MEDICAL EDUCATION RESOURCE

Hemoglobin (Structure, Oxygen and Carbon Dioxide, Transport, Abnormal Hemoglobins)

? HEMOGLOBIN

(Structure, Oxygen & CO? Transport, Oxygen Dissociation Curve)

This is written in clean MedMentor MBBS/PG style — crisp, conceptual, and ready for use in your platform.

? STRUCTURE OF HEMOGLOBIN

? Basic Composition

- Hemoglobin (Hb) is a **tetrameric protein**.
- Consists of **4 globin chains** + **4 heme groups**.
- Each heme contains **protoporphyrin IX + Fe²?**.
- One molecule of Hb binds **4 O? molecules**.

? Adult Hemoglobins

- **HbA (????)** — main adult Hb (~97%).
- **HbA? (????)** — ~2%.
- **HbF (????)** — <1% in adults; predominant in fetus.

? Globin Chains

- Globin is a **protein** with helical regions.
- Each chain surrounds one **heme pocket**.
- Fe²? is held by:
    - Proximal histidine (F8)
    - Distal histidine (E7) helps binding O?.

? Quaternary Structure

- Hb has **two ?? dimers**.
- Exists in two states:
    - **T-state (Tense):** low O? affinity
    - **R-state (Relaxed):** high O? affinity
- Binding of O? shifts Hb ? **T ? R transition** (cooperative binding).

? TRANSPORT OF OXYGEN

? How much O? is carried?

- Each Hb carries **4 O? molecules** (one per heme iron).
- Hb carries **98% of total oxygen**; plasma carries 2%.

? Mechanism of O? Binding

- O? binds reversibly to **$Fe^{2?}$** without oxidation.
- $Fe^{2?}$ remains in reduced state (oxyhemoglobin is NOT $Fe^{3?}$).

? Factors Affecting O? Binding (Bohr Effect)

? pH (acidic)
? CO?
? Temperature
? 2,3-BPG
? **Shift O? curve to the right** (? affinity, ? release).

? TRANSPORT OF CARBON DIOXIDE

CO? is transported in three forms:

? 1. As Bicarbonate (HCO??) — 70%

- CO? + H?O ? H?CO? ? H? + HCO??
- Enzyme: **Carbonic anhydrase** (RBC cytosol).

? 2. As Carbaminohemoglobin — 20%

- CO? binds to **terminal amino groups** of globin chains (not heme).
- Deoxygenated Hb carries more CO? (**Haldane effect**).

? 3. Dissolved CO? — 10%

- Directly dissolved in plasma.

? OXYGEN DISSOCIATION CURVE (ODC)

The ODC is **sigmoid** due to **cooperative binding** of oxygen.

? Right Shift (? O? affinity — easier release)

Memory: **CADET ? right shift**
CO? ?
Acid ? (? pH)
DPG ? (2,3-BPG)
Exercise ?
Temperature ?

Seen in:

- Exercise
- Anemia
- High altitude
- Fever
- Acidosis (DKA, sepsis)

? Left Shift (? O? affinity — harder release)

- ? 2,3-BPG
- ? Temperature
- ? CO?

- ? pH (alkalosis)
- **HbF (fetal hemoglobin)**
- CO poisoning
- Methemoglobinemia

Left shift means **less O? delivered to tissues**.

? P50 Value (Very Important)

- **P50 = PO? at which Hb is 50% saturated**.
- Normal P50 ? **26 mmHg**.

Interpretation:

- **Right shift:** ? P50
- **Left shift:** ? P50

? Fetal Hemoglobin (HbF)

- Structure: **????**
- Higher O? affinity due to **low 2,3-BPG binding**.
- Facilitates transfer of O? from mother to fetus.
- Curve is shifted **left**.

? Myoglobin vs Hemoglobin

- Myoglobin = **monomer**, hyperbolic curve, no cooperativity.
- Has **higher O? affinity** than Hb.
- Acts as O? reservoir in muscle.

? HEMOGLOBIN INTERACTION (ALLOSTERIC BEHAVIOR)

Hemoglobin is an **allosteric protein**, meaning its activity changes when molecules bind at sites other than the oxygen-binding site.

? 1. Cooperative Binding (O?–O? Interaction)

- Binding of the **first O? increases the affinity** for the next O?.
- Called **positive cooperativity**.
- Responsible for the **sigmoid shape** of the O? dissociation curve.

? 2. T-state ? R-state Transition

- Deoxygenated Hb = **T-state (tense)** ? low O? affinity.
- Oxygenated Hb = **R-state (relaxed)** ? high O? affinity.
- O? binding causes **conformational change** that breaks salt bridges ? R-form.

