

Simple, Hydroxy and Sulfur Containing Amino Acids (Glycine, Serine, Methionine, Cysteine)

? GLYCINE

Structure

- Simplest amino acid
- $\text{H}-\text{CH}_2-\text{COOH}$
- No chiral carbon
- Both glucogenic & non-essential

Synthesis

- From **serine**
 - Serine → glycine (via **serine hydroxymethyltransferase**, requires PLP & THF)
- From **threonine** (minor pathway)

Functions

- Component of **collagen** (1 in every 3 residues = glycine)

- Required for **heme synthesis** (glycine + succinyl-CoA → δ -ALA)
- Required for **glutathione synthesis**
- Precursor of **purines**
- Component of **bile salts (glycocholate)**
- Neurotransmitter (inhibitory) in spinal cord

Clinical Notes

- Defects in glycine cleavage → **non-ketotic hyperglycinemia**
 - Severe neonatal seizures
 - ↑ CSF glycine
 - “Glycine encephalopathy”

↑ CREATINE

What is it?

A nitrogenous compound present mainly in **muscle & brain**; stores high-energy phosphate.

Synthesis (two-organ pathway)

Occurs in **kidney + liver**:

1. **Arginine + glycine → guanidinoacetate**
(Kidney)
2. Guanidinoacetate → **creatine**
(Liver; requires **SAM**)

Creatine travels to **muscle**, where it is phosphorylated:

Creatine + ATP → Phosphocreatine

Enzyme: **Creatine kinase (CK)**

Functions

- Rapid energy buffer in muscle
- Helps regenerate ATP during contraction
- Used clinically to assess **muscle injury** (CK leaks into blood)

? CREATININE

What is creatinine?

A cyclic **spontaneous breakdown product** of creatine and phosphocreatine.

Key Facts

- Produced at a **constant rate**
- **Proportional to muscle mass**
- **Freely filtered** by kidney

- Not reabsorbed ? excellent marker of **GFR**

Clinical Uses

- Best routine blood test for GFR
- High creatinine = kidney dysfunction
- Creatinine clearance = estimate of GFR

? PRIMARY HYPEROXALURIA

Definition

A group of genetic disorders where excess **oxalate** is produced ? kidney stones, renal failure.

Types

1. Type I

- Defect: **Alanine–glyoxylate aminotransferase (AGT)**
- Glyoxylate ? oxalate
- Most severe

2. Type II

- Glyoxylate reductase deficiency

3. Type III

- HOGA1 deficiency

Features

- Early-onset **calcium oxalate stones**
- Nephrocalcinosis
- Progressive renal failure
- High urinary oxalate

Biochemical Basis

Normally:

- Glycine ? glyoxylate
- Glyoxylate is detoxified to **glycine**

In disease:

- Glyoxylate ? **oxalate**
- Oxalate forms **stones** (insoluble)

? SERINE

Structure

- Hydroxy amino acid
- Polar, uncharged
- Precursor of glycine

Synthesis

- From **3-phosphoglycerate (glycolysis intermediate)**

Functions

- Donor of **one-carbon units** (via conversion to glycine)
- Essential for **phosphatidylserine** synthesis
- Component of **sphingolipids**
- Required for folate-dependent pathways
- Serine → pyruvate (gluconeogenic)

Clinical Point

Cancer cells up-regulate serine synthesis for rapid nucleotide production.

? SERINE-CHOLINE-GLYCINE CYCLE

(This is sometimes called the **one-carbon exchange between serine, glycine & choline.**)

Purpose

To generate **one-carbon units** and maintain **methylation reactions**.

Steps

1. Serine ? Glycine

- Via **serine hydroxymethyltransferase**
- Produces **methylene-THF**

2. Choline ? Betaine

- Betaine donates a methyl group to homocysteine ? **methionine**
- Maintains SAM cycle

3. Glycine ? Serine

- Reversible conversion
- Supports **THF cycle**
- Generates one-carbon units

Importance

- Major supplier of **one-carbon units** for DNA synthesis

- Links amino acid & methylation metabolism
- Crucial during pregnancy, growth, cancer cell proliferation

? Selenocysteine (Sec / U-amino acid)

What is it?

- Known as the **21st amino acid**.
- Similar to cysteine but **sulfur is replaced by selenium**.
- Incorporated **during translation**, not post-translationally.

Special Features

- Coded by the **UGA codon**, which normally signals *stop*.
- Presence of a special **SECIS element** (Selenocysteine Insertion Sequence) in mRNA allows recoding of UGA ? selenocysteine.
- Requires a dedicated **tRNA-Sec**.

