

CHAPTER

Metabolism of Proteins and Amino Acids

Q.1. What is meant by amino acid pool?

Amino acids in the blood are obtained from:

- ***From dietary proteins:*** absorption of amino acids from intestine.
- ***Breakdown of tissue proteins:*** both structural and functional.
- ***Synthesis of amino acids*** in liver mainly except essential amino acids.

Amino acids from all these sources get mixed up to constitute ***amino acid pool***. It has no anatomical reality but represents an availability of amino acid building units. No functional distinction can be made between the fate of the amino acids derived from dietary source and those derived from tissue breakdown.

Q.2. What is meant by “circadian” changes in plasma amino acid levels?

The plasma levels of most amino acids do not remain constant throughout 24 hours period; but change by varying in a ***circadian*** rhythm, about a mean value. In general plasma amino acids levels are lowest at early morning and rise 15 to 35% by afternoon.

Q.3. What is the level of amino acids in blood?

- Blood amino acid level varies from 30 to 50 mg/dl in the postabsorptive state. In terms of amino acid N₂ it is 4 to 5 mg %.
- Following protein meal, the amino acid levels rise to 45 to 100 mg % (amino acid N₂ 6 to 10 mg %).

Q.4. How tissues take up amino acids?

The amino acids are taken up by the tissues *actively*. Pyridoxal-P (B_6 - PO_4) is required for the active transport.

Q.5. Name the hormones which favour tissue uptake of amino acids.

- Insulin
- Growth hormone (GH) and
- Testosterone favour the uptake of amino acids by tissues. Hence these hormones are called “anabolic” hormones.
- Estradiol stimulates selectively the uptake of a.a by uterus.
- Epinephrine and Glucocorticoids (GC) stimulate uptake of a.a by the liver only.

Q.6. What is meant by nitrogen balance or nitrogen equilibrium?

- In an adult healthy individual maintaining a constant weight, the amount of intake of ‘N’ in food (as dietary proteins mainly) will be balanced by an excretion of an equal amount of ‘N’ in urine (in the form of urea mainly, uric acid, creatine and to a small extent by amino acids) and
- In feces (mainly as unabsorbed N)
- Such an individual is then said to be in nitrogen balance or in nitrogen equilibrium.

Q.7. What is meant by positive nitrogen balance?

- If the amount of nitrogen consumed exceeds the amount of nitrogen lost, the person is said to be in *positive nitrogen balance*. This happens in:
 - Growing children
 - Pregnancy
 - Convalescence after illness/surgery, and
 - After administration of anabolic hormones.
- In positive nitrogen balance, the body puts on weight and N-intake will be greater than N-output since new cells are formed and N is retained as tissue proteins.

Q.8. What is meant by negative nitrogen balance?

- A subject whose intake of N is less than the output of N is said to have a *negative nitrogen balance*. The person loses weight and the tissue proteins are catabolized to a

greater extent than they are formed. Such a situation occurs in:

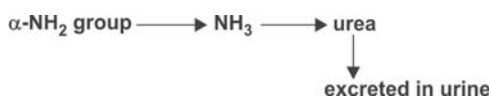
- Old age
- Starvation
- Wasting diseases like tuberculosis
- Cancer
- Prolonged illness
- Postoperative conditions and burns.

Q.9. What non-protein nitrogenous substances are synthesized from amino acids? List them.

- *Creatine* from glycine, arginine and methionine.
- *Heme* from glycine and succinyl CoA.
- *Melanins* from tyrosine.
- *Choline* from serine through ethanolamine.
- *Purine nucleotides* from glycine with 5-Phosphoribosylamine.
- *Pyrimidine nucleotides*: from aspartate and carbamoyl phosphate.

Q.10. What happens to the N-Part of an amino acid?

In mammalian tissues, α -NH₂ group of amino acids, derived either from the diet or breakdown of tissue proteins, is first converted to NH₃ and then to urea and excreted in urine.



Humans are therefore called *ureotelic*.

Q.11. What is the fate of α -NH₂ group of amino acid in other animals?

- Reptiles and birds produce uric acid in place of urea and they are called *uricotelic* organisms.
- Bony fishes produce NH₃ only and excrete it in urine. They are called *ammonotelic* organisms.

Q.12. What is transamination?

Transamination is a *reversible reaction* in which α -NH₂ group of one amino acid is transferred to an α -keto acid resulting in the formation of a new amino acid and a new ketoacid.

Q.13. Does formation of NH_3 take place in transamination reaction?

NH_3 formation does not take place in transamination reaction. The process represents only an *“intermolecular” transfer of $-\text{NH}_2$ group without splitting out of N as NH_3 .*

Q.14. Name the tissues in which transamination reaction occur.

Transamination takes place principally in

- Liver
- Kidney
- Heart
- Brain, but to a small extent transamination can take place in all tissues.

Q.15. Name the enzyme and co-enzyme required in transamination reaction.

- *Enzyme: Transaminases* (Now called as *“aminotransferases”*)
- *Co-enzyme: Pyridoxal-P ($\text{B}_6 - \text{PO}_4$).*

Q.16. Name the amino acids which do not participate in transamination reaction.

The amino acids which do not participate in transamination reaction are:

- Lysine
- Threonine
- Cyclic imino acids-Proline and OH-Proline.

Q.17. Name two specific transaminases which are of clinical importance. What are the substrates and end-products?

- *Aspartate transaminase* (or aspartate aminotransferase): Previously used to be called as *“S-GOT”*— serum glutamate oxaloacetate transaminase.



(Donor	a.a)	(recipient	(New keto	(New a.a)
		keto acid)	acid)	

- *Alanine transaminase* (or Alanine aminotransferase): Previously used to be called as *“S-GPT”*— serum glutamate *“pyruvate transaminase”*

Alanine + α -oxoglutarate	Pyruvic Acid + Glutamate
(Donor a.a) (recipient K.A)	(New K.A) (New a.a)

Note: In both the cases, glutamic acid is produced as new amino acid.

Q.18. What are normal levels of S-GOT and S-GPT?

- **S-GOT** (aspartate transaminase): Normal serum activity is 4 to 7 I.u/L (7 to 35 Karmen units/ml).
- **S-GPT** (alanine transaminase): Normal serum activity is 3 to 15 I.u/L (6 to 32 Karmen units/ml).

Q.19. What is deamination? What are the types?

Deamination is the process by which N of amino acid is removed as NH_3

2 types of deamination:

- Oxidative deamination
- Non-oxidative deamination.

Q.20. What is the site of oxidative deamination?

- Liver and
- Kidney are the main organs where oxidative deamination takes place. 

Q.21. What is the nature of enzyme and coenzyme that take part in oxidative deamination?

- **Enzyme:** *L-amino acid oxidase* which acts specifically on L-amino acids and oxidatively deaminate to form NH_3 .
- **Coenzyme:** is Flavoprotein (FMN) which acts as H-acceptor.
- **Nature of the enzyme:** The *L-amino acid oxidases* are *auto-oxidizable* flavoproteins. The reduced flavoproteins FMN.H₂ are re-oxidized at substrate level directly by molecular O_2 forming H_2O_2 which is converted to H_2O by the enzyme *catalase*.

