CONCEPT: BPG REGULATION OF HEMOGLOBIN

BPG Effect on Oxygen Binding

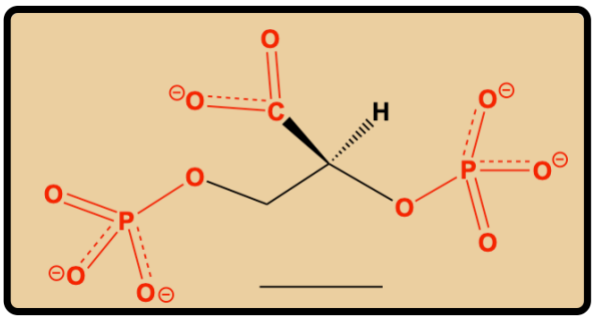
●*2,3-Bisphosphoglycerate* (_____): inhibitor *reducing* Hb's O_2 affinity in the *tissues* (allows _____ O_2 to be released).

□ BPG: *negative* _____*-otropic allosteric inhibitor* of Hb's O_2 binding, shifting the curve to the _____.

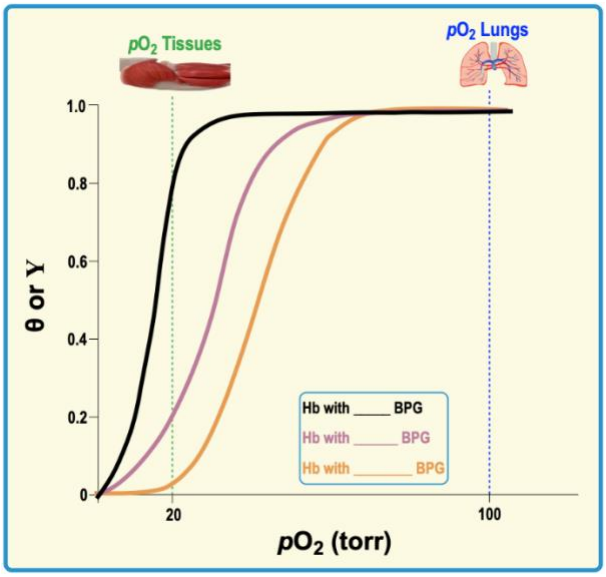
□ BPG is present within erythrocytes, but it's binding site to Hb is only available when Hb is in the _____ state.

□ BPG binds to _____ hemoglobin via electrostatic interactions & *stabilizes* Hb's T State.

EXAMPLE: Effect of BPG on O_2-binding.



$HbO_2 + BPG \rightleftharpoons HbBPG + O_2$



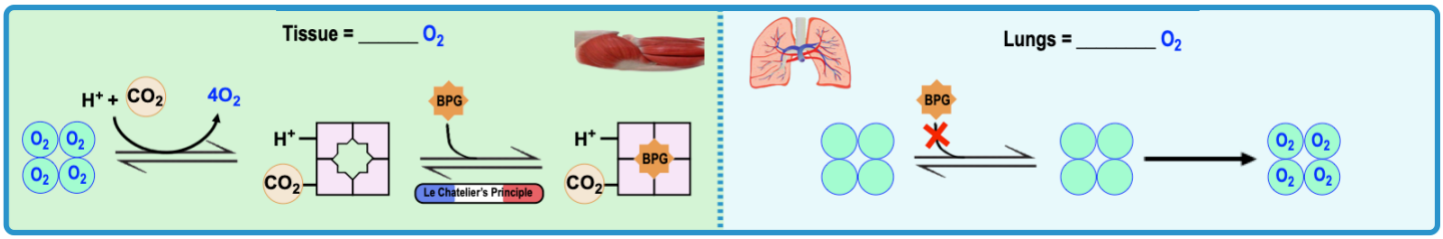
BPG Only Affects Hb in the Tissues

●BPG ONLY *decreases* Hb's O_2 binding in the _____ where Hb is mainly in the ____ state.

□ BPG has very _____ effect on O_2-binding in the lungs since Hb is mainly in ____ state in the lungs.

□ One BPG molecule binds per Hb tetramer & stabilizes the ___ State in the tissues, causing Hb to release O_2.

□ Due to high [O_2] in the lungs, Hb is mainly in the ___ State, which _____ BPG's binding-site.



PRACTICE: Under which of the following conditions will hemoglobin bind less oxygen?

a) The pH increases from 7.0 to 7.2.

b) The oxygen pressure increases from 20 torr to 100 torr.

c) The concentration of carbon dioxide increases.

d) BPG is removed.

e) None of the above.

