Clinical respiratory physiology

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Hypoxia vs Hypoxemia

- Hypoxia is defined as a decrease in O2 delivery to, or utilization by, the tissues (deficiency of O2 at the tissue level).
- Hypoxemia is a decrease in arterial PO2.
- Hypoxemia is one cause of tissue hypoxia, although it is not the only cause.

Hypoxia

- Because O2 delivery is the product of **cardiac output** and **O2 content** of blood, hypoxia is caused by decreased cardiac output (blood flow) or decreased O2 content of blood.

- O2 content of blood is determined primarily by the amount of O2-hemoglobin.

Hypoxia

- Based on the cause, it can be classified into four types, as follows:

- 1. **Hypoxic hypoxia** is caused by a low PO2 in arterial blood as a result of high altitude, airway obstruction, or fluid in the lungs.

- 2. In **anemic hypoxia**, too little functioning hemoglobin is present in the blood, which reduces O2 transport to tissue cells. Among the causes are hemorrhage, anemia, and failure of hemoglobin to carry its normal complement of O2, as in CO poisoning.

Hypoxia

- 3. In **ischemic hypoxia**, blood flow to a tissue is so reduced that too little O2 is delivered to it, even though PO2 and oxyhemoglobin levels are normal.

- 4. In **histotoxic hypoxia**, the blood delivers adequate O2 to tissues, but the tissues are unable to use it properly because of the action of some toxic agent. One cause is cyanide poisoning, in which cyanide blocks an enzyme required for the use of O2 during ATP synthesis.

Causes of Hypoxia

Cause	Mechanism	Pa_{O_2}
↓ Cardiac output	↓ Blood flow	—
Hypoxemia	↓ Pa_{O_2} ↓ O_2 saturation of hemoglobin ↓ O_2 content of blood	↓
Anemia	↓ Hemoglobin concentration ↓ O_2 content of blood	—
Carbon monoxide poisoning	↓ O_2 content of blood Left shift of O_2-hemoglobin curve	—
Cyanide poisoning	↓ O_2 utilization by tissues	—

Hypoxemia

- Hypoxemia, a decrease in arterial PO2, has multiple causes.
- One useful tool for comparing the various causes of hypoxemia is the A − a gradient.
- The A − a gradient is the difference between the PO2 of alveolar gas (PAO2) and the PO2 of systemic arterial blood (PaO2).

Hypoxemia

- Briefly, the A − a gradient describes whether there has been equilibration of O2 between alveolar gas and pulmonary capillary blood (which becomes systemic arterial blood).

- Normally, O2 equilibrates across the alveolar/pulmonary capillary barrier and the A − a gradient is close to zero.

