# Pulmonary Ventilation

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## Page 1. Introduction

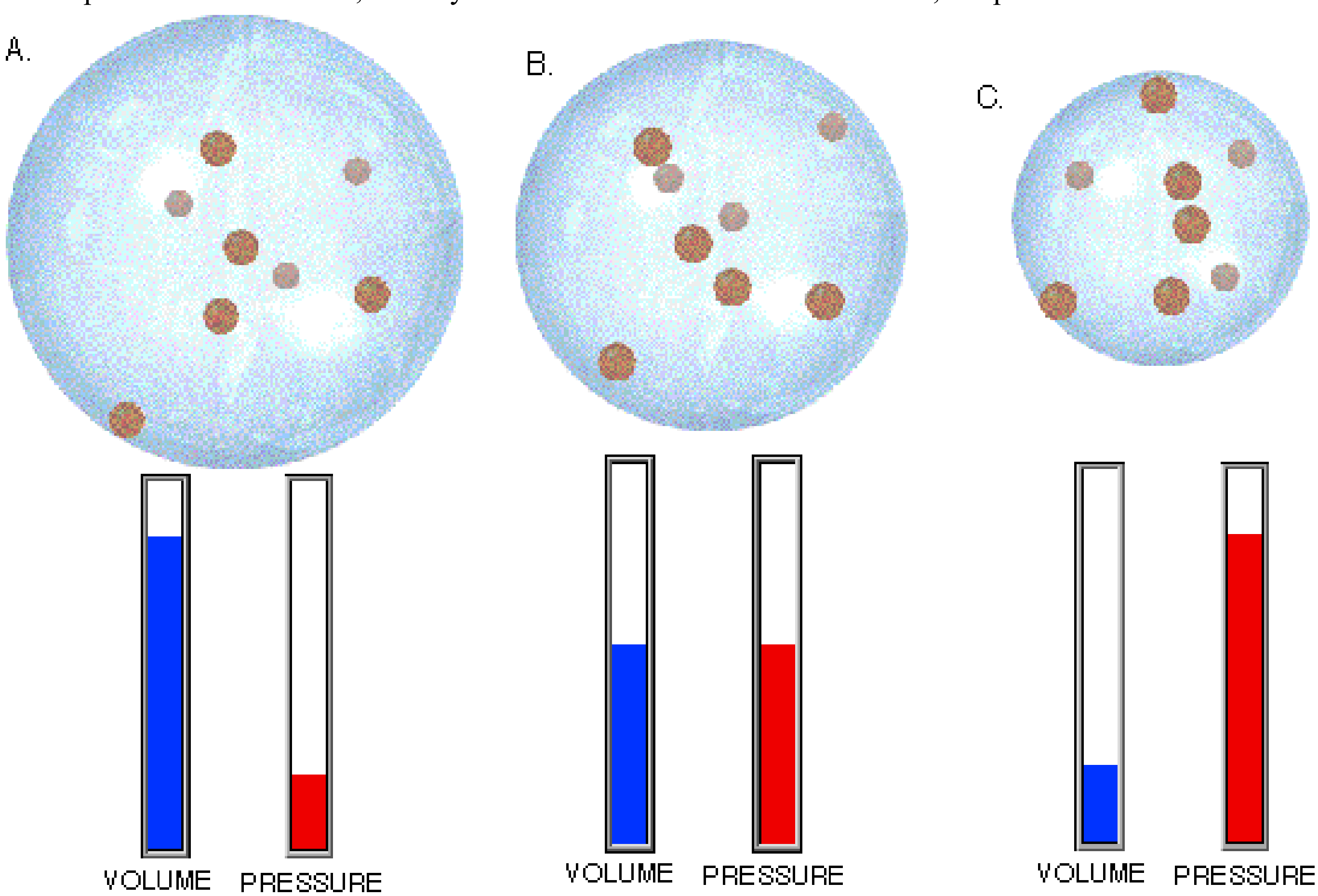
- Pulmonary ventilation, or breathing, is the exchange of air between the atmosphere and the lungs.
- As air moves into and out of the lungs, it travels from regions of high air pressure to regions of low air pressure

## Page 2. Goals

- To relate Boyle's law to ventilation.
- To identify the muscles used during ventilation.
- To understand how volume changes in the thoracic cavity cause pressure changes that lead to air flow.
- To identify factors which influence airway resistance and lung compliance.

## Page 3. Boyle's Law: Relationship Between Pressure and Volume

- In order to understand ventilation, we must first look at the relationship between pressure and volume.
- Pressure is caused by gas molecules striking the walls of a container.
- The pressure exerted by the gas molecules is related to the volume of the container.
- This large sphere contains the same number of gas molecules as the original sphere. Notice that in this larger volume, the gas molecules strike the wall less frequently, thus exerting less pressure.
- In this small sphere, the gas molecules strike the wall more frequently, thus exerting more pressure. Notice that the number of gas molecules has not changed.
- These demonstrations illustrate Boyle's Law, which states that the pressure of a gas is inversely proportional to the volume of its container. Thus, if you increase the volume of a container, the pressure will decrease, and if you decrease the volume of a container, the pressure will increase.



