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GENOSYS–Exam Preparatory Manual for Undergraduates

BIOCHEMISTRY

(A Simplified Approach)

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- Cell and Subcellular Organelles
- Enzymology
- Carbohydrates
- Proteins and Amino Acids
- Lipids
- Cellular Energetics
- Nutrition
- Tissue Biochemistry
- Molecular Biology
- Xenobiotics
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- Biochemical Pathways

Viva Voce

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Chapter

4

Proteins and Amino Acids

AMINO ACIDS

All proteins are polymers of amino acids. Proteins are composed of a number of amino acids linked by peptide bonds.

Classification

Based on Structure

1. Aliphatic amino acids:
   a. Monoamino monocarboxylic acids:
      - Simple amino acids: Glycine, alanine
      - Branched-chain amino acids: Valine, leucine, isoleucine
      - Hydroxy amino acids: Serine, threonine
      - Sulfur-containing amino acids BCA: Cysteine, methionine
      - Amino acids with amide group: Asparagine, glutamine.
   b. Monoamino dicarboxylic acids: Aspartic acid, glutamic acid.
   c. Dibasic monocarboxylic acids: Lysine, arginine.
2. Aromatic amino acids: Phenylalanine, tyrosine.
3. Heterocyclic amino acids: Tryptophan, histidine.
4. Imino acid: Proline.
5. Derived amino acids:
   a. Derived amino acids found in proteins: After the synthesis of proteins, some of the amino acids are modified, e.g. hydroxyproline, hydroxylysine, γ-carboxyglutamic acid.
   b. Derived amino acids not seen in proteins (non-protein amino acids), e.g. ornithine, citrulline, homocysteine.
   c. Non-α amino acids: Gamma-aminobutyric acid (GABA) is derived from glutamic acid. β-alanine, is a constituent of pantothenic acid (vitamin) and coenzyme A.

Based on Side Chain

1. Amino acids having non-polar side chains: These include alanine, valine, leucine, isoleucine, methionine, proline, phenylalanine and tryptophan. The groups are hydrophobic and lipophilic.
2. Amino acids having uncharged or non-ionic polar side chains: Glycine, serine, threonine, cysteine, tyrosine, glutamine and asparagine.
3. Amino acids having charged or ionic polar side chains:
   a. Acidic amino acids: Aspartic acid, glutamic acid.
   b. Basic amino acids: Lysine, arginine, histidine.

Based on Metabolism

1. Purely ketogenic: Leucine.
2. Ketogenic and glucogenic: Lysine, isoleucine, phenylalanine, tyrosine, tryptophan.
3. Purely glucogenic: Remaining 14 amino acids.

Based on Nutrition

1. Essential amino acids: Isoleucine, leucine, threonine, lysine, methionine, phenylalanine, tryptophan, valine.
2. Semi-essential: Histidine, arginine.
3. Nonessential: Remaining 10 amino acids.

Structure

There are 20 common amino acids called α-amino acids because they all have an amino (NH_3^+) group and a carboxyl group (COOH) attached to C-2 carbon (α-carbon).

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At pH of 7, amino group is protonated ($-NH_3^+$) and carboxyl group is ionized (COO–). The amino acid is called zwitterion.

- pKa of a carboxyl group = 1.8–2.5
- pKa of a amino group = 8.7–10.7.

The α-carbon is chiral or asymmetric (four different groups are attached to the carbon; exception is glycine).

Amino acids exist as stereoisomers (same molecular formula, but differ in arrangement of groups). Designated as D (right) or L (left). Amino acids used in nature are of L configuration.

Ionization of Amino Acids

All amino acids are having a neutral net charge at physiological pH (7.4). The carboxyl and amino groups or any other ionizable groups determine charge. Each amino acid has 2 or 3 pKa values (seven amino acids have side chains that are ionizable). This complicates the basic titration curve, so that there are three inflection points rather than two. At a given pH, amino acids have different net charges. Titration curves can be used for amino acids to show ionizable groups.

The isoelectric point (pI) is the pH at which the amino acid has no net charge = zwitterion:

- If pH > pI, amino acid would be negatively charged
- If pH < pI, amino acid would be positively charged
- If pH is = pI, amino acid would have no charge.

