms.

- **Amino acids and other reduced nitrogen-carbon compounds**

The diagram illustrates the flow of nitrogen through these processes, indicating the conversion and movement of nitrogen compounds in the environment.
Ammonia is incorporated into biomolecules through Glutamate and Glutamine they provide the critical entry point. These same amino acids play a central role in catabolism. They are present at high conc. in extracellular fluid up to an order of magnitude higher
incorporation of NH4 into glutamate requires glutamine synthetase

\[ \text{L-Glutamate} \]

\[ \text{ATP} \xrightarrow{\text{glutamine synthetase}} \text{ADP} \]

\[ \text{NH}_3 \]

\[ \text{gamma-Glutamyl phosphate} \]

\[ \text{NH}_4^+ \]

\[ \text{glutamine synthetase} \]

\[ P_i \]

\[ \text{NH}_3 \]

\[ \text{H}_2\text{N} \]

\[ \text{L-Glutamine} \]

\[ \text{glutaminase (liver mitochondria)} \]

\[ \text{H}_2\text{O} \]

\[ \text{NH}_4^+ \xrightarrow{\text{Urea}} \]

\[ \text{L-Glutamate} \]
concerted inhibition more than additive
second level regulation of the enzyme
Glutamine synthetase
adenylylation (AMP) of Tyr 397 covalent
binding increases sensitivity to inhibitors
adenylyltransferase (AT next figure)
this enzyme responds to levels of glutamine, alpha ketoglutarate, ATP and Pi
Uridyltransferase induces gene transcription of glutamine synthetase through protein interaction.
Glutamine amidotransferase

Glutamine binding domain

NH$_3^-$ acceptor domain

Glutamine

Cys-SH

NH$_2$

COO$^-$

H$_3$N-CH

CH$_2$

CH$_2$

C

H$^+$

NH$_3$

Glutamine amidotransferase

1. R$^-$OH or R$^1$C=O

Accepter

Activated substrate

2. R$^-$OX or

C=C=O

Glutamyl enzyme intermediate

H$_2$O

NH$_3$

COO$^-$

H$_3$N-CH

CH$_2$

CH$_2$

C

NH$_2$

Glutamate

R$^-$NH$_2$ + H-OX or

C=NH + H$_2$O
<table>
<thead>
<tr>
<th><strong>TABLE 22–1</strong> Amino Acid Biosynthetic Families, Grouped by Metabolic Precursor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>α-Ketoglutarate</strong></td>
</tr>
<tr>
<td>Glutamate</td>
</tr>
<tr>
<td>Glutamine</td>
</tr>
<tr>
<td>Proline</td>
</tr>
<tr>
<td>Arginine</td>
</tr>
<tr>
<td><strong>3-Phosphoglycerate</strong></td>
</tr>
<tr>
<td>Serine</td>
</tr>
<tr>
<td>Glycine</td>
</tr>
<tr>
<td>Cysteine</td>
</tr>
<tr>
<td><strong>Oxaloacetate</strong></td>
</tr>
<tr>
<td>Aspartate</td>
</tr>
<tr>
<td>Asparagine</td>
</tr>
<tr>
<td>Methionine*</td>
</tr>
<tr>
<td>Threonine*</td>
</tr>
<tr>
<td>Lysine*</td>
</tr>
<tr>
<td><strong>Pyruvate</strong></td>
</tr>
<tr>
<td>Alanine</td>
</tr>
<tr>
<td>Valine*</td>
</tr>
<tr>
<td>Leucine*</td>
</tr>
<tr>
<td>Isoleucine*</td>
</tr>
<tr>
<td><strong>Phosphoenolpyruvate and erythrose 4-phosphate</strong></td>
</tr>
<tr>
<td>Tryptophan*</td>
</tr>
<tr>
<td>Phenylalanine*</td>
</tr>
<tr>
<td>Tyrosine†</td>
</tr>
<tr>
<td><strong>Ribose 5-phosphate</strong></td>
</tr>
<tr>
<td>Histidine*</td>
</tr>
</tbody>
</table>

*Essential amino acids.
†Derived from phenylalanine in mammals.
Synthesis of Glutamate, Glutamine, Proline and Arginine

α-Ketoglutarate

Glutamate

Glutamine  Proline  Arginine
Biosynthesis of Proline
Biosynthesis of Proline

Nonenzymatic

Glutamate γ-semialdehyde

Δ¹-Pyrroline-5-carboxylate (P5C)

Pyrroline carboxylate reductase

NAD(P)H + H⁺

Proline
Biosynthesis of Arginine

Glutamate

\[ \text{Glutamate} \rightarrow \text{N-Acetylglutamate} \]

N-acetylglutamate synthase

\[ \text{ATP} \rightarrow \text{ADP} \]

Glutamate kinase

\[ \text{γ-Glutamyl phosphate} \]

Glutamate dehydrogenase

\[ \text{NAD(P)H} + \text{H}^+ \]