**Page 4. Quiet Inspiration: Muscle Contraction**

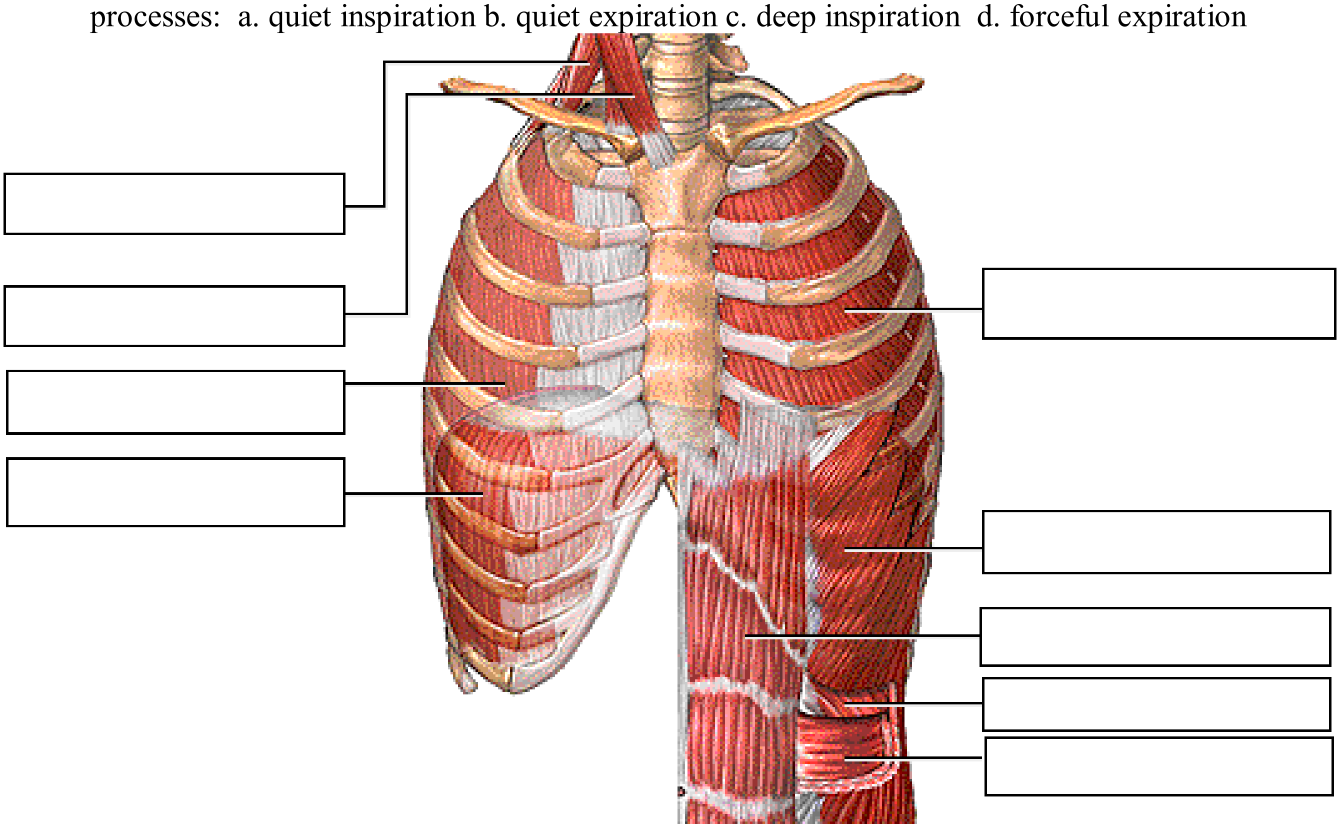
- The volume of the thoracic cavity is changed by muscle contraction and relaxation.
- During quiet inspiration, the diaphragm and the external intercostal muscles contract, slightly enlarging the thoracic cavity.
- As we learned from Boyle's Law, increasing the volume decreases the pressure within the thoracic cavity and the lungs.
- Notice how the diaphragm flattens and moves inferiorly while the external intercostal muscles elevate the rib cage and move the sternum anteriorly. These actions enlarge the thoracic cavity in all dimensions.
- As we learned from Boyle's Law, increasing the volume decreases the pressure within the thoracic cavity and the lungs.

**Page 5. Quiet Expiration: Muscle Relaxation**

- Quiet expiration is a passive process, in which the diaphragm and the external intercostal muscles relax, and the elastic lungs and thoracic wall recoil inward.
- This decreases the volume and therefore increases the pressure in the thoracic cavity.
- As the diaphragm relaxes, it moves superiorly. As the external intercostal muscles relax, the rib cage and sternum return to their resting positions. These actions decrease the size of the thoracic cavity in all dimensions, and therefore increase the pressure in the thoracic cavity.

**Page 6. Muscles of Deep Inspiration and Expiration**

- Deep breathing uses forceful contractions of the inspiratory muscles and additional accessory muscles to produce larger changes in the volume of the thoracic cavity during both inspiration and expiration.
- Label the muscles in this diagram. Indicate which muscles are used during each of the following processes: a. quiet inspiration b. quiet expiration c. deep inspiration d. forceful expiration



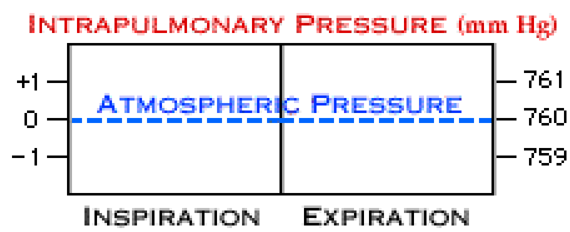
- During deep inspiration, the diaphragm and the external intercostal muscles contract more forcefully than during quiet breathing. Additionally, the sternocleidomastoid and scalenes contract, lifting the rib cage higher. These actions further increase the volume. As we learned from Boyle's Law, this decreases the pressure within the thoracic cavity.