Functions

Present in several **antioxidant enzymes**:

- **Glutathione peroxidase**
- **Thioredoxin reductase**
- **Iodothyronine deiodinases** (thyroid hormone activation)

Clinical Point

- Selenium deficiency → glutathione peroxidase → oxidative stress.
- Seen in TPN without selenium supplementation.

? ALANINE

Properties

- Non-essential amino acid
- Formed mainly by transamination:
Pyruvate + glutamate → alanine + α-ketoglutarate

Major Functions

- **Carrier of nitrogen** from muscle → liver
- Important in fasting and exercise
- Component of the **glucose–alanine cycle**

- Amino group disposal (safely transported as alanine)

Clinical Note

- ALT (Alanine transaminase) is a sensitive marker of **liver cell injury**.

? GLUCOSE-ALANINE CYCLE

Purpose

- Transport nitrogen from **muscle ? liver**
- Provide **glucose back to muscle**
- Prevent toxic ammonia buildup in muscle

Steps

? In Muscle

1. Amino acids ? lose NH_2 ? **form glutamate**
2. Glutamate transfers NH_2 to pyruvate ? **alanine**
3. Alanine travels to liver

? In Liver

1. Alanine → pyruvate + NH₄⁺
2. NH₄⁺ → **urea cycle**
3. Pyruvate → **glucose** (via gluconeogenesis)
4. Glucose returns to muscle

Importance

- Active in **fasting, exercise, catabolic states**
- Clears nitrogen safely
- Provides energy substrate to muscle

? BETA-ALANINE

What is it?

- β-isomer of alanine
- **Not** used in protein synthesis
- Formed from **uracil degradation**

Functions

- Component of:
 - **Coenzyme A (CoA)**
 - **Carnosine** (muscle buffer)
 - **Pantothenic acid (Vitamin B5)**

Clinical Relevance

- Beta-alanine supplementation increases **carnosine**, improving muscle buffering.

? THREONINE

Properties

- **Essential amino acid**
- Both **glucogenic & ketogenic**

Catabolism

Threonine can be metabolized via three pathways:

1. To Glycine + Acetaldehyde

- Involves **threonine aldolase**

2. To Propionyl-CoA

- Leads to **succinyl-CoA**
- Vitamin B12 dependent
- Important glucogenic route

3. To ?-ketobutyrate ? propionyl-CoA

- Via **threonine dehydratase**

Functions

- Component of **mucins** (O-linked glycosylation)
- Required for **one-carbon metabolism** (via conversion to glycine)
- Supports gut immunity

Clinical Point

- Threonine deficiency ? poor mucin production ? impaired intestinal barrier function.

? Super-High-Yield Summary

- **Selenocysteine** ? encoded by UGA; in glutathione peroxidase.
- **Alanine** ? primary nitrogen carrier from muscle to liver.

- **Glucose–Alanine cycle** ? runs in fasting; prevents ammonia buildup in muscle.
- **Beta-alanine** ? part of CoA & carnosine.
- **Threonine** ? essential; forms glycine and propionyl-CoA.

? METHIONINE

Properties

- Essential amino acid
- **Sulfur-containing**
- Precursor of **S-adenosylmethionine (SAM)** — the universal methyl donor
- Both **glucogenic** and **ketogenic**

Functions

- Methyl group donor (via SAM)
- Precursor of **cysteine**
- Required for synthesis of:
 - Carnitine

- Creatine
- Adrenaline
- Phosphatidylcholine (lecithin)
- Polyamines
- DNA/RNA methylation

Metabolism Overview

1. **Methionine ? SAM**
(via methionine adenosyltransferase)
2. **SAM ? SAH (S-adenosylhomocysteine)**
(after donating methyl groups)
3. **SAH ? Homocysteine**
4. Homocysteine has 2 fates:
 - **Remethylation to methionine**
(Requires folate + B12)
 - **Transsulfuration to cysteine**
(Requires vitamin B6)

? TRANSMETHYLATION REACTIONS (via SAM)

SAM — Universal Methyl Donor

- SAM has **high-energy sulfonium bond**
- Donates **CH₃** group to various acceptors

Major Transmethylation Reactions

- Norepinephrine → Epinephrine
- Phosphatidylethanolamine → Phosphatidylcholine
- Guanidinoacetate → Creatine
- DNA methylation (epigenetics)
- RNA methylation
- Melatonin synthesis
- Carnitine synthesis

Regeneration of Methionine

- Homocysteine + methyl-THF → methionine
- Enzyme: **Methionine synthase**
- Cofactor: **Vitamin B₁₂**

Clinical Notes

- Folate or B12 deficiency ? ? homocysteine
- Hyperhomocysteinemia ? cardiovascular risk

