3

Amino Acid and its Metabolism

The general structure of an amino acid contains a central alpha (α) carbon atom to which a carboxylic group, an amino group, a hydrogen atom and a side chain (R) which uniquely defines each of the 20 common amino acids are attached (Diagram 3.1a).

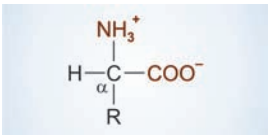


Diagram 3.1a: Structure of an amino acid

Peptide bond formation (Diagram 3.1b).

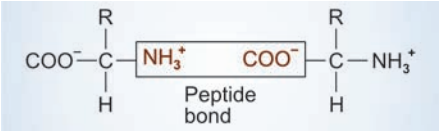


Diagram 3.1b: Peptide bond formation

α-amino group of one amino acid and α-carboxyl group of another amino acid make a peptide bond.

Characteristic of peptide bond[Q]

- Partial double bond (distance is 1.32Å)
- Rigid and planar
- C-N bond *trans* in nature
- Uncharged but polar
- The free NH_2 group of the terminal amino acids is called N-terminal end and free—COOH end is called C-terminal end (Diagram 3.1b).

Zwitter Ions (Ampholyte) and Isoelectric pH (pI)

Amino acids in solution are predominantly present as dipolar ions (zwitter ions/ampholytes) rather than as unionized molecules. Net charge on the amino acid depends

upon the pH of the medium. **pH at which amino acids are electrically neutral (equal positive and negative charges present) is known as isoelectric pH (pI).**Q

Values of pI of various amino acids are given in Table 3.1.Q

Table 3.1: Isoelectric pH (pI) of various amino acids

Amino acid with pI <7	*pI*	*Amino acid with pI >7*	*pI*
Aspartic acid	3.0	Arginine	10.8
Glutamic acid	3.2	Lysine	9.7
Cysteine	5.1	HistidineQ	7.6
Glutamine	5.6		
Serine	5.7		
Tyrosine	5.7		
Tryptophan	5.9		
Phenylalanine	5.9		
Valine	6.0		
Glycine	6.1		

At isoelectric pH amino acids show following characteristics

1. No net charge
2. No mobility on electrophoresis
3. Minimum solubility (maximum precipitability)
4. Least buffering capacity

CLASSIFICATION OF AMINO ACIDS

They are classified based on following 4 characters

1. Based on structure
2. Based on side chain character
3. Based on metabolic fate
4. Based on nutritional requirements

1. Classification of Amino Acid Based on StructureQ

A. Aliphatic amino acidQ

1. Monoamino monocarboxylic acid
   - Simple: Glycine, alanine
   - Branched: Valine, leucine, isoleucine
   - Hydroxyl: Serine, threonine
   - Sulfur containing: Cysteine, methionine
   - Amide group containing: Glutamine, asparagine
2. Monoamino dicarboxylic acid: Aspartic acid, glutamic acid
3. Dibasic monocarboxylic acid: Arginine, lysine

B. Aromatic amino acid: Phenylalanine, tyrosine

C. Heterocyclic amino acid: Histidine, tryptophan

D. Imino amino acid: Proline

E. Derived amino acid: Hydroxyproline, hydroxylysine, ornithine, citrulline, homocysteine.

Special group present in some amino acid[Q]

Amino acids	*Special groups*	*Carbon atom at which special group is present*
Arginine	Guanidium	δ
Tryptophan	Indole	β
Histidine	Imidazole	β
Proline	Pyrrolidine	α
Tyrosine	Phenol	β

2. Classification of Amino Acid Based on Side Chain Character[Q]

Nonpolar: Mnemonic—**PP TT MILAV**.

Phenylalanine, **p**roline, **t**ryptophan, **t**yrosine, **m**ethionine, **i**soleucine, **l**eucine, **a**lanine, **v**aline.

Polar: Uncharged = Glycine, serine, threonine, cysteine
Acidic = Aspartic acid, glutamic acid
Basic = Arginine, lysine, histidine

3. Classification of Amino Acid Based on Metabolic Fate[Q]

Purely ketogenic—leucine, lysine

Ketogenic and glucogenic—phenylalanine, isoleucine, tyrosine, tryptophan (PITT)

Glucogenic—rest 14 amino acids are glucogenic

4. Classification of Amino Acid Based on Nutritional Requirement[Q]

Essential	*Nonessential*
Methionine	Rest 10
Arginine—semi-essential	
Threonine	
Tryptophan	
Valine	
Isoleucine	
Leucine	
Phenylalanine	
Histidine—semi-essential	
Lysine	

*(Mnemonic for essential amino acid is **MATT VIL PHLY**)*

BIOSYNTHESIS OF UREA

Urea synthesis occurs in the following **4 stages**:[Q] (i) Transamination, (ii) oxidative deamination of glutamate, (iii) ammonia transport, (iv) reactions of urea cycle.

i. ***Transamination*:** The transfer of an amino group from an amino acid to a keto acid. This process involves the inter conversion of a pair of amino acids and a pair of keto acids, catalysed by a group of enzymes called transaminase (amino transferases).

Important features of transamination

1. All transaminases require pyridoxal phosphate **(PLP) as cofactor**,[Q] which resides at the catalytic site.
2. Specific transaminase exists for each pair of amino and keto acids. These are specific for only one pair, but non-specific for the other pair.
3. No free ammonia is liberated. Only the transfer of amino group occurs.
4. This reaction is reversible
5. It is not restricted to α-amino groups.
6. Amino acids undergo transamination, transferring nitrogen mostly to the α-ketoglutarate synthesizing glutamate, which is the only amino acid that undergoes oxidative deamination to a significant extent to liberate free NH_3 for urea synthesis.

   1. Aspartate + α-ketoglutarate $\xrightleftharpoons{\text{AST/SGOT}}$ Oxaloacetate + glutamate

   2. Alanine + α-ketoglutarate $\xrightleftharpoons{\text{ALT/SGPT}}$ Pyruvate + glutamate

   All amino acids undergo transamination reaction except lysine, threonine (they undergo deamination)

ii. ***Deamination*:** The removal of amino group from the amino acid as ammonia is called deamination. Simultaneously, the carbon skeleton of amino acid is converted to keto acids.

***Oxidative deamination*:** Liberation of free ammonia from the amino group of amino acids coupled with oxidation is catalysed by glutamate dehydrogenase enzyme found in the liver and kidney.

GDH is unique in that it can utilize both NAD^+ or $NADP^+$ as coenzyme[Q]

GDH is inhibited by GTP and is activated by ADP. (Low energy activates amino acid catabolism.)

iii. ***Transport of ammonia***

- It is transported in the form of **glutamine and alanine.**
- A mitochondrial enzyme glutamine synthase is responsible for the synthesis of glutamine from glutamate and ammonia. **Glutamine synthase is abundantly found in brain cells**

$$\text{Glutamate + ammonia} \xrightarrow[\text{ATP, } Mg^+]{\text{Glutamine synthase}} \text{Glutamine}$$

In the liver, kidney and intestinal cells, an enzyme **glutaminase** removes NH_3 from glutamine. In the liver this NH_3 is incorporated in the urea and in renal cells this NH_3 is used in maintaining the acid–base balance.

iv. ***The urea cycle (Krebs-Henseleit cycle/ornithine cycle).***

REACTIONS OF THE UREA CYCLE

The first two reactions (a) CPS I and (b) OTC leading to the synthesis of urea occur in the mitochondria, whereas remaining enzymes are located in the cytoplasm.

a. **Carbamoyl phosphate synthetase I (CPS I)** catalyzes the formation of carbamoyl phosphate formed from ammonia and carbon dioxide (as HCO_3^-)
   i. Energy requirement: Two molecules of ATP are required for this reaction.
   ii. **N-Acetylglutamate is a positive allosteric effector of CPS I**
b. **Ornithine transcarbamoylase** (OTC) catalyzes the formation of citrulline from carbamoyl phosphate and ornithine.
c. **Argininosuccinate synthetase** catalyzes the formation of argininosuccinate from citrulline and aspartate. One molecule of ATP is required which is cleaved to AMP + PPi (equivalent to 2 ATP). The amino group of aspartate provides one of the two nitrogen atoms that appear in urea.Q
d. **Argininosuccinate lyase** catalyzes the formation of arginine and fumarate from the cleavage of argininosuccinate.
e. **Arginase** catalyzes the formation of urea and ornithine from the cleavage of arginine.

Note

1. Urea is highly soluble and nontoxic. It enters the blood and is excreted in the urine.
2. Ornithine continues to act as an intermediate in the urea cycle. Ornithine is considered as catalyst in urea cycle.

Diagram 3.2 shows the various reactions of urea cycle.