- Deep or forceful expiration is an active process. The internal intercostal muscles depress the rib cage, and the external oblique, internal oblique, transversus abdominis and rectus abdominis muscles compress the abdominal organs, forcing them superiorly against the diaphragm. These actions can dramatically decrease the volume, and further increase the pressure within the thoracic cavity, producing forceful expiration.

** Now is a good time to go to quiz questions 1-3:
- Click the Quiz button on the left side of the screen.
- Work through questions 1-3.
- After answering question 3, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "7. Intrapulmonary Pressure Changes".

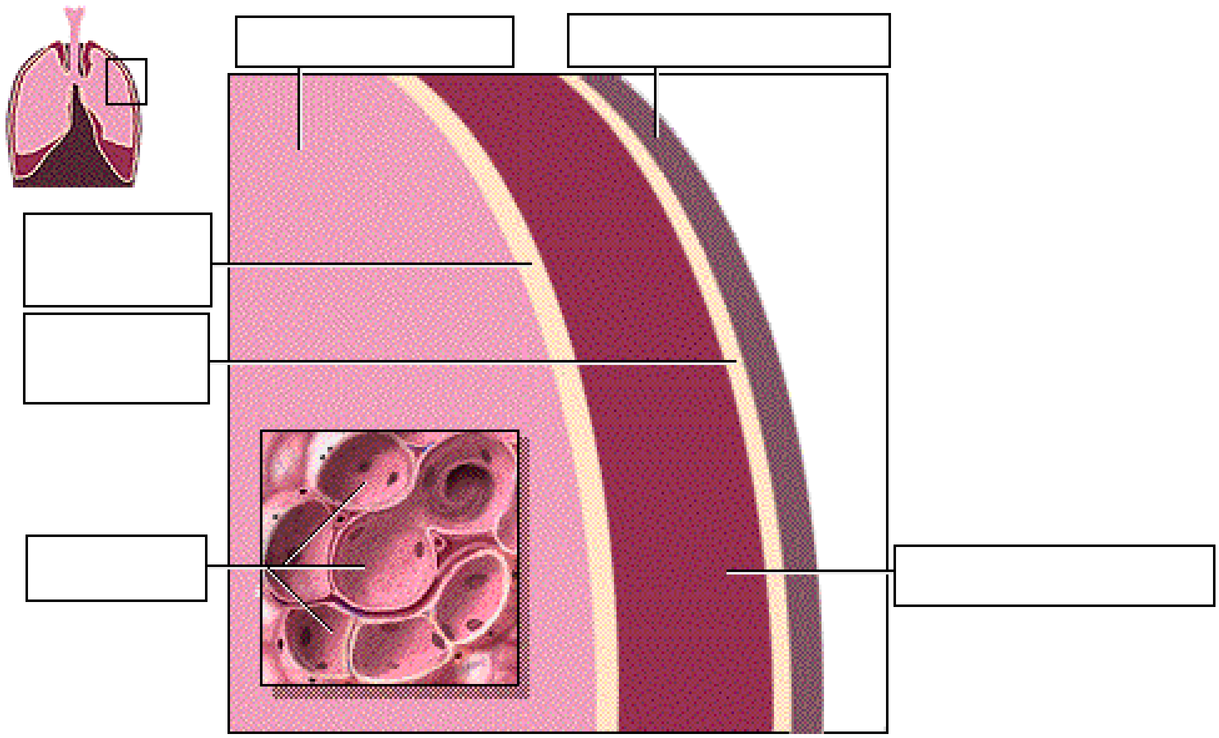
## Page 7. Intrapulmonary Pressure Changes

- Now let's look at the specific pressure changes that occur in the lungs during breathing. For reasons described later, the lungs closely follow the movements of the thoracic wall.
- The pressure within the lungs is called the intrapulmonary, or intra-alveolar, pressure.
- Between breaths, it equals atmospheric pressure, which has a value of 760 millimeters of mercury at sea level. When discussing respiratory pressures, this is generally referred to as zero.
- During inspiration, the volume of the thoracic cavity increases, causing intrapulmonary pressure to fall below atmospheric pressure. This is also known as a negative pressure. Since air moves from areas of high to low air pressure, air flows into the lungs. Notice that at the end of inspiration, when the intrapulmonary pressure again equals atmospheric pressure, airflow stops.
- During expiration, the volume of the thoracic cavity decreases, causing the intrapulmonary pressure to rise above atmospheric pressure. Following its pressure gradient, air flows out of the lungs, until, at the end of expiration, the intrapulmonary pressure again equals atmospheric pressure.
- Draw the pressure changes that occur during inspiration and expiration on this graph:




## Page 8. Intrapleural Pressure

- Label this diagram:



• Intrapleural pressure is the pressure within the pleural cavity. Intrapleural pressure is always negative, which acts like a suction to keep the lungs inflated.

• The negative intrapleural pressure is due to three main factors:

1. The surface tension of the alveolar fluid.
   • The surface tension of the alveolar fluid tends to pull each of the alveoli inward and therefore pulls the entire lung inward. Surfactant reduces this force.
2. The elasticity of the lungs.
   • The abundant elastic tissue in the lungs tends to recoil and pull the lung inward. As the lung moves away from the thoracic wall, the cavity becomes slightly larger. The negative pressure this creates acts like a suction to keep the lungs inflated.
3. The elasticity of the thoracic wall.
   • The elastic thoracic wall tends to pull away from the lung, further enlarging the pleural cavity and creating this negative pressure. The surface tension of pleural fluid resists the actual separation of the lung and thoracic wall.