? CYSTEINE

Properties

- Sulfur-containing amino acid
- **Non-essential**, but depends on methionine ? “semi-essential”
- Precursor of glutathione

Synthesis

- From **methionine ? homocysteine ? cystathionine ? cysteine**
- Requires **Vitamin B6 (PLP)**

Functions

- Component of **glutathione**
- Required for **coenzyme A** synthesis

- Part of disulfide bonds ? stabilizes **protein tertiary structure**
- Precursor of **taurine** (bile salts)
- Detoxification reactions

Clinical Points

- Defect in cystathionine γ -synthase ? **homocystinuria**
 - High homocysteine
 - Lens dislocation, thrombosis, developmental delay

? GLUTATHIONE (GSH)

Structure

A tripeptide:

- **Glutamate – Cysteine – Glycine**

Functions

- Major **intracellular antioxidant**
- Neutralizes H_2O_2 (via **glutathione peroxidase**)

- Regenerated by **glutathione reductase** (uses NADPH)
- Maintains **RBC membrane integrity**
- Required for:
 - Transport of amino acids (?-glutamyl cycle)
 - Detoxification (conjugation reactions)
 - Leukotriene synthesis
 - Protection against oxidative drugs (e.g., sulfonamides)

Clinical Notes

- Deficiency ? hemolysis
- Glutathione peroxidase contains **selenocysteine**
- NADPH (from HMP shunt) is necessary to maintain GSH in reduced form

? SULPHUR METABOLISM

Sources of Sulfur

- Sulfur-containing amino acids:
 - **Methionine**

- **Cysteine**

- Diet: onions, garlic, pulses

Fates of Sulfur

1. Formation of cysteine & taurine

- Taurine needed for **taurocholic acid (bile salt)**

2. Synthesis of Coenzyme A

- Requires cysteine for the **thiol (–SH)** group

3. Synthesis of glutathione

- Essential antioxidant

4. Sulfation reactions

- Detoxification in liver (phase II reactions)
- Inactivation of hormones (e.g., catecholamines)
- Sulfated steroids, bile acids

5. Excretion

- Sulfate is excreted as **inorganic sulfate** in urine

Clinical Points

- Defect in cystathionine synthase ? accumulation of homocysteine
- Vitamin B6 deficiency ? impaired cysteine synthesis
- High sulfur intake ? odor in urine (benign)

? Ultra-Short Revision (Perfect for Last 5 Minutes)

- Methionine ? SAM ? methyl transfer ? homocysteine ? cysteine.
- SAM is the **universal methyl donor**.
- Cysteine is **non-essential but methionine-dependent**.
- Glutathione = glutamate + cysteine + glycine.
- Glutathione peroxidase contains **selenocysteine**.
- Sulfur used in glutathione, CoA, taurine, detoxification.
- Homocystinuria = CBS deficiency, requires **B6**.

? CYSTINURIA

Definition

A hereditary disorder of **renal reabsorption of dibasic amino acids**.

Transport Defect

Defective transporter for:

- Cystine
- Ornithine
- Lysine
- Arginine

(remember: **COLA**)

Pathology

- Cystine is least soluble ? forms **hexagonal crystals**
- Leads to **recurrent kidney stones**

Clinical Features

- Flank pain
- Hematuria

- Recurrent **cystine stones**
- Stones begin in childhood or adolescence

Diagnosis

- Urine microscopy ? **hexagonal cystine crystals**
- Cyanide–nitroprusside test positive

Treatment

- High fluid intake
- Urinary alkalinization (potassium citrate)
- Penicillamine in severe cases ? forms soluble complexes

? HOMOCYSTINURIAS

Homocysteine is an intermediate between **methionine** and **cysteine**.
Defects in its metabolism ? **homocystinuria**.

? 1. Classical Homocystinuria (Type I)

Most common.

Enzyme Defect

Cystathionine β -synthase (CBS) deficiency.

Requirements

- **Vitamin B6 (PLP)** as cofactor
- Some patients respond to **high-dose B6**

Metabolic Consequences

- Methionine ?
- Homocysteine ??
- Cystathionine ?
- Cysteine ? (becomes essential)

Clinical Features

Very similar to Marfan syndrome but with **thrombosis**:

- Tall, long limbs
- Intellectual disability
- **Downward lens dislocation** (Marfan ? upward)

- Osteoporosis
- **Thromboembolism (most dangerous)**

Treatment

- High-dose B6
- Restrict methionine
- Supplement cysteine
- Betaine (donates methyl groups ? remethylates homocysteine)

? 2. Homocystinuria (Type II) — Methylcobalamin Defect

Defect

Impaired conversion of

Homocysteine ? Methionine

due to lack of **B12-dependent methionine synthase** activity.