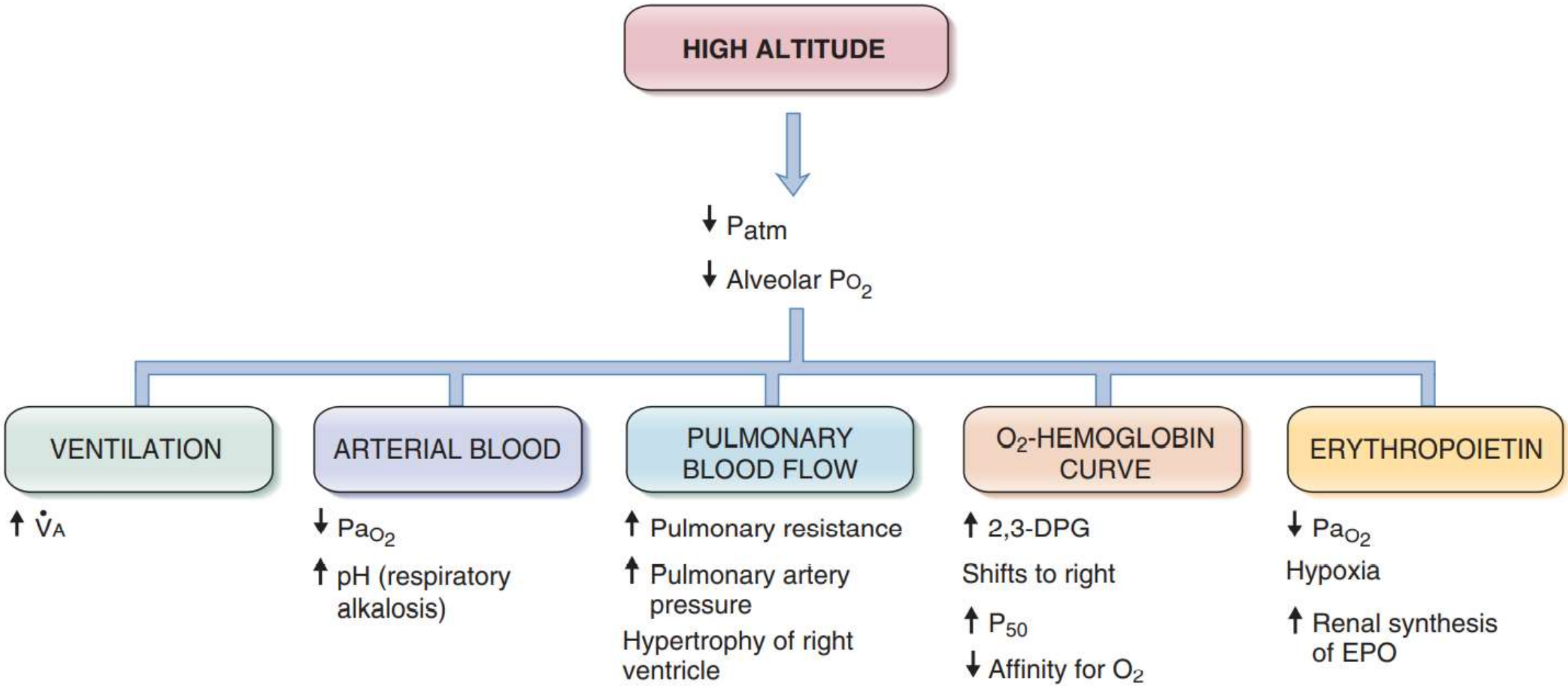
- In some but not all causes of hypoxemia, the A − a gradient is increased, or widened, signifying a defect in O2 equilibration.

Causes of Hypoxemia

Cause	Pa_{O_2}	A – a Gradient	Supplemental O_2 Helpful?
High altitude (↓ P_B; ↓ PI_{O_2})	Decreased	Normal	Yes
Hypoventilation (↓ PA_{O_2})	Decreased	Normal	Yes
Diffusion defect (e.g., fibrosis)	Decreased	Increased	Yes
$\dot{V}/\dot{Q}$ defect	Decreased	Increased	Yes
Right-to-left shunt	Decreased	Increased	Limited

High altitude

DESCRIPTION OF CASE. A 28-year-old man moves from his sea level residence in Durham, North Carolina to work at a ski resort in Aspen, Colorado, where the base altitude is 8000 feet above sea level. The man is in excellent physical condition and passes a complete physical examination before the move with flying colors. When he first arrives in Aspen, he experiences fatigue and nausea, especially on exertion; he even has periods of "fuzzy thinking." With time, he gradually begins to feel better.


HIGH ALTITUDE
↓ P_{atm}
↓ Alveolar P_{O_2}
VENTILATION
↑ $\dot{V}_A$
ARTERIAL BLOOD
↓ Pa_{O_2}
↑ pH (respiratory alkalosis)
PULMONARY BLOOD FLOW
↑ Pulmonary resistance
↑ Pulmonary artery pressure
Hypertrophy of right ventricle
O_2-HEMOGLOBIN CURVE
↑ 2,3-DPG
Shifts to right
↑ P_{50}
↓ Affinity for O_2
ERYTHROPOIETIN
↓ Pa_{O_2}
Hypoxia
↑ Renal synthesis of EPO