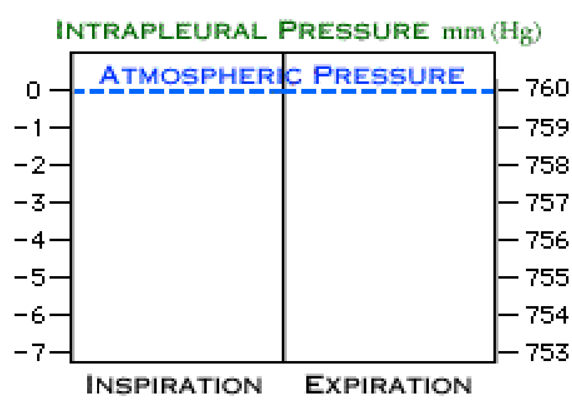
## Page 9. Intrapleural Pressure Changes

• Intrapleural pressure changes during breathing:

• As the thoracic wall moves outward during inspiration, the volume of the pleural cavity increases slightly, decreasing intrapleural pressure.

• As the thoracic wall recoils during expiration, the volume of the pleural cavity decreases, returning the pressure to minus 4, or 756 millimeters of mercury.

• Draw the changes in intrapleural pressure on this graph:

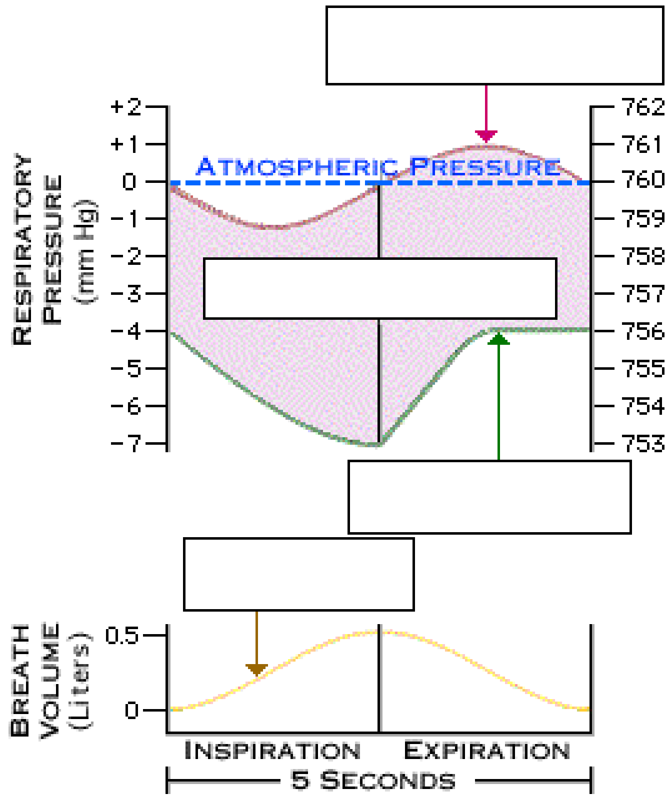



## Page 10. Effect of Pneumothorax

• If you cut through the thoracic wall into its pleural cavity, air enters the pleural cavity as it moves from high pressure to low pressure. This is called a pneumothorax.
• Normally, there is a difference between the intrapleural and intrapulmonary pressures, which is called transpulmonary pressure. The transpulmonary pressure creates the suction to keep the lungs inflated. In this case, when there is no pressure difference there is no suction and the lung collapses.
• The lungs are completely separate from one another, each surrounded by its own pleural cavity and pleural membranes. Therefore, changes in the intrapleural pressure of one lung do not affect the other lung.

## Page 11. Events During Inspiration

• Label this graph as you work through this page.
• Let's review all the events that occur during inspiration. The upper graph shows the intrapulmonary pressure, that is, the pressure within the lungs. The middle graph shows the intrapleural pressure, the pressure within the pleural cavity. The region between the two graphs is the transpulmonary pressure, the pressure difference between the intrapulmonary and intrapleural pressures. The lower graph shows the volume of air which enters and leaves the lungs during quiet breathing. This is called the tidal volume.
• During inspiration, the diaphragm and external intercostal muscles contract, increasing the volume of the thoracic cavity. This causes the intrapleural pressure to become more negative, which increases the transpulmonary pressure, causing the lungs to expand. The expansion of the lungs lowers the intrapulmonary pressure below atmospheric pressure. Air, following its pressure gradient, now flows into the lungs.




## Page 12. Events During Expiration

• During expiration, the diaphragm and external intercostal muscles relax, decreasing the volume of the thoracic cavity. The intrapleural pressure becomes less negative, the transpulmonary pressure decreases, and the lungs passively recoil. This increases the intrapulmonary pressure so that it rises above atmospheric pressure. Air, following its pressure gradient, moves out of the lungs. Watch how the three pressures change together on the graph.

## Page 13. Events During Inspiration and Expiration

• Let's correlate the graphs with the movements of the thoracic cavity during inspiration and expiration.

** Now is a good time to go to quiz questions 4-6:
• Click the Quiz button on the left side of the screen.
• Click on the scrolling page list at the top of the screen and choose "4. Sequence of Inspiration and Expiration".
• Work through questions 4-6.
• After answering question 6, click the Back to Topic button on the left side of the screen.
• To get back to where you left off, click on the scrolling page list at the top of the screen and choose "14. Other Factors Effecting Ventilation".

## Page 14. Other Factors Affecting Ventilation

- Two other important factors play roles in ventilation:
  1. The resistance within the airways.
  2. Lung compliance.