Biochemical Pattern

- Homocysteine ?
- Methionine ?
- Methylmalonic acid **normal**

Clinical Features

- Megaloblastic anemia
- Developmental delay
- Homocysteine accumulation

? 3. Homocystinuria (Type III) — Methylenetetrahydrofolate Reductase (MTHFR) Deficiency

Defect

Reduced conversion of methyl-THF ? impaired homocysteine remethylation.

Biochemical Pattern

- Homocysteine ?
- Methionine ?
- Methylmalonic acid normal

Features

- Neurological problems
 - Megaloblastic changes
-

? High-Yield Summary of Homocystinurias

TYPE	ENZYME DEFECT	METHIONINE	HOMOCYSTEINE	KEY FEATURE
Type I	CBS	?	??	Lens dislocation, thrombosis
Type II	Methionine synthase	?	?	Megaloblastic anemia
Type III	MTHFR	?	?	Neuro symptoms

? CYSTATHIONINURIA

Definition

Rare defect in **cystathionine γ -lyase**, the enzyme that converts:
Cystathionine $\rightarrow$ Cysteine + α -ketobutyrate

Biochemical Findings

- **Cystathionine ??** in blood and urine
- Homocysteine normal or mildly ?
- Cysteine ? (may become conditionally essential)

Clinical Features

Most cases are **benign** and asymptomatic.
Occasionally mild developmental delay or growth issues.

Triggers

- Low vitamin B6
- Premature birth
- Liver disease

Management

- **Vitamin B6 supplementation**
- No strict diet needed (unlike homocystinuria)

? Ultra-Short Revision (Perfect for Last-Minute)

- **Cystinuria**: COLA transport defect ? cystine stones ? hexagonal crystals.
- **Homocystinuria Type I**: CBS deficiency ? methionine ? ? downward lens dislocation + thrombosis.
- **Type II & III**: Remethylation defects ? methionine ? + megaloblastic features.
- **Cystathioninuria**: Cystathionine γ -lyase deficiency ? benign, B6 responsive.

? IMPORTANT POINTS TO REMEMBER (Whole Chapter)

? Glycine

- Simplest amino acid; **no chiral carbon**.
- Major component of **collagen** (every third residue).
- Required for **heme synthesis** (glycine + succinyl-CoA → ?-ALA).
- Part of **glutathione** and **purine rings**.
- Inhibitory neurotransmitter in **spinal cord**.
- Defect in glycine cleavage → **non-ketotic hyperglycinemia** (seizures, ↑ CSF glycine).

? Creatine / Creatinine

- Creatine synthesized from **arginine + glycine**, methylated by **SAM**.
- Converted in muscle to **phosphocreatine** (energy reservoir).
- **Creatinine** is spontaneous breakdown product → marker of **GFR** (constant rate).

? Primary Hyperoxaluria

- Due to defect in **alanine–glyoxylate aminotransferase** (type I).
 - Excess oxalate ? **calcium oxalate stones**, nephrocalcinosis, renal failure.
 - Glyoxylate diverted ? oxalate (instead of ? glycine).
-

? Serine

- Synthesized from **3-phosphoglycerate**.
 - Major donor of **one-carbon units** (via conversion to glycine).
 - Precursor of **phosphatidylserine** and sphingolipids.
 - Serine hydroxymethyltransferase requires **PLP + THF**.
-

? Serine–Choline–Glycine Cycle

- Central route for generating **one-carbon units**.
 - Choline ? betaine ? donates methyl group to homocysteine ? methionine.
 - Important for **DNA synthesis** and **methylation balance**.
-

? Alanine

- Main amino acid released by muscle during fasting.
 - Major carrier of **nitrogen from muscle ? liver**.
 - Formed by transamination of pyruvate (ALT).
 - Part of the **glucose–alanine cycle**.
-

? Glucose–Alanine Cycle

- Muscle forms **alanine** to transport NH_4^+ safely.
 - Liver converts alanine ? pyruvate + NH_4^+ ? urea.
 - Pyruvate ? glucose ? back to muscle.
 - Active in **exercise and fasting**.
-

? Beta-Alanine

- Component of **Coenzyme A** and **pantothenic acid**.
 - NOT used in proteins.
 - Formed from **uracil degradation**.
-

? Threonine

- **Essential** amino acid.
 - Both glucogenic and ketogenic.
 - Converted to **glycine, acetaldehyde, propionyl-CoA**.
 - Important in **mucin** proteins (O-glycosylation).
-

? Methionine

- Essential sulfur amino acid.
 - Precursor of **SAM** (universal methyl donor).
 - Converted to **homocysteine**, which either:
 - **Remethylates** to methionine (B₁₂ + folate), or
 - Enters **transsulfuration** to cysteine (B₆).
-

? Transmethylation (via SAM)

SAM donates methyl group for:

- **Epinephrine** synthesis (from norepinephrine)
- **Creatine** synthesis

- **Phosphatidylcholine** formation
- **DNA & RNA methylation**
- **Melatonin** synthesis
- **Carnitine** synthesis

SAM ? SAH ? homocysteine ? methionine (requires B12).