? 3. Interaction with Hydrogen Ions (H?)

- ? H? (acidosis) stabilizes T-form ? Hb releases more O?.

- This is the **Bohr effect**.

? 4. Interaction with CO?

- CO? binds to **terminal amino groups** ? carbaminohemoglobin.
- Stabilizes T-form ? promotes O? release (Haldane effect).

? 5. Interaction with 2,3-BPG

- 2,3-BPG binds between ?-chains ? stabilizes T-form ? ? O? affinity.
- Helps unloading of O? in tissues.

? EFFECT OF 2,3-BPG (KEY REGULATOR OF OXYGEN AFFINITY)

2,3-BPG is produced in RBCs via the **Rapoport–Luebering shunt**.

? Role

- Binds to the **central cavity** of deoxygenated Hb.
- Binds only to **?-chains** ? therefore:
  - HbA (????) ? strongly affected
  - HbF (????) ? weakly affected ? **higher O? affinity**

? Effects on Hemoglobin

- **Decreases hemoglobin's affinity for oxygen**.

- Shifts the **O? dissociation curve to the right**.
- Increases **P50** (more O? needed for 50% saturation).
- Improves O? delivery to tissues.

? Conditions with ? 2,3-BPG

- High altitude
- Anemia
- Hypoxia
- Chronic lung disease
- Exercise
- Hyperthyroidism

? Conditions with ? 2,3-BPG

- Stored blood (banked blood)
- Hypothermia
- HbF presence (poor binding of 2,3-BPG)
- Alkalosis

? ISOHYDRIC TRANSPORT OF CARBON DIOXIDE

Isohydric transport refers to **CO? being carried in blood without altering the pH dramatically**, thanks to buffering by hemoglobin.

? Mechanism

1. CO? enters RBC.
2. Combined with water ? H?CO? ? H? + HCO??
    - Catalyzed by **carbonic anhydrase**.
3. **H? is buffered by deoxygenated hemoglobin**.
    - Hb acts as a **buffer** ? prevents drastic change in pH.
4. HCO?? leaves RBC and is carried in plasma.

? Importance

- Allows **70% of CO?** to be transported as bicarbonate without making the blood acidic.
- Hemoglobin binding of H? is key.

? Relationship With O?

- Deoxygenated Hb (in tissues) binds H? better ? favors CO? transport.
- This is part of the **Haldane effect**.

? CHLORIDE SHIFT (HAMBURGER PHENOMENON)

This is the **exchange of bicarbonate and chloride ions** between RBCs and plasma to maintain electrical neutrality.

? At Tissues (High CO?) – “Forward Chloride Shift”

1. CO? diffuses into RBC.
2. Converts to HCO?? + H? (carbonic anhydrase).
3. HCO?? leaves RBC into plasma.
4. **Cl? enters RBC** to maintain charge balance.

? RBC becomes **chloride-rich** in tissues.

? At Lungs (Low CO?) – “Reverse Chloride Shift”

1. CO? is expelled from blood.
2. HCO?? enters RBC from plasma.
3. **Cl? moves out** of RBC to maintain neutrality.
4. HCO?? + H? ? H?CO? ? CO? (exhaled).

? RBC loses chloride in lungs.

? Significance of Chloride Shift

- Maintains **electrical neutrality**.

- Enables **maximum transport of CO? as bicarbonate**.
- Essential for acid-base homeostasis.
- Occurs in **all RBCs during CO? transport**.

? FETAL HEMOGLOBIN (HbF)

? Structure

- HbF = **????**
- ?-chains replace ?-chains of adult Hb.
- Predominant Hb in fetus and newborn.

? Key Properties

- **Higher affinity for oxygen** than HbA.
- Curve shifted **left**.
- Because 2,3-BPG binds poorly to ?-chains.
- Facilitates O? uptake from maternal blood.

? Physiological Importance

- Allows fetal RBCs to extract oxygen across the placenta.
- Protects fetus from low oxygen tension in utero.

? When does HbF disappear?

- HbF declines rapidly after birth.
- Major switch from **? ? ? chains** completed by 6 months.
- Adult pattern (HbA) predominates thereafter.

? Conditions with Increased HbF

- ?-thalassemia major
- Hereditary persistence of fetal Hb (HPFH)
- Sickle cell disease (after hydroxyurea therapy)

? HEMOGLOBIN DERIVATIVES

(Abnormal chemical forms of hemoglobin)

? 1. Oxyhemoglobin

- Hb + O?
- Normal physiologic oxygenated form.

? 2. Deoxyhemoglobin

- Hb without oxygen.
- Found in venous blood.