Q.22. What are the toxic substances that can form in oxidative deamination of L-amino acids by “L-amino acid oxidase”?

- **Superoxide anion O_2^- :** This is scavenged by the enzyme *superoxide dismutase*.
- **H_2O_2 :** Scavenged by the enzyme *catalase*.
Both superoxide anion O_2^- and H_2O_2 are toxic and they can oxidize membrane proteins, lipids, -SH groups and methionine sulphur and produce harmful effects.

Q.23. What is the function of presence of *D-amino acid oxidase* in cells, when it is known there is absence of D-amino acids in cells?

There is no D-amino acids in the body tissues, hence it is not clear about the presence of *D-amino acid oxidase* in cells and its functions. Probably the dietary D-amino acids may be oxidized by *D-amino acid oxidase* and be isomerized through their keto acids to L-amino acids.

Q.24. Does oxidative deamination fulfil a major role in formation of NH_3 as:

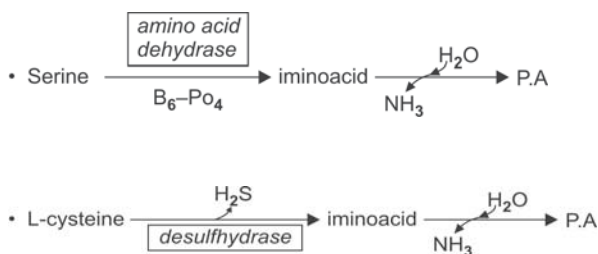
L-amino acid oxidase does not fulfil a major role in mammalian amino acid catabolism and formation of NH_3 as:

- It is restricted only to liver and kidney.
- Activity of the enzyme in these tissues is low.
- It does not have any effect on glycine or the L-isomers of the dicarboxylic acid or $\beta\text{-OH-}\alpha\text{-amino acids}$.
- It does contribute to formation of NH_3 to some extent.

Q.25. What is Non-oxidative deamination? Give two examples.

Certain amino acids like OH-amino acids, histidine and S-containing a.a can be deaminated non-oxidatively by specific enzymes to form NH_3 . They also do not fulfil major role in NH_3 formation.

- Two examples:



Q.26. State the principal method by which NH_3 is formed from L-amino acids.

- **By transdeamination:** It is combination of transamination + Deamination.
- The- NH_2 group of most L-amino acids are transferred to $\alpha\text{-oxoglutarate}$ by specific transaminases by the process

of transamination **forming L-glutamate** as end-product. L-glutamate is oxidatively deaminated by a specific Zn-containing enzyme *glutamate dehydrogenase*, of high activity and wide distribution, which requires NAD^+ or NADP^+ as coenzyme, to form NH_3 .

- As the process involves first transamination and coupled with oxidative deamination, it is called as *transdeamination*.

Q.27. List the sources of NH_3 in the body.

- Transdeamination—the major pathway.
- Oxidative deamination by *L-amino acid oxidase*
- Non-oxidative deamination
- Absorption of NH_3 from gut produced by intestinal bacterial flora:
 - From dietary proteins
 - From urea present in fluids secreted into the gut
 - From uric acid secreted in bile (This assumes importance in intestinal obstruction and portocaval shunt)
- Pyrimidine catabolism (small fraction).

Q.28. What is the normal blood ammonia level?

- In man, normal blood level of NH_3 varies from 40 to 70 $\mu\text{g}/\text{dl}$.
- Free NH_4^+ (ammonium ion) concentration of fresh plasma is less than 20 $\mu\text{g}/\text{dl}$.

Q.29. Why NH_3 is toxic?

Exact cause is not known. The following associated biochemical changes are important:

- Increased NH_3 concentration enhances amination of α -oxoglutarate, thus decreasing the α -oxoglutarate, an intermediate of TCA cycle. This depresses TCA cycle affecting cellular respiration.
- Increased NH_3 concentration enhances glutamine formation from glutamate thus **reduces “brain cells pool” of glutamic acid**, which decreases formation of inhibitory neurotransmitter “**GABA**” (γ -amino butyric acid).
- Rise in brain glutamine level enhances the overflow of glutamine from brain which allows entry of tryptophan by the same “transporter”. *Hence tryptophan concentration in brain cells increases which leads to increased synthesis of serotonin.*

Q.30. What are the metabolic fate of NH_3 in the body?

- **Main fate:** toxic NH_3 is detoxicated to form nontoxic urea in liver by urea cycle and excreted in urine.
- **Formation of glutamine**, which acts as a reservoir of NH_3 .
- **Amination** of α -keto acids to form α -amino acids.

Q.31. What is the other name of urea cycle?

- Krebs-Henseleit cycle.

Q.32. Why urea formation is called cyclic process?

One molecule of NH_3 and one molecule of CO_2 are converted to urea by Five sequential enzymatic reactions. In each turn of the cycle, Ornithine is regenerated in the last reaction which acts as a **catalytic agent** and repeats the cycle again. Hence it is a cyclic process.

Q.33. Which organ is associated with urea formation?

Liver is the only organ which can form urea and all the enzymes involved have been isolated from the liver tissue.

Q.34. Can other organs like kidney and brain synthesize urea?

- **Kidney:** Can form upto arginine but cannot form urea as enzyme "*arginase*" is absent in kidney tissues.
- **Brain:** Can synthesize urea if citrulline is available but lacks the enzyme *ornithine transcarbamoylase* which forms citrulline from ornithine.

Q.35. State the five steps of urea cycle indicating the enzymes involved and location of the enzyme.

	<i>Enzyme</i>	<i>Location</i>
• Reaction 1 : Synthesis of Carbamoyl-P	Carbamoyl-P Synthetase I	Mitochondria
• Reaction 2 : Synthesis of Citrulline	Ornithine transcarbamoylase	Mitochondria
• Reaction 3 : Synthesis of Arginino-succinate	Arginino-succinate Synthetase	Cytosol
• Reaction 4 : Cleavage of Argininosuccinate	Arginino-Succinase	Cytosol
• Reaction 5 : Cleavage of arginine to form urea and ornithine	Arginase	Cytosol

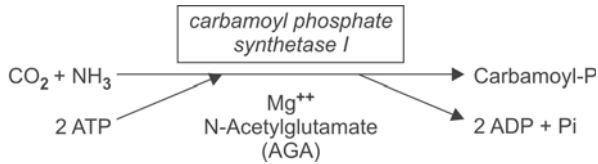
Q.36. What is the role of N-acetyl glutamate (AGA) in the first reaction in formation of carbamoyl-P?

N-acetyl glutamate (AGA) acts as an **allosteric activator** of the enzyme *carbamoyl synthetase I*, it brings about

conformational changes in the enzyme so that the second molecule of ATP can bind.

Q.37. Show schematically the first reaction, synthesis of carbamoyl-P. What are the starting materials? Is biotin necessary?

- **Starting materials:** CO_2 and NH_3
- **Biotin is not required.**



Q.38. How many amino acids take part in the urea cycle? 5 amino acids participate in urea cycle. They are:

- Ornithine
- Citrulline
- Glutamic acid
- Aspartic acid
- Arginine.