? Homocysteine Metabolism

- Requires **B6, B12, folate**.
 - High homocysteine ? thrombosis, endothelial injury.
 - **Classical homocystinuria (CBS deficiency)**: methionine ?, lens dislocation (downward), thrombosis.
-

? Cysteine

- Formed from **homocysteine + serine** (requires B6).
- “**Semi-essential**” — dependent on methionine.
- Precursor of:
 - **Glutathione**
 - **Coenzyme A**

- **Taurine** (for bile salts)
 - **Disulfide bonds** (protein structure)
-

? Selenocysteine

- **21st amino acid.**
 - Encoded by **UGA** (normally a stop codon).
 - Requires **SECIS element** in mRNA.
 - Present in key **antioxidant enzymes**:
 - Glutathione peroxidase
 - Thioredoxin reductase
 - Iodothyronine deiodinase (T? ? T?)
-

? Glutathione (GSH)

- Tripeptide: **Glu–Cys–Gly**.
 - Most important intracellular antioxidant.
 - Detoxifies H₂O₂ (glutathione peroxidase + selenium).
 - Regenerated by **glutathione reductase** using **NADPH** (from HMP shunt).
-

- Protects RBCs from oxidative damage.
 - Essential in **drug detoxification**.
-

? Sulphur Metabolism

- Sulfur comes from **methionine & cysteine**.
 - Used in:
 - **Glutathione**
 - **CoA**
 - **Taurine** (bile salts)
 - **Detoxification (sulfation)**
 - Excreted as **inorganic sulfate**.
-

? Cystinuria

- Defect in renal reabsorption of **COLA** amino acids (Cystine, Ornithine, Lysine, Arginine).
 - Leads to **cystine stones** ? hexagonal crystals.
-

? Homocystinurias

- **Type I (CBS deficiency)** ? methionine ?, homocysteine ??
 - **Type II (B12 defect)** ? methionine ?
 - **Type III (MTHFR defect)** ? methionine ?
 - Classical presentation: thrombosis + downward lens dislocation.
-

? Cystathioninuria

- Defect of **cystathionine ?-lyase**.
 - Usually **benign**, B6 responsive.
-

? Ultra-Short Revision (Memory Capsule)

- Glycine: heme, collagen, glutathione, purines.
- Serine ? glycine ? one-carbon units.
- Alanine: nitrogen carrier; glucose–alanine cycle.
- Methionine ? SAM ? methyl transfer ? homocysteine ? cysteine.
- Cysteine: precursor of glutathione, CoA, taurine.
- Selenocysteine: antioxidant enzymes, coded by UGA.

- Glutathione: antioxidant; uses NADPH.
- Cystinuria: COLA defect, hexagonal stones.
- Homocystinuria: CBS deficiency ? thrombosis + lens dislocation.

? CLINICAL CASE–BASED PROBLEMS (Whole Chapter)

1. Neonate with severe seizures + high CSF glycine

A newborn within 24 hours of life develops **intractable seizures**, apnea, and hypotonia.

Investigations:

- **Very high CSF glycine**
- Serum glycine mildly elevated
- Normal ketones

Diagnosis:

Non-ketotic hyperglycinemia

Explanation:

Defect in **glycine cleavage enzyme** ? glycine accumulates in CSF ? severe encephalopathy.

2. Teenager with recurrent kidney stones + hexagonal crystals

A 15-year-old presents with flank pain.

Urinalysis shows **hexagonal, flat crystals**.

Family history positive for renal stones.

Diagnosis:

Cystinuria

Explanation:

Defect in renal tubular reabsorption of **COLA amino acids**.

Cystine is poorly soluble ? stone formation.

3. Adult with muscle injury after strenuous exercise

A young athlete collapses after marathon running.

Blood shows:

- CK extremely high
- Creatinine mildly elevated
- Myoglobinuria present

Diagnosis:

Rhabdomyolysis

Explanation:

Creatine/phosphocreatine breakdown ? increased creatinine; CK leaks from damaged muscle.

4. Child with early-onset calcium oxalate stones + nephrocalcinosis

A 3-year-old has recurrent kidney stones.

Urinary oxalate extremely high.

Renal biopsy shows oxalate deposition.