? 3. Methemoglobin (MetHb)

- Hb where iron is **Fe³?** (ferric).
- Cannot bind oxygen.

? 4. Carboxyhemoglobin (CO-Hb)

- Hb bound to **carbon monoxide (CO)**.

? 5. Carbaminohemoglobin

- CO? bound to terminal NH? groups of globin chains.

? 6. Sulfhemoglobin

- Hb with sulfur atom incorporated.
- Irreversible.
- Seen with sulfur-containing drugs.

? 7. Cyanmethemoglobin

- MetHb + cyanide ion.
- Used in laboratory estimation of Hb.

? CARBOXYHEMOGLOBIN (CO-Hb)

(A highly important exam topic)

? Definition

Hemoglobin bound to **carbon monoxide**.

? Affinity

- Hb has **200–250 times higher affinity** for CO than for O?.
- CO shifts the O? dissociation curve **left** ? reduced O? unloading.

? Features

- Causes **tissue hypoxia** without anemia.
- CO poisoning symptoms:
    - Headache
    - Cherry-red skin
    - Confusion
    - Seizures
    - Coma
- Pulse oximetry is **normal** (false reading).
- CO-Hb gives blood a **bright red** color.

? Sources

- Car exhaust
- Fire/smoke inhalation
- Tobacco smoke

- Generators used in closed rooms

? Treatment

- 100% oxygen
- Hyperbaric oxygen (severe cases)
- Remove exposure

? METHEMOGLOBIN (Met-Hb)

? Definition

Hemoglobin with **iron oxidized to Fe^{3}?** instead of Fe^{2}?.
Fe^{3}? **cannot bind O?** ? functional anemia.

? Causes

- Drugs/chemicals:
  - Nitrites
  - Dapsone
  - Nitrates
  - Aniline dyes
  - Local anesthetics (benzocaine)
- Congenital:

- Cytochrome b? reductase deficiency

? Clinical Features

- Cyanosis with **normal PaO?**.
- Chocolate-brown colored blood.
- Low pulse oximetry readings (85% “methemoglobin saturation plateau”).
- Shortness of breath, headache, fatigue.

? Diagnosis

- Co-oximetry (gold standard).
- Methemoglobin level measurement.

? Treatment

- **Methylene blue** (reduces Fe^{3}? ? Fe^{2}?).
- Vitamin C (adjunct).
- Avoid causative drugs.

? KEY DIFFERENTIATION (Very High Yield)

CONDITION	IRON STATE	O? BINDING	BLOOD COLOR	O? CURVE
Oxy-Hb	Fe^{2}?	Yes	Bright red	Normal

CONDITION	IRON STATE	O? BINDING	BLOOD COLOR	O? CURVE
Deoxy-Hb	$Fe^{2?}$	No O? bound	Dark red	Normal
Met-Hb	**$Fe^{3?}$**	**Cannot bind O?**	Chocolate brown	Left shift
CO-Hb	$Fe^{2?}$ + CO	O? blocked	Bright red	Left shift

? HEMOGLOBIN VARIANTS

Hemoglobin variants are **structural abnormalities** of globin chains due to **single amino acid substitutions** or deletions.

? Examples of important variants:

- **HbS** (sickle cell hemoglobin) – ?6 Glu ? Val
- **HbC** – ?6 Glu ? Lys
- **HbE** – ?26 Glu ? Lys (common in NE India)
- **HbD-Punjab** – another ?-chain variant
- **Hb M** – oxidation of $Fe^{2?}$? $Fe^{3?}$ (methemoglobinemia)
- **HbF persistence** – Hereditary persistence of fetal Hb (HPFH)

? Why variants cause disease:

- Affect **solubility**, **stability**, or **oxygen affinity** of Hb.

- Some variants cause **hemolysis**, **polymerization**, or **decreased oxygen delivery**.

? SICKLE CELL HEMOGLOBIN (HbS)

(Most important hemoglobinopathy)

? Genetic Defect

- Point mutation in ?-globin gene: **Valine replaces Glutamic acid at position 6** (Glu ? Val).
- Produces abnormal HbS.

? Mechanism of Sickling

- In low O? ? HbS polymerizes ? forms **rigid, sickle-shaped RBCs**.
- Sickled cells cause:
  - Hemolysis
  - Vaso-occlusion
  - Microinfarcts

? Clinical Features

- Painful crises
- Avascular necrosis
- Acute chest syndrome

- Anemia
- Dactylitis in children
- Autosplenectomy ? Howell–Jolly bodies

? Lab Findings

- Sickle cells on smear
- ? Reticulocytes
- ? Indirect bilirubin
- ? LDH
- Positive sickling test

? Treatment

- **Hydroxyurea** ? ? HbF (reduces sickling)
- Blood transfusion
- Pain control
- Bone marrow transplant (curative)

? THALASSEMIAS

Genetic disorders causing **reduced synthesis** of ?- or ?-globin chains.