## Page 15. Resistance Within Airways

- As air flows into the lungs, the gas molecules encounter resistance when they strike the walls of the airway. Therefore the diameter of the airway affects resistance.
- When the bronchiole constricts, the diameter decreases, and the resistance increases. This is because more gas molecules encounter the airway wall. Airflow is inversely related to resistance.
- This relationship is shown by the equation:

$$\text{AIRFLOW} = \frac{\text{PRESSURE}}{\text{RESISTANCE}}$$

- Airflow equals the pressure difference between atmosphere and intrapulmonary pressure, divided by the resistance.
- As the resistance increases, the airflow decreases.
- As the resistance decreases, the airflow increases.
- In healthy lungs, the airways typically offer little resistance, so air flows easily into and out of the lungs.

## Page 16. Factors Affecting Airway Resistance

- Several factors change airway resistance by affecting the diameter of the airways. They do this by contracting or relaxing the smooth muscle in the airway walls, especially the bronchioles.
- Parasympathetic neurons release the neurotransmitter acetylcholine, which constricts bronchioles. As you can see in the equation, increased airway resistance decreases airflow.
- Histamine, released during allergic reactions, constricts bronchioles. This increases airway resistance and decreases airflow, making it harder to breathe.
- Epinephrine, released by the adrenal medulla during exercise or stress, dilates bronchioles, thereby decreasing airway resistance. This greatly increases airflow, ensuring adequate gas exchange.

## Page 17. Lung Compliance: Elastic Fibers

- Another important factor affecting ventilation is the ease with which the lungs expand, also known as lung compliance. It is primarily determined by two factors:
  1. The stretchability of the elastic fibers within the lungs.
  2. The surface tension within the alveoli.
- Healthy lungs have high compliance because of their abundant elastic connective tissue.
- Low lung compliance occurs in some pathological conditions, such as fibrosis, in which increasing amounts of less flexible connective tissue develop.

## Page 18. Lung Compliance: Surface Tension

- The second factor affecting lung compliance is surface tension within the alveoli.
- Some premature infants do not produce surfactant. Is their lung compliance high or low?
- Without surfactant, alveoli have high surface tension, and they tend to collapse. Collapsed alveoli resist expansion, so lung compliance is low. This condition is known as respiratory distress syndrome of the newborn. Natural or synthetic surfactant may be sprayed into the infant's respiratory passageways. Surfactant lowers surface tension and increases lung compliance.

## Page 19. Summary

- Muscle activity causes changes in the volume of the thoracic cavity during breathing.
- Changing the thoracic cavity volume causes intrapulmonary and intrapleural pressure changes, which allow air to move from high pressure to low pressure regions.
- Airway resistance is normally low, but nervous stimulation and chemical factors can change the diameter of bronchioles, thereby altering resistance and airflow.

• Lung compliance is normally high due to the lung's abundant elastic tissue and surfactant's ability to lower the surface tension of the alveolar fluid.

** Now is a good time to go to quiz questions 7 and 8:
• Click the Quiz button on the left side of the screen.
• Click on the scrolling page list at the top of the screen and choose "7. Bronchiole Airflow and Resistance".
• Work through quiz questions 7 and 8.

## Notes on Quiz Questions:

### Quiz Question #1a,b: Pressure and Volume Changes

• This question asks you to watch animations of deep inspiration or expiration and note the pressure and volume changes that occur.

### Quiz Question 2: Muscles of Deep Inspiration and Expiration

• This question asks you to label the muscles involved during deep inspiration and expiration.

### Quiz Question 3: Blow Out the Candles

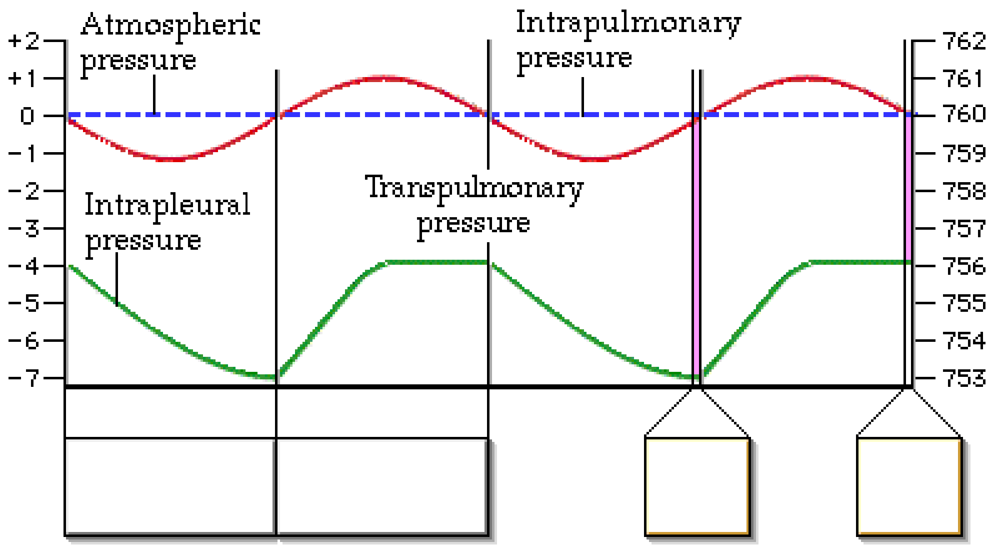
• This question asks you to identify the muscles involved when one blows out the candles on birthday cake.

### Quiz Question 4: Sequence of Inspiration and Expiration

• This question asks you to list the sequence of events that occur during inspiration and expiration.

### Quiz Question 5a,b,c,d,e: Pressure Graph - Airflow In, Airflow Out, No Airflow

• This question asks you to identify the parts of the graph of pressure changes during respiration.
• Make notes on this graph as you do this question:




### Quiz Question 6: Reinflate the Collapsed Lung

• This question asks you to chose the best way to reinflate a collapsed lung.