If pH is more than pKa, there is a greater ionization and a greater amount of amino acid can use Henderson-Hasselbalch equation to calculate the fraction of group ionized at a given pH:

- A carboxyl group pKa 1.8–2.5
- A amino group pKa 8.7–10.7.

If pH is less than pKa, a greater amount of the group is protonated (NH_3^+ or COOH). Unprotonated or anion form (NH_2 or COO^-).

If pH = pKa, then [conjugate base] = [weak acid].

Reactions of Amino Acids

Decarboxylation

The amino acids will undergo α-decarboxylation to form the corresponding amine. For example:

Histidine ⟶ Histamine + CO_2
Tyrosine ⟶ Tyramine + CO_2
Tryptophan ⟶ Tryptamine + CO_2
Lysine ⟶ Cadaverine + CO_2
Glutamic acid ⟶ Gamma-aminobutyric acid + CO_2

Amide Formation

The -COOH group of dicarboxylic amino acids (other than α-carboxyl) can combine with ammonia to form the corresponding amide. For example:

Aspartic acid + NH_3 ⟶ Asparagine
Glutamic acid + NH_3 ⟶ Glutamine

Transamination

The α-amino group of amino acid can be transferred to α-keto acid to form the corresponding new amino acid and α -keto acid. This is an important reaction in the body for the interconversion of amino acids and for synthesis of non-essential amino acids.

Oxidative Deamination

The α-amino group is removed from the amino acid to form the corresponding keto acid and ammonia. Glutamic acid undergoes oxidative deamination.

Formation of Carbamino Compound

Carbon dioxide adds to the α-amino group of amino acids to form carbamino compounds.

Transmethylation

The methyl group of methionine, after activation, may be transferred to an acceptor, which becomes methylated.

Methionine + Acceptor ⟶ Methylated acceptor + Homocysteine.

Ester Formation by the -OH Group

The hydroxyl amino acids can form esters with phosphoric acid. In this manner, the serine and threonine residues of proteins are involved in the formation of phosphoproteins.

Reaction of the Amide Group

The amide groups of glutamine and asparagine can form N-glycosidic bonds with carbohydrate residues to form glycoproteins.

Reactions of -SH Group

Cysteine has a sulfhydryl (SH) group and it can form a disulfide (S-S) bond with another cysteine residue. The two cysteine residues can connect two polypeptide chains by the formation of interchain disulfide bonds. The dimer formed by two cysteine residues is sometimes called cystine.

Amino Acid Derivatives

1. Gamma-aminobutyric acid (derivative of glutamic acid) and dopamine (derived from tyrosine) are neurotransmitters.

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2. Histamine (synthesized from histidine) is the mediator of allergic reactions.
3. Thyroxine (from tyrosine) is an important thyroid hormone.
4. Cycloserine, a derivative of serine is an antituberculosis drug. Azaserine inhibits reactions where amide groups are added and so acts as an anticancer drug.
5. Histidine residues are important in the buffering activity of proteins.
6. Ornithine and citrulline are derivatives of arginine, and are essential for urea synthesis.

PROTEINS

Proteins are polypeptides of amino acids linked by peptide bond.

Structure of Proteins

Primary Structure

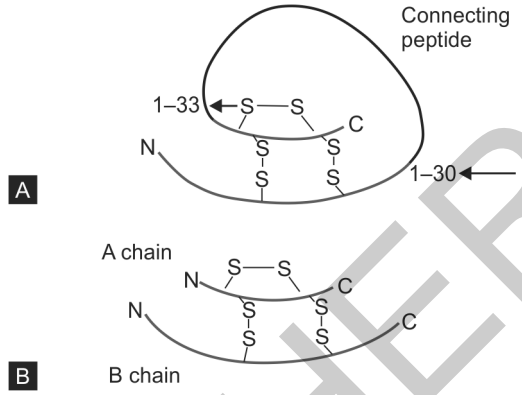
Primary structure of protein denotes the number and sequence of amino acids in the protein and location of disulfide bonds if any. Primary structure determines biological activity. It is maintained by the covalent peptide bonds. The peptide bond is a partial double bond. The C—N bond is 'trans' in nature and there is no freedom of rotation because of the partial double bond character. The side chains are free to rotate on either side of the peptide bond. The angles of rotation are known as Ramachandran angles. At one end, a free α-amino group is present, this end is called amino terminal (N-terminal). Other end with free carboxyl group is called carboxy-terminal end (C-terminal).