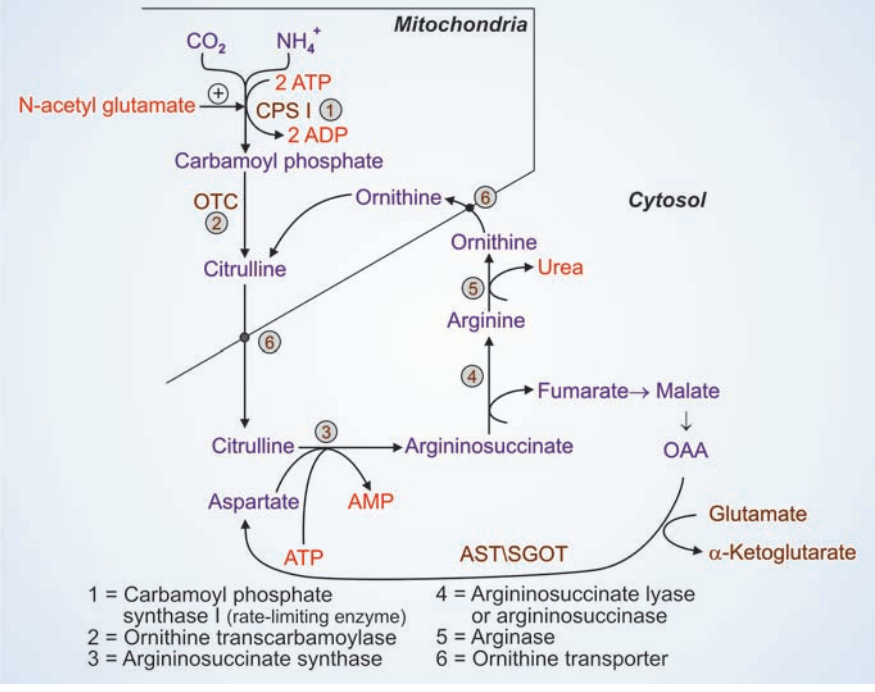


Diagram 3.2: Urea cycle reactions

Regulation of the urea cycle

N-Acetylglutamate is a positive allosteric effector for carbamoyl phosphate synthetase I. It is the rate-limiting step in the urea cycle.[Q]

N-Acetylglutamate is synthesized from acetyl CoA and glutamate, in a reaction for which arginine is needed.

So, protein intake increases the concentration of agrinine and thus of N-acetyl glutamate, leading to increased urea formation.

Urea Cycle Disorder[Q]

- **Type I** hyperammonemia is due to a defect in carbamoyl phosphate synthetase I.
- **Type II** hyperammonemia is due to a defect in ornithine transcarbamoylase.
- **Citrullinemia** is due to a defect in argininosuccinate synthetase.
- **Argininosuccinic aciduria** is due to a defect in argininosuccinate lyase.
- **Hyperarginemia** is due to a defect in arginase.

Phenyl butyrate is given in the treatment of urea cycle disorder.

1. *Glycine*

- Nonessential, polar and glycogenic[Q]
- It is the only amino acid which is optically inactive[Q]

Synthesis[Q]

It can be synthesized in mammalian tissues by serine, threonine, choline, glyoxylate.

$$\text{Glycine} \xrightarrow{\text{Serine hydroxymethyl transferase}} \text{Serine} \xrightarrow{\text{Serine dehydratase}} \text{Pyruvate}$$

$$\text{Threonine} \xrightarrow{\text{Aldolase}} \text{Glycine} + \text{acetaldehyde}$$

$$\text{Glyoxylate} + \text{glutamate/alanine} \longrightarrow \text{Glycine}$$

Specialized Products of Glycine[Q]

1. Purine (C_4, C_5, N_7 atoms of purine ring comes from glycine)
2. Glutathione
3. Heme
4. Creatine (glycine + arginine + methionine)[Q]
5. Conjugation — With bile acids, so that to increase their amphipathic properties
   Detoxification, e.g. glycine + benzoic acid → hippuric acid.

2. *Alanine*

Nonessential, glucogenic amino acid[Q]

Quantitatively most important amino acid taken up by liver from peripheral tissues specially skeletal muscle during fasting state[Q].

β alanine formed due to catabolism of pyrimidine nucleotide. It is used for coenzyme A synthesis.

3. *Serine*

Nonessential, glucogenic amino acid.Q

Synthesis

- 3 phosphoglycerates (an intermediate of the glycolysis) are major source of serine.Q
- Glycine
- Alanine

Catabolism: Serine is deaminated to give pyruvate

Serine contributes in the formation of the following compounds

- Glycine
- Cysteine
- Alanine
- Phosphatidylserine
- Sphingosine
- Selenocysteine
- Ethanolamine
- Choline

Selenocysteine: Selenocysteine is considered as 21st amino acid.Q

Biosynthesis of selenocysteine is **by replacing the oxygen of hydroxyl group of serine by selenium**. Selenocysteine is derived from serine and it is incorporated in the protein during translation (cotranslational process). One of the codons of mRNA **UGA** is read as selenocysteine incorporation codon, for which a selenocysteine insertion element (a loop structure) is needed at the 3′ region of the mRNA.

Selenocysteine is found at the **active site of the following enzymes**Q

- Thioredoxine reductase
- Glutathione peroxidase (GPO)
- De-iodinase
- Selenoprotein P

4. *Threonine:* *Essential, glucogenic amino acid*Q

5. *Branched Chain Amino Acids*

Valine: Essential, glucogenic

Leucine: Essential, ketogenic

Isoleucine: Essential, glucogenic + ketogenic

During degradation of the branched chain amino acid, the first three metabolic reactions are common to all the three amino acids. These three reactions are:

1. Transamination
2. Oxidative decarboxylation
3. FAD dependent dehydrogenation (Diagram 3.3).

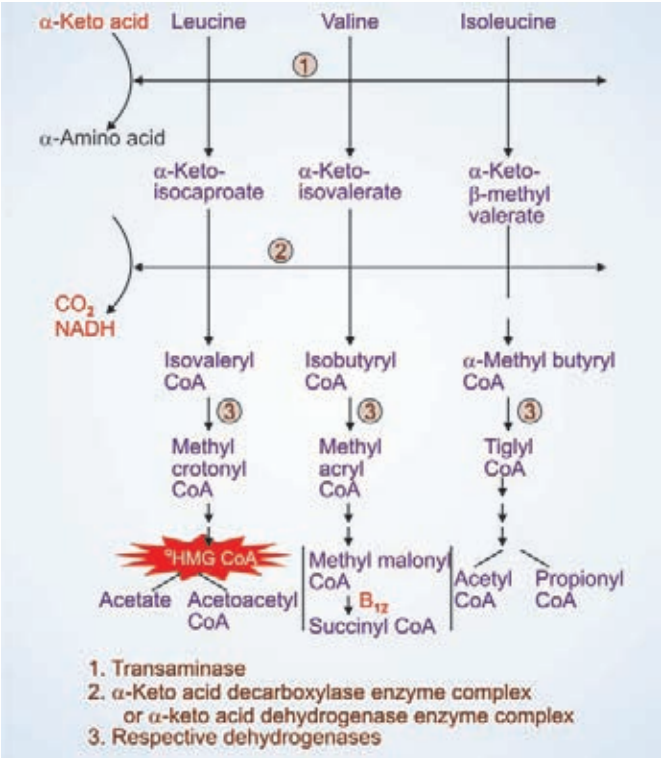


Diagram 3.3: Catabolism of branched chain amino acid

Metabolic Defects in Branched Chain Amino Acid Degradation

Maple syrup urine disease/branched chain ketonuria (MSUD)[Q]

- Defect is in the enzyme **α-keto acid dehydrogenase (also known as α-keto acid decarboxylase)**[Q]
- Elevated plasma concentration of branched chain amino acids and their respective keto acids
- Urine of patients has maple syrup or burnt sugar smell.

Isovaleric Aciduria

- Here only **leucine catabolism is affected.**[Q] Enzyme affected is isovaleryl CoA dehydrogenase.
- Urine gives cheesy odor.

6. Phenylalanine and Tyrosine

→ Structurally related aromatic amino acids. They are glucogenic + ketogenic.[Q]
→ Phenylalanine: Essential
→ Tyrosine: Nonessential
→ Phenylalanine gets converted to tyrosine and ingestion of tyrosine can reduce dietary requirement of phenylalanine.

Following physiological products are produced from tyrosine

1. Melanin (Diagram 3.5).
2. Catecholamine (Diagram 3.6).
3. In addition, thyroid hormone synthesis also requires tyrosine as a precursor.

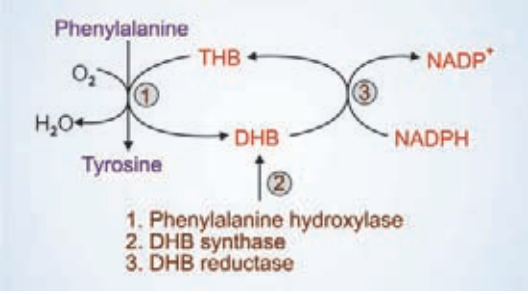


Diagram 3.4: Conversion of phenylalanine to tyrosine

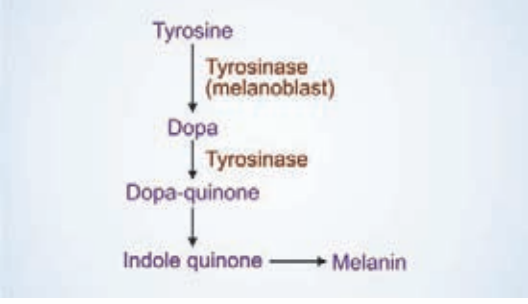


Diagram 3.5: Tyrosine to melanin

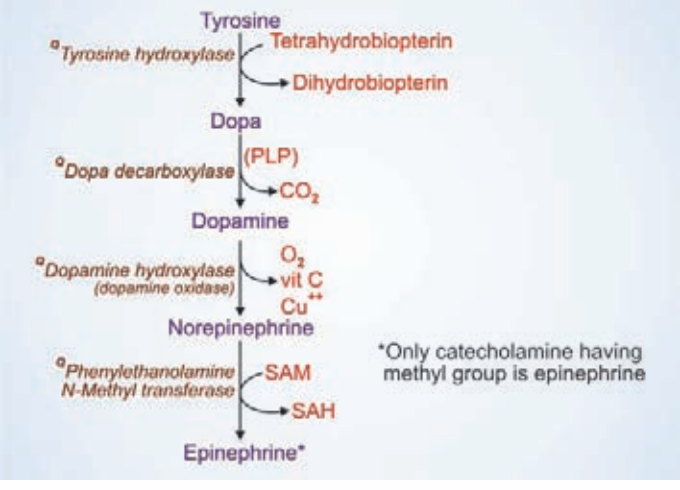


Diagram 3.6: Tyrosine to catecholamine

Degradation of Tyrosine (Phenylalanine)

As phenylalanine is converted to tyrosine, a single pathway is responsible for the degradation of both these amino acids, which occurs mostly in liver (Diagram 3.7).