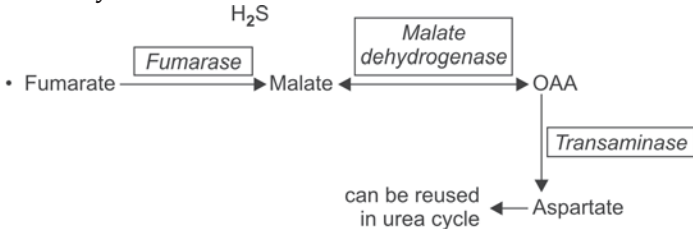
Q.39. What is the energy requirement in formation of one molecule of urea in urea cycle?

Three molecules of ATP are utilized for the formation of one molecule of urea. As one ATP is converted to AMP, it is equivalent to utilizing 4 high energy bonds.

Q.40. Urea contains two nitrogen (NH_2 groups), what are the sources of the two nitrogens?

- One nitrogen of NH_2 group is derived from the NH_4^+ ion (Reaction 1)
- Other nitrogen of NH_2 group is provided by aspartic acid (Reaction 3).

Q.41. How fumarate a by-product in fourth reaction can be converted to Aspartic acid required in the third reaction of urea cycle?



Q.42. What is the normal blood level of urea in the body?

- Normal level ranges from 20 to 40 mg%.
- Indians take less proteins in diet, hence in Indians normal level is taken as 15 to 40 mg%.

Q.43. In what conditions the blood level of urea increase:

Causes may be:

- Pre-renal
- Renal
- Postrenal

Q.44. Mention some pre-renal causes.

Conditions in which plasma volume/body fluid are reduced, e.g.:

- Salt and water depletion
- Severe and protracted vomiting as in pyloric/intestinal obstruction,
- Severe and prolonged diarrhea,
- Hemorrhage and shock,
- In burns.

Q.45. State some renal causes:

- *In acute glomerulonephritis.*
- In Type II nephritis (nephrotic syndrome)-in later stages.
- Chronic pyelonephritis.
- Malignant nephrosclerosis.
- Mercurial poisoning.

Q.46. Mention some post renal causes.

- Enlargement of prostate—benign and malignant
- Stone in urinary tract (urinary lithiasis)
- Stricture of urethra
- Tumors of the bladder affecting urinary flow.

Q.47. What is glutamine?

- Glutamine is chemically δ -amide of α -amino glutaric acid. Glutamine formation helps in removal of NH_3 which is toxic (detoxication of NH_3).
- Glutamine serves as an important reservoir of nitrogen in tissues which is readily available and can be drawn upon for various synthetic processes, when the body needs.

Q.48. How glutamine is synthesized in the body? Name the tissues involved in synthesis of glutamine.

Glutamine is synthesized in tissues like:

- Liver
- Kidney
- Brain and retina. It is formed from:
 - Glutamic acid and
 - NH_3 by the action of a mitochondrial enzyme "*Glutamine synthetase*" in presence of **ATP** and **Mg⁺⁺**.
- The reaction is "**irreversible**", so that glutamine cannot reform glutamic acid and NH_3 by the same enzyme.

Q.49. What is the normal blood level of glutamine?

Normal blood level in a healthy adult ranges from 6 to 12 mg%.

Q.50. How NH_3 can be obtained from glutamine?

- Glutamine is **reservoir of NH_3** and **readily available source of NH_3** .
- Glutamine is hydrolyzed readily by a specific enzyme *glutaminase*. The reaction is 'irreversible' and can occur in various tissues like liver, kidney, brain and retina.

Q.51. State some important functions of glutamine in the body.

- **Transamidation:** The amide N of glutamine can be transferred to keto-group of fructose-6-P to form glucosamine-P.
- **Formation of guanylate (GMP).**
- **Role of glutamine in kidney:** in conservation of Na^+ ($\text{NH}_4 \rightarrow \text{Na}^+$ exchange)
- **Role of glutamine in brain:** Brain tissues cannot detoxicate NH_3 to form urea. Excess NH_3 entering brain, e.g. in hepatic failure is detoxicated by Glutamine formation.
- **Role of Glutamine in conjugation reaction** (Detoxication).
- **Role in cancer:** Certain tumors exhibit abnormally high requirement of glutamine/asparagine for their growth.

Q.52. What is the normal level of glutamine in CS fluid in health?

- Normal range of CSF glutamine is 6 to 14 mg%.

Q.53. What are the clinical manifestations of ammonia intoxication?

The symptoms of NH_3 intoxication include:

- A peculiar flapping tremor
- Slurring of speech
- Blurring of vision
- In severe cases lead to coma and death.

Q.54. How much urea is excreted daily in urine?

- 20 to 30 gm in 24 hours urine.

Q.55. Name the inherited disorders associated with urea cycle.

- Hyperammonemia Type I
- Hyperammonemia Type II, (also called ornithinemia)
- Citrullinemia
- Arginino-succinic aciduria
- Hyperargininemia.

Q.56. What are the fates of C-skeleton of amino acids after removal of NH_3 ?

The fates are:

- **Reamination** to form amino acid e.g. PA $\rightarrow$ Alanine, OAA $\rightarrow$ Aspartic acid, α -oxoglutarate $\rightarrow$ Glutamic acid.
- **Formation of CO_2 , H_2O and energy**, after entering TCA cycle.
- **Formation of glucose** (glucogenic), or ketone bodies (ketogenic) or both.

Q.57. How much protein is potentially glucogenic?

It has been shown by experimental studies that 60 gm (approximately 58 gm) of glucose are formed and excreted in urine for 100 gm of proteins metabolized. Thus **60% of proteins (amino acids) is potentially glucogenic.**

Q.58. Name at least ten amino acids which are glucogenic.

Glycine, alanine, serine, cysteine/cystine, threonine, methionine, proline, valine, arginine, glutamate.

Q.59. Name the only amino acid which is ketogenic.

- L-leucine.

Q.60. Name at least three amino acids which are both glucogenic and ketogenic.

- Phenylalanine/tyrosine, tryptophan, isoleucine.

Q.61. What is decarboxylation reaction?

Decarboxylation is the reaction by which CO_2 is removed from the $-\text{COOH}$ group of an amino acid resulting to formation of a biogenic amine. the reaction is catalyzed by the enzyme *decarboxylase* which requires pyridoxal-P ($\text{B}_6\text{-PO}_4$) as coenzyme.

Q.62. Name at least five biogenic amines of clinical importance. State the amino acid from which it is derived and mention biological importance in the body.

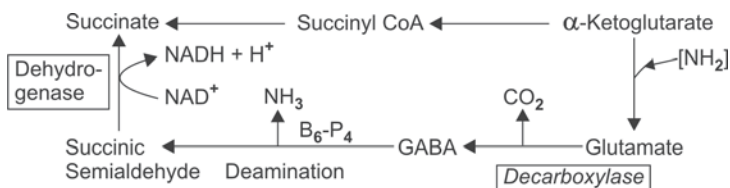
Biogenic amine	Name of the amino acid	Biologic importance
• Histamine	Histidine	• Vasodilator, $\text{B.P}\downarrow$ • $\text{HCL}\uparrow$ • $\text{Pepsin}\uparrow$, • Liberated in anaphylactic reaction
• γ-amino butyric acid (GABA)	Glutamic acid	• Presynaptic inhibitor in brain • Forms a by-pass in TCA cycle (GABA shunt)
• Taurine	Cysteic acid (derived from cysteine)	• Constituent of bile acid (taurocholic acid)
• Tryptamine	Tryptophan	• Tissue hormone, a derivative of 5-OH tryptamine (serotonin) • Vasoconstriction, $\text{BP}\uparrow$
• Ethanol-amine	Serine	• Forms choline • Constituent of PL like cephalin.