? 1. ?-Thalassemia

? Cause

- Gene deletion of ?-globin genes (4 total).

? Severity

- 1 gene deleted ? Silent carrier
- 2 deleted ? ?-thalassemia trait
- 3 deleted ? HbH disease (?? tetramers)
- 4 deleted ? Hydrops fetalis (Hb Bart’s; ??) ? fatal

? 2. ?-Thalassemia

? Cause

- Mutations causing decreased ?-chain production.

? Types

- **??** (partial reduction)
- **??** (complete absence)

? ?-Thalassemia Minor

- Mild anemia

- Very high HbA? (>3.5%)

? ?-Thalassemia Major (Cooley’s anemia)

- Severe microcytic anemia
- Extramedullary hematopoiesis ? chipmunk facies
- Splenomegaly
- High HbF levels
- Iron overload from transfusions

? Treatment

- Regular transfusions
- Iron chelation (deferoxamine)
- Bone marrow transplant (curative)

? MYOGLOBIN

? Structure

- **Monomer** (single polypeptide).
- Contains **one heme group** ? binds **one O?**.

? Oxygen Binding

- **Very high O? affinity**.
- No cooperativity (hyperbolic curve).
- Acts as an **oxygen reservoir** in muscle.

? Clinical Importance

- **Myoglobinuria** seen in:
  - Rhabdomyolysis
  - Crush injuries
  - Severe muscle damage
- Causes **dark red/brown urine**.
- Can precipitate in kidneys ? acute renal failure.

? ANEMIAS

(From the hemoglobin perspective)

? Definition

Reduced **oxygen-carrying capacity** of blood.

? Classification Based on Hb Issues

? 1. Hemolytic Anemia

- Premature RBC destruction.
- Causes: HbS, HbC, G6PD deficiency, thalassemia, autoimmune.
- Features:
  - ? unconjugated bilirubin
  - ? LDH
  - ? haptoglobin
  - Reticulocytosis

? 2. Hypochromic Microcytic Anemia

- Reduced Hb synthesis ? small, pale RBCs.
- Causes:
  - Iron deficiency
  - Thalassemias
  - Sideroblastic anemia
  - Chronic disease

? 3. Normocytic Normochromic Anemia

- Acute blood loss
- Hemolysis
- Chronic kidney disease (? EPO)

? 4. Macrocytic Anemia

- Vitamin B12 or folate deficiency
- Alcoholism
- Liver disease
- Reticulocytosis

? KEY DIFFERENCES — HbS vs Thalassemia vs Myoglobin

FEATURE	HBS	THALASSEMIA	MYOGLOBIN
Defect	Structural mutation	Reduced synthesis	Structural monomer
O? Affinity	Low	Normal/high	Very high
Curve	Right-shift & polymerization	Affected by chain imbalance	Hyperbolic

FEATURE	HBS	THALASSEMIA	MYOGLOBIN
Clinical	Pain crises, hemolysis	Microcytosis, marrow expansion	Muscle oxygen store

? IMPORTANT POINTS TO REMEMBER (Whole Hemoglobin Chapter)

? Structure of Hemoglobin

- Hb is a **tetramer**: ???? in adults.
- Each chain contains a **heme group with Fe²?**.
- **Fe²?** binds O?; **Fe³?** cannot.
- Exists in two states:
  - **T-state** (tense, low O? affinity)
  - **R-state** (relaxed, high O? affinity)

? Oxygen Transport

- Hb carries **98% of oxygen** in blood.
- O? binding is **cooperative** ? sigmoid O? dissociation curve.

- Exchange of one O? changes affinity of other subunits.

? Oxygen Dissociation Curve (ODC)

- Sigmoid shape due to **cooperative binding**.
- **Right shift (? affinity, ? O? release):**
  - ? CO?, ? H? (? pH), ? Temperature, ? 2,3-BPG, Exercise.
- **Left shift (? affinity):**
  - HbF, CO-Hb, Met-Hb, ? CO?, ? Temperature, ? 2,3-BPG.
- **P50 = 26 mmHg**; increased by right shift.

? Bohr Effect

- ? CO? or ? pH ? Hb releases O? (right shift).
- Helps oxygen delivery to tissues.

? Haldane Effect

- Deoxygenated Hb binds **more CO? and H?**.
- Oxygenated Hb releases CO?.
- Important for CO? unloading in lungs.