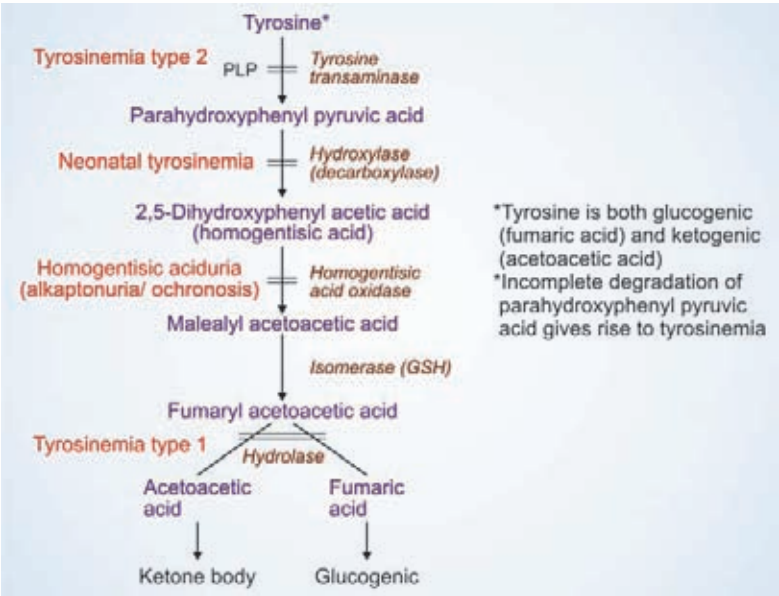


Diagram 3.7: Degradation of tyrosine

Disorders

1. **Phenylketonuria**
   a. Deficiency of phen
ylalanine hydroxylase: Classic PKU (PKU I), II, III.
   b. Deficiency of dihydrobiopterin reductase: Atypical PKU IV.
   c. Deficiency of dihydrobiopterin synthase: PKU V.

→ Phenylalanine cannot be converted to tyrosine and so there is increased concentration of phenylalanine and its metabolites in the body. It causes seizures and tremors, mental retardation, eczema, psychosis and mousy odor urine.

Diagnostic test for phenylketonuria

DNA probe facilitates **prenatal diagnosis** of defect of phenylalanine hydroxylase or dihydrobiopterin reductase enzyme.

- **Blood phenylalanine level:** Level increases from normal 1 mg/dl to >20 mg/dl
- **Guthrie test:** *Bacillus subtilis* is grown in media containing patient blood. *Bacillus subtilis* requires phenylalanine for its growth and hence it grows in patient blood.
- **Urine ferric chloride test:** $FeCl_3$ in the urine gives green discoloration to the urine.

Treatment

→ Diet low in phenylalanine to be given lifelong.

2. **Alkaptonuria**
   - Deficiency of homogentisate oxidase

- Characteristic finding: Darkening of urine, when exposed to air.
- Generalised pigmentation of connective tissues (ochronosis and a form of arthritis (ochre colored pigmentation of tissue).

3. **Albinisms:** Deficiencies of tyrosinase (Cu containing enzyme) cause albinisms. In this disease there is universal absence of melanin from whole body.

7. *Tryptophan*

- Essential
- Glucogenic and ketogenic
- Metabolism of tryptophan is divided into:
  a. Kynurenine pathway
  b. Serotonin pathway

Kynurenine Pathway[Q]

Diagram 3.8 shows kynurenine pathway.

Xanthurenic acid is produced by tryptophan in a shunt pathway in deficiency of vitamin B_6.

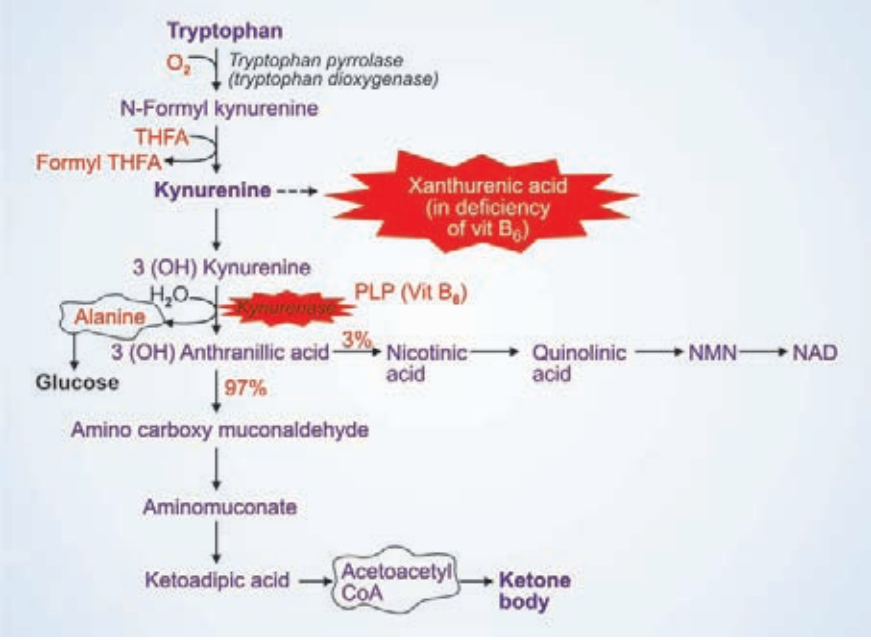


Diagram 3.8: Kynurenine pathway

Serotonin/Melatonin Pathway

Serotonin (also known as 5-hydroxytryptamine)

- It is a neurotransmitter
- Normally, ~1% of Trp is converted to serotonin (Diagram 3.9)
- 5-HIAA (5-hydroxyindoleacetic acid) is produced from serotonin when MAO acts on it.

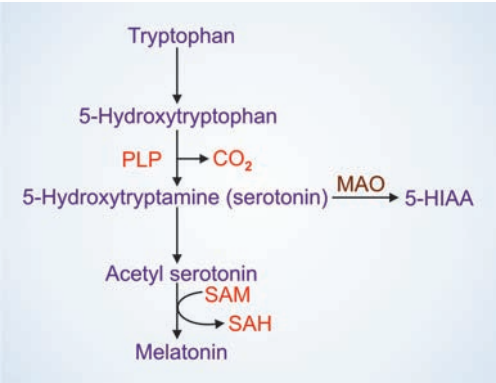


Diagram 3.9: Serotonin/melatonin pathway

8. *Arginine*

Semiessential, glucogenic[Q]
Contain guanidium group[Q]
Special product
1. Creatine
2. NO (Diagram 3.10)

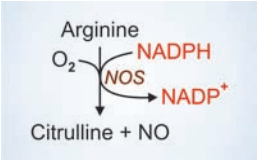


Diagram 3.10: NO synthesis from arginine

NOS (Nitric Ooxide Synthase)

Mono-oxygenase, cytosolic enzyme
It contains NADPH, FAD, FMN, tetrahydrobiopterin and heme.

Isoenzymes of NOS

- Neuronal: Constitutive, calcium stimulates its activity
- Inducible (macrophages): Induced by inflammation, IL-1 and TNF. Does not require calcium for its activation.
- Endothelial: Constitutive, calcium stimulates its activity.
  NO acts in **paracrine fashion** and acts via **cGMP.**

9. *Methionine*

- Essential amino acid.[Q]
- Serves as a precursor for the synthesis of cysteine and cystine.[Q]

Metabolism of Methionine

Methionine forms S-adenosyl methionine (SAM) which acts as a methyl donor and after donation of the methyl group SAM is converted back to SAH (S-adenosyl homocysteine).

SAH is hydrolysed into homocysteine and adenosine.

Homocysteine has got two fates:

1. May get converted into methionine
2. May form cysteine

1. ***Resynthesis of methionine:*** **N_5-methyl THF** acts as a methyl donor for conversion of homocysteine to methionine. Enzyme needed here is **methionine synthetase (homocysteine methyl transferase)**. Vitamin B_{12} is required as a cofactor.
2. **Synthesis of cysteine:** See Diagrams 3.11 and 3.12.

Metabolic Disorders

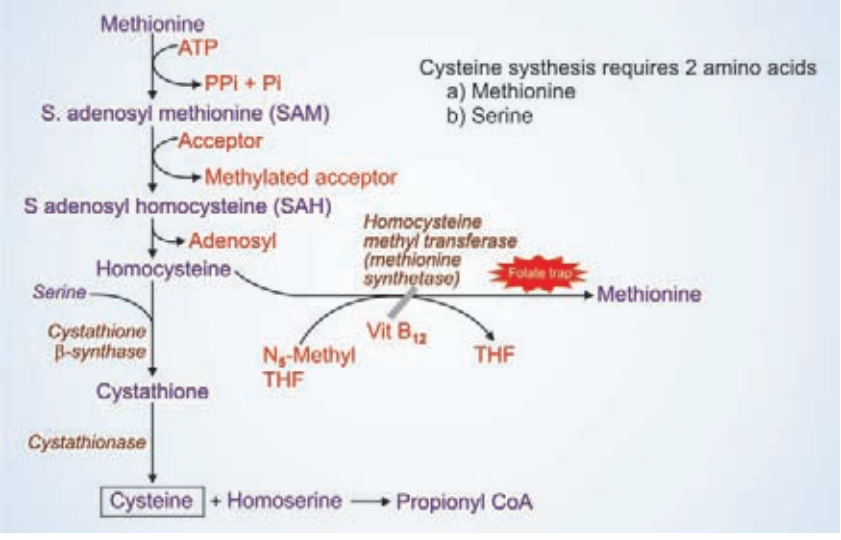
1. Homocystinurias

- Heritable defects of methionine metabolism.
- Up to 300 mg of homocystine (disulfide form) is excreted in the urine.
- Cyanide nitroprusside test is done in the urine.