### Quiz Question 7: Bronchiole Airflow and Resistance

• This question asks you to predict what happens to airflow and resistance when bronchioles dilate.

### Quiz Question 8: Asthma and Bronchioles

• This question asks you to chose a treatment for asthma.

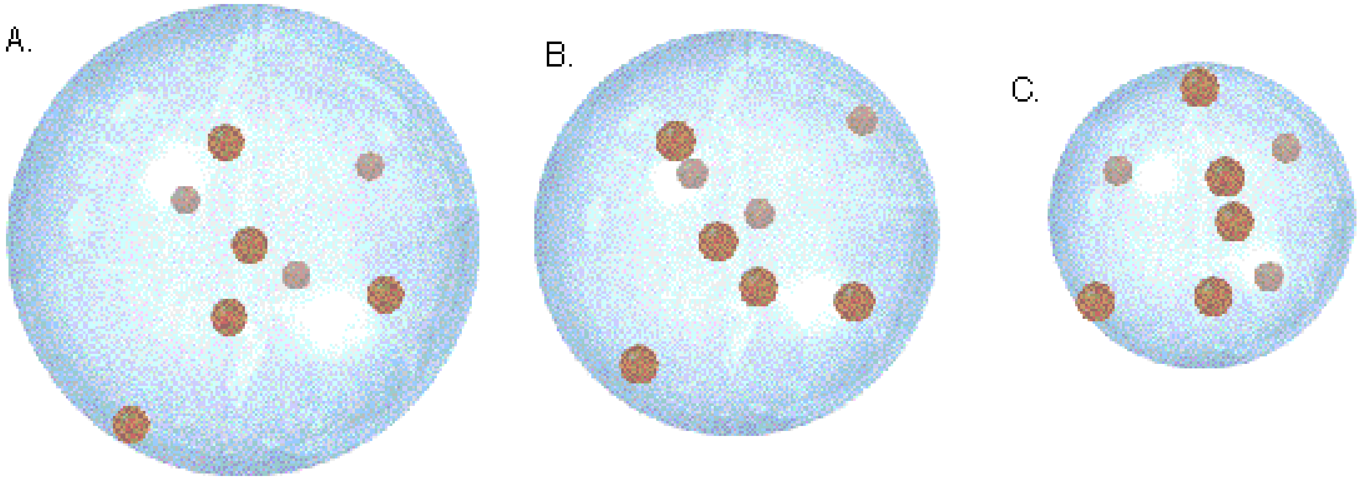
## Study Questions on Pulmonary Ventilation:

1. (Page 1.) What is another term for pulmonary ventilation?

2. (Page 1.) Define pulmonary ventilation in simple terms.

3. (Page 3.) What causes pressure within a gas sample?

4. (Page 3.) Which of these three samples of gas would have the highest pressure, and which would have the lowest pressure?.




5. (Page 3.) Define Boyle's Law.

6. a. What happens to the pressure of a gas if you increase the size of a container? b. What happens to the pressure of a gas if you decrease the size of a container?

7. (Page 4.) How is the volume of the thoracic cavity changed?

8. (Page 4.) What two muscles contract during quiet inspiration? What is the effect of their contraction?

9. (Page 4.) What happens to pressure when we increase the volume within the thoracic cavity and the lungs?

10. (Page 4.) a. What happens to the diaphragm muscle when it contracts? b. What happens to the external intercostal muscles when they contract?

11. (Page 5.) Explain what happens in quiet expiration.

12. (Page 5.) What effect does quiet expiration have on the volume of the thoracic cavity? How does this effect the pressure within the cavity?

13. (Page 6.) Which of these are active and which are passive processes?
a. quiet inspiration b. quiet expiration c. deep inspiration d. forceful expiration

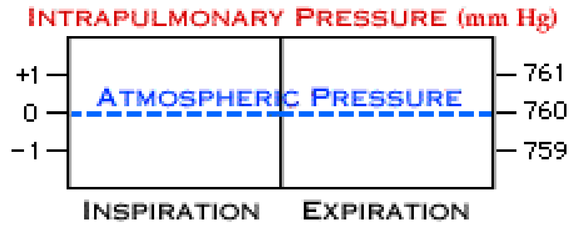
14. (Page 6.) Label the diagram on p. 6. Indicate which muscles contract in these processes:
a. quiet inspiration b. quiet expiration c. deep inspiration d. forceful expiration

15. (Page 7.) What is the pressure within the lungs called?

16. (Page 7.) What is a typical value for intrapulmonary, or intra-alveolar, pressure during normal breathing at these times. Assume the atmospheric pressure is 760 mm Hg. a. before inspiration b. during inspiration c. after inspiration and before expiration d. during expiration

17. (Page 7.) When discussing respiratory pressures, what do these pressures mean? a. 0 b. -1 c. +1

18. (Page 7.) Draw the pressure changes that occur during inspiration and expiration on this graph:



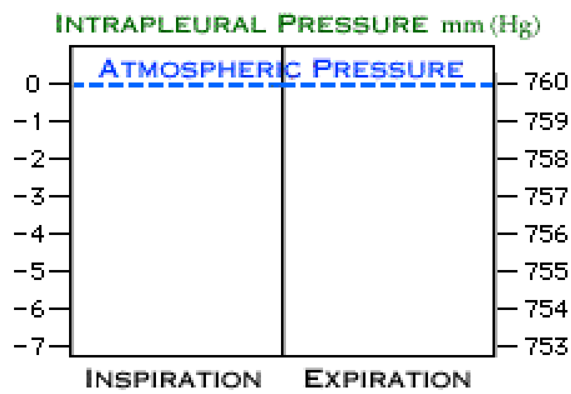

19. (Page 8.) Label the diagram on p. 8.

