MEDICAL EDUCATION RESOURCE

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

? GLYCINE

Structure

- Simplest amino acid
- **H–CH?–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 ? ?-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 + ?-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? ? **form glutamate**
2. Glutamate transfers NH? to pyruvate ? **alanine**
3. Alanine travels to liver

? In Liver

1. Alanine ? pyruvate + NH?
2. NH? ? **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?

- ?-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 **CH?** 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 B??**

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 ?-synthase ? **homocystinuria**
  - High homocysteine
  - Lens dislocation, thrombosis, developmental delay

? GLUTATHIONE (GSH)

Structure

A tripeptide:

- **Glutamate – Cysteine – Glycine**

Functions

- Major **intracellular antioxidant**
- Neutralizes H?O? (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 ?-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 ?-lyase**, the enzyme that converts:
Cystathionine ? Cysteine + ?-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 ?-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? safely.
- Liver converts alanine ? pyruvate + NH? ? 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 (B?? + folate), or
  - Enters **transsulfuration** to cysteine (B?).

? 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 H?O? (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.

Notes downloaded from **Medmentoredu**

- 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.

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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.

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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.

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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.

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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 ?

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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.

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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)

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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 ?-lyase deficiency)

Explanation:

Usually **benign**, B6 dependent.

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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.

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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).

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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).

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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.

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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 ?-synthase and ?-lyase require B6.

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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.

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16. Young boy with delayed puberty + hyperhomocysteinemia

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

Diagnosis:

Type III homocystinuria — MTHFR deficiency

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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)

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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.

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19. Patient with recurrent infections + poor detoxification

Tracing reveals low glutathione levels due to cysteine deficiency.

Diagnosis:

Cysteine-dependent glutathione deficiency

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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

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

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

Answer: D

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

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

Answer: C

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

A. Serine
B. **Alanine**

C. Glycine
D. Ornithine

Answer: B

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5. The glucose–alanine cycle occurs between:

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

Answer: B

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

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

Answer: B

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7. Creatinine is best described as:

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

Answer: B

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8. Phosphocreatine acts as:

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

Answer: B

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9. Serine ? Glycine requires:

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

Answer: C

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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**.

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11. The universal methyl donor in the body is:

A. THF
B. **SAM**

C. SAH
D. Methyl-B12

Answer: B

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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 ?-synthase**
D. Cystathionine ?-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 ? **?-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 ?-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.

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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).