Diagnosis:

Primary hyperoxaluria (Type I)

Explanation:

Defect in **alanine–glyoxylate aminotransferase** ? glyoxylate ? oxalate.

5. Alcoholic patient with GGT elevation

A chronic alcoholic with normal AST/ALT but **very high GGT**.

Diagnosis:

GGT elevation due to **induction of ?-glutamyl cycle enzymes**

Explanation:

GGT participates in the **Meister cycle** for amino acid transport.

6. Marfanoid patient with thrombosis + lens dislocation (downward)

A 14-year-old tall, thin boy with long limbs, intellectual disability, and **downward lens dislocation**.

There is history of **recurrent DVT**.

Diagnosis:

Classical Homocystinuria (CBS deficiency)

Biochemical Signature:

- Methionine ?
- Homocysteine ??

- Cysteine ?
-

7. Patient with megaloblastic anemia + high homocysteine + normal methylmalonic acid

A 22-year-old vegetarian female has:

- Macrocytic anemia
- Very high plasma homocysteine
- Normal methylmalonic acid
- No neurologic symptoms

Diagnosis:

Folate deficiency or impaired remethylation (Type II Homocystinuria)

Explanation:

Remethylation requires folate + B12; MMA normal ? not B12 deficiency.

8. Infant with hepatomegaly + high methionine + developmental delay

A 6-month-old child has failure to thrive, hepatomegaly, and delayed milestones.

Plasma: Methionine ?, Homocysteine ??, Cystine ?.

Diagnosis:

Homocystinuria (CBS deficiency)

9. Child with cystathionine elevation but no major symptoms

A child evaluated for urinary amino acids shows markedly elevated **cystathionine**, but normal development and no vascular events.

Diagnosis:

Cystathioninuria (cystathionine γ -lyase deficiency)

Explanation:

Usually **benign**, B6 dependent.

10. Patient with recurrent oxidative hemolysis

A patient treated with sulfonamides develops jaundice and anemia.
Peripheral smear shows bite cells.

Diagnosis:

Glutathione deficiency–induced hemolysis

Explanation:

Drugs generate oxidative stress.
Glutathione protects RBCs.
G6PD deficiency can worsen it.

11. Patient with hypothyroidism symptoms but normal TSH

A patient on long-term parenteral nutrition develops fatigue, bradycardia, and mild goiter despite normal TSH.
Biochemistry shows low T3.

Diagnosis:

Selenium deficiency ? low selenocysteine-dependent deiodinase activity

Explanation:

Selenocysteine is essential for **5'-deiodinase** (T4 ? T3).

12. Muscle pain during exercise + rapid recovery

A bodybuilder reports fatigue during high-intensity exercise but improves after taking **beta-alanine supplements**.

Diagnosis:

Improved **carnosine** levels (a muscle buffer).

13. Neonate with severe acidosis + abnormal sulfur metabolism

A newborn with lethargy and seizures shows elevated **sulfite** in urine.

Diagnosis:

Sulfite oxidase deficiency

Explanation:

Inability to convert sulfite ? sulfate; sulfur amino acid catabolism disturbed.

14. Patient with mild tremors + low plasma cysteine

A patient with poor nutrition and alcoholism has low cysteine levels, fatigue, and oxidative stress.

Diagnosis:

Reduced transsulfuration due to B6 deficiency

Explanation:

Cystathionine γ -synthase and γ -lyase require B6.

15. Cancer patient with rapidly dividing tumor cells

Tumor biopsy shows extremely high demand for **serine and glycine**.

Diagnosis:

Tumor relies on **serine–glycine one-carbon metabolism** for nucleotide synthesis.

16. Young boy with delayed puberty + hyperhomocysteinemia

Homocysteine is very high, methionine is low, methylmalonic acid is **normal**.

Diagnosis:

Type III homocystinuria — MTHFR deficiency

17. Patient with severe oxidative stress after acetaminophen overdose

A patient with overdose shows liver enzyme elevation.

Glutathione levels are extremely low.

Diagnosis:

Glutathione depletion leading to hepatotoxicity

(Treatment = N-acetylcysteine)

18. Vegetarian adult with peripheral neuropathy + glossitis

Labs show:

- Homocysteine ?
- Methylmalonic acid ?
- Methionine ?

Diagnosis:

Vitamin B12 deficiency

Explanation:

Both remethylation and methylmalonyl-CoA pathway affected.

19. Patient with recurrent infections + poor detoxification

Tracing reveals low glutathione levels due to cysteine deficiency.

Diagnosis:

Cysteine-dependent glutathione deficiency

20. Patient with unusual sulfur smell urine

A man presents with urine smelling like rotten eggs.