Primary structure of insulin: It has two polypeptide chains. The chain (glycine chain) has 21 amino acids and B (phenylalanine) chain has 30 amino acids. They are held together by two interchain disulfide bonds. There is another intrachain disulfide bond between 6th and 11th cysteine residues of A chain. Proinsulin has an additional C peptide (connecting peptide) which is removed during maturation (Figs 4.1A and B).

Secondary Structure

Secondary structure is the steric relationship of amino acids, close to each other. They are preserved by non-covalent forces or bonds like hydrogen bonds, electrostatic bonds, hydrophobic interactions and van der Waals forces. Three types are there (Fig. 4.2).

Alpha helix: It is the most common and stable conformation for a polypeptide chain. In proteins like hemoglobin and myoglobin, the α-helix is abundant. The α-helix is a spiral structure. The α-helix is generally right handed. Left handed α-helix is rare, because amino acids found in proteins are of L-variety.



Figs 4.1A and B: Primary structure of insulin. **A.** Proinsulin; **B.** Active insulin.

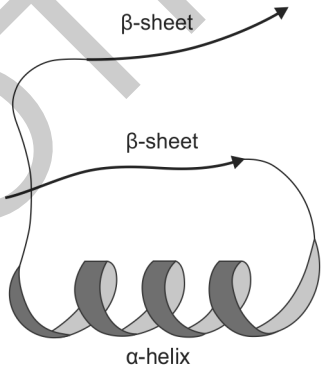


Fig. 4.2: Secondary structure of protein

Beta-pleated sheet: The polypeptide chains in β-pleated sheet is almost fully extended. β-pleated sheet is the major structural motif in proteins like silk fibroin (antiparallel), flavodoxin (parallel) and carbonic anhydrase (both).

Collagen helix: It is a triple helical structure found in collagen.

Tertiary Structure

Tertiary structure denotes the overall arrangement and inter-relationship of the various regions or domains of a single polypeptide chain. The tertiary structure is maintained by non-covalent interactions such as hydrophobic bonds, electrostatic bonds and van der Waals forces. Domain is the term used to denote a compact globular functional unit of a protein.

Quaternary Structure

Quaternary structure results when the proteins consist of two or more polypeptide chains held together by non-covalent forces. They are functional proteins. Examples are hemoglobin, immunoglobulin, etc.

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Classification of Proteins

Based on Functions

1. Contractile proteins, e.g. myosin, actin.
2. Transport proteins, e.g. hemoglobin, myoglobin, albumin, transferrin.
3. Regulatory proteins or hormones, e.g. adrenocorticotropic hormone (ACTH), insulin growth hormone.
4. Genetic proteins, e.g. histones.
5. Protective proteins, e.g. immunoglobulins, interferons, clotting factors.
6. Catalytic proteins, e.g. enzymes.
7. Structural proteins, e.g. collagen, elastin.