? 2,3-BPG (Key Modulator)

- Produced in RBCs via **Rapoport–Luebering shunt**.
- Binds to **?-chains** ? stabilizes T-state ? ? O? affinity.
- ? in high altitude, hypoxia, anemia, exercise.
- ? in stored blood, alkalosis, HbF presence (?-chains do not bind it).

? Isohydric Transport of CO?

- CO? + H?O ? H?CO? ? H? + HCO?? (carbonic anhydrase).
- **H? buffered by deoxygenated Hb** ? prevents acidosis.
- Allows 70% of CO? transport as bicarbonate.

? Chloride Shift

- At tissues: HCO?? leaves RBC ? **Cl? enters** (forward shift).
- At lungs: HCO?? enters RBC ? **Cl? exits** (reverse shift).
- Maintains electrical neutrality.

? Fetal Hemoglobin (HbF)

- Structure: **????**.

- Binds O? more strongly (left shift).
- Poor interaction with 2,3-BPG.
- High levels in fetus ? facilitates placental oxygen transfer.
- ? in HPFH, ?-thalassemia, hydroxyurea therapy.

? Hemoglobin Derivatives

- **Oxyhemoglobin:** normal oxygenated form.
- **Deoxyhemoglobin:** venous blood.
- **Carboxyhemoglobin:** Hb + CO (bright red).
- **Methemoglobin:** Fe^{3}? form, cannot bind O?.
- **Carbaminohemoglobin:** Hb + CO? (globin binding).
- **Sulfhemoglobin:** irreversible sulfur binding.

? Carboxyhemoglobin (CO-Hb)

- CO binds Hb **200–250 times** more strongly than O?.
- Causes tissue hypoxia despite normal PaO?.
- Pulse oximeter is falsely normal.
- Treat with **100% oxygen** or hyperbaric O?.

- Seen in smoke inhalation, exhaust exposure, smoking.

? Methemoglobin (Met-Hb)

- Iron is oxidized to **Fe³?** ? cannot bind O?.
- Blood becomes **chocolate brown**.
- Causes: nitrates, nitrites, dapsone, benzocaine.
- Treated with **methylene blue**.

? Hemoglobin Variants

- Structural changes in globin chains.
- Examples: HbS, HbC, HbE, HbD-Punjab, HbM.
- May affect solubility, stability, or O? affinity.

? Sickle Cell Hemoglobin (HbS)

- Mutation: **?6 Glu ? Val**.
- Polymerizes in low O? ? sickling.
- Causes hemolysis, vaso-occlusion, pain crises.
- HbF reduces sickling ? hydroxyurea benefits.

- Spleen becomes auto-infarcted ? Howell–Jolly bodies.

? Thalassemias

- ? Synthesis of ?- or ?-globin chains.

? ?-Thalassemia

- One gene deletion ? silent carrier.
- Four deletions ? Hb Bart’s ? hydrops fetalis (fatal).

? ?-Thalassemia

- ? ?-chain synthesis.
- Major: severe anemia, crew-cut skull, hepatosplenomegaly, ? HbF.
- Minor: mild anemia, ? HbA? (>3.5%).

? Myoglobin

- Monomeric, one heme group.
- **Very high O? affinity** (hyperbolic curve).
- O? storage protein in muscle.

- Elevated in rhabdomyolysis ? myoglobinuria ? renal damage.

? Anemias Related to Hemoglobin Issues

- **Hemolytic anemia:** HbS, G6PD deficiency, thalassemia.
- **Microcytic anemia:** iron deficiency, ?-thalassemia, chronic disease.
- **Normocytic anemia:** acute blood loss, CKD.
- **Macrocytic anemia:** B12/folate deficiency.

? Ultra-Short Rapid Revision

- HbA = ????; HbF = ???? (left shift).
- P50 = 26 mmHg.
- CO binds Hb 200–250× stronger than O?.
- Met-Hb = Fe^{3}?; treat with methylene blue.
- Right shift = CADET ? (CO?, Acid, DPG, Exercise, Temp).
- HbS = Glu ? Val (?6).
- ?-thalassemia major ? ? HbF, skeletal deformities.
- Chloride shift = HCO?? ? Cl? exchange.
- Myoglobin = monomer, hyperbolic curve, high affinity.