Q.63. State the biogenic amines produced by putrefaction in the gut by intestinal bacterial action.

- *Cadaverine*: derived from lysine.
- *Putrescine*: derived from ornithine.
- *Agmatine*: derived from arginine.

Q.64. What is GABA shunt? Show schematically.

GABA by its conversion to succinic acid can form a “bypass” in TCA cycle and this is called as **GABA shunt**.



Q.65. Give an example of decarboxylation which occurs spontaneously without an enzyme.

- Formation of acetone from acetoacetate



Q.66. Name the polyamines.

- Spermidine
- Spermine and
- Their precursor putrescine.

Q.67. Name the amino acids required in polyamine synthesis.

- *Ornithine*: The starting amino acid
- *Methionine*: Required as S-adenosyl methionine (“active” methionine).

Q.68. State clinical significance of polyamines.

- *Increased urinary polyamine excretion claimed to be characteristic of malignant diseases.* It has been reported to be increased in:
 - Leukemias
 - Carcinoma of ovaries, lungs, colon, rectum, prostate, GI tract, kidney, bladder and testes.
- *Spermidine is the best “marker” of tumor cells destruction.*
- *Putrescine is the best “marker” for cell proliferation.*

Q.69. What is carbamoyl-P synthetase II? What is its function?

Carbamoyl-P-synthetase II is an enzyme present in cytosol. It can form carbamoyl-P from CO_2 and amide-N of glutamine, which is used in pyrimidine synthesis.

Q.70. What are the aromatic amino acids? Name them, which is essential and which is not.

- Aromatic amino acids are:
 - Phenylalanine and
 - Tyrosine
- Phenylalanine is essential and must be provided in the diet
- Tyrosine is not essential as it can be formed from phenylalanine in the Liver.

Q.71. What are the enzymes and coenzymes/cofactors required for conversion of phenylalanine to tyrosine?

- **Enzyme:** *phenylalanine hydroxylase*.
- **Coenzymes/cofactors:**
 - Molecular O_2
 - NADPH
 - Fe^{++} and
 - FH_4 (Tetrahydrobiopterin).

Q.72. State how phenylalanine is converted to tyrosine in the body.

Reactions occur in two stages:

- **Stage 1:** Reduction of molecular O_2 to H_2O and conversion of Phenylalanine $\longrightarrow$ to tyrosine. Reduced form of folic acid $F.H_4$ acts as H-donor to molecular O_2 and is converted to $F.H_2$. In this stage, there is incorporation of one atom of molecular O_2 to p-position of phenyl alanine to form tyrosine, while other atom of O_2 is reduced to H_2O .
- **Stage 2:** Reduction of $F.H_2$ to reform $F.H_4$ takes place by NADPH, acting as a H-donor, catalyzed by the enzyme *dihydrobiopterin reductase*.

Note: Both the reactions are irreversible.

Q.73. What is meant by sparing action?

The feeding of tyrosine/or cysteine decreases the need of phenylalanine/or methionine in the diet respectively. This is called “sparing” action. Phenylalanine/or methionine is spared from synthesis of tyrosine/or cysteine respectively.

Q.74. Tyrosine is a non-essential amino acid. In which condition it becomes an essential amino acid?

In phenylketonurias, where phenylalanine cannot be converted to tyrosine in the body due to inherited absence

of the enzyme *phenylalanine hydroxylase*, tyrosine becomes an essential amino acid to the patient.

Q.75. Enumerate the metabolic role/or biomedical importance of tyrosine in the body.

Though tyrosine is a non-essential amino acid, it is of great metabolic importance as many *“biologically” important compounds are formed from tyrosine*. They are:

- *Synthesis of thyroid hormones*: Thyroxine (T_4), tri-iodo thyronine (T_3) and “reverse” T_3 .
- *Synthesis of catecholamines*: Epinephrine and norepinephrine.
- *Synthesis of melanin* pigments in skin.
- *Formation of biogenic amine* tyramine.
- *Formation of phenol and cresol*.
- *Formation of tyrosine-o-sulphate*, a constituent of fibrinogen molecule.

Q.76. What is phenylketonuria?

Phenylketonuria is an inherited disease due to inherited deficiency of the enzyme *phenylalanine hydroxylase*.

- Due to the deficiency of the enzyme, phenylalanine cannot be converted to tyrosine resulting to accumulation of phenylalanine in blood and tissues. Phenylalanine undergoes transamination producing,
- Phenyl pyruvic acid
- Phenyl lactic acid
- Phenyl acetic acid

Which are excreted in urine, hence called as phenyl ketonuria.

Q.77. Why the urine of phenylketonuric patient has a mousy odour?

Phenyl acetic acid is conjugated with glutamine and excreted as *phenyl acetyl glutamine* in urine which is responsible for the “mousy” odour.

Q.78. What other biochemical changes occur due to accumulation of phenylalanine in phenylketonurics?

Accumulation of phenylalanine leads to:

- Defective serotonin formation
- Impaired melanin synthesis that is the reason for fair skin and hairs

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- Excretion of phenylalanine into the intestine competes with tryptophan for absorption. Tryptophan becomes subject to action of intestinal bacteria resulting in formation of indole derivatives which are absorbed and excreted in urine.

Q.79. What are the clinical presentation of a phenylketonuric child?

Child is *mentally retarded*. May have other features like, eczema, psychoses and seizures.

Q.80. What treatment you will suggest for a phenylketonuric child?

Child should be given diet with very low or absent phenylalanine. The diet can be terminated after six years of age, when high concentration of phenylalanine and its derivatives are not injurious to brain.

Q.81. A lady reports to you with the complaints her baby's napkin soiled with urine turns black on exposure to air. Which disease you will suspect?

- Alkaptonuria.

Q.82. What is alkaptonuria? What is the enzyme deficiency?

Alkaptonuria is an **inherited disorder** of phenylalanine/tyrosine metabolism in which homogentisic acid, a metabolite in the metabolic pathway, cannot be oxidized to Maleylacetoacetate due to the inherited deficiency of the enzyme *homogentisate oxidase*.

Q.83. Why the urine becomes dark on standing in alkaptonuria?

Urine of alkaptonuric patient turns black gradually from top to down when exposed to air and on standing. Homogentisic acid excreted in urine gets oxidized to **black pigment (alkapton)**.

Q.84. How will you produce alkaptonuria experimentally?

Experimental alkaptonuria can be produced by administering " **α - α' -dipyridil**", a chelating agent that binds strongly to Fe^{++} of the enzyme *homogentisate oxidase* and inhibits the reaction i.e. conversion of homogentisic acid to maleyl acetoacetate. Thus homogentisic acid accumulates and appears in urine.

