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Hemoglobin Physiology: Bohr Shift, pH, Cooperativity & Sickle Cell

Study Guide — Blood & Hemoglobin

High-school/Pre-med/IB questions on hemoglobin structure, oxygen binding cooperativity, Bohr shift (CO_2/pH effects), alkalosis/acidosis, fetal hemoglobin, and sickle cell basics.

30 items — Study Guide with Answers

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1 **Which statement about ADULT human hemoglobin (HbA) is correct?**

A HbA is a monomer with one heme group, similar to myoglobin.

B **HbA is a tetramer (2 2) with four heme groups, each able to bind one O_2.** ✓

C HbA is made of four identical subunits only.

D HbA binds oxygen only after being transported into mitochondria.

E HbA binds oxygen covalently and cannot release it in tissues.

▶ **Explanation:** Adult hemoglobin (HbA) is a tetramer with two and two chains. Each subunit contains a heme group that can bind one O_2 reversibly. Myoglobin is a monomer; oxygen binding is not covalent and does not require mitochondria.

2 **A single hemoglobin molecule can carry a maximum of how many oxygen molecules?**

A 1

B 2

C 3

D **4** ✓

E 8

▶ **Explanation:** Hemoglobin has four heme groups (one per subunit). Each heme binds one O_2, so the maximum is 4 O_2 per hemoglobin molecule.

3 **Oxygen binds to iron in heme when the iron is in which oxidation state?**

A Fe^{3+} only

B **Fe^{2+} (ferrous)** ✓

C Fe^{0} (metallic iron)

D Any oxidation state equally

E Iron is not involved in oxygen binding

▶ **Explanation:** O_2 binds reversibly to Fe^{2+} in the heme group. Fe^{3+} (methemoglobin) cannot bind O_2 effectively, so it is not the normal oxygen-carrying form.

4 **The oxygen–hemoglobin dissociation curve is sigmoidal (S-shaped) primarily because hemoglobin shows:**

A Simple diffusion of O_2 through the membrane

B **Cooperative binding: binding of one O_2 increases affinity for the next O_2** ✓

C ATP production by red blood cells

D O_2 binding only in the lungs and never in tissues

E Irreversible binding of O_2 to heme

▶ **Explanation:** Cooperativity means each O_2 bound makes the next binding easier, producing an S-shaped curve. If binding were non-cooperative, the curve would be more hyperbolic (like myoglobin).

5 **Which statement best describes cooperative binding in hemoglobin?**

A Hemoglobin binds four O_2 molecules at exactly the same strength, regardless of how many are already bound.

B Binding of the first O_2 decreases the affinity of hemoglobin for the remaining O_2 molecules.

C **Binding of one O_2 increases hemoglobin's affinity for additional O_2 molecules.** ✓

D Only myoglobin shows cooperativity; hemoglobin does not.

E Cooperativity means hemoglobin binds CO_2 more strongly than O_2.

▶ **Explanation:** Cooperativity in hemoglobin is positive: the first O_2 binding promotes a conformational change that increases affinity at the other sites. It is not about CO_2 binding and does not occur in myoglobin.

6 **Compared with hemoglobin, myoglobin is BEST described as:**

A A tetramer with a sigmoidal binding curve

B **A monomer with a hyperbolic binding curve and generally higher O_2 affinity** ✓

C A monomer that shows strong cooperativity

D A protein that carries oxygen only in the blood plasma

E A protein found only in red blood cells

▶ **Explanation:** Myoglobin is a single polypeptide (monomer) in muscle, with one heme and no cooperativity, giving a hyperbolic curve and higher O_2 affinity—useful for O_2 storage in muscle.

7 **The Bohr effect (Bohr shift) refers to the phenomenon that increasing CO_2 or H^+ (lower pH) causes hemoglobin to:**

A Bind O_2 more tightly (left shift)

B **Bind O_2 less tightly (right shift), promoting O_2 release in tissues** ✓

C Carry more O_2 by increasing the number of heme groups

D Stop binding CO_2 entirely

E Become unable to bind any gases

▶ **Explanation:** Higher CO_2 and lower pH (more H^+) decrease hemoglobin's O_2 affinity (right shift), making O_2 unloading easier in active tissues that produce CO_2 and acid.