erythropoietin

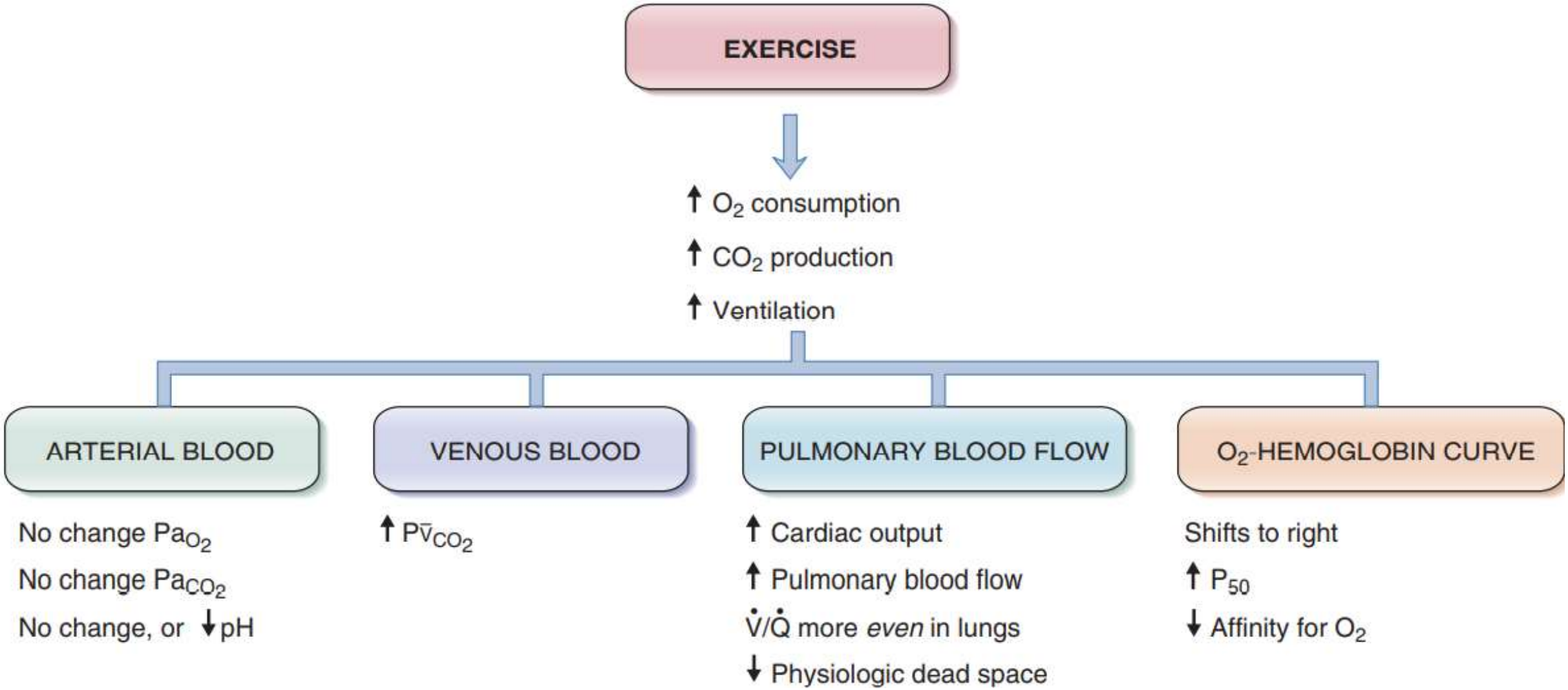
- EPO synthesis is induced in the kidney in response to hypoxia.

- Erythropoietin (EPO) is a glycoprotein growth factor that is synthesized in the kidneys (and to a lesser extent in the liver) and serves as the major stimulus for erythropoiesis by promoting the differentiation of proerythroblasts into red blood cells.

Summary of Adaptive Respiratory Responses to High Altitude

Parameter	Response to High Altitude
Alveolar P_{O_2}	↓ (due to decreased barometric pressure)
Arterial P_{O_2}	↓ (hypoxemia)
Ventilation rate	↑ (hyperventilation due to hypoxemia)
Arterial pH	↑ (respiratory alkalosis due to hyperventilation)
Hemoglobin concentration	↑ (increased red blood cell concentration)
2,3-DPG concentration	↑
O_2-hemoglobin dissociation curve	Shifts to right; increased P_{50}; decreased affinity
Pulmonary vascular resistance	↑ (due to hypoxic vasoconstriction)
Pulmonary arterial pressure	↑ (secondary to increased pulmonary resistance)

Exercise


EXERCISE
↑ O_2 consumption
↑ CO_2 production
↑ Ventilation
ARTERIAL BLOOD
No change Pa_{O_2}
No change Pa_{CO_2}
No change, or ↓ pH
VENOUS BLOOD
↑ $P\bar{v}_{CO_2}$
PULMONARY BLOOD FLOW
↑ Cardiac output
↑ Pulmonary blood flow
$\dot{V}/\dot{Q}$ more *even* in lungs
↓ Physiologic dead space
O_2-HEMOGLOBIN CURVE
Shifts to right
↑ P_{50}
↓ Affinity for O_2