Q.85. What is ochronosis?

In longstanding cases of alkaptonuria, *homogentisic acid derivatives get deposited in cartilages* of ears, nose and other exposed parts of the body leading to generalized pigmentation of connective tissues. Also gets deposited in joints leading to arthritis. This condition is called ochronosis.

Q.86. What is the mechanism of ochronosis?

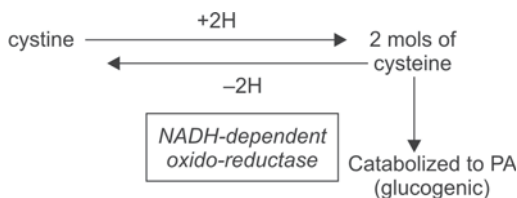
Exact mechanism is not known. Probably the homogentisic acid gets oxidized by *polyphenol oxidase* forming benzo-quinone acetate, which polymerizes and binds to connective tissue macromolecules.

Q.87. What is albinism?

It is an **inherited disorder** of tyrosine metabolism in which the enzyme *tyrosinase* is lacking resulting to non-formation of melanin pigment for which the hair, skin and retina of eye are not black.

Q.88. What is the relationship between cysteine and cystine?

- Two molecules of L-cysteine oxidized to give one molecule of cystine which is joined by S–S-bond.
- One molecule of cystine is reduced to form two molecules of cysteine.



Q.89. What are the end-products of methionine degradation? What are the fate of end products?

End products are:

- *Propionyl CoA*: Converted to succinyl CoA through formation of Methyl malonyl CoA (glucogenic).
- *α -amino butyric acid*: Excreted in urine.

Q.90. What is active methionine? What is it known as chemically?

- “**Active methionine**” is an active compound in which CH_3 group is *biologically labile* and it acts as a methyl

(CH₃) group donor to a suitable “acceptor” so that it can form biologically important compounds.

- Chemically “active methionine” is *S-adenosyl methionine*.

Q.91. How active methionine is formed?

Activation of methionine occurs in presence of ATP, catalyzed by the enzyme called “*L-methionine-adenosyl transferase*”. It requires presence of Mg⁺⁺ and G-SH. In the process of activation, ATP donates the entire adenosine moiety to methionine and loses three molecules of PO₄, one as orthophosphate and two as pyrophosphates.

Q.92. Why methyl group in active methionine is labile and can be donated easily?

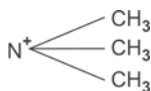
In “**active**” methionine, CH₃ group forms a “*high energy*” bond with sulphur (-S ~ CH₃) and *not* with carbon. This attributes to the lability of the CH₃ group which can be easily donated to a suitable acceptor.

Q.93. What is meant by transmethylation reaction?

Certain compounds of the body, with structures containing CH₃ group attached to an atom other than carbon can take part in enzymic reactions, whereby these CH₃ groups are transferred to a suitable “acceptor” which have no methyl group. Such reactions are called as *transmethylation reaction*.

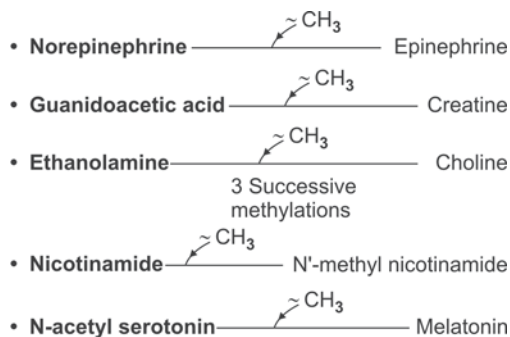
Q.94. Name the compounds which possess biologically labile methyl group.

- **Active methionine (S-adenosyl methionine):** containing -S ~ CH₃ group.
- **Choline:** containing -CH₃ groups attached to N as follows:



- **Betaine:** an oxidation product of choline.

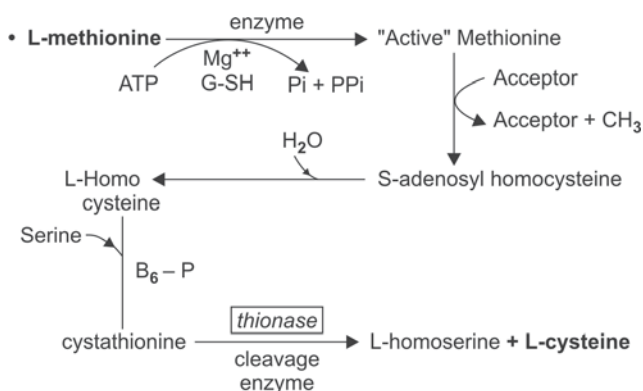
Q.95. Give Five examples of transmethylation reactions, where active methionine acts as methyl donor.



Q.96. Enumerate the metabolic role or biomedical importance of L-methionine.

- Methionine is **glucogenic**.
- Methionine is converted to L-cysteine in the body.
- **Lipotropic function**: provides choline, a lipotropic agent, by methylations of ethanolamine.
- **Transmethylation reactions**: by forming active methionine.
- **In polyamine synthesis**.
- **Formation of methyl mercaptan** in liver diseases, which accounts for foul odour in breath (foetor hepaticus).

Q.97. Show schematically how L-cysteine is formed from L-methionine.



Q.98. What contributes to C-skeleton and sulphur of L-cysteine?

- Sulphur of methionine is directly contributed to formation of L-cysteine.
- Carbon skeleton is derived from the amino acid serine.

Q.99. What is the end product of L-cysteine catabolism?

- Pyruvic acid (Thus it is glucogenic).

Q.100. Enumerate the metabolic role/or biomedical importance of cysteine.

- Cysteine is **glucogenic**.
- **Formation of glutathione**.
- **Formation of taurine** which is required for formation of taurocholic acid.
- **Formation of mercaptoethanolamine** by decarboxylation which is an important constituent of CoA-SH.
- **Role in detoxication:** involved in detoxication of aromatic compounds and forms mercapturic acids which are excreted in urine.
- Cysteine is an important constituents of **Scleroproteins**. It is present in proteins of nails, hairs, hoofs, and keratin of skin.

Q.101. Differentiate cystinuria and cystinosis.

Both are inherited disorders of cysteine metabolism.

Cystinuria

- Due to renal transport defect.
- Excretion of cystine in urine increases 20 to 30 times of normal.
- Also there is increased excretion of dibasic amino acids:
 - Lysine • arginine, and
 - ornithine
- May form cystine stones.

Cystinosis

- Also called as “cystine storage disease.
- Defect: impaired conversion of cystine to cysteine (deficiency of “*cystine reductase*”).
- Widespread deposition of cystine in various tissues like liver, spleen, kidney, bone marrow, lymphnodes, and cornea.
- Cystine accumulates in lysosomes of cells of RE system.

Q.102. What is homocystinuria? What is the enzyme deficiency?

- An **inherited** disorder of metabolism of L-methionine or more specifically its metabolic intermediates homocysteine/or homocystine.