Based on Composition and Solubility

1. Simple proteins: They contain only amino acids:
   a. Albumins: They are soluble in water and coagulated by heat, e.g. human serum albumin, lactalbumin of milk and egg albumin.
   b. Globulins: These are insoluble in pure water, but soluble in dilute salt solutions. They are also coagulated by heat, e.g. egg globulin, serum globulins, legumin of peas.
   c. Protamines: These are soluble in water, dilute acids and alkalis. They contain large number of arginine and lysine residues, and so are strongly basic, e.g. protamine zinc insulinate.
   d. Prolamins: They are soluble in alcohol. They are rich in prolines, but lack, in lysine, e.g. zein from corn, gliadin of wheat, hordein of barley.
   e. Lectins: These are precipitated by ammonium sulfate. They have high affinity to sugar groups.
   f. Scleroproteins: They are insoluble in water, salt solutions and organic solvents; soluble only in hot strong acids. They form supporting tissues. For example, collagen of bone, cartilage and tendon, keratin of hair, horn, nail and hoof.
2. Conjugated proteins: They are combinations of protein with a non-protein part called prosthetic group:
   a. Glycoproteins: These are proteins combined with carbohydrates. Blood group antigens and many serum proteins are glycoproteins.
   b. Lipoproteins: These are proteins loosely combined with lipid components.
   c. Nucleoproteins: These are proteins attached to nucleic acids, e.g. histones.
   d. Chromoproteins: These are proteins with colored prosthetic groups, e.g. hemoglobin (heme, red).
   e. Phosphoproteins: These contain phosphorus casein of milk and vitellin of egg yolk, e.g.
   f. Metalloproteins: They contain metal ions. For example, hemoglobin (iron), cytochrome (iron), tyrosinase (copper) and carbonic anhydrase (zinc).
3. Derived proteins: They are degradation products of native proteins.

Based on the Shape

1. Globular proteins: Spherical or oval in shape and easily soluble, e.g. albumins, globulins and protamines.
2. Fibrous proteins: Elongated or needle-shaped, and solubility is minimum; they resist digestion, e.g. collagen, elastin and keratins.

Based on Nutritional Value

1. Nutritionally rich proteins (complete proteins or first class proteins): They contain all the essential amino acids in the required proportion, e.g. casein.
2. Incomplete proteins: They lack one essential amino acid. Proteins from pulses are deficient in methionine, while proteins of cereals lack lysine.
3. Poor proteins: They lack in many essential amino acids. Zein from corn lacks tryptophan and lysine.

Biologically Important Peptides

1. Thyrotropin-releasing hormone (TRH) is a tripeptide with the sequence of Glu-His-Pro.
2. Glutathione is a tripeptide. It is γ-glutamyl-cysteinyl-glycine. It is involved in erythrocyte membrane integrity and is important in keeping enzymes in active state.
3. Oxytocin and vasopressin antidiuretic hormone (ADH) are nanopeptides with nine amino acids.
4. Angiotensin.

METABOLISM OF AMINO ACIDS

Amino acids are either derived from diet or are synthesized by the body. The body amino acid pool is always in a steady state, the rate of synthesis of proteins balances the rate of degradation.

Digestion of Proteins

The major proteolytic enzymes are:
1. Endopeptidases: Pepsin, trypsin, chymotrypsin.
2. Exopeptidases: Carboxypeptidases, aminopeptidases.

1. Gastric Digestion of Proteins

In the stomach, hydrochloric acid is secreted. It makes the pH optimum for the action of pepsin and also activates pepsin.

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The acid also denatures the proteins. Rennin, otherwise called chymosin, is active in infants and is involved in the curdling of milk. It is absent in adults. Milk protein, casein is converted to paracasein by the action of rennin. Pepsin is secreted by the chief cells of stomach as inactive pepsinogen. The optimum pH for activity of pepsin is around 2.

2. Pancreatic Digestion of Proteins

The optimum pH for the activity of pancreatic enzymes (pH 8) is provided by the alkaline bile and pancreatic juice. The secretion of pancreatic juice is stimulated by the peptide hormones, cholecystokinin and pancreozymin. Pancreatic juice contains the important endopeptidases namely trypsin, chymotrypsin, elastase and carboxypeptidase. Trypsinogen is activated by enterokinase, which activates trypsin.

3. Intestinal Digestion of Proteins

Complete digestion of the small peptides to amino acids is by enzymes present in intestinal juice (succus entericus). Leucine aminopeptidase, proline aminopeptidase, dipeptidases and tripeptidases are involved.

Absorption of Amino Acids

Five different carriers are involved for the transport of amino acids:

- Neutral amino acids (alanine, valine, leucine, methionine, phenylalanine, tyrosine, isoleucine)
- Basic amino acids (Lys, Arg and cysteine)
- Imino acids and glycine
- Acidic amino acids (Asp, Glu)
- Beta-amino acids (β-alanine).