? MCQs — Hemoglobin (Whole Chapter)

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1. The quaternary structure of adult hemoglobin (HbA) is:

A. ????
B. ????
C. **????**
D. ??

Answer: C

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2. Iron in heme that binds oxygen must be in the:

A. Ferric state
B. **Ferrous state**
C. Elemental state
D. Ferritin-bound state

Answer: B

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3. The sigmoid shape of the oxygen dissociation curve is due to:

A. Bohr effect
B. Haldane effect
C. **Cooperative binding of oxygen**
D. Binding of CO?

Answer: C

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4. A right shift in the O? dissociation curve indicates:

A. Increased affinity for oxygen
B. Left shift of curve
C. Reduced tissue oxygenation
D. **Reduced affinity ? increased O? delivery to tissues**

Answer: D

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5. Which of the following causes a right shift of the O? curve?

A. Low temperature
B. High pH
C. Low 2,3-BPG
D. **High CO?**

Answer: D

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6. P50 is increased when:

A. Affinity for O? is increased
B. **Affinity for O? is decreased**
C. HbF is dominant
D. CO is bound

Answer: B

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7. 2,3-BPG binds to which part of hemoglobin?

A. Heme iron
B. ?-chains
C. **?-chains in the central cavity**
D. ?-chains

Answer: C

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8. 2,3-BPG has the weakest binding with:

A. HbA
B. HbA?
C. **HbF**
D. Methemoglobin

Answer: C

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9. Isohydric transport refers to:

A. CO bound to hemoglobin
B. Shifting of chloride across RBC membrane
C. CO? dissolved in plasma
D. **CO? transport as HCO?? while H? is buffered by hemoglobin**

Answer: D

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10. Chloride shift at the tissues results in:

A. Chloride leaving RBC
B. **Chloride entering RBC**
C. Potassium entering RBC
D. CO? entering plasma

Answer: B

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11. HbF has higher oxygen affinity because:

A. It has more ?-chains
B. It has more iron
C. **It binds poorly to 2,3-BPG**
D. It contains ferric iron

Answer: C

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12. Which form of hemoglobin cannot bind oxygen?

A. Oxyhemoglobin
B. Deoxyhemoglobin
C. Carboxyhemoglobin
D. **Methemoglobin (Fe^{3}?)**

Answer: D

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13. Carboxyhemoglobin forms due to:

A. Nitrite exposure

B. Iron deficiency

C. **Carbon monoxide exposure**

D. ATP depletion in RBCs

Answer: C

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14. Carboxyhemoglobin shifts O? curve to:

A. Right

B. **Left**

C. Flat

D. Hyperbolic

Answer: B

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15. The mutation in sickle cell disease is:

A. ?26 Glu ? Lys

B. **?6 Glu ? Val**

C. ?6 Glu ? Asp

D. ?1 deletion

Answer: B

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16. Sickling occurs most readily during:

A. High oxygen tension

B. Cold exposure only

C. **Low oxygen tension**

D. High HbF

Answer: C

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17. Thalassemias are disorders of:

A. Heme synthesis

B. Iron absorption

C. **Globin chain synthesis**

D. Chloride transport

Answer: C

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18. ?-thalassemia major typically shows:

A. High HbA?

B. Normal HbF

C. **Markedly increased HbF**

D. High 2,3-BPG deficiency

Answer: C

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19. ?-thalassemia with all four ?-genes deleted produces:

A. HbH disease

B. HbC disease

C. **Hydrops fetalis (Hb Bart's)**

D. Mild anemia

Answer: C

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20. Myoglobin differs from hemoglobin because:

A. It has 4 heme groups

B. It is a tetramer

C. **It has a hyperbolic O? curve**

D. It has lower affinity for oxygen

Answer: C

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21. Myoglobinuria is most commonly seen in:

A. Malaria

B. Iron deficiency

C. **Rhabdomyolysis**

D. Pneumonia

Answer: C

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22. A patient shows chocolate brown blood and normal PaO?. Diagnosis?

A. Carboxyhemoglobin

B. Anemia

C. **Methemoglobinemia**

D. HbE disease

Answer: C

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23. Treatment of methemoglobinemia is:

A. Hydroxyurea

B. Blood transfusion

C. Iron therapy

D. **Methylene blue**

Answer: D

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24. In CO poisoning, pulse oximetry:

A. Falls to zero

B. Shows high CO?

C. **May remain falsely normal**

D. Shows low pH

Answer: C

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25. Which hemoglobinopathy gives a "crew-cut skull" on X-ray?

A. HbS

B. HbC

C. **?-Thalassemia major**

D. HbE trait

Answer: C

? CLINICAL CASE–BASED QUESTIONS (Whole Hemoglobin Chapter)

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1. A 22-year-old man presents with severe chest pain, bone pain, and fatigue. Smear shows sickled RBCs. Hemoglobin electrophoresis shows increased HbS and elevated HbF.