Causes

1. Type I: Deficiency of—cystathionine beta synthase.
2. Type II: Defect in homocysteine methyl transferase.
3. Type III: Unavailability of N_5-methyl THF, due to defect in N_5, N_{10}-methylenetetrahydrofolate reductase

2. **Cystathioninuria:** Due to cystathionase deficiency.
3. **Cystinuria (cystine–lysinuria)**
   - Inherited metabolic disease, characterized by urinary excretion of cystine up to 30 times than normal.



Diagrams 3.11 and 3.12: Synthesis of SAM and synthesis of cysteine from methionine

- Excretion of ornithine, lysine and arginine also rises, suggesting a defect in the renal reabsorption mechanisms for these four amino acids **(COLA)**.
- Since cystine is relatively insoluble, **cystine calculi** form in the renal tubules of these patients.

4. **Cystinosis (cystine storage disease)**
   - Rare lysosomal disorder characterized by defective carrier-mediated transport of cystine.
   - Cystine crystals are deposited in tissues and organs, particularly the RE system.

Cysteine

Synthesis of cysteine from methionine:
Refer to Diagram 3.12.

Special products of cysteine[Q]

- Cystine
- Glutathione (γ-glutamyl-cysteinyl-glycine)
- PAPS (3′-Phosphoadenosine 5′-phosphosulfate)
- Taurine
- Coenzyme A

10. *Histidine*

- Semiessential, basic amino acid[Q]
- Glucogenic

Diagram 3.13 shows histidine catabolism

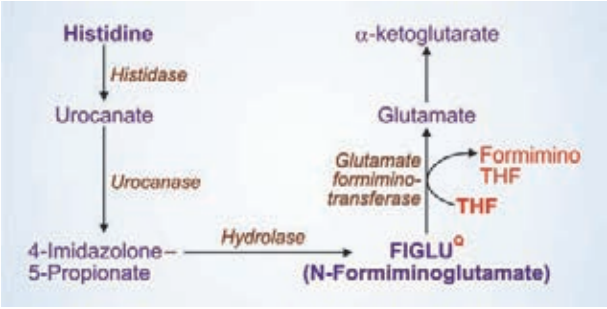


Diagram 3.13: Histidine catabolism

FIGLU is the **intermediate of catabolism of histidine amino acid**[Q] which needs folic acid for its further metabolism. In deficiency of folic acid, FIGLU is excreted in urine.

FIGLU Excretion Test/Histidine Load Test

- Sensitive indicator for folic acid deficiency.
- 5 gm of histidine is given 3 times at the interval of 8 hours.
- 24 hours urine is collected after the last dose.

- Normally <30 mg of FIGLU is excreted in the urine.
- Excretion of ≥30 mg of FIGLU in the urine indicates folic acid deficiency.

11. *Glutamic Acid*

Nonessential and glucogenic amino acid.Q

- Glutamic acid is the excitatory neurotransmitter and its alpha-decarboxylation gives rise to GABA (gamma-aminobutyric acid) which is an inhibitory neurotransmitter.
- Glutamate fixes NH_3 in brain and intestine with the help of glutamine synthase enzyme.
- Glutaminase enzyme is found in renal tubular cell and it releases NH_3 which helps in maintaining acid–base balance.

12. *Aspartic Acid*

Nonessential and glucogenic amino acid.

13. *Lysine*

Essential and basic amino acid.Q

Now please memorise Table 3.2 which may prove useful to you:

Table 3.2: List of amino acids giving rise to various intermediates of TCA cycle

Intermediate	*Amino acids which may produce them*
1. OxaloacetateQ	Asparagine Aspartate
2. α-ketoglutarate	Glutamine Glutamate Proline Arginine Histidine
3. Pyruvate	Alanine Serine Glycine Cystine Threonine
4. Fumarate	Phenylalanine Tyrosine
5. Succinyl CoAQ	Methionine, threonine, valine, isoleucine [MTVIs succinyl CoA]
6. Acetyl CoA or acetoacetyl CoA	Leucine Isoleucine Lysine Tryptophan

MULTIPLE CHOICE QUESTIONS

Q 1. Second messenger for smooth muscle relaxation mediated by NO is: ***(May 2016 AIIMS)***

a. cGMP
b. cAMP
c. Ca^{2+}
d. Magnesium

Ans. a: cGMP

Ref: Harper's Illustrated Biochemistry, 30/e, p 660.

NO is having paracrine role. Once it is diffused to underlying cell it activates guanylyl cyclase enzyme which converts GTP to cGMP. This cGMP phosphorylates muscle protein which relaxes smooth muscle and leads to vasodilatation.

Q 2. Which of these amino acid does not enter the Krebs cycle by forming acetyl-CoA via pyruvate: ***(May 2016 AIIMS)***

a. Tyrosine
b. Hydroxyproline
c. Glycine
d. Alanine

Ans. a: Tyrosine

Ref: Harper's Illustrated Biochemistry, 30/e, p 165.

Tyrosine rather enters the TCA cycle after giving rise to fumarate during its catabolism. Diagram 3.14 may help you.

Q 3. Detoxification of ammonia in the brain is by formation of: ***(Nov 2016 AIIMS)***

a. Glutamine
b. Glutamate
c. Urea
d. Alanine

Ans. a: Glutamine

- During catabolism of amino acid, **glutamate** is formed during transamination process in many of the cells. This glutamate is further converted to glutamine by **glutamine synthetase** enzyme found in brain and many other cells.
- This glutamine is poured in the blood where is carries the ammonia in a nontoxic form to liver.

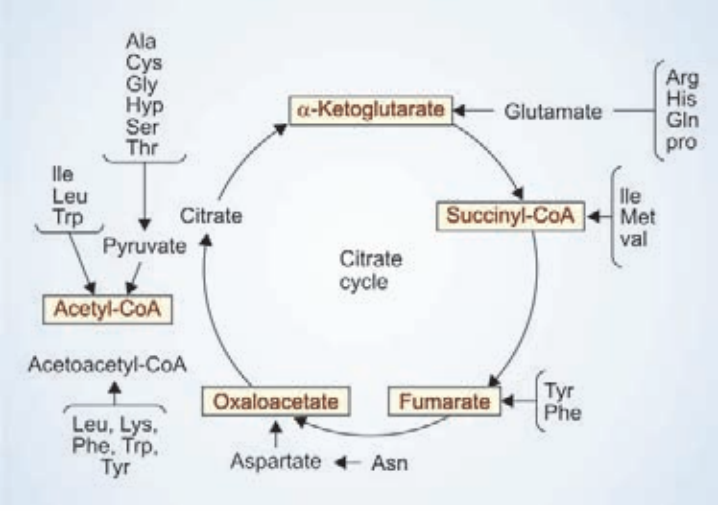


Diagram 3.14

- In the liver mitochondria **glutaminase** is the enzyme which acts on this glutamine to release the free ammonia which goes for urea synthesis.
- In skeletal muscle, pyruvate is the major acceptor of amino group which after accepting the amino group gets converted to **alanine**. So, from skeletal muscle the major transporter of ammonia to the liver is alanine.

Ref. Harper's Biochemistry, 28th/ed, p 242.

Q 4. Which of the amino acid has a net positive charge at physiological pH?

a. Alanine
b. Serine
c. Arginine
d. Aspartic acid

Ans. c: Arginine

- Alanine is nonpolar
- Serine is polar but neutral
- Aspartic acid is negatively charged

Ref. Harper's Illustrated Biochemistry, 28th ed, Chapter 3, p 16.

Q 5. Hyperphenylalaninemia is seen in: ***(PGI)***

a. Phenylalanine hydroxylase deficiency
b. Dihydrobiopterin reductase deficiency
c. Homogentisic oxidase deficiency
d. Phenylalanine-rich diet

Ans. a, b

a: Phenylalanine hydroxylase deficiency results in phenylketonuria where phenylalanine is utilised in the alternate route to give rise to phenyl ketones.

b: Dihydrobiopterin reductase deficiency also results in phenylketonuria due to reduced regeneration of THB, which impairs the phenylalanine metabolism.

Q 6. HCO_3/H_2CO_3 is the best physiological buffer, because of:

a. Combination of weak acid and weak bases
b. pK is close to the physiological pH
c. The component of the combination buffer can increase or decrease as per body's need
d. It is a good acceptor as well as donor of H^+

Ans. c: The component of the combination buffer can increase or decrease as per body's need

Ref. Harper's Biochemistry, Chapter 2.

Q 7. Which of the following vitamins is synthesized in the body by *de novo* metabolism of an amino acid? ***(Nov 2016 AIIMS)***

a. Niacin
b. Pantothenic acid
c. Cyanocobalamin
d. Folic acid

Ans. a: Niacin

Niacin is produced in the body by *de novo* metabolism of tryptophan (kynurenine pathway).