20. (Page 8.) What is the value of intrapleural pressure compared to intrapulmonary (alveolar) pressure?

21. (Page 8.) What three factors cause the intrapleural pressure to be less than intrapulmonary (alveolar) pressure?

22. (Page 8.) How do each of the following decrease the pressure inside the pleural cavity: a. the surface tension of the alveolar fluid b. The elasticity of the lungs. c. The elasticity of the thoracic wall.

23. (Page 9.) Draw the changes in intrapleural pressure on this graph:




24. (Page 9.) What happens to the volume of the pleural cavity and the intrapleural pressure during a. inspiration? b. expiration?

25. (Page 10.) Why does a lung collapse if you cut into the pleural cavity?

26. (Page 10.) a. What is the transpulmonary pressure? b. What is the function of the transpulmonary pressure?

27. (Page 10.) If a pneumothorax occurs in one lung, why doesn't it also occur in the other lung?

28. (Page 11.) Label the diagram on page 11.

29. (Page 11.) Match the pressures to their definition:

• Intrapulmonary Pressure
• Transpulmonary Pressure
• Intrapleural Pressure

a. The pressure within the pleural cavity.
b. The pressure within the alveoli.
c. The difference between the pressure within the pleural cavity and the pressure within the alveoli.

30. (Page 11.) What is the tidal volume?

31. (Page 11.) Chose the proper words to explain what happens during inspiration.

The diaphragm and external intercostal muscles __________ (contract, relax).

↓

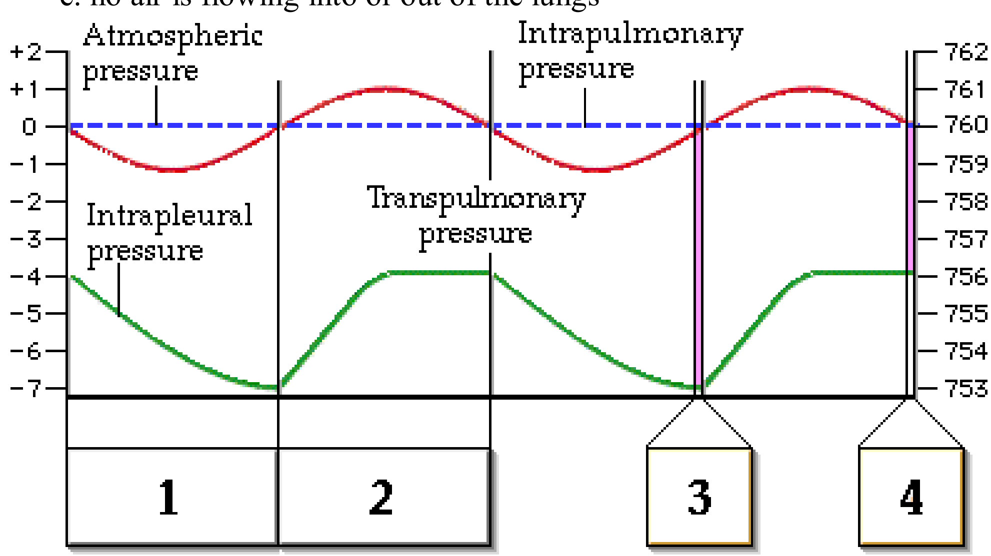
The volume of the thoracic cavity _________ (increases, decreases).

↓
Intrapleural pressure becomes ________ (more, less) negative.
↓
Lungs ________ (recoil, expand).
↓
Intrapulmonary pressure __________ (increases, decreases).
↓
Air flows _________ (into, out of) the lungs.

32. (Page 12.) Chose the proper words to explain what happens during expiration.

The diaphragm and external intercostal muscles __________ (contract, relax).
↓
The volume of the thoracic cavity _________ (increases, decreases).
↓
Intrapleural pressure becomes ________ (more, less) negative.
↓
Lungs ________ (recoil, expand).
↓
Intrapulmonary pressure __________ (increases, decreases).
↓
Air flows _________ (into, out of) the lungs.

33. (Summary) Which numbers correspond to regions of the graph where:
   a. the external intercostal muscles and diaphragm are relaxed.
   b. the external intercostal muscles and diaphragm are contracted.
   c. air is flowing into the lungs.
   d. air is flowing out of the lungs.
   e. no air is flowing into or out of the lungs




34. (Page 14.) What two factors play roles in ventilation besides muscle contraction?

35. (Page 15.) What is airway resistance due to?

36. (Page 15.) What happens to the airway resistance as the bronchiole constricts?

37. (Page 16.) Does histamine constrict or dilate bronchioles?

38. (Page 16.) Does epinephrine constrict or dilate bronchioles?

39. (Page 17.) What term is used to describe the ease with which the lungs expand?

40. (Page 17.) What two factors is lung compliance dependent upon?

41. (Page 18.) What happens to alveoli when there is not enough surfactant?