8 **A RIGHT shift of the oxygen–hemoglobin dissociation curve means that at a given partial pressure of oxygen (pO_2), hemoglobin will have:**

A Higher saturation (more O_2 bound)

B **Lower saturation (less O_2 bound)** ✓

C Exactly the same saturation, but faster diffusion

D No binding to O_2 at all

E Higher affinity and stronger binding

▶ **Explanation:** A right shift indicates decreased affinity. Therefore, at the same pO_2, hemoglobin is less saturated and more willing to release oxygen.

9 **A LEFT shift of the oxygen–hemoglobin dissociation curve most directly indicates:**

A Decreased O_2 affinity and easier unloading

B **Increased O_2 affinity and harder unloading in tissues** ✓

C No change in affinity, only change in hemoglobin amount

D Less cooperativity

E More oxygen binding sites per hemoglobin molecule

▶ **Explanation:** A left shift means hemoglobin binds O_2 more tightly (higher affinity). This helps loading in lungs but can make unloading in tissues harder.

10 **During intense exercise in muscle, CO_2 production increases and pH may decrease (lactic acid). What is the expected effect on hemoglobin's O_2 affinity in that muscle?**

A Affinity increases; O_2 unloading decreases (left shift)

B **Affinity decreases; O_2 unloading increases (right shift)** ✓

C Affinity becomes zero; no O_2 can bind anywhere

D Hemoglobin becomes identical to myoglobin

E There is no effect of pH on oxygen binding

▶ **Explanation:** Exercise increases CO_2 and H^+, producing a Bohr right shift. That lowers affinity and helps deliver more O_2 to hard-working muscle.

11 **Which situation most likely causes a LEFT shift of the oxygen–hemoglobin dissociation curve?**

A Increased CO_2 in tissues

B Decreased pH (acidosis)

C Increased body temperature

D **Decreased CO_2 and increased pH (alkalosis)** ✓

E Increased 2,3-BPG in red blood cells

▶ **Explanation:** Lower CO_2 and higher pH (more alkaline) increase hemoglobin's O_2 affinity (left shift). The other options generally decrease affinity (right shift).

12 **A patient is hyperventilating due to anxiety. Their blood CO_2 falls and blood pH rises (respiratory alkalosis). What is the most likely effect on O_2 delivery to tissues?**

A Improved O_2 unloading because the curve shifts right

B **Reduced O_2 unloading because the curve shifts left** ✓

C No change because pH never affects hemoglobin

D Hemoglobin releases all its oxygen immediately

E Hemoglobin can bind only 2 O_2 molecules in alkalosis

▶ **Explanation:** Hyperventilation lowers CO_2 and raises pH, causing a left shift (higher affinity). This can make unloading O_2 in tissues harder, potentially contributing to dizziness.

13 **Which statement about fetal hemoglobin (HbF) is correct?**

A HbF has lower O_2 affinity than adult hemoglobin, helping it release O_2 to the fetus.

B **HbF has higher O_2 affinity than adult hemoglobin, helping it take O_2 from maternal blood.** ✓

C HbF contains no heme groups.

D HbF is a single-chain protein like myoglobin.

E HbF cannot bind oxygen until after birth.

▶ **Explanation:** Fetal hemoglobin binds oxygen more strongly (left-shifted curve), which supports O_2 transfer from maternal to fetal blood across the placenta. HbF still contains heme and is not a monomer.

14 **Which subunit composition is correct for normal ADULT hemoglobin (HbA) and FETAL hemoglobin (HbF)?**

A HbA = 2 2; HbF = 2 2

B **HbA = 2 2; HbF = 2 2** ✓

C HbA = 4; HbF = 4

D HbA = 2 2 only; HbF = 2 2

E HbA = 1 1; HbF = 1 1

▶ **Explanation:** The standard adult hemoglobin is HbA (2 2). Fetal hemoglobin is HbF (2 2). The other subunit combinations are incorrect for normal HbA/HbF at this level.

15 **The term P50 (in hemoglobin physiology) refers to:**

A **The pO_2 at which hemoglobin is 50% saturated** ✓

B The pH at which hemoglobin releases 50% of its oxygen

C The percent of oxygen in the atmosphere at sea level

D The number of amino acids in a hemoglobin subunit

E The pressure of CO_2 in venous blood

▶ **Explanation:** P50 is the partial pressure of oxygen at which hemoglobin is half-saturated. It is a useful measure of hemoglobin's oxygen affinity.