Nonenzymatic

\[ \text{Glutamate} \rightarrow \text{γ-semialdehyde} \]

\[ \Delta^1\text{-Pyrroline-5-carboxylate (PSC)} \]

N-acetylglutamate dehydrogenase

\[ \text{NAD(P)H} + \text{H}^+ \]

Aminotransferase

\[ \text{α-Ketoglutarate} \]

Pyroline carboxylate reductase

\[ \text{NAD(P)H} + \text{H}^+ \]

\[ \text{N-acetylornithine} \rightarrow \text{N-Acetylglutamate} \]

\[ \text{N-acetylglutamate kinase} \rightarrow \text{ATP} \]

\[ \text{ADP} \]

\[ \text{N-Acetyl-γ-glutamyl phosphate} \]

N-acetylglutamate dehydrogenase

\[ \text{NAD(P)H} + \text{H}^+ \]

\[ \text{P}_{\text{i}} \]

Urea cycle

\[ \text{Ornithine} \rightarrow \text{Carbamoyl phosphate} \]

\[ \text{L-Citrulline} \]

\[ \text{Argininosuccinate synthetase} + \text{ATP} + \text{aspartate} \]

\[ \text{AMP} + \text{PP}_{\text{i}} \]

\[ \text{Argininosuccinate} \rightarrow \text{Fumarate} \]

\[ \text{Fumarate} + \text{NH}_3 \]

\[ \text{Arginine} \]

\[ \text{N-Acetylglutamate γ-semialdehyde} \]
Biosynthesis of Serine, Glycine and Cysteine

3-Phosphoglycerate

Serine

Glycine
Cysteine
Removal of the B-C (C-3) accepted by H4 folate oxidation of the OH group

transamination

hydrolysis

Removal of the B-C (C-3) accepted by H4 folate
Methionine

S-adenosylmethionine

\[-\text{OOC}\cdot\text{CH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{SH} + \text{HOCH}_2\cdot\text{CH}\cdot\text{COO}^-\]

Homocysteine

\[\text{Serine}\]

\[\text{cystathionine } \beta-\text{synthase}\]

\[\text{PLP}\]

\[\text{H}_2\text{O}\]

\[-\text{OOC}\cdot\text{CH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{S}\cdot\text{CH}_2\cdot\text{CH}\cdot\text{COO}^-\]

Cystathionine

\[\text{cystathionine } \gamma-\text{lyase}\]

\[\text{PLP}\]

\[\text{H}_2\text{O}\]

\[\text{NH}_4^+\]

\[-\text{OOC}\cdot\text{C}\cdot\text{CH}_2\cdot\text{CH}_3 + \text{HS}\cdot\text{CH}_2\cdot\text{CH}\cdot\text{COO}^-\]

\[\alpha-\text{Ketobutyrate}\]

\[\text{Cysteine}\]
Biosynthesis of Three Nonessential and Six Essential From Oxaloacetate and Pyruvate
L-Phenylalanine

PKU

Phenylalanine hydroxylase

Tetrahydro-biopterin + O₂

Dihydro-biopterin + H₂O

L-Tyrosine
Biosynthesis of Alanine

Aminotransferase

\[
\text{\(\alpha\)-Amino acid} \xrightarrow{\text{Aminotransferase}} \text{\(\alpha\)-Ketoglutarate}
\]

\[
\text{\(\alpha\)-Keto acid} \xrightarrow{\alpha\text{-Keto acid}} \text{Glutamate}
\]

\[
\text{L-Alanine} \xrightarrow{\alpha\text{-KETOGLUTARATE}} \text{Glutamate}
\]

\[
\text{PYRUVATE}
\]

\[
\text{CH}_3
\]

\[
\text{HCNH}_3^+
\]

\[
\text{COO}^-
\]

\[
\text{CH}_2
\]

\[
\text{CH}_2
\]

\[
\text{O=C}
\]

\[
\text{COO}^-
\]

\[
\text{H}_3\text{N}-\text{CH}
\]

\[
\text{COO}^-
\]
amidation

Glutamine donates NH₄⁺
Biosynthesis on non-essential amino acids

They are synthesized from intermediates of metabolism or from essential amino acids like the case of tyrosine and cysteine. Histidine and arginine are generally classified as non-essential depending on conc.

From -keto acids

From amidation (glutamine) formed from glutamate important in synthesis and degradation providing detoxification of ammonia in liver and brain as previously discussed in Urea cycle. Asparagine formed from aspartate

Proline formed from glutamate

Serine (from 3 phosphoglycerate-3 phosphopyruvate-3 phosphoserine-serine and glycine), glycine(serine) and cysteine (homocysteine-cystathionine-cysteine depends on methionine (essential)

Tyrosine (20.7) phenylalanine (essential) requires BH4 tetrahydrobiopterin
Allosteric regulation of amino acid biosynthesis