-
- **Enzyme deficiency: cystathionine synthetase** enzyme deficiency leads to accumulation of homocystine which is excreted in urine.

Q.103. State the salient clinical features of a case of homocystinuria.

- **Mental retardation** in children and surviving adults.
- Enlargement of liver (**hepatomegaly**).
- Affected individuals are extra-ordinarily tall, with long extremities frequently with flat feet with toes out ("**Charlie-Chaplin**" gait).
- Skeletal deformities involving spinal vertebrae (X-ray shows "**cod-fish**" appearance)
- Dislocation of lens of the eye (**Ectopia lentis**).
- **Life threatening arterial/venous thrombosis**.

Q.104. State the metabolic role of glycine (aminoacetic acid).

Though glycine is the simplest and non-essential amino acid, but it is of great importance as it forms many biologically important compounds in the body. They are:

- **Synthesis of heme**
- **Synthesis of purine nucleus**, it contributes C₄, C₅ and N₇ of purine ring
- **Synthesis of glutathione**
- **Synthesis of creatine**
- **Conjugation reaction**: detoxicates benzoic acid to form hippuric acid which is excreted in urine.
- Formation of glycocholic acid (**bile acid**).
- **Glucogenic**: Glycine is converted to serine which is converted to PA (glucogenic).
- Source of **oxalate** and **formate** (one carbon metabolism).

Q.105. Name the histidine compounds present in the body.

- **Histamine**: a biogenic amine formed by decarboxylation.
- **Ergothioneine**: Present in RB cells and liver. Ruptured red cells liberate ergothioneine which can reduce Benedict's qualitative reagent.
- **Carnosine**: a dipeptide of histidine and β -alanine.
- **Anserine**: a methyl derivative of carnosine.

Q.106. What is glutathione?

Glutathione is a **tripeptide** of three amino acids:

- Glutamic acid, • Cysteine and • Glycine (Glutamyl-cysteinyl-glycine).

Q.107. State five metabolic role/or biomedical importance of glutathione in the body.

- Reduced Glutathione (G-SH) is necessary for maintaining *integrity of red cell membranes* and *lens protein*.
- It *helps to destroy* H_2O_2 and other peroxides in cells. The reaction is catalyzed by selenium containing enzyme *glutathione peroxidase*.
- *Acts as coenzyme* with liver enzyme *glutathione-insulin transhydrogenase* which helps in catabolism of Insulin.
- Glutathione takes part in " **γ -glutamyl cycle**" for absorption of amino acids from gut.
- Reduced glutathione (G-SH) is required as **coenzyme/cofactor** for *PG synthetase system* in PG synthesis and also for formation of "active methionine".

Q.108. What is serotonin?

Serotonin is chemically 5-OH tryptamine (5-HT), and it is formed from amino acid tryptophan. It is present in blood and is produced in tissues like gastric mucosa, intestine, brain, mastcells and platelets. (Probably stored in Platelets?)

Q.109. State the cells that produce serotonin.

Serotonin is produced by special cells present in serotonin producing tissues, called as serotonin-producing cells" (also called *argentaaffin cells* or *Kultchitsky's cells*).

Q.110. How much tryptophan is converted to serotonin normally?

Only 1% of tryptophan is utilized for serotonin synthesis normally.

Q.111. How Serotonin is synthesized by the serotonin-producing cells in the body?

- Tryptophan is first hydroxylated to form 5-OH tryptophan in liver by *hydroxylase* enzyme in presence of O_2 and NADPH.
- 5-OH tryptophan is next **decarboxylated** by the enzyme *decarboxylase* to form 5-OH tryptamine (5-HT), called serotonin, the reaction requires B_6 -P as coenzyme.

Q.112. What are the functions of Serotonin?

- It is a potent **vasoconstrictor**, increases B.P↑
- Produces **contraction of smooth muscles**.
- **Stimulates cerebral activity↑ (excitation)**. Deficiency of serotonin in brain produces depressed activity (Depression).

Q.113. Name the enzyme which degrades serotonin. What is the degradation product?

- Enzyme is *monoamine oxidase (MAO)*
- Degradation product is 5-OH-Indole acetic acid (5-HIAA) which is excreted in urine.

Q.114. In which condition excessive amount of serotonin is produced in the body?

- Excessive amount of serotonin is produced in *carcinoids*. a malignant tumour of serotonin-producing cells. It is also called as *argentaffinoma*.
- The clinical features associated with it is called as *carcinoid syndrome*.
- *In carcinoids, 60% of tryptophan is utilized for serotonin formation* as compared to 1% in normals.

Q.115. State the clinical features seen in carcinoid syndrome.

Symptoms are mainly due to excessive production of serotonin and its effects on smooth muscle. The clinical features are:

- Cutaneous vasomotor episodes of “flushing”
- Occasionally cyanotic appearance
- Chronic diarrhea
- Respiratory distress and bronchospasm
- Some may have right-sided heart failure. Serotonin passing through lungs is destroyed by “MAO” hence left side is not affected.

Q.116. What is melatonin?

- Chemically melatonin is “N-acetyl-5-methoxy serotonin”. It is a hormone produced by the pineal gland and peripheral nerves of man and some other higher animals.
- The hormone lightens the color of melanocytes in the skin of frog and blocks the action of MSH (Melanocyte stimulating hormone) and ACTH.

Q.117. What is Hartnup's disease?

- It is an **inherited disorder** associated with the metabolism of tryptophan. The clinical symptoms are **mental retardation**, intermittent cerebellar ataxia and skin rash.
- Urine of patients with Hartnup's disease contains increased amounts of indoleacetic acid and tryptophan.

Q.118. Why it is called as Hartnup's disease?

The disease is *named after the Hartnup family* in which it was discovered.

Q.119. What is the metabolic defect in Hartnup's disease?

- An inherited deficiency of the enzyme *tryptophan dioxygenase* in liver.
- Could also be due to a defective indole transport and consequent impairment of tryptophan metabolism.

Q.120. What is the relationship between creatine-P and creatinine?

- Both are nonprotein nitrogenous compounds.
- Creatinine-P is chemically methyl guanidino acetic acid".
- Creatinine is *anhydride of creatine*, the reaction is **irreversible** and **non-enzymatic**. Creatinine has a ring structure.

Q.121. In which tissues creatine is found and in what form?

- Creatine is a normal constituent of the body and is present principally **in muscles**, also found in brain, liver, testes and blood.
- It can occur in "free" form and mainly as "phosphorylated" form called creatine-P (also called as **phosphocreatine** or **phosphagen**).

Q.122. How much creatine is present in the body?

- Total amount in an adult human is approximately 120 gm.
- Of the total amount, 98% is present in muscles, of which 80% occurs in phosphorylated form, 1.3% in nervous tissues including brain and 0.5 to 0.7% in other tissues.

Q.123. In what form creatine is excreted in urine in normal health?

- As creatinine and NOT creatine.

Q.124. What is blood and plasma level of creatine?

- **In whole blood:** Creatine level varies from 2.0 to 7.0 mg%.
- **In plasma:** It is less than 1 mg%.
 - In males: It varies from 0.2 to 0.6 mg%.
 - In females: 0.35 to 0.9 mg%.