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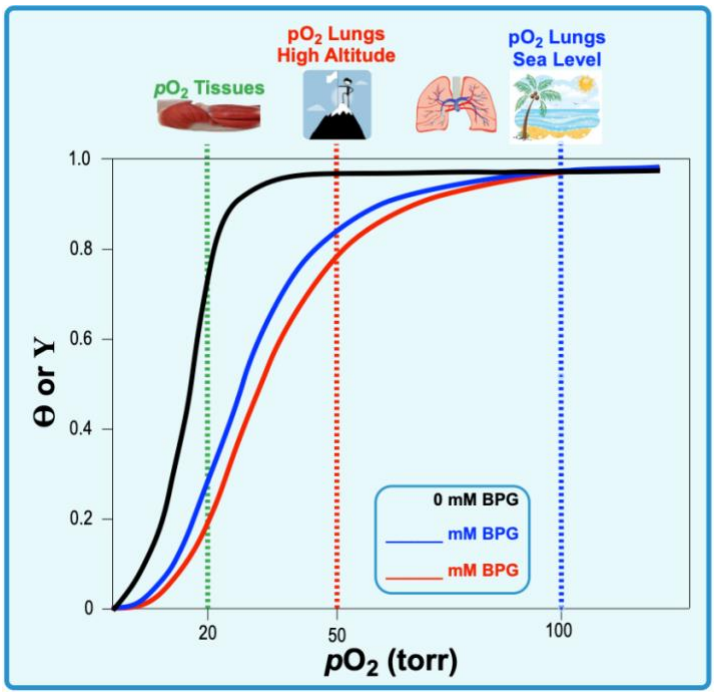
Physiological Regulation of [BPG]

●*Normal* [BPG] ≈ 5 mM in erythrocytes (red blood cells), but [BPG] can be modified to _____ Hb's O_2-binding.

□ At _____ altitudes, there is less O_2 available in atmosphere for Hb to bind than at sea level.

□ To account for *low* pO_2 at *high altitudes*, blood [BPG] _____ to 8 mM to *maintain* similar O_2 release.

EXAMPLE: Regulation of [BPG] based on elevation.



●People with _____ (*low* red blood cell count) also have *higher* [BPG] in the blood to *increase* O_2 *release*.

●Athletes train at high altitudes to acclimate cells to high BPG, allowing _____ O_2 *release* upon returning to sea level.

PRACTICE: In hemoglobin, the equilibrium transition from R state to T state is triggered by:

a) Fe^{2+} binding. b) Heme binding. c) Oxygen binding. d) 2,3-BPG binding.

PRACTICE: Some patients with erythrocytosis (excess red blood cells) have a mutation that converts a lysine to alanine at residue 82 in the β-subunit of hemoglobin. This particular lysine normally protrudes into the central cavity of deoxyhemoglobin, where it participates in binding 2,3-bisphosphoglycerate (BPG). Which of the following effects would you predict this mutation (Lys82Ala) to have on hemoglobin's affinity for BPG and for O_2 in patients with erythrocytosis? Hint: The terms "increased" and "decreased" below are relative to normal (without mutation).

a) Increased BPG affinity and decreased O_2 affinity.
b) Increased BPG affinity and increased O_2 affinity.
c) Decreased BPG affinity and increased O_2 affinity.
d) Decreased BPG affinity and decreased O_2 affinity.

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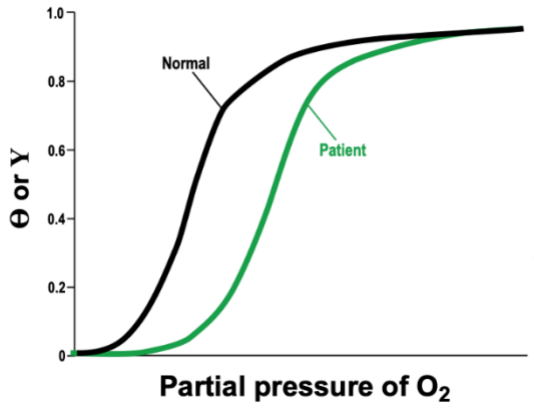
PRACTICE: A 9-month old girl with hemolytic anemia is found to have a deficiency in the enzyme responsible for the conversion of molecule-B to pyruvate. Shown below is the oxygen saturation curve for hemoglobin in the erythrocytes of this patient (green curve), compared to the corresponding black curve in normal red blood cells. Which of the following is the most likely explanation for the observed oxygen saturation curve in this patient?

a) Decreased [BPG].
b) Increased [BPG].
c) Decreased blood glucose.
d) Increased blood glucose.



PRACTICE: What is the effect of the following changes on the O_2 affinity of hemoglobin?

A) A drop in the pH of blood plasma from 7.4 to 7.2.

a) Lower the O_2 Affinity. b) Increase the O_2 Affinity.

B) A decrease in the partial pressure of CO_2 in the lungs from 6 kPa (holding one's breath) to 2 kPa (normal).

a) Lower the O_2 Affinity. b) Increase the O_2 Affinity.

C) An increase in [BPG] from 5 mM (normal altitudes) to 8 mM (high altitudes).

a) Lower the O_2 Affinity. b) Increase the O_2 Affinity.