Q 8. Amino acids with aliphatic side chains are:

a. Threonine
b. Valine
c. Cysteine
d. Proline
e. Histidine

Ans. b: Valine

Explanation: Summary of important amino acids

Aliphatic side chains	*Glycine, alanine, valine, leucine and isoleucine*
Hydroxyl (OH) groups	Serine, threonine tyrosine
Sulphur atoms	Cysteine, methionine
Acidic groups/amides	Aspartic acid, asparagine glutamic acid, glutamine
Basic groups	Lysine, arginine, histidine
Aromatic rings	Histidine, phenylalanine, tyrosine, tryptophan
Imino acid	Proline

Ref: Harper's 30th ed.

Q 9. Incorrect statement(s) regarding urea cycle is/are: *(PGI)*

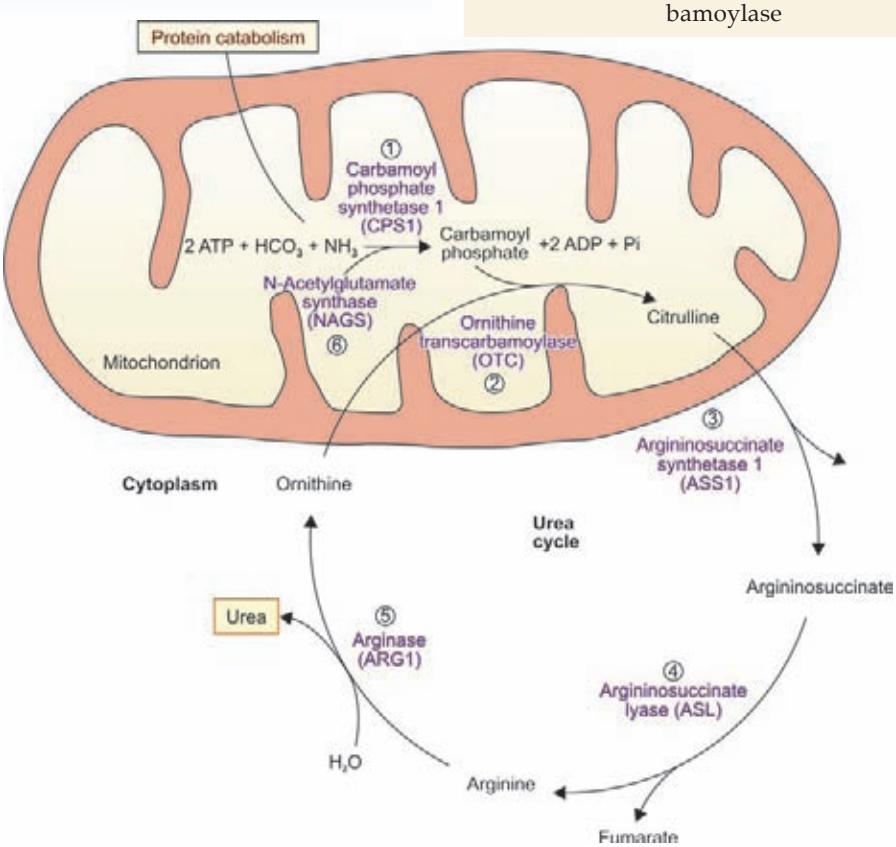
a. Ornithine transcarbamoylase is a cytoplasmic enzyme
b. Arginase is directly involved in urea formation
c. Citrullinemia occurs due to OTC deficiency
d. Raised ammonia is seen in all varieties of urea cycle disorders
e. CPS-1 utilises 2 ATPs per cycle

Ans: a, c:

a. Ornithine transcarbamoylase is infact a mitochondrial enzyme
b. Citrullinemia occurs due to deficiency of argininosuccinate synthase enzyme.

Disorders	*Defective enzymes*	*Product accumulated*
Hyperammonemia 1	Carbamoyl phosphate synthase 1	Ammonia
Hyperammonemia 2	Ornithine transcarbamoylase	Ammonia

Contd.



Contd.

Citrullinemia	Arginino-succinate synthase	Citrulline
Argininosuccinic aciduria	Arginase	Argino-succinate
Argininemia	Arginase	Arginine

Q 10. Which among the following amino acids absorbs UV light?

a. Leucine
b. Lysine
c. Tyrosine
d. Valine

Ans. c: Tyrosine

Amino acids which absorb 250–290 nm UV light are:
a. Tryptophan
b. Tyrosine
c. Phenylalanine

(In decreasing order of extent of absorbtion of UV light).

Important Biomolecules and the Wavelength of Light which they Absorb

- Nucleotides—260 nm
- Aromatic amino acids—250–290 nm
- NADH—340 nm
- Porphyrin—400 nm (Soret band)

Q 11. Phenylbutyrate is used in urea cycle disorders because it: ***(May 2017 AIIMS)***

a. Scavenges nitrogen
b. Activates enzymes
c. Maintains renal output
d. Maintains energy production

Ans. a: Scavenges nitrogen

Sodium phenylbutyrate metabolites allow the kidneys to excrete excess nitrogen in place of urea and coupled with dialysis, amino acid supplements and a protein-restricted diet, children born with urea cycle disorders can usually survive beyond 12 months.

Q 12. Urea is formed from which substrate?

a. Arginine
b. Ornithine
c. Citrulline
d. Aspartate

Ans. a: Arginine

Ref: Harper's Illustrated Biochemistry, 27th ed, p 246–49.

Some important point about urea cycle

- Urea is the major end product of nitrogen catabolism in humans.
- Some reactions of urea synthesis occur in matrix of the mitochondrion, other reactions in cytosol.
- Synthesis of one mol of urea requires 3 mol of ATP plus 1 mol each of ammonium ion and of the amino nitrogen of aspartate.

Q 13. Which vitamin deficiency can result in homocystinuria?

a. Vit B_1
b. Vit B_2
c. Vit B_5
d. Vit B_{12}

Ans. d: Vit B_{12}

HOMOCYSTINURIA

Classic Homocystinuria

Due to cystathionine β-synthetase deficiency.

Clinical Features

- MR, skeletal deformities
- Ectopia lentis, CAD

Screening: Cyanide nitroprusside test.

Non-classic Homocystinuria

- Homocystinuria due to defects in methyl cobalamin formation
- **R_x:** Vit B_{12} in the form of hydroxycobalamin
- Homocystinuria the to deficiency of methylene tetrahydrofolate reductase
- **R_x:** Folic acid + vit B_6 + vit B_{12}, betaine and methionine supplementation.

Q 14. Which one of the following is a feature of homocystinuria?

a. A high incidence of renal calculi
b. An association with dissecting aortic aneurysms
c. Upward dislocation of the lens
d. Elevated plasma methionine levels

Ans. d: Elevated plasma methionine levels

- Homocystinuria is caused by an inborn metabolic block in the conversion of homocystine and serine to cystathionine, due to a deficiency of cystathione β-synthetase.
- Its clinical features include mental retardation, seizures, osteoporosis, spastic paraplegia, cataracts, downward dislocation of the lens, a high arched palate, arachnodactyly and recurrent thromboembolic disease, but not dissecting aortic disease.
- Plasma methionine and urinary homocystine levels are elevated. Treatment is by dietary restriction of methionine and supplementation with cystine.

Q 15. Amino acid used in carnitine synthesis is:

a. Alanine
b. Lysine
c. Arginine
d. Tyrosine

Ans. b: Lysine

Carnitine is a quarternary ammonium compound biosynthesized from the amino acids lysine and methionine.
(Mnemonic: CML)

Q 16. A genetic defect in the ability to synthesize tetrahydrobiopterin would affect each of the following conversions *except*:

a. Phenylalanine to tyrosine
b. Tyrosine to dopamine
c. Dopa to melanin
d. Tryptophan to serotonin

Ans. c: Dopa to melanin

Tetrahydrobiopterin is involved in hydroxylation reactions that occur in phenylalanine to tyrosine, tyrosine to dopamine, and tryptophan to serotonin, but not in the conversion of dopa to melanin.

Q 17. Which of following is most likely in an untreated child with PKU?

a. Elevated tyrosine
b. Increased skin pigmentation
c. Decreased skin pigmentation
d. Normal phenylalanine

Ans. c: Decreased skin pigmentation

In PKU phenylalanine is not converted to tyrosine due to lack of phenylalanine hydroxylase enzyme. At times lack of biopterin cofactor due to lack of its synthetic enzyme may also be a responsible cause for PKU. All types of PKU is AR.

Deficiency of tyrosine in untreated child results in lack of melanin synthesis (skin depigmentation).

Level of phenylalanine is high and can be tested by positive Gutherie test.

Q 18. All of the following techniques can precipitate proteins *except*:

(November 2015 AIIMS)

a. Adjusting pH to other than isoelectric point
b. Addition of alcohol and acetone
c. Addition of tricholoroacetic acid
d. Using salts of heavy metals

Ans. a: Adjusting pH to other than isoelectric point

At pH other than isoelectric pH, proteins are either positive or negatively charged which makes it soluble.

Methods to precipitate the proteins are as follows

a. Neutralization of charge of protein (isoelectric pH)
b. Removal of shell of hydration (alcohol or acetone)
c. Denaturation

Q 19. Maple syrup urine disease is due to deficiency of:

a. Decarboxylation
b. Dehydroxylation
c. Transamination
d. Deamination

Ans. a: Decarboxylation

- Alpha keto acid decarboxylase enzyme also known as alpha keto acid, dehydrogenase enzyme is a multienzyme complex similar to PDH complex.
- Deficiency of this enzyme complex impairs degradation of branched chain amino acid.
- This leads to excretion of keto acids of all 3 branched chain amino acid.
- This is responsible for branched chain ketonuria. This will have maple syrup or burnt sugar smell of the urine.