Summary of Respiratory Responses to Exercise

Parameter	Response to Exercise
O_2 consumption	↑
CO_2 production	↑
Ventilation rate	↑
Arterial P_{O_2} and P_{CO_2}	No change
Arterial pH	No change during moderate exercise ↓ During strenuous exercise
Venous P_{CO_2}	↑
Pulmonary blood flow and cardiac output	↑
$\dot{V}/\dot{Q}$ ratio	More evenly distributed throughout the lung
Physiologic dead space	↓
O_2-hemoglobin dissociation curve	Shifts to the right; ↑ P_{50}; decreased affinity

DESCRIPTION OF CASE. A 65-year-old man has smoked two packs of cigarettes a day for more than 40 years. He has a long history of producing morning sputum, cough, and progressive shortness of breath on exertion (dyspnea). For the past decade, each fall and winter he has had bouts of bronchitis with dyspnea and wheezing, which have gradually worsened over the years. When admitted to the hospital, he is short of breath and cyanotic. He is barrel-chested. His breathing rate is 25 breaths/min, and his tidal volume is 400 mL. His vital capacity is 80% of the normal value for a man his age and size, and FEV_1 is 60% of normal. The following arterial blood values were measured (normal values are in parentheses):

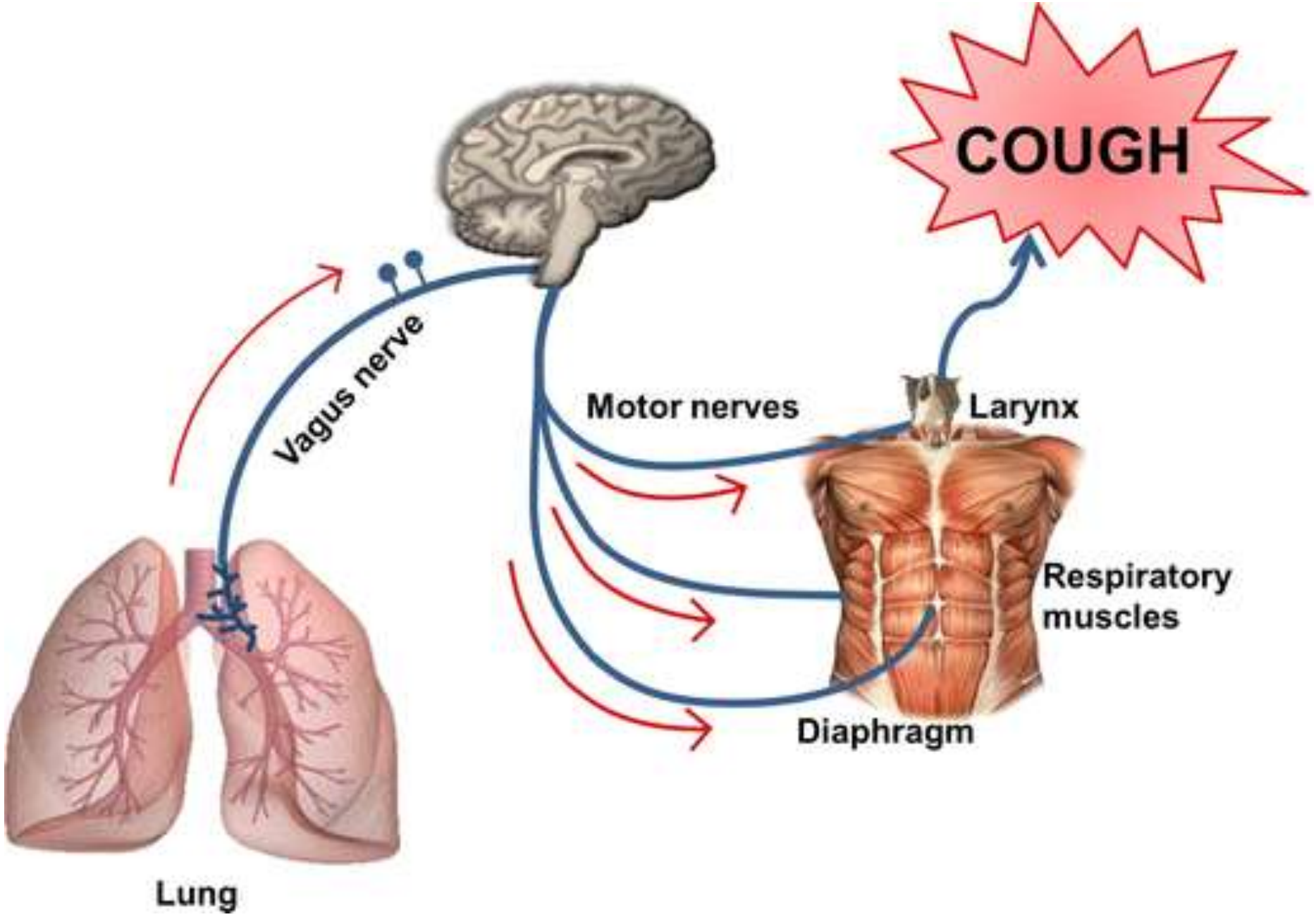
pH, 7.47 (normal, 7.4)