Amino Acid Pool

Amino acid pool of the body depends on the input and output of amino acids (Fig. 4.3).

Metabolism of Ammonia

Ammonia is a toxic product released during amino acid metabolism. Sources and fate of ammonia are shown in Figure 4.4. Detoxification of ammonia is by conversion to urea and excretion through urine.

1. Transamination

Transamination is the exchange of the α-amino group between one α-amino acid and another α-keto acid, forming a new α-amino acid (Fig. 4.5).

Significance of transamination: These are the following:

1. In this first step, ammonia is removed and the carbon skeleton of the amino acid enters into catabolic pathway.
2. By means of transamination, all non-essential amino acids can be synthesized. For example, pyruvate can be transaminated to synthesize alanine.
3. Interconversion of amino acids.
4. Transamination is reversible and requires pyridoxal phosphate.
5. Exception: Lysine, threonine and proline are not transaminated. They follow direct degradative pathways.
6. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are induced by glucocorticoids, which favor gluconeogenesis. AST and ALT are markers of liver injury.

2. Transdeamination

a. The amino group of most of the amino acids is released by a coupled reaction, transdeamination, i.e. transamination followed by oxidative deamination. Transamination takes place in the cytoplasm. The amino group is transported to liver as glutamic acid, which is finally oxidatively deaminated in the mitochondria of hepatocytes.
b. Only liver mitochondria contain glutamate dehydrogenase (GDH), which deaminates glutamate to α-ketoglutarate plus ammonia. So, all amino acids are first transaminated to glutamate, which is then finally deaminated (transdeamination).

Urea Cycle

Urea is the end product of protein metabolism. The nitrogen in amino acid is converted into toxic ammonia, which

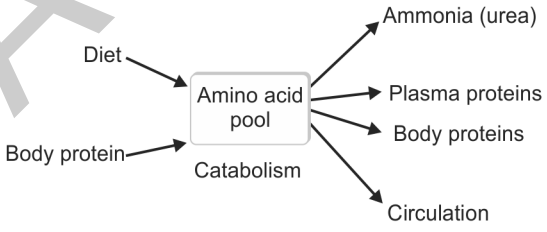

Fig. 4.3: Amino acid pool

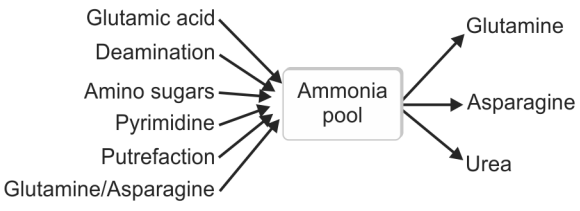

Fig. 4.4: Fate of ammonia

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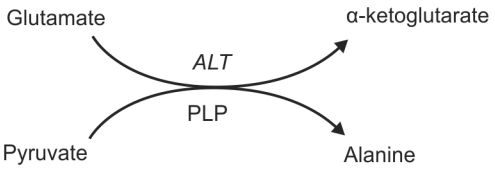

Fig. 4.5: Transamination (ALT, alanine aminotransferase; PLP, pyridoxal phosphate).

then detoxifies to urea by urea cycle. The urea cycle is the first metabolic pathway to be elucidated. The cycle is known as Krebs-Henseleit urea cycle. As ornithine is the first member of the reaction, it is also called ornithine cycle (Fig. 4.6).

Steps

Urea synthesis is a five-step cyclic process, with five distinct enzymes. The first two enzymes are present in mitochondria, while the rest are localized in cytosol.

Step 1: Formation of carbamoyl phosphate
One molecule of ammonia condenses with CO_2 in the presence of two molecules of adenosine triphosphate (ATP) to form carbamoyl phosphate. The reaction is catalyzed by the mitochondrial enzyme carbamoyl phosphate synthetase I (CPS I). An entirely different cytoplasmic enzyme, carbamoyl phosphate synthetase II, (CPS II) is involved in pyrimidine nucleotide synthesis. CPS I reaction is the rate-limiting step in urea formation. It is irreversible and allosterically regulated.