Q 20. Age-related deterioration of cognitive function is due to increase in which of the following? *(AIIMS Nov 2012)*

a. Homocystine b. Cystine
c. Taurine d. Methionine

Ans. a: Homocystine

Q 21. Urea cycle occurs in the: *(AI 2011, 2012)*

a. Liver b. Gastrointestinal tract
c. Spleen d. Kidney

Ans. a: Liver

- Urea synthesis is a process which takes place in the liver cell.
- This is a partly cytosolic and partly mitochondrial process.
- Two ammonia and one CO_2 is responsible for urea synthesis. One ammonia is coming from glutamate and the other is coming from aspartate.
- Glutamate dehydrogenase enzyme presents in the liver cell is responsible for oxidative deamination of the glutamate.

Q 22. Which of the following does not undergo phosphorylation by protein kinases? *(AI 2012)*

a. Threonine b. Tyrosine
c. Asparagine d. Serine

Ans. c: Asparagine

Phosphorylation occurs at the hydroxyl group of serine, threonine and tyrosine.

Q 23. Which of the following amino acids in a protein acts as a potential O-glycosylation site for attachment of an oligosaccharide unit? *(AI 2012)*

a. Glutamine b. Cysteine
c. Serine d. Asparagine

Ans. c: Serine

There are three major classes of glycoproteins:

1. Those containing an **O-glycosidic linkage** involving the hydroxyl side chain of serine–threonine or hydroxylysine and a sugar such as *N-acetylgalactosamine* **(GalNAc-Ser[Thr])**.
2. Those containing an **N-glycosidic linkage** involving the amide nitrogen of asparagine and *N-acetylglucosamine* **(GlcNAc-Asn).**
3. **GPI linked glycoprotein**

Q 24. Glycoproteins may have protein linked to the carbohydrate moiety through any of the following bonds: *(AI 2012)*

a. O-glycosidic linkage
b. N-glycosidic linkage
c. GPI linkage
d. Either O- or N-glycosidic linkage

Ans. d: Either O- or N-glycosidic linkage

O-glycosylation occurs between OH group of the amino acid and oligosaccharide, while N-glycosylation occurs between amino group of the amino acid and a oligosaccharide chain.

Serine, threonine and hydroxylysine are OH group containing amino acid which gets attached with the oligosaccharide chain with the help of **O-glycosidic linkage.**

Asparagine is amide group containing amino acid which gets attached with the oligosaccharide chain with the help of **N-glycosidic linkage.**

Q 25. Which of the following side chains is least polar? ***(AI 2009)***

a. Methyl
b. Carboxyl
c. Amino
d. Phosphate

Ans. a: Methyl

Methyl side chain is rather nonpolar.

Carboxyl group is polar group of acidic tendency. They are found in aspartic acid and glutamic acid.

Amino group is polar group of basic tendency. They are found in arginine, lysine and histidine.

Q 26. Homologous substitution of the isoleucine in a protein sequence is the: ***(AI 2006)***

a. Methionine
b. Aspartic acid
c. Valine
d. Arginine

Ans. c: Valine

Substitution of isoleucine to valine is an example of conservative or homologous substitution.

Q 27. All of the following amino acids are converted to succinyl CoA *except*: ***(AI 2006)***

a. Methionine
b. Isoleucine
c. Valine
d. Histidine

Ans. d: Histidine

Remember: Following amino acids are converted to succinyl CoA:

1. Methionine
2. Threonine
3. Valine
4. Isoleucine

Mnemonic (MTV is succinyl CoA)

Q 28. The amino acid which serves as a carrier of ammonia from skeletal muscle to the liver is: ***(AII 2006)***

a. Alanine
b. Methionine
c. Arginine
d. Glutamine

Ans. a: Alanine

During exercise excessive alanine is produced from the skeletal muscle, either due to protein breakdown or due to transamination of pyruvate produced via glycolysis.

This alanine is carried to the liver where it synthesizes glucose via gluconeogenesis.

Q 29. Replacing alanine by which amino acid will increase UV absorbance of protein at 280 nm wavelength? ***(AIIMS 05, 08, 09)***

a. Leucine
b. Praline
c. Arginine
d. Tryptophan

Ans. d: Tryptophan

Aromatic amino acid having aromatic ring shows increase absorbance of UV light at 280 nm.

Q 30. All are true about glutathione *except*: *(AIIMS 2008)*

a. It is a tripeptide
b. It converts hemoglobin to methemoglobin
c. It conjugates xenobiotics
d. It is a cofactor of various enzymes

Ans. b: It converts hemoglobin to methemoglobin

- Glutathione is a tripeptide (γ-glutamyl-cysteinyl-glycine)
- It helps in conjugation reaction
- It is a cofactor of various enzymes

Its reduced form is necessary for converting methemoglobin to hemoglobin.

(Not the hemoglobin to methemoglobin)

Q 31. Amino acid producing ammonia in the kidney is: *(AIIMS 96, May 2007)*

a. Glutamine
b. Alanine
c. Methionine
d. Glycine

Ans. a: Glutamine

Enzyme glutaminase is responsible for removal of NH_3 from the glutamine in the kidney tubules.

Q 32. Which is not the essential amino acid? *(AIIMS Nov 07)*

a. Methionine
b. Lysine
c. Alanine
d. Leucine

Ans. c: Alanine

Q 33. A 40-year-old woman presents with progressive palmoplantar pigmentation. X-ray spine shows calcification of intervertebral discs. On adding Benedict's reagent to urine, it gives greenish brown precipitate and blue black supernatant fluid. What is the diagnosis? *(AIIMS Nov 2009, May 2010)*

a. Phenylketonuria
b. Alkaptonuria
c. Tyrosinemia type 2
d. Argininosuccinic aciduria

Ans. b: Alkaptonuria

Homogentisic acid oxidase deficiency leads to excretion of homogentisic acid in the urine. This compound gets oxidised in the presence of air and urine turns black on standing. Alkali medium enhances black discoloration.

Ochronosis is the condition where oxidised product of homogentisic acid "benzoquinone acetate" is accumulated in the connective tissues.

Q 34. Hepatomegaly is the essential feature for all of the following *except*: *(AIIMS Nov 2009)*

a. Hepatic porphyria
b. Niemann-Pick disease
c. von Gierke's disease
d. Hurler syndrome

Ans. a: Hepatic porphyria

It is very rare to find hepatomegaly in hepatic porphyria.

Niemann-Pick disease, von Gierke's disease and Hurler syndrome are all associated with hepatomegaly.

Q 35. All of the following are true about sickle cell disease *except*: *(AIIMS Nov 2009)*

a. Single nucleotide change results in change of glutamine to valine
b. RFLP results from a single base change

c. Sticky patch is generated as a result of replacement of nonpolar residue with a polar residue
d. HbS confers resistance against malaria in heterozygotes

Ans. c: Sticky patch is generated as a result of replacement of nonpolar residue with a polar residue

In sickle cell disease valine (nonpolar) appears at the place of glutamic acid (polar), so the above statement is wrong.

All other statements are right, RFLP pattern is observed due to polymorphism or mutation.

Q 36. Amino acid residue having imino side chain is: ***(AI 2005)***

a. Lysine
b. Histidine
c. Tyrosine
d. Proline

Ans. d: Proline

The side chain of the proline makes **pyrrolidine ring** structure with the imino group.

Q 37. Phenylalanine is the precursor of all of the following *except*: ***(AI 2002)***

a. Tyrosine
b. Epinephrine
c. Thyroxine
d. Melatonin

Ans. d: Melatonin

Melatonin is synthesized from tryptophan.

Tyrosine, epinephrine, thyroxine as well as melanin are all synthesized from phenylalanine.

Q 38. Basic amino acids are: ***(PGI 92, AI 01)***

a. Aspartate and glutamate
b. Serine and glycine
c. Lysine and arginine
d. None of the above

Ans. c: Lysine and arginine

Arginine, lysine and histidine are all basic amino acids.

Q 39. Transamination of pyruvate with glutamate produces: ***(AI 1998)***

a. Oxaloacetate and aspartate
b. Alanine and aspartate
c. Oxaloacetate and α-ketoglutarate
d. Alanine and α-ketoglutarate

Ans. d: Alanine and α-ketoglutarate

Q 40. One week infant, having classic phenylketonuria, which of the following statements is correct?

a. Tyrosine is nonessential amino acid for this infant
b. High levels of phenylpyruvate is appearing in the urine
c. Therapy must begin within the first year of life
d. Diet therapy should be discontinued once infant reaches adulthood

Ans. b: High levels of phenylpyruvate is appearing in the urine

Tyrosine becomes essential amino acid for this infant as phenylalanine cannot be converted to tyrosine.

Phenylalanine is converted to phenylpyruvate, phenylacetate and phenyllactate in this disorder.

Therapy of phenylalanine restricted diet should be started within 7 to 10 days of life to avoid mental retardation.

Adult PKU patient shows deterioration of attention and thinking process after discontinuation of diet, so lifelong restriction of dietary phenylalanine is recommended.

Q 41. Xanthurenic acid in the urine is suggestive of deficiency of which vitamin?

a. Vitamin B_6
b. Vitamin B_{12}
c. Folic acid
d. Thiamine

Ans. a: Vitamin B_6

Xanthurenic acid is formed in the side reaction of kynurenine. Kynurenine which is a intermediate of tryptophan metabolism requires vitamin B_6 dependent enzyme kynureinase for its normal metabolism. In pyridoxine (vit B_6) deficiency kynurenine is metabolized to xanthurenic acid which is excreted unchanged in the urine.