Q.125. What is the normal creatinine level in whole blood?

In whole blood creatinine level varies from 1.0 to 2.0 mg%.
Creatinine is evenly distributed in blood and plasma.

Q.126. What is the urinary excretion of creatinine in normal health:

Urinary excretion of creatinine in normal health is as follows:

- In males: 1.5 to 2.0 gm in 24 hours urine.
- In females: 0.8 to 1.5 gm in 24 hours urine.

Q.127. Name the amino acids required for creatine synthesis in the body.

Three amino acids are required:

- Glycine
- Arginine
- Methionine.

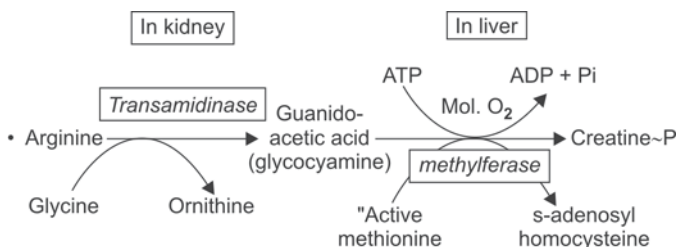
Q.128. Which are the starting amino acids?

- Arginine and
- Glycine.

Q.129. What are sites of synthesis of creatine in the body?

- First reaction occurs in **kidney**. The product formed is guanidoacetic acid (glycocyamine), which passes to blood.
- Second reaction occurs **in liver** where creatine-P is formed, which goes from liver to muscles and stored there.

Q.130. Show schematically the biosynthesis of creatine.



Q.131. Where does the formation of creatinine occur?

- In Liver and in Kidney.

Q.132. What is meant by transamidination?



Transfer of an amidine group $\text{NH}=\text{C}$, from an amino acid to another amino acid, e.g. from arginine to glycine under the influence of an enzyme *transamidinase* to form guanido-acetic acid (also called glyco-cyamine).

Q.133. What is creatinuria? List the conditions where creatinuria occur?

Excretion of creatine in urine is called creatinuria.

Creatinuria can occur under following conditions:

- In children: Probably due to lack of ability to convert creatine to creatinine.
- Adult females: in pregnancy and maximum after parturition (2 to 3 weeks).
- **Thyrotoxicosis:** Probably due to associated thyrotoxic myopathy.
- Muscular dystrophies, in myositis and in myasthenia gravis
- Wasting diseases, e.g. in malignancies
- In febrile conditions
- Starvation
- Subjects lacking carbohydrates in diets and in diabetics.

Q.134. What is creatinine coefficient?

- It is the ratio of total creatinine in 24 hours urine in mg and total body weight in kg. Thus,

=

- The value is 20 to 26 for males and 14 to 22 in females.

Q.135. What is Jaffe's reaction?

- When serum is treated with alkaline picrate solution a red color develops. It is called as *Jaffe's reaction*.
- The color is read against a "standard" similarly treated in a colorimeter and calculated to get the serum creatinine value.

Q.136. What is the fallacy with Jaffe's reaction?

Serum creatinine estimation by Jaffe's reaction *does not give "true" creatinine value*. It measures also certain "non-creatinine chromogens", up to 20% in blood and 5% in urine.

Q.137. How will you exclude the chromogens from estimation and get "True" creatinine value?

For excluding the chromogens and to get "True" creatinine after precipitating proteins, creatinine is adsorbed on to Lloyd's reagent (Fuller's earth), a hydrated aluminium silicate, and then color developed with alkaline picrate and measured.

Q.138. What is Löhman reaction?

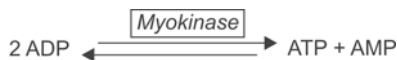
- Creatinine ~ P is the reservoir of energy in muscles. When muscles contract, energy is derived from breakdown of ATP to ADP and Pi. ATP must be reformed quickly to supply the energy.



- The high energy phosphate of creatine-P is transferred to ADP and ATP is reformed. This reaction is called as *Löhman reaction* and it takes place during muscle activity.

Q.139. What is myokinase reaction?

Two ADP molecules react to produce one molecule of ATP and AMP, the reaction is catalyzed by the enzyme *myokinase (adenylate Kinase)*.



Q.140. What is meant by creatinine clearance test.

Endogenous creatinine clearance is used as a renal function test. At normal levels of creatinine in the blood, this metabolite is filtered at the glomerulus but neither secreted nor reabsorbed by the tubules. Hence its clearance measures the glomerular filtration rate (GFR).

Q.141. What is the normal endogenous clearance?

Normal values for creatinine clearance varies from 95 to 105 ml/mt.

Q.142. What are the biological importance and metabolic role of arginine?

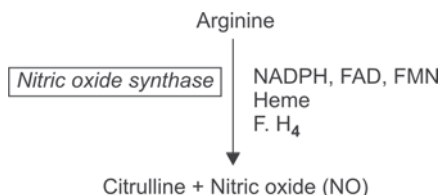
- Semiessential amino acid required in growing children, in pregnancy and lactation
- Required for creatine synthesis
- Required in urea formation (an intermediate metabolite)
- Tissue protein formation
- Glucogenic amino acid.
- Formation of Nitric oxide (NO).

Q.143. Is nitric oxide found in our body?

Yes, it is found in our body. It is formed from the amino acid arginine.

Q.144. How nitric oxide (NO) is formed in the body?

Arginine is acted upon by an enzyme called "*Nitrogen oxide synthase*", a cytosolic enzyme which converts arginine to citrulline and nitric oxide.



Q.145. State the mechanism of the action of the enzyme.

- Nitric oxide synthase catalyzes a five electron oxidation of an amidine nitrogen of arginine.
- **Cofactors** required for the oxidation are NADPH, FAD, FMN, heme and F.H₄.

Q.146. Name the isoenzymes of Nitric oxide synthase enzyme (NOS).

Three isoenzymes have been isolated and described. They are:

- *Endothelial NOS (eNOS)*
- *Neuronal NOS (nNOS)*
- *Macrophage NOS (iNOS)*

Q.147. Mention some important functions of Nitric Oxide (NO) in the body.

- Acts as a vasodilator and causes relaxation of smooth muscle.
- It has important role in the regulation of blood flow and maintenance of blood pressure.
- Inhibits adhesion, activation and aggregation of platelets.
- Acts as a neurotransmitter in the brain and peripheral autonomic nervous system.

Q.148. State the mechanism of action of Nitric oxide (NO).

Vasodilatation effect of Nitric oxide (NO) and inhibition of Platelets aggregation are mediated through increased cGMP $\uparrow$ and protein kinase activity.

Q.149. What is EDRF? Has it any relation with Nitric oxide?

- EDRF is endothelium derived relaxing factor which produces vasodilatation.
- It is claimed that EDRF is same as Nitric oxide (NO).

Q.150. Mention some inhibitors of NO and NO synthase.

Inhibitors are as follows:

- Nitric oxide (NO) is inhibited by hemoglobin and other heme proteins which bind it tightly.
- **ADMA** (Asymmetric dimethyl arginine): an endogenous arginine analogue may function as a competitive inhibitor of NO synthase enzyme.

Q.151. State three clinical application of Nitric oxides.