Diagnosis: Sickle cell disease
Mechanism: ?6 Glu ? Val mutation ? polymerization of HbS in low O?
Why high HbF helps: HbF inhibits sickling

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2. A 6-month-old infant has severe anemia, frontal bossing, hepatosplenomegaly, and "crew-cut" skull X-ray. Hb electrophoresis shows very high HbF.

Diagnosis: ?-Thalassemia major
Mechanism: Absent ?-chains ? excess ?-chains ? ineffective erythropoiesis

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3. A newborn presents with hydrops fetalis and dies hours after birth. Hemoglobin electrophoresis shows Hb Bart's (??).

Diagnosis: ?-Thalassemia — deletion of all four ?-genes
Mechanism: No ?-chains ? Hb Bart's has extremely high O? affinity ? no O? delivery

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4. A mountain climber at 14,000 ft experiences tachycardia and dyspnea. Labs show increased 2,3-BPG.

Diagnosis: Physiological adaptation to high altitude
Mechanism: 2,3-BPG ? ? right shift ? enhanced O? release

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5. A patient trapped in a house fire has headache, dizziness, and bright red skin. Pulse oximeter shows 100% saturation.

Diagnosis: CO poisoning (Carboxyhemoglobin)
Mechanism: CO binds Hb 250× stronger than O? ? tissue hypoxia
Treatment: 100% O? or hyperbaric O?

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6. A child eats nitrate-contaminated well water. Blood sample appears chocolate-brown. Pulse ox ~85% regardless of O?.

Diagnosis: Methemoglobinemia (Fe^{3}? state)
Mechanism: Oxidation of Fe^{2}? ? Fe^{3}?
Treatment: Methylene blue

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7. A neonate has persistent cyanosis since birth but normal PaO?. Family history positive.

Diagnosis: Congenital methemoglobinemia
Mechanism: Cytochrome b? reductase deficiency

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8. A patient with pneumonia shows right shift of O? dissociation curve. Which factor explains this?

Diagnosis: Tissue hypoxia due to infection
Mechanism: Fever + acidosis ? ? O? affinity ? better tissue delivery

---

9. A patient with COPD has elevated carbaminohemoglobin.

Diagnosis: Chronic CO? retention
Mechanism: CO? binding to amino terminals of globin chains
Relevance: Haldane effect ? deoxygenated Hb binds more CO?

---

10. A man collapses after using benzocaine throat spray. Cyanosis does not improve with oxygen.

Diagnosis: Benzocaine-induced methemoglobinemia
Reason: Fe^{3}? cannot bind oxygen
Treatment: Methylene blue

---

11. A child has pallor, fatigue, and microcytic hypochromic RBCs. Iron therapy shows no improvement. HbA? is elevated.

Diagnosis: ?-Thalassemia minor
Mechanism: Reduced ?-chain synthesis ? compensatory ? HbA?

---

12. An adult presents with dark urine after a crush injury. Serum CK is high.

Diagnosis: Myoglobinuria due to rhabdomyolysis
Mechanism: Myoglobin released from muscle ? renal toxicity

---

13. A 25-year-old athlete has high myoglobin in muscle but normal hemoglobin.

Diagnosis: Physiological adaptation
Mechanism: Myoglobin acts as muscle O? reservoir

---

14. A smoker has chronically elevated carboxyhemoglobin.

Diagnosis: CO exposure from cigarettes
Result: Tissue hypoxia despite normal Hb
Long-term risk: Polycythemia (compensatory)

---

15. A patient with severe anemia has normal MCV and normal RDW. Hemoglobin is low but RBC count normal.

Diagnosis: Dilutional/acute blood loss anemia
Mechanism: RBCs normal size; loss due to hemorrhage

---

16. A baby born to a diabetic mother shows oxygen saturation drop despite normal PaO ?. Hb electrophoresis shows high HbF.

Diagnosis: High fetal hemoglobin level
Mechanism: HbF has high O? affinity ? less O? released to tissues

---

17. A patient has dyspnea and confusion after taking dapsone. Blood is chocolate-brown.

Diagnosis: Methemoglobinemia
Mechanism: Oxidation of Fe^{2}? ? Fe^{3}?
Best test: Co-oximetry

---

18. A young man with G6PD deficiency develops severe jaundice after malaria treatment.

Diagnosis: Hemolytic anemia
Mechanism: Hb breakdown ? ? unconjugated bilirubin

---

19. A child from NE India presents with mild anemia and target cells on smear. Hb electrophoresis shows HbE.

Diagnosis: HbE disease
Mechanism: ?26 Glu ? Lys mutation
Prevalent in: Assam, Bengal, Thailand

---

20. A patient has cyanosis, but PaO? is normal and pulse oximetry shows 85–88% plateau.

Diagnosis: Methemoglobinemia
Clue: Saturation plateau at 85% is diagnostic

? VIVA VOCE — Hemoglobin (Whole Chapter)

1. What is the basic structure of hemoglobin?

A tetramer of **two ? and two ? chains**, each containing a heme group with Fe²?.