Diagnosis:

High sulfur amino acid metabolism ? **benign sulfur excretion**
(seen after high garlic/onion diet)

? MCQs — Full Chapter

1. The simplest amino acid without a chiral carbon is:

- A. Alanine
- B. Serine
- C. **Glycine**
- D. Threonine

Answer: C

2. Glycine + Succinyl-CoA forms γ -ALA. This reaction requires:

- A. B6
- B. B12
- C. Folate
- D. **Pyridoxal phosphate**

Answer: D

3. Hexagonal, flat crystals in urine are characteristic of:

- A. Cystathioninuria
- B. Homocystinuria
- C. **Cystinuria**
- D. Tyrosinemia

Answer: C

4. Which amino acid is the major nitrogen carrier from muscle to liver?

- A. Serine
- B. **Alanine**

- C. Glycine
- D. Ornithine

Answer: B

5. The glucose–alanine cycle occurs between:

- A. Liver ? Kidney
- B. **Muscle ? Liver**
- C. Intestine ? Muscle
- D. Brain ? Blood

Answer: B

6. Primary hyperoxaluria Type I is due to deficiency of:

- A. Glycine transaminase
- B. **Alanine–glyoxylate aminotransferase**
- C. DOPA oxidase
- D. Glyoxylase

Answer: B

7. Creatinine is best described as:

- A. Enzyme product
- B. **Spontaneous breakdown product of creatine phosphate**
- C. Hormone
- D. RNA precursor

Answer: B

8. Phosphocreatine acts as:

- A. Enzyme inhibitor
- B. **Energy buffer**
- C. Neurotransmitter
- D. Lipid precursor

Answer: B

9. Serine ? Glycine requires:

- A. B1
- B. B2
- C. **PLP + THF**
- D. Biotin

Answer: C

10. Selenocysteine is inserted into protein using codon:

- A. AUG
- B. UAA
- C. **UGA**
- D. UAG

Answer: C

UGA normally stops, but becomes Sec in presence of **SECIS element**.

11. The universal methyl donor in the body is:

- A. THF
- B. **SAM**

- C. SAH
- D. Methyl-B12

Answer: B

12. Homocysteine ? Methionine requires which vitamins?

- A. B6 only
- B. B2 + folate
- C. **B12 + folate**
- D. Vitamin C

Answer: C

13. Classical homocystinuria (Type I) shows all EXCEPT:

- A. Thrombosis
- B. Downward lens dislocation
- C. High homocysteine
- D. **High cysteine**

Answer: D

(Cysteine ? because transsulfuration is blocked)

14. Patient with high homocysteine, low methionine, normal methylmalonic acid — diagnosis?

- A. CBS deficiency
- B. B12 deficiency
- C. **MTHFR deficiency**
- D. Vitamin C deficiency

Answer: C

15. A child has elevated cystathionine but is asymptomatic. Diagnosis?

- A. Homocystinuria
- B. **Cystathioninuria**
- C. MSUD
- D. Tyrosinemia

Answer: B

16. Which amino acid is sulfur-containing but non-essential?

- A. Methionine
- B. **Cysteine**
- C. Threonine
- D. Alanine

Answer: B

17. Which amino acid becomes essential if methionine is deficient?

- A. Glycine
- B. Glutamate
- C. **Cysteine**
- D. Serine

Answer: C

18. Glutathione is composed of:

- A. Glu–Ala–Gly
- B. Gly–Met–Ser

C. **Glu–Cys–Gly**

D. Ala–Cys–Gly

Answer: C

19. Glutathione peroxidase contains which special amino acid?

A. Tyrosine

B. **Selenocysteine**

C. Hydroxyproline

D. Homocysteine

Answer: B

20. The major urinary end product of sulfur metabolism is:

A. Homocysteine

B. Cystathionine

C. Thiosulfate

D. **Inorganic sulfate**

Answer: D

21. Homocystinuria Type I results from deficiency of:

A. Methionine synthase

B. MTHFR

C. **Cystathionine γ -synthase**

D. Cystathionine γ -lyase

Answer: C

22. Methionine ? SAM uses which enzyme?

- A. SAM lyase
- B. **Methionine adenosyltransferase**
- C. Methionine reductase
- D. SAM synthase

Answer: B

23. Which amino acid forms bile salt taurine?

- A. Alanine
- B. Glycine
- C. Serine
- D. **Cysteine**

Answer: D

24. Choline metabolism contributes mainly to:

- A. Urea cycle
- B. **One-carbon pool (via betaine)**
- C. Ketogenesis
- D. Pyruvate metabolism