Pa_{O_2}, 60 mm Hg (normal, 100 mm Hg)

Pa_{CO_2}, 30 mm Hg (normal, 40 mm Hg)

Hemoglobin saturation, 90%

Hemoglobin concentration, 14 g/L (normal, 15 g/L)



https://link.springer.com/article/10.1007/s00210-014-1082-1

Cough reflex

- 1. Up to 2.5 liters of air are rapidly inspired.
- 2. The epiglottis closes, and the vocal cords shut tightly to entrap the air within the lungs.
- 3. The abdominal muscles contract forcefully, pushing against the diaphragm while other expiratory muscles, such as the internal intercostals, also contract forcefully. Consequently, the pressure in the lungs rises rapidly.
- 4. The vocal cords and epiglottis suddenly open widely, so that air under this high pressure in the lungs explodes outward. Sometimes this air is expelled at velocities ranging from 75 to 100 miles/hour.

$$
\begin{aligned}
P_{I_{O_2}} &= (P_B - P_{H_2O}) \times F_{I_{O_2}} \\
&= (760 \text{ mm Hg} - 47 \text{ mm Hg}) \times 0.21 \\
&= 150 \text{ mm Hg}
\end{aligned}
$$

$$
\begin{aligned}
P_{A_{O_2}} &= P_{I_{O_2}} - \frac{P_{A_{CO_2}}}{R} \\
&= 150 \text{ mm Hg} - \frac{30 \text{ mm Hg}}{0.8} \\
&= 113 \text{ mm Hg}
\end{aligned}
$$

Revision Questions

- 1. A 12-year-old boy has a severe asthmatic attack with wheezing. He experiences rapid breathing and becomes cyanotic. His arterial PO2 is 60 mm Hg and his PCO2 is 30 mm Hg.

  Which of the following statements about this patient is most likely to be true?

- (A) Forced expiratory volume1/forced vital capacity (FEV1/FVC) is increased
- (B) Ventilation/perfusion (V/Q) ratio is increased in the affected areas of his lungs
- (C) His arterial PCO2 is higher than normal because of inadequate gas exchange
- (D) His arterial PCO2 is lower than normal because hypoxemia is causing him to hyperventilate
- (E) His residual volume (RV) is decreased

Revision Questions

- 2. When a person is standing, blood flow in the lungs is

- (A) equal at the apex and the base
- (B) highest at the apex owing to the effects of gravity on arteria pressure
- (C) highest at the base because that is where the difference between arterial and venous pressure is greatest
- (D) lowest at the base because that is where alveolar pressure is greater than arterial pressure

Revision Questions

- 3. A 49-year-old man has a pulmonary embolism that completely blocks blood flow to his left lung. As a result, which of the following will occur?

- (A) Ventilation/perfusion (V/Q) ratio in the left lung will be zero
- (B) Systemic arterial PO_2 will be elevated
- (C) V/Q ratio in the left lung will be lower than in the right lung
- (D) Alveolar PO_2 in the left lung will be approximately equal to the PO_2 in inspired air
- (E) Alveolar PO_2 in the right lung will be approximately equal to the PO_2 in venous blood

Revision Questions

- 4. Compared with the systemic circulation, the pulmonary circulation has a

- (A) higher blood flow
- (B) lower resistance
- (C) higher arterial pressure
- (D) higher capillary pressure
- (E) higher cardiac output

Revision Questions

- 5. Compared with the apex of the lung, the base of the lung has

- (A) a higher pulmonary capillary PO_2
- (B) a higher pulmonary capillary PCO_2
- (C) a higher ventilation/perfusion (V/Q) ratio
- (D) the same V/Q ratio

Revision Questions

- 6. Hypoxemia produces hyperventilation by a direct effect on the

- (A) phrenic nerve
- (B) J receptors
- (C) lung stretch receptors
- (D) medullary chemoreceptors
- (E) carotid and aortic body chemoreceptors

Revision Questions

- 7. Which of the following changes occurs during strenuous exercise?