Q 42. Xanthurenic acid is metabolic end product in the metabolism of:

a. Xanthine
b. Tryptophan
c. Uric acid
d. Uronic acid

Ans. b: Tryptophan

See explanation of question above.

Q 43. VMA is excreted excessively in the urine. What may be the diagnosis?

a. Carcinoid syndrome
b. Phaeochromocytoma
c. Cushing's syndrome
d. None of the above

Ans. b: Phaeochromocytoma

VMA is the end product of catabolism of catecholamines. In phaeochromocytoma and neuroblastoma there is excessive synthesis of catecholamines which causes enhanced synthesis of VMA and its excretion in the urine.

Q 44. Glycine is present in:

a. Hemoglobin
b. Glutathione
c. Purine
d. All of the above

Ans. d: All of the above

Glycine is required for the synthesis of hemoglobin, purine and glutathione.

Q 45. Which of the following combinations is wrong?

a. Phenylalanine–niacin
b. Tryptophan–serotonin
c. Phenylalanine–melanin
d. Tyrosine–epinephrine

Ans. a: Phenylalanine–niacin

Niacin is synthesized from tryptophan and not from tyrosine. So this combination is wrong. Rest other combinations are correct because respective compounds are synthesized from corresponding amino acids.

Q 46. Dopamine beta-hydroxylase catalyses:

a. Dopa to dopamine
b. Norepinephrine to dopamine
c. Epinephrine to norepinephrine
d. Dopamine to norepinephrine

Ans. d: Dopamine to norepinephrine

Dopamine hydroxylase catalyses conversion of dopamine to norepinephrine.

Q 47. Guanidium group is present on which carbon of the side chain?

a. Alpha
b. Epsilon
c. Gamma
d. Delta

Ans. d: Delta

Guanidium is the special group in arginine which is found on delta carbon atom.

Q 48. FIGLU is a metabolite of:

a. Folic acid
b. Tyrosine
c. Histidine
d. Alanine

Ans. c: Histidine

FIGLU is an intermediate metabolite of histidine catabolism. It is excreted in urine in increased quantity when there is folic acid deficiency as folic acid is required for further metabolism of FIGLU.
(Refer to Diagram 3.13)

Q 49. Catecholamines:

a. Production terminates with dopamine in the brain but epinephrine in the adrenal gland
b. Production begins with the action of tyrosinase on tyrosine
c. Are metabolized to both glucogenic and ketogenic fragments
d. All contain methyl group donated by S adenosyl methionine

Ans. a: Production terminates with dopamine in the brain but epinephrine in the adrenal gland

- Synthesis of catecholamine is organ specific, so ***option a*** is correct.
- Production of catecholamine begins once tyrosine hydroxylase enzyme acts on tyrosine and forms dopa so ***option b*** is wrong. (Tyrosinase action on tyrosine which forms dopa synthesizes melanin.)
- All catecholamines are metabolized to vanillylmandelic acid (VMA) which gets excreted in urine unchanged. VMA has neither glucogenic nor ketogenic fate. So ***option c*** is also wrong.
- Out of various catecholamine, **only epinephrine has got one methyl group**. Dopamine and norepinephrine do not contain any methyl group. So, ***option d*** is also wrong.

Q 50. Tyrosinemia type II is due to deficiency of: ***(JIPMER 91)***

a. Tyrosine transaminase
b. Fumaryl acetoacetyl hydrolase
c. Tyrosine hydroxylase
d. Tyrosinase

Ans. a: Tyrosine transaminase

Tyrosinemia type II is due to deficiency of tyrosine transaminase and tyrosinemia type I is due to deficiency of fumaryl acetoacetyl hydrolase.

Q 51. In maple syrup urine disease the amino acids excreted in the urine are:

a. Leucine
b. Isoleucine
c. Valine
d. All of the above

Ans. d: All of the above

Maple syrup urine disease is due to excretion of α-keto acid of all branched amino acid (valine, leucine, isoleucine). It is due to deficiency of α-keto acid decarboxylase (also called α-keto acid dehydrogenase) which is an example of multifunctional enzyme having catalytic domain of decarboxylase activity for all the three keto acids.

Q 52. What is false about tryptophan?

a. Nonessential amino acid
b. Involved in serotonin synthesis
c. Involved in niacin synthesis
d. Involved in melatonin synthesis

Ans. a: Nonessential amino acid

Tryptophan is an essential amino acid, as its synthesis in body does not take place. Tryptophan is involved in synthesis of melatonin, serotonin, and niacin by various pathways.

Q 53. Kynurenine is formed from:

a. Phenylalanine b. Tryptophan
c. Tyrosine d. Histidine

Ans. b: Tryptophan

Kynurenin is synthesized from tryptophan as an intermediate of its metabolic pathway. This pathway is also known as kynurenine pathway.

Q 54. Cabbage odor urine is found in:

a. Leucine catabolism defect
b. Valine catabolism defect
c. Tyrosinemia type 1
d. None of the above

Ans. c: Tyrosinemia type 1

Tyrosinemia type 1 is due to defect of hydrolase enzyme, in this disorder there occurs cabbage odor urine (rancid butter smell).

Q 55. In arginase enzyme defect of urea cycle the amino acid excreted in the urine is:

a. Lysine
b. Cystine
c. Both a and b
d. Arginine

Ans. c: Both a and b

In arginase defect of urea cycle arginine is accumulated in the plasma and it is excreted in the urine in the PCT of the kidney. In the DCT, this arginine is reabsorbed in exchange for lysine and cystine which then gets excreted in the urine. So, in arginase defect amino acid accumulated in the plasma is **arginine but the one that is excreted in the urine are lysine and cystine.**

Q 56. Melatonin is synthesized from: *(AIIMS 97, PGI 98)*

a. Tryptophan
b. Serotonin
c. Phenylalanine
d. Histidine
e. Leucine

Ans. a: Tryptophan

Q 57. Which amino acid is excreted in the urine in cystinosis?

a. Cystine
b. Ornithine
c. Arginine
d. Lysine
e. All of the above

Ans. e: All of the above

Q 58. In maple syrup urine disease amino acids excreted In the urine are: *(PGI 95, 97)*

a. Leucine
b. Isoleucine
c. Valine
d. a, b and c
e. Arginine

Ans. d: a, b and c

Q 59. In Hartnup's disease..... is excreted in the urine.

a. Ornithine
b. Glycine
c. Tryptophan
d. Phenylalanine
e. Cystine

Ans. c: Tryptophan

Q 60. In alkaptonuria the urine contains:

a. Homogentisic acid
b. Phenylalanine
c. Ketone
d. Acetates
e. None of the above

Ans. a: Homogentisic acid

Q 61. Glycine is used in the synthesis of all *except*: *(AIIMS 97)*

a. Heme
b. Glycocholic acid
c. Taurocholic acid
d. Purines

Ans. c: Taurocholic acid

Q 62. Which of the following is metalloporphyrin? *(PGI)*

a. Hemoglobin
b. Catalase
c. Bilirubin
d. Cytochrome
e. Pyrrolase

Ans. a, b, d, e

Q 63. The immediate precursor of norepinephrine is:

a. Epinephrine
b. Tyrosine
c. Dopamine
d. Phenylalanine

Ans. c: Dopamine

Q 64. Metabolite of epinephrine is:

a. Metanephrine
b. Normetanephrine
c. Hydroxymandelic acid
d. 3-methoxy 2-hydroxy glycol

Ans. a: Metanephrine

Q 65. Glutathione is a:

a. Monopeptide
b. Dipeptide
c. Tripeptide
d. None of the above

Ans. c: Tripeptide

Glutathione is γ-glutamyl-cysteinyl-glycine (tripeptide)

Q 66. Ammonia is detoxified in brain to: *(AI 99)*

a. Uric acid
b. Glutamine
c. Creatinine
d. Urea

Ans. b: Glutamine

Q 67. S adenosyl methionine is necessary for synthesis of: *(PGI)*

a. Serine
b. Cysteine
c. Homocysteine
d. Choline

Ans. b and c

Q 68. Melanin is synthesized from:

a. Glycine
b. Leucine
c. Tyrosine
d. Phenylalanine

Ans. c: Tyrosine

Q 69. Decarboxylation yields a vasodilator from:

a. Aspartate
b. Arginine
c. Histidine
d. Serine
e. Glutamate

Ans. c: Histidine

Q 70. Which of the following is precursor of adrenaline and thyroxine synthesis? *(AIIMS 94, 98, UP 06)*

a. Phenylalanine
b. Tyrosine
c. Tryptophan
d. None of the above

Ans. b: Tyrosine

Q 71. Which is the byproduct of the urea cycle?

a. Aspartate
b. Succinate
c. Ornithine
d. Fumarate

Ans. d: Fumarate

Q 72. Urea is produced by the enzyme: *(PGI 93, UP 02)*

a. Urease
b. Uricase
c. Arginase
d. Glutaminase

Ans. c: Arginase

Q 73. Which of the following is found in conjugation with bile acids?

a. Cholic acid
b. Pregnenolone
c. Glycine
d. Chloroacetyl

Ans. c: Glycine

Q 74. An essential amino acid in man is:

a. Hippuric acid
b. Phenyl pyruvic acid
c. Phenylalanine
d. Noradrenaline

Ans. c: Phenylalanine

Q 75. A plasma albumin concentration of less than 2 g/L would affect specifically the transport of:

a. Glucose
b. Iron
c. Bilirubin
d. Cholesterol

Ans. c: Bilirubin

Q 76. An amino acid not involved in urea synthesis is: *(PGI)*

a. Ornithine
b. Citrulline
c. Histidine
d. Arginine
e. Aspartic acid

Ans. c: Histidine

Q 77. The rationale for feeding benzoic acids to subjects with an urea cycle enzyme defect is:

a. It provides an alternative route for N_2 excretion through glycine conjugate, hippuric acid
b. It provides an alternative route for N_2 excretion through the N-acetyl glucuronic acid conjugate kynurenine
c. It inhibits adenylate deaminase
d. It inhibits glutamate dehydrogenase
e. It neutralized NH_3 in both blood as well as urine