Step 2: Formation of citrulline
Citrulline is synthesized from carbamoyl phosphate and ornithine by ornithine transcarbomylase. Ornithine is regenerated and used in urea cycle. The citrulline leaves the mitochondria and further reactions are taking place in cytoplasm.

Step 3: Synthesis of argininosuccinate
Argininosuccinate synthase condenses citrulline with aspartate to produce argininosuccinate. The second amino group of urea is incorporated in this reaction. This step requires ATP, which is cleaved to adenosine monophosphate (AMP) and inorganic pyrophosphate (PPi). The PPi is an inhibitor of this step.

Step 4: Formation of arginine
Argininosuccinate is cleaved by argininosuccinate lyase (argininosuccinate) to arginine and fumarate. The enzyme is inhibited by fumarate. The fumarate formed may be funneled into TCA cycle to be converted to malate and then to oxaloacetate to be transaminated to aspartate. Thus the urea cycle is linked to tricarboxylic acid (TCA) cycle through fumarate.

Citrulline + Aspartate ⟶ Arginine + Fumarate

Step 5: Formation of urea
The final reaction of the cycle is the hydrolysis of arginine to urea and ornithine by arginase. The ornithine returns to the mitochondria to react with another molecule of carbamoyl phosphate, so that the cycle will proceed. Thus, ornithine may be considered as a catalyst, which enters the reaction and is regenerated.

Overall Reaction and Energetics of Urea Cycle

The urea cycle is irreversible and consumes four ATP. Two ATP are utilized for the synthesis of carbamoyl phosphate. One ATP is converted to AMP and PPi to produce argininosuccinate, which equals to two ATP. Four ATP are actually consumed.

$NH_4^+ + CO_2$ + Aspartate + 3ATP ⟶ urea + Fumarate + 2ADP + 2Pi + AMP + PPi

Regulation of the Urea Cycle

Coarse regulation: The enzyme levels change with the protein content of diet. During starvation, the activity of urea cycle enzymes is elevated to meet the increased rate of protein catabolism.

Fine regulation: The major regulatory step is catalyzed by CPS I, where the positive effector is N-acetylglutamate (NAG). It is formed from glutamate and acetyl-CoA. Arginine is an activator of NAG synthase.

Compartmentalization: The urea cycle enzymes are located in such a way that the first two enzymes are in the mitochondrial matrix. The inhibitory effect of fumarase on its own formation is minimized because argininosuccinate lyase is in the cytoplasm, while fumarase is in mitochondria.

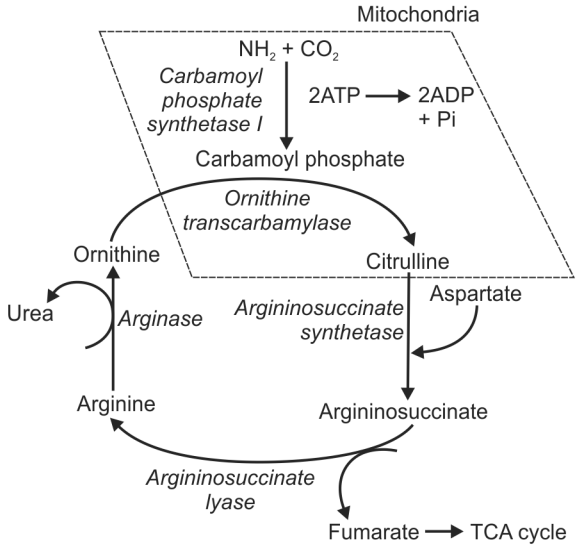

Fig. 4.6: Urea cycle (ADP, adenosine diphosphate; ATP, adenosine triphosphate; TCA, tricarboxylic cycle; Pi, inorganic phosphate).

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Disorders of Urea Cycle

Disorders of urea cycle are summarized in Table 4.1.

Urea Level in Blood

In clinical practice, blood urea level is taken as an indicator of renal function. The normal urea level in plasma is from 20 to 40 mg/dL. Urinary excretion of urea is 15–30 g/day (6–15 g nitrogen/day).