16 **If the oxygen–hemoglobin dissociation curve shifts RIGHT, what happens to P50?**

A P50 decreases

B **P50 increases** ✓

C P50 becomes zero

D P50 has no relationship to curve shifts

E P50 changes only with hemoglobin concentration, not affinity

▶ **Explanation:** A right shift means lower affinity, so a higher pO_2 is required to reach 50% saturation—therefore P50 increases. A left shift would decrease P50.

17 **Carbon monoxide (CO) poisoning reduces oxygen delivery to tissues mainly because CO:**

A Destroys red blood cells immediately

B **Binds hemoglobin strongly and also makes remaining sites hold O_2 more tightly (left shift)** ✓

C Increases 2,3-BPG binding and shifts the curve right

D Turns hemoglobin into myoglobin

E Replaces iron with calcium in heme

▶ **Explanation:** CO binds hemoglobin with very high affinity, blocking O_2 binding sites. It also increases the O_2 affinity of remaining sites (left shift), making O_2 unloading to tissues even harder. It does not immediately destroy RBCs or replace iron with calcium.

18 **A patient has anemia (low hemoglobin concentration). Which statement is MOST accurate about their arterial oxygen saturation (SaO_2) vs oxygen content?**

A SaO_2 must be low, and oxygen content must be normal

B **SaO_2 can be normal, but oxygen content can be low because there is less hemoglobin to carry O_2** ✓

C SaO_2 and oxygen content are always identical measurements

D Oxygen content increases because each hemoglobin binds extra O_2

E Anemia has no effect on oxygen delivery because dissolved O_2 is enough

▶ **Explanation:** Saturation measures the percent of hemoglobin binding sites occupied, which can be normal even if hemoglobin quantity is low. Oxygen content depends strongly on hemoglobin concentration, so it can be reduced in anemia.

19 **Most oxygen in blood is transported:**

A Dissolved in plasma

B **Bound reversibly to hemoglobin in red blood cells** ✓

C As bicarbonate (HCO_3^-)

D Bound to albumin

E In the form of glucose

▶ **Explanation:** The vast majority of O_2 is carried by hemoglobin. Only a small fraction is dissolved in plasma. Bicarbonate transport is mainly for CO_2, not O_2.

20 **Most carbon dioxide (CO_2) in blood is transported to the lungs mainly as:**

A CO_2 dissolved directly in plasma

B Carbon monoxide (CO)

C **Bicarbonate ions (HCO_3^-)** ✓

D Oxygen bound to hemoglobin

E Glucose bound to albumin

▶ **Explanation:** Most CO_2 is converted to bicarbonate (HCO_3^-) in red blood cells and carried in plasma. Only smaller amounts are dissolved as CO_2 or bound to hemoglobin (carbaminohemoglobin).

21 **The enzyme in red blood cells that rapidly converts CO_2 and water into carbonic acid (which then forms H^+ and HCO_3^-) is:**

A Amylase

B **Carbonic anhydrase** ✓

C Acetylcholinesterase

D DNA polymerase

E ATP synthase

▶ **Explanation:** Carbonic anhydrase catalyzes $CO_2 + H_2O \rightleftharpoons H_2CO_3$, speeding CO_2 transport as bicarbonate. The other enzymes are unrelated to CO_2 chemistry in blood.

22 **Carbaminohemoglobin refers to CO_2 bound to which part of hemoglobin?**

A The iron (Fe^{2+}) in the heme group

B **The globin (protein) chains, not the heme iron** ✓

C The red blood cell membrane

D The phosphate group of ATP

E The plasma protein albumin

▶ **Explanation:** CO_2 can bind to amino groups on the globin chains (forming carbaminohemoglobin). O_2 binds to the heme iron, not to globin amino groups.

23 **At the level of tissues, the Bohr effect is useful because it:**

A Prevents oxygen release where CO_2 is high

B **Promotes oxygen release where CO_2 is high and pH is low** ✓

C Forces hemoglobin to bind oxygen covalently

D Stops CO_2 production in cells

E Converts CO_2 into O_2

▶ **Explanation:** Active tissues produce CO_2 and H^+, which lower hemoglobin's O_2 affinity. This right shift promotes unloading exactly where oxygen is needed most.