Ans. a: It provides an alternative route for N_2 excretion through glycine conjugate, hippuric acid

Q 78. Creatinine is synthesized from: *(Kerala 94)*

a. Glycine, arginine and methionine
b. Glycine and methionine
c. Ornithine and glycine
d. Thymine and ornithine

Ans. a: Glycine, arginine and methionine (Mnemonic: GAM)

Q 79. Homocystinuria is due to abnormal metabolism of:

a. Methionine
b. Valine
c. Tryptophan
d. Leucine

Ans. a: Methionine

Q 80. Tyrosinemia type II is due to deficiency of:

a. Tyrosine transaminase
b. Fumarylacetoacetyl hydrolase
c. Tyrosine hydroxylase
d. Tyrosinase

Ans. a: Tyrosine transaminase

Q 81. Mousy odor urine is seen in: *(UP 04)*

a. Phenylketonuria
b. Maple syrup urine disease
c. Isovaleric aciduria
d. None of the above

Ans. a: Phenylketonuria

Q 82. Which metabolite of TCA cycle is used in detoxification of ammonia in brain?

a. Alpha-ketoglutarate
b. Ornithine
c. Oxaloacetate
d. Glycine

Ans. a: Alpha- ketoglutarate

Q 83. Regarding glutathione, which of the following is/are true? *(PGI 2000)*

a. It helps in the absorption of certain amino acids
b. It inactivates some enzymes
c. It helps in membrane transport
d. It helps in conjugation reactions

Ans. a and d

Q 84. Which of the following is not synthesized from tyrosine? *(TN 03, WB 06)*

a. Norepinephrine
b. Melatonin
c. Thyroxine
d. Dopamine

Ans. b: Melatonin

Q 85. Carbamoyl phosphate is used in synthesis of:

a. Urea
b. Uric acid
c. Pyruvic acid
d. Stearic acid

Ans. a: Urea

Q 86. Methyl donor is: *(PGI)*

a. N_5-methyl tetrahydrofolate
b. Homocysteine
c. Adenosyl methionine
d. Tetrahydrofolate

Ans: a and c

Q 87. Which of the following amino acids is essential for synthesis of nitric oxide? *(AI 2001)*

a. Arginine
b. Aspartate
c. Alanine
d. Glycine

Ans. a: Arginine

Q 88. Pigment providing color to stool is: *(Kerala 99)*

a. Stercobilinogen
b. Urobilinogen
c. Mesobilirubin
d. Bilirubin

Ans. a: Stercobilinogen

Q 89. The conjugation of bilirubin to glucuronic acid in the liver:

a. Converts a hydrophilic compound to a hydrophobic one
b. Converts a hydrophobic compound to a hydrophilic one
c. Enables the bilirubin molecule to cross the cell membrane
d. Is increased during neonatal jaundice

Ans. b: Converts a hydrophobic compound to a hydrophilic one

Q 90. Which is false about alkaptonuria? *(AI 2001)*

a. Genitourinary system is not involved
b. Homogentisic oxidase deficiency
c. Black urine
d. Calcification in vertebral bodies

Ans. a: Genitourinary system is not involved

Q 91. Which of the following gives a positive reaction with ferrous chloride? *(PGI 97)*

a. Phenylketonuria
b. Alkaptonuria
c. Maple syrup urine disease
d. None of the above

Ans. a and b

(Ref Vasudevan 7th ed, pages 237, 238)

Q 92. A 45-year-old male, blood sample gives purple brown color in Ehrlich's solution, the substance is:

a. Urobilinogen
b. Conjugated bilirubin
c. Unconjugated bilirubin
d. Hemosiderin

Ans. a: Urobilinogen

Q 93. Which of the following amino acids is purely ketogenic?

a. Tyrosine
b. Tryptophan
c. Leucine
d. Alanine

Ans. c: Leucine

Q 94. All are true about glutathione *except*: *(AIIMS 2003)*

a. It is a tripeptide
b. It converts hemoglobin to methemoglobin
c. It conjugates xenobiotics
d. It scavenges free radicals and superoxide ions

Ans. b: It converts hemoglobin to methemoglobin

Q 95. All are aromatic amino acids *except*: *(PGI 93, UP 99)*

a. Lysine
b. Phenylalanine
c. Tyrosine
d. Tryptophan

Ans. a: Lysine

Q 96. Replacing alanine by which amino acids will increase UV absorbance of protein at 280 nm wavelength? *(AIIMS Nov 2008)*

a. Leucine
b. Proline
c. Arginine
d. Tryptophan

Ans. d: Tryptophan

Q 97. Dopamine beta-hydroxylase catalyzes: *(AI 2004)*

a. Dopa to dopamine
b. Norepinephrine to dopamine
c. Epinephrine to norepinephrine
d. Dopamine to norepinephrine

Ans. d: Dopamine to norepinephrine

Q 98. The rate-limiting step for norepinephrine synthesis:

a. Conversion of phenylalanine to tyrosine
b. Conversion of tyrosine to dopa
c. Conversion of dopa to dopamine
d. Conversion of dopamine to norepinephrine

Ans. b: Conversion of tyrosine to dopa

Q 99. A 9-month-old child has pellagra-like features and mild amino aciduria. Her elder sister has the same complaints. The parents are asymptomatic and other four siblings are normal. The most likely diagnosis is: *(Nov 2014)*

a. Phenylketonuria
b. Alkaptonuria
c. Hartnup disease
d. Maple syrup urine disease

Ans. c: Hartnup disease

Hartnup disease is an autosomal recessive disorder caused by impaired neutral (i.e. monoaminomonocarboxylic) amino acid transport in the apical brush border membrane of the small intestine and the proximal tubule of the kidney.

Patient presents with pellagra-like skin eruptions, cerebellar ataxia, and gross aminoaciduria.

Also know: **Cystinuria:** Cysteine absorption is defective in both GIT and kidney. In urine cysteine is oxidized to cystine, which can crystallize forming kidney stone.

Q 100. Assertion (A): Urea synthesis is an energy requiring process. It consumes total 4 high energy phosphates.

Reasoning (R): 2 ATPs are needed to restore 2 ADP, produced at carbamoyl phosphate synthetase 1, and 2 ATPs are used to restore AMP produced from argininosuccinate synthase step which converts L-citrulline to argininosuccinate. So, total 4 ATPs are required to synthesize one molecule of urea.

a. A and R both are right but R is not the correct explanation of A
b. A as well as R are right and R is a correct explanation of A
c. A is wrong but R is a right statement
d. A and R both are wrong

Ans. b: A as well as R are right and R is a correct explanation of A

Q 101. Assertion (A): FIGLU excretion test is done to find out folic acid deficiency.

Reasoning (R): FIGLU is the intermediate of histidine catabolism and it needs tetrahydrofolic acid (THF) for its further catabolism, so in deficiency of THF, FIGLU is excreted in the urine.

a. A and R both are right but R is not the correct explanation of A
b. A as well as R are right and R is a correct explanation of A
c. A is wrong but R is a right statement
d. A and R both are wrong

Ans. b: A as well as R are right and R is a correct explanation of A

Q 102. Assertion (A): Conversion of homocysteine to methionine requires folate and vitamin B_{12} as cofactor, this reaction is a transmethylation process.

Reasoning (R): Enzyme required for this remethylation process is homocysteine methyl transferase which requires methyl group from methylcobalamin. Methylcobalamin in turn, acquires the methyl group from N_5-methyl-THF.

a. A and R both are right but R is not the correct explanation of A
b. A as well as R are right and R is a correct explanation of A
c. A is wrong but R is a right statement
d. A and R both are wrong

Ans. b: A as well as R are right and R is a correct explanation of A

That is why deficiency of vitamin B_{12} leads to accumulation of N_5-methyl-THF. Free THF becomes deficient **(folate trap)**.Ⓠ TMP synthesis requires N_5-, N_{10}-methylene-THF which is derivatized from free THF. This leads to defective DNA synthesis and so megaloblastic anemia.

So, **B_{12} deficiency leads to megaloblastic anemia due to folate trap.**

Q 103. Assertion (A): Branched chain α-keto acid dehydrogenase complex uses TPP, lipoic acid, FAD^+, NAD^+ and CoA.

Reasoning (R): This complex is similar to the PDH complex which converts pyruvate to acetyl CoA, and also to α-ketoglutarate dehydrogenase complex converting α-ketoglutarate to succinyl CoA.

a. A and R both are right but R is not the correct explanation of A
b. A as well as R are right and R is a correct explanation of A

c. A is wrong but R is a right statement
d. A and R both are wrong

Ans. b: A as well as R are right and R is a correct explanation of A.

Q 104. Assertion (A): Cheesy odor urine is due to isovalerate being excreted in the urine. Isovaleric acid is one of the intermediates derived during catabolism of leucine.

Reasoning (R): The enzyme defective in isovaleric academia is isovaleryl CoA dehydrogenase which is FAD^+ requiring enzyme.

a. A and R both are right but R is not the correct explanation of A
b. A as well as R are right and R is a correct explanation of A
c. A is wrong but R is a right statement
d. A and R both are wrong

Ans. b: A as well as R are right and R is a correct explanation of A.