Elevation of blood urea may be broadly classified as:

1. **Pre-renal:** This is associated with increased protein breakdown leading to a negative nitrogen balance, as seen after major surgeries, prolonged fever, diabetic coma, etc.
2. **Renal:** In renal disorders like acute glomerulonephritis, chronic nephritis, nephrosclerosis, polycystic kidney, blood urea is increased.
3. **Postrenal:** When there is obstruction in urinary tract, blood urea is elevated. This is due to increased reabsorption of urea from renal tubules.
4. **Uremia:** Increased blood urea levels mostly due to renal failure.
5. **Azotemia:** A condition with elevation in blood urea or other nitrogen metabolites, which may or may not be associated with renal disease.

ONE-CARBON METABOLISM

The different one-carbon groups of the 'one-carbon pool' of the body are:

- Formyl group
- Formimino group
- Methenyl group
- Hydroxymethyl group
- Methylene group
- Methyl group.

The one-carbon groups, except methyl group, are carried by tetrahydrofolic acid (THFA). The THFA is produced from folic acid. Generation of one-carbon group is shown in Figure 4.7.

Generation of One-carbon Groups

The one-carbon groups are contributed to the one-carbon pool by amino acids:

1. Serine to glycine (serine hydroxymethyltransferase reaction) is the primary contributor for methylene THFA.
2. Glycine cleavage system also produces methylene groups.
3. Histidine contributes to N^5-formimino THFA through formiminoglutamic acid (FIGLU).
4. Tryptophan donates formyl-THFA.
5. Choline and betaine are donors of hydroxymethyl groups.

As serine is converted to choline, three one-carbon units are used up. During the conversion of choline to glycine, these methyl groups are recovered. Hence, this pathway is called 'salvage pathway' for one-carbon units.

Role of Methionine and Vitamin B_{12} in One-carbon Metabolism

Methyl ($-CH_3$) group is an important one-carbon unit. After the release of methyl group, methionine is converted to homocysteine. For the regeneration of methionine, free homocysteine and N-methyltetrahydrofolate (THF) are required and this reaction is dependent on methylcobalamin (vitamin B_{12}). The one-carbon pool, under the control of THF, is linked with methionine metabolism (transmethylation) through vitamin B_{12}. Hence vitamin B_{12} is also involved in one-carbon metabolism (refer Fig. 4.7).

Utilization of One-carbon Groups

The carbon units are used for synthesis of the following compounds:

Table 4.1: Disorders of urea cycle

Diseases	Enzyme deficit	Features
Hyperammonemia type I	Carbamoyl phosphate synthetase I	High NH_3 level in blood, autosomal recessive, mental retardation
Hyperammonemia type II	Ornithine transcarbamylase	High NH_3 level in blood, orotic aciduria
Hyperornithinemia	Defective ornithine transporter protein	Hyperornithinemia, hyperammonemia Homocitrullinuria Autosomal recessive
Citrullinemia	Argininosuccinate synthetase	Autosomal recessive, citrullinuria, high blood levels of NH_3 and citrulline
Argininosuccinic aciduria	Argininosuccinate lyase	Argininosuccinate in blood and urine
Hyperargininemia	Arginase	Arginine increased in blood and cerebrospinal fluid (CSF); cysteine and lysine in urine

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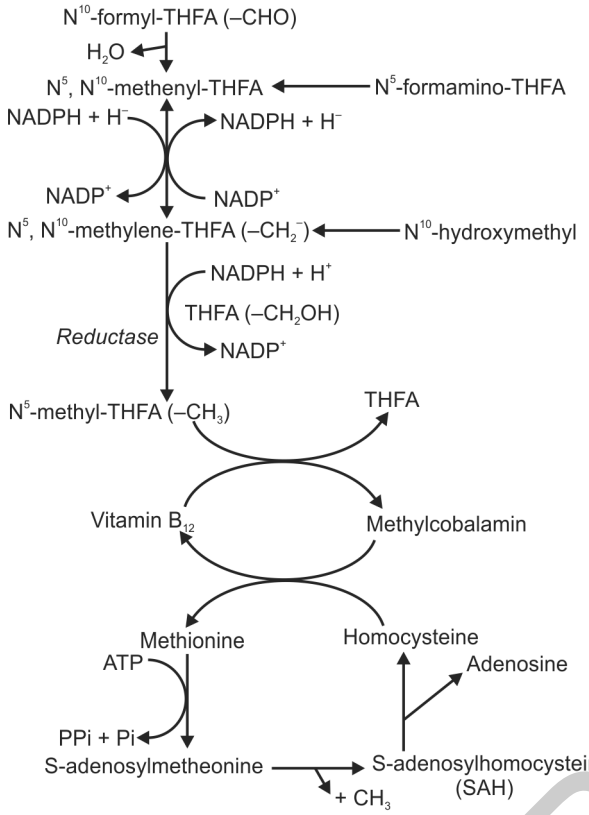