Answer: B

25. The most important intracellular antioxidant is:

- A. Catalase
- B. Peroxidase
- C. **Glutathione**

D. Uric acid

Answer: C

26. A sulfur-rich amino acid important for disulfide bond formation is:

- A. Glycine
- B. **Cysteine**
- C. Serine
- D. Alanine

Answer: B

27. Defect in cystine, ornithine, lysine, arginine reabsorption occurs in:

- A. Homocystinuria
- B. **Cystinuria**
- C. MSUD
- D. Phenylketonuria

Answer: B

28. Beta-alanine is a component of:

- A. NAD
- B. FAD
- C. **Coenzyme A**
- D. ATP

Answer: C

29. Selenocysteine incorporation requires:

- A. Riboswitch
- B. **SECIS element**
- C. Telomerase
- D. Thiamine

Answer: B

30. Serum creatinine is used clinically to estimate:

- A. Liver function
- B. **Glomerular filtration rate (GFR)**
- C. Thyroid function
- D. Lipid oxidation

Answer: B

? VIVA VOCE – Simple, Hydroxy & Sulfur-Containing Amino Acids

1. What is the simplest amino acid?

Glycine.

2. Does glycine have a chiral carbon?

No, it is the only amino acid without one.

3. What is the role of glycine in heme synthesis?

Glycine + succinyl-CoA → **δ-ALA**, first step of heme synthesis.

4. Which amino acid is found at every third position in collagen?

Glycine.

5. Name the disease caused by defect in glycine cleavage enzyme.

Non-ketotic hyperglycinemia.

6. What is creatine synthesized from?

Arginine + glycine, later methylated by **SAM**.

7. What is creatinine?

Spontaneous breakdown product of **creatine phosphate**, marker of **GFR**.

8. What is primary hyperoxaluria?

Genetic defect in **alanine-glyoxylate aminotransferase**, causing excess oxalate.

9. Which type of crystal is seen in cystinuria?

Hexagonal crystals.

10. Which amino acids are defective in reabsorption in cystinuria?

Cystine, Ornithine, Lysine, Arginine (COLA).

11. What is the main nitrogen carrier from muscle to liver?

Alanine.

12. Which cycle detoxifies muscle ammonia during fasting?

Glucose–alanine cycle.

13. From which glycolysis intermediate is serine synthesized?

3-phosphoglycerate.

14. Serine ? Glycine requires which cofactors?

PLP (B6) and THF.

15. What is the metabolic role of the Serine–Choline–Glycine cycle?

Generation of **one-carbon units** for nucleotide synthesis.

16. Is threonine essential?

Yes, **threonine** is an essential amino acid.

17. Which amino acid is precursor of taurine?

Cysteine.

18. Why is cysteine called “semi-essential”?

Because it depends on **methionine** for synthesis.

19. What is the universal methyl donor?

SAM (S-adenosylmethionine).

20. Which enzyme converts homocysteine ? cystathionine?

Cystathionine ?-synthase (CBS), B6-dependent.

21. What is the biochemical hallmark of classical homocystinuria?

Homocysteine ?? and **methionine ?**.

22. Which direction does lens dislocate in homocystinuria?

Downward.

23. Which homocystinuria presents with low methionine?

Type II and Type III (remethylation defects — methionine synthase or MTHFR).

24. What is cystathioninuria?

Deficiency of **cystathionine γ -lyase**, usually benign.

25. Name the amino acid inserted at UGA codon.

Selenocysteine.

26. What special mRNA sequence is needed for selenocysteine insertion?

SECIS element.

27. Which important enzyme contains selenocysteine?

Glutathione peroxidase.

28. What is the structure of glutathione?

Tripeptide: **Glu–Cys–Gly.**

29. Which enzyme regenerates glutathione?

Glutathione reductase, using NADPH.

30. What is the major intracellular antioxidant?

Glutathione (GSH).

31. Sulfur from amino acids is excreted in which form?

Inorganic sulfate.

32. Which vitamin is required for transsulfuration?

Vitamin B6.

33. Methionine ? SAM requires which enzyme?

Methionine adenosyltransferase.

34. Which amino acid becomes essential in methionine deficiency?

Cysteine.

35. Name a transmethylation reaction involving SAM.

Norepinephrine ? **Epinephrine.**

36. Why does deficiency of B12 cause high homocysteine?

Because **methionine synthase** cannot remethylate homocysteine.

37. What causes the marfanoid habitus in homocystinuria?

Defective connective tissue ? **weak collagen cross-linking**.

38. Which lab test detects cystine in urine?

Cyanide–nitroprusside test.

39. Beta-alanine is a component of which coenzyme?

Coenzyme A.

40. Threonine is important for synthesis of which mucosal protein?

Mucins (O-linked glycoproteins).