---

2. Why must iron be in the Fe²? state?

Only **Fe²?** can bind oxygen; Fe³? cannot.

---

3. What bonds hold O? in hemoglobin?

Reversible coordination bond between **O? and Fe²?** in heme.

---

4. What is the T-state of hemoglobin?

Tense state ? **low oxygen affinity**.

---

5. What is the R-state?

Relaxed state ? **high oxygen affinity**.

---

6. What causes the sigmoid shape of the O? dissociation curve?

Cooperative binding of oxygen.

---

7. What is P50?

PO? at which Hb is **50% saturated**; normal ~26 mmHg.

---

8. What does an increased P50 indicate?

Decreased oxygen affinity (right shift).

---

9. What shifts the O? curve to the right?

? CO?, ? H?, ? Temperature, ? 2,3-BPG.

---

10. What is the Bohr effect?

H? and CO? decrease Hb’s O? affinity ? O? release in tissues.

---

11. What is the Haldane effect?

Oxygenated blood carries less CO?; deoxygenated blood carries more.

---

12. What is the role of 2,3-BPG?

Binds ?-chains ? stabilizes T-state ? **reduces O? affinity**.

---

13. Why does HbF have higher O? affinity than HbA?

HbF (????) binds 2,3-BPG weakly ? O? affinity rises ? left shift.

---

14. What is the Rapoport–Luebering shunt?

Pathway in RBCs producing **2,3-BPG**.

---

15. What is carbaminohemoglobin?

CO? bound to terminal **amino groups** of globin chains.

---

16. What is isohydric transport?

Transport of CO? as **HCO??** while H? is buffered by Hb.

---

17. What is the chloride shift?

Exchange of **HCO?? and Cl?** across RBC membrane for neutrality.

---

18. What is HbF useful for clinically?

Protects against sickling ? increased by **hydroxyurea** in sickle cell disease.

---

19. Name hemoglobin derivatives.

Oxy-Hb, Deoxy-Hb, **Carboxy-Hb**, **Met-Hb**, Sulf-Hb, Carbamino-Hb.

---

20. What is carboxyhemoglobin?

Hb combined with **carbon monoxide**.

---

21. Why is CO dangerous?

CO binds Hb **200–250×** stronger than O? ? severe tissue hypoxia.

---

22. What is the treatment of CO poisoning?

100% oxygen or hyperbaric oxygen.

---

23. What is methemoglobin?

Hemoglobin with iron in **Fe³?** state ? cannot bind oxygen.

---

24. What causes methemoglobinemia?

Nitrates, nitrites, benzocaine, dapsone, aniline dyes.

---

25. What color is blood in methemoglobinemia?

Chocolate-brown.

---

26. Treatment of methemoglobinemia?

Methylene blue.

---

27. What is the mutation in sickle cell disease?

?6 Glutamic acid ? **Valine**.

---

28. Why do RBCs sickle in HbS disease?

HbS polymerizes in **low O?**, forming rigid fibers.

---

29. What protects infants with sickle cell disease early in life?

High levels of **HbF**.

---

30. What is Howell–Jolly body?

Nuclear remnants seen after **autosplenectomy** in sickle cell.

---

31. What is the defect in thalassemias?

Reduced **synthesis** of ?- or ?-globin chains.

---

32. What is elevated in ?-thalassemia minor?

HbA? (>3.5%).

---

33. What is HbH?

?? tetramers seen in **?-thalassemia (3 gene deletion)**.

---

34. What forms in complete ?-gene deletion (4 genes)?

Hb Bart's (??) ? causes **hydrops fetalis**.

---

35. Why is HbF increased in ?-thalassemia major?

Compensation due to absent ?-chains.

---

36. What differentiates myoglobin from hemoglobin?

Myoglobin is **monomeric**, binds one O?, and has hyperbolic curve.

---

37. What is myoglobinuria?

Myoglobin in urine after muscle damage (rhabdomyolysis).

---

38. What type of anemia is caused by thalassemia?

Microcytic hypochromic anemia.

---

39. Why is stored blood poor at O? delivery?

Stored RBCs have **low 2,3-BPG** ? left shift.

---

40. Which form of Hb cannot bind oxygen?

Methemoglobin (Fe^{3}?).