Fig. 4.7: One-carbon metabolism (ATP, adenosine triphosphate; NADPH, nicotinamide adenine dinucleotide phosphate; THFA, tetrahydrofolic acid).

- C2 of purine
- Formylation of methionyl-tRNA
- C8 of purine
- Glycine
- Serine
- Choline
- Deoxythymidine monophosphate (TMP)
- Transmethylation reactions including creatine, choline and epinephrine synthesis
- Excreted as carbon dioxide.

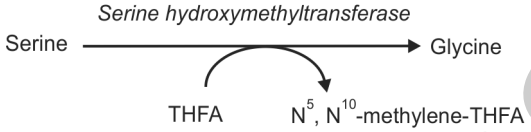
AMINO ACID METABOLISM

Glycine (G)

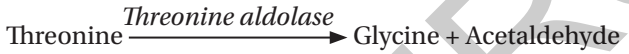
Glycine (G) is the simplest amino acid. It is non-essential and glucogenic.

Synthesis of Glycine

1. From serine: The β-carbon of serine is channeled into the one-carbon pool, carried by THFA. The α-carbon of serine becomes the α-carbon of glycine.



2. From threonine by the activity of threonine aldolase.



3. From glycine synthase: Glycine can be synthesized by the glycine synthase reaction from CO_2, NH_3 and one carbon unit. This is the reversal of the glycine cleavage system.

Metabolism of Glycine

1. From glycine cleavage system: Glycine undergoes oxidative deamination (reversal of glycine synthase) to form NH_3, CO_2 and one-carbon unit methylene-THFA. This pathway is the major catabolic route for glycine (Fig. 4.8). It consist of:
   a. Glycine decarboxylase with pyridoxal phosphate (PLP).
   b. Lipoamide-containing amino methyltransferase.
   c. Methylene THFA-synthesizing enzyme.
   d. NAD^+-dependent lipoamide dehydrogenase.
2. Glucogenic pathway: Glycine is mainly channeled into the glucogenic pathway by getting first converted to serine. This is the reversal of serine hydroxymethyltransferase reaction. The serine is then converted to pyruvate by serine dehydratase.
3. Creatine and creatine phosphate: Creatine constitutes about 0.5% of total muscle weight. It is synthesized from three amino acids, glycine, arginine and methionine (Fig. 4.9).
4. Synthesis of heme: The enzyme aminolevulinic acid (ALA) synthase condenses glycine with succinyl-CoA to form delta ALA. It is the key enzyme of heme synthesis.
5. Synthesis of purines: The whole molecule of glycine is incorporated into the purine ring (C_4, C_5 and N_7).

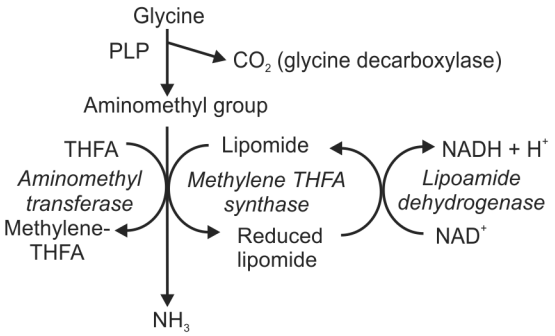


Fig. 4.8: Glycine cleavage (NADH, nicotinamide adenine dinucleotide; PLP, pyridoxal phosphate; THFA, tetrahydrofolic acid)

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