- (A) Ventilation rate and O2 consumption increase to the same extent
- (B) Systemic arterial PO2 decreases to about 70 mm Hg
- (C) Systemic arterial PCO2 increases to about 60 mm Hg
- (D) Systemic venous PCO2 decreases to about 20 mm Hg
- (E) Pulmonary blood flow decreases at the expense of systemic blood flow

Revision Questions

- 8. If an area of the lung is not ventilated because of bronchial obstruction, the pulmonary capillary blood serving that area will have a PO2 that is

- (A) equal to atmospheric PO2
- (B) equal to mixed venous PO2
- (C) equal to normal systemic arterial PO2
- (D) higher than inspired PO2
- (E) lower than mixed venous PO2

Revision Questions

- 9. Which of the following causes of hypoxia is characterized by a decreased arterial PO2 and an increased A–a gradient?

- (A) Hypoventilation
- (B) Right-to-left cardiac shunt
- (C) Anemia
- (D) Carbon monoxide poisoning
- (E) Ascent to high altitude

Revision Questions

- 10. A 42-year-old woman with severe pulmonary fibrosis is evaluated by her physician and has the following arterial blood gases: pH = 7.48, PaO_2 = 55 mm Hg, and $PaCO_2$ = 32 mm Hg. Which statement best explains the observed value of $PaCO_2$?

- (A) The increased pH stimulates breathing via peripheral chemoreceptors
- (B) The increased pH stimulates breathing via central chemoreceptors
- (C) The decreased PaO_2 inhibits breathing via peripheral chemoreceptors
- (D) The decreased PaO_2 stimulates breathing via peripheral chemoreceptors
- (E) The decreased PaO_2 stimulates breathing via central chemoreceptors

Revision Questions

- 11. A 38-year-old woman moves with her family from New York City (sea level) to Leadville, Colorado (10,200 feet above sea level). Which of the following will occur as a result of residing at high altitude?

- (A) Hypoventilation
- (B) Arterial PO_2 greater than 100 mm Hg
- (C) Decreased 2,3-diphosphoglycerate (DPG) concentration
- (D) Shift to the right of the hemoglobin–O_2 dissociation curve
- (E) Pulmonary vasodilation
- (F) Hypertrophy of the left ventricle
- (G) Respiratory acidosis

Revision Questions

- 12. A person with a ventilation/perfusion (V/Q) defect has hypoxemia and is treated with supplemental O2. The supplemental O2 will be most helpful if the person's predominant V/Q defect is

- (A) dead space
- (B) shunt
- (C) high V/Q
- (D) low V/Q
- (E) V/Q = 0
- (F) V/Q = ∞

Revision Questions

- 13. Which person would be expected to have the largest A–a gradient?

- (A) Person with pulmonary fibrosis
- (B) Person who is hypoventilating due to morphine overdose
- (C) Person at 12,000 feet above sea level
- (D) Person with normal lungs breathing 50% O2
- (E) Person with normal lungs breathing 100% O2

Revision Questions

- 14. A 48-year-old woman at sea level breaths a gas mixture containing 21% O2. She has the following arterial blood gas values:
- PaO2 = 60 mm Hg
- PaCO2 = 45 mm Hg
- Her measured DLCO is normal. Which of the following is the cause of her hypoxemia?

- (A) The values demonstrate normal lung function
- (B) Hypoventilation
- (C) Fibrosis
- (D) Carbon monoxide poisoning
- (E) Right-to-left shunt

Revision Questions

- 15. A 62-year-old man at sea level breaths a gas mixture containing 21% O2. He has the following arterial blood gas values:
- PaO2 = 60 mm Hg
- PaCO2 = 70 mm Hg
- Which of the following is the cause of his hypoxemia?

- (A) Hypoventilation
- (B) Fibrosis
- (C) V/Q defect
- (D) Right-to-left shunt
- (E) Anemia

Answer key

- 1. D
- 2. C
- 3. D
- 4. B
- 5. B
- 6. E
- 7. A
- 8. B
- 9. B
- 10. D
- 11. D
- 12. D
- 13. A
- 14. D
- 15. A

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