24 **Sickle cell disease is caused by hemoglobin molecules that tend to:**

A Bind oxygen irreversibly in the lungs

B **Polymerize when deoxygenated, distorting red blood cells into a sickle shape** ✓

C Lose their heme groups at high oxygen levels

D Convert oxygen into carbon dioxide

E Become soluble only at low temperatures

▶ **Explanation:** Hemoglobin S (HbS) can polymerize when oxygen is low, forming fibers that deform RBCs into sickle shapes. This can block capillaries and reduce oxygen delivery.

25 **The most common mutation underlying sickle cell disease is best described as:**

A A large deletion removing the entire -globin gene

B **A point mutation causing a single amino acid substitution in the -globin chain** ✓

C A chromosome duplication that doubles hemoglobin subunits

D A mutation that changes iron (Fe^{2+}) into Fe^{3+} permanently

E A mutation in mitochondrial DNA

▶ **Explanation:** Sickle cell disease results from a point mutation in the -globin gene that changes one amino acid (classically Glu → Val). It is not a whole-gene deletion or mitochondrial mutation.

26 **Why is deoxygenation especially important in triggering sickling in sickle cell disease?**

A Oxygenated HbS is more likely to polymerize than deoxygenated HbS

B **Deoxygenated HbS exposes regions that promote hemoglobin–hemoglobin sticking (polymer formation)** ✓

C Low oxygen directly breaks red blood cells apart by osmosis

D Deoxygenation removes iron from heme

E Deoxygenation prevents hemoglobin from being a tetramer

▶ **Explanation:** When HbS is deoxygenated, it adopts a conformation that promotes polymerization, causing sickling. Oxygenation reduces polymer formation. Osmosis and iron loss are not the primary triggers here.

27 **Which factor would MOST likely shift the oxygen–hemoglobin dissociation curve to the RIGHT (promoting O_2 release)?**

A Decreased temperature

B Decreased CO_2

C Increased pH (alkalosis)

D **Increased temperature and increased CO_2 in tissues** ✓

E Fetal hemoglobin replacing adult hemoglobin

▶ **Explanation:** Higher temperature and higher CO_2 (often with lower pH) shift the curve right to help unload oxygen in active tissues. Lower temperature, alkalosis, and fetal hemoglobin tend to shift left.

28 **Which statement best explains why hemoglobin's cooperativity is useful for oxygen transport?**

A It makes hemoglobin bind O_2 equally well at all pO_2 values, so delivery is constant everywhere

B It allows high saturation at high pO_2 (lungs) but significant unloading with small pO_2 drops in tissues ✓

C It prevents any oxygen unloading until hemoglobin is completely full

D It makes hemoglobin a better oxygen storage molecule than myoglobin

E It removes the need for a pressure gradient

▶ **Explanation:** The sigmoidal curve means hemoglobin loads efficiently in the lungs and unloads efficiently in tissues (steep region of the curve). That's better for transport than a simple hyperbola.

29 At very low tissue pO_2, myoglobin remains more saturated with O_2 than hemoglobin. The best explanation is that myoglobin:

A Has multiple subunits that increase affinity when O_2 binds

B Has a higher O_2 affinity and does not show cooperativity, so it holds onto O_2 at low pO_2 ✓

C Cannot bind O_2 at all, so its saturation is irrelevant

D Binds O_2 only when CO_2 is high

E Is found only in blood, so it must stay saturated

▶ **Explanation:** Myoglobin is a monomer with high affinity and a hyperbolic curve. It serves as an O_2 store in muscle, releasing O_2 mainly when pO_2 becomes very low.

30 Which paired change would most likely REDUCE oxygen unloading in tissues (make hemoglobin hold onto oxygen more strongly)?

A Increased CO_2 and decreased pH

B Increased temperature and increased CO_2

C **Decreased CO_2 and increased pH** ✓

D Decreased pH and increased 2,3-BPG

E Increased CO_2 and increased 2,3-BPG

▶ **Explanation:** Lower CO_2 and higher pH cause a left shift (higher affinity), which reduces unloading in tissues. The other combinations generally cause right shifts and increase unloading.