- **Nitroglycerine:** The important coronary artery vasodilator used in Angina Pectoris acts to increase intracellular release of NO.
- **In eclampsia and pre-eclampsia:** The hypertension is due to increased production of NO due to probably formation of ADMA, which acts as competitive inhibitor of enzyme "NO synthase".
- **In septic shock:** Bacterial lipopolysaccharide present in blood causes uncontrolled production of NO leading to dilatation of blood vessels and lowering of BP.

Q.152. What are the metabolic role/or biomedical importance of threonine?

- An essential amino acid, must be provided in the diet.
- Required for tissue protein formation.

- By non-oxidative deamination forms α -keto butyric acid, which on oxidative decarboxylation gives Propionyl CoA (glucogenic).
- Cleaved by the enzyme *threonine aldolase* to form glycine and acetaldehyde.
- It can be converted to PA (thus glucogenic).
- It is a -OH amino acid like serine and acts as PO_4 carrier.

Q.153. What are the metabolic role/or biomedical importance of serine?

- Serine produces PA (**glucogenic**).
- Tissue protein formation.
- "Carrier" of PO_4 group.
- Serine contributes to C-skeleton to form cysteine from methionine.
- Serine on decarboxylation **forms ethanolamine** which on methylations form choline (lipotropic agent).
- Serine and glycine are interconvertible.
- Serine is used for *synthesis of sphingol*.
- β -carbon of Serine is used for **thymine formation**.
- -OH group of serine in an enzyme protein is phosphorylated/dephosphorylated *to form active/inactive forms of the enzyme*.

Q.154. What is Proteinuria?

When proteins appear in urine in detectable quantities, it is called proteinuria. Albumin having the smallest size of the plasma proteins passes easily through damaged epithelia in kidney diseases. Hence, commonly called as "albuminuria".

Q.155. What are the types of proteinurias?

Two types:

- Functional proteinurias
- Organic proteinurias.

Q.156. State some causes of functional proteinuria.

- Violent exercise, long marches
- Pregnancy
- Orthostatic/postural proteinuria
- Alimentary proteinuria-rare.

Note: Usually temporary excretion of proteins in very small amounts less than 2%.

Q.157. State a few causes of organic proteinuria.

Found in many pathological conditions, grouped as:

- Prerenal
- Renal
- Post renal.
- **Pre-renal causes:** Cardiac diseases, liver diseases, abdominal tumors, malignancies.
- **Renal causes:** Acute and chronic glomerulonephritis, nephrotic syndrome (heavy albuminuria). In nephrosclerosis, TB of kidney and carcinoma of kidney.
- **Postrenal causes:** may be due to inflammatory, degenerative and traumatic lesions of ureter, bladder, prostate and urethra.

Q.158. What is Tamm-Horsfall protein? What is its function?

- Tamm-Horsfall protein, a glycoprotein, molecular wt—approximately 30,000 is found in relatively small amount in normal urine. It is secreted by the mucous glands of the normal genitourinary tract.
- **Function:** Probably it serves to protect the epithelia of the genitourinary tract.

Q.159. What is the most common bed-side test used for detecting albumin in urine?

- **Heat test:** Take 2/3 test-tube full of urine sample. Hold the test-tube from the bottom and heat the top portion of the tube. Add a few drops of 1% acetic acid drop by drop. Do not mix.
- Appearance of white turbidity/floccules in the heated portion indicate presence of albumin. If no turbidity/floccules occur, albumin is not detected.

Q.160. Why 1% acetic acid is added drop by drop after heating? What is the purpose?

It serves two purposes:

- If the urine is alkaline, on heating, phosphates may be precipitated which may be taken mistakenly as albumin. On acidification of heated urine, the phosphate if present disappears.
- By acidification of heated urine, the denatured albumin appears as floccules when PI of albumin is reached.
Denatured albumin forms floccules at PI of the protein.

Q.161. Does amino acids are excreted in urine?

Small amounts of amino acids, both free and combined, are excreted in urine. The free amino acid normally amounts to 1.4 mg/kg for men and 2.3 mg/kg for women.

Q.162. What is aminoaciduria?

Increased excretion of amino acids in urine than normal is called aminoaciduria.

Q.163. What are the types of aminoaciduria?

Amino acidurias can be divided into **two main groups**:

- Over-flow aminoaciduria.
- Renal amino aciduria.

Q.164. What is overflow amino aciduria?

In this, due to some metabolic defect/or other defects there occurs an increase in plasma level of one or more amino acids, which are excreted in urine, as it exceeds the capacity of normal renal tubules to reabsorb them.

Q.165. Give three examples of overflow amino aciduria.

- **In severe liver diseases**, e.g. acute yellow atrophy of liver and sometimes in cirrhosis liver, leucine and tyrosine are excreted in urine.
- Can occur in **wasting diseases**.
- **Metabolic defects affecting a single amino acid** or a small group, include inherited disorders, e.g. in phenylketonuria, histidinaemia with histidinuria, glycinuria, maple-syrup disease, etc.

Q.166. What is renal amino aciduria?

In this condition, plasma concentration of amino acids is normal, but because of defects in renal tubular reabsorption of amino acids, an increase amount of one, several or all amino acids escape in urine.

Q.167. Give some examples of renal amino aciduria.

The defect may be specific or non-specific.

- **Specific defect:**
 - *Cystinuria*: due to common renal transport defect:
 - Cystine
 - Lysine
 - Arginine
 - Ornithine are excreted in urine.

-
- *Hartnup disease*: monoamino monocarboxylic acids are excreted.

- **Non-specific defect:**

- In Fanconi's syndrome
- In Wilson's disease
- In patients suffering from muscular dystrophies.
- Heavy metal poisoning like Pb, Hg, Cd, etc.

Q.168. What are the sulphur compounds excreted in urine?

Sulphur is excreted in urine in **three forms**:

- **Inorganic SO_4** : 80 to 85%.
- **Organic esters or ethereal SO_4** : 5%
- **Neutral sulphur**: 15 to 20%.

Q.169. How much sulphur is excreted in urine?

Total urinary sulphur varies from 0.8 to 1.4 gm per 24 hours (average = 1.0 gm).

Q.170. What is the urinary N : S ratio?

Urinary N : S ratio = 13 to 16 on a high meat diet and during fasting.

Q.171. What are Ethereal SO_4 sulphur?

- It consists of Na and K salts of sulphuric acid esters of phenols such as indoxyl, skatoxyl, phenol and cresol. These ethereal SO_4 represent detoxication compounds of above and are formed in liver.
- Indoxyl and skatoxyl are formed by putrefactive decomposition of tryptophan in the gut, and phenol and cresol from tyrosine.

Q.172. What is indican?

K-salt of indoxyl sulphuric acid is called as indican and excreted in urine.

Q.173. What is the clinical significance of increased excretion of ethereal SO_4 and indican?

Excretion of Indican in urine is taken as a rough index of intestinal putrefaction. In acute intestinal obstruction, carcinoma of liver, cholera, typhus, excretion of ethereal SO_4 and Indican increases. In cholera and typhus sufficient indican is excreted to cause urine to assume a bluish tinge on standing.