# Gas Exchange

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**Page 1. Introduction**

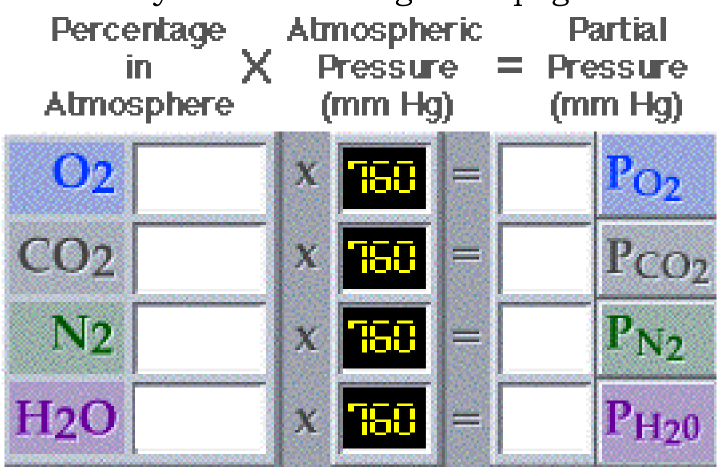
- Oxygen and carbon dioxide diffuse between the alveoli and pulmonary capillaries in the lungs, and between the systemic capillaries and cells throughout the body.
- The diffusion of these gases, moving in opposite directions, is called gas exchange.

**Page 2. Goals**

- To apply gas law relationships - between partial pressure, solubility, and concentration - to gas exchange.
- To explore the factors which affect external and internal respiration.

**Page 3. Dalton's Law of Partial Pressures**

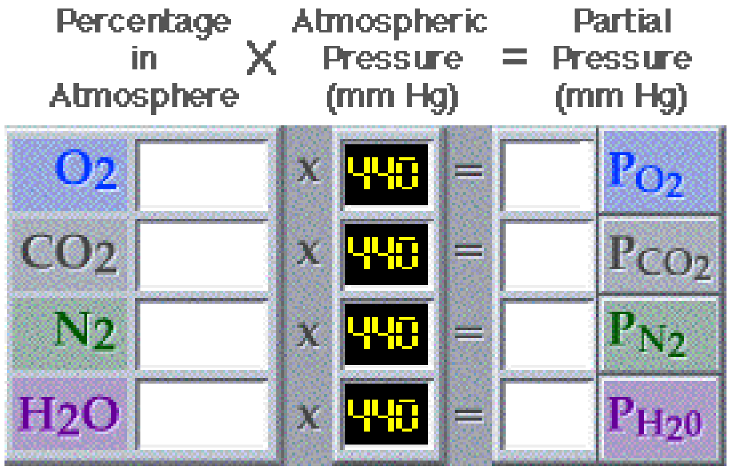
- Fill out this chart as you work through this page:




- In order to understand gas exchange, we must first understand the air we breathe. The atmosphere is a mixture of gases, including oxygen, carbon dioxide, nitrogen, and water.
- The combined pressure of these gases equals atmospheric pressure.
- At sea level, atmospheric pressure is 760 mm Hg, which means that the atmosphere pushes a column of mercury to a height of 760 millimeters. Each gas within the atmosphere is responsible for part of that pressure in proportion to its percentage in the atmosphere.
- Oxygen comprises 20.9% of the atmosphere. The pressure exerted by oxygen is 20.9% of the total pressure of 760 millimeters of mercury, which equals 159 millimeters of mercury. This value is known as the partial pressure of oxygen, and is written as "P" with the subscript "$O_2$".
- Notice that the partial pressures of the four gases add up to 760 millimeters of mercury, the total atmospheric pressure. This demonstrates Dalton's Law of Partial Pressures, which states that in a mixture of gases, the total pressure equals the sum of the partial pressures exerted by each gas. The partial pressure of each gas is directly proportional to its percentage in the total gas mixture.

**Page 4. Effect of High Altitude on Partial Pressures**

- Fill out this chart as you work through this page:




- Atmospheric pressure decreases with increasing altitude. For example, on the top of Mt. Whitney, atmospheric pressure drops to approximately 440 millimeters of mercury.
- Oxygen still makes up 20.9% of the atmosphere, but the $P_{O_2}$ is 20.9% of 440 millimeters of mercury, or about 92 millimeters of mercury. Compare that to the $P_{O_2}$ at sea level of 159 millimeters of mercury. Lower atmospheric pressure means fewer gas molecules, and therefore fewer oxygen molecules, are available. That explains why you may gasp for breath at high altitudes.
- As you can see, at high altitudes the partial pressures of all gases are lower than at sea level.

**Page 5. Henry's Law**

- Within the lungs, oxygen and carbon dioxide diffuse between the air in the alveoli and the blood, that is between a gas and a liquid.
- This movement is governed by Henry's Law, which states that the amount of gas which dissolves in a liquid is proportional to:
    1. the partial pressure of the gas
    2. the solubility of the gas
- In this container, the oxygen in the air is at equilibrium with the oxygen in the liquid. At equilibrium, the pressure of the oxygen in the air is the same as in the liquid, with the gas molecules diffusing at the same rate in both directions.
- If you increase the pressure in the container more oxygen molecules dissolve in the liquid, moving from a region of high pressure to a region of low pressure. Diffusion continues until a new equilibrium is reached. This is what happens when oxygen moves from the alveoli into the blood.
- Now let's look at the diffusion of carbon dioxide. Although both gases are at the same pressure, far more carbon dioxide dissolves in the liquid than oxygen. This occurs because carbon dioxide is much more soluble than oxygen. As stated in Henry's Law, the amount of oxygen and carbon dioxide which dissolves is proportional to the partial pressure and the solubility of each gas.

** Now is a good time to go to quiz questions 1-3:

- Click the Quiz button on the left side of the screen..
- Work through questions 1-3.
- After answering question 3, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "6. Sites of Gas Exchange".

### Page 6. Sites of Gas Exchange

Sites of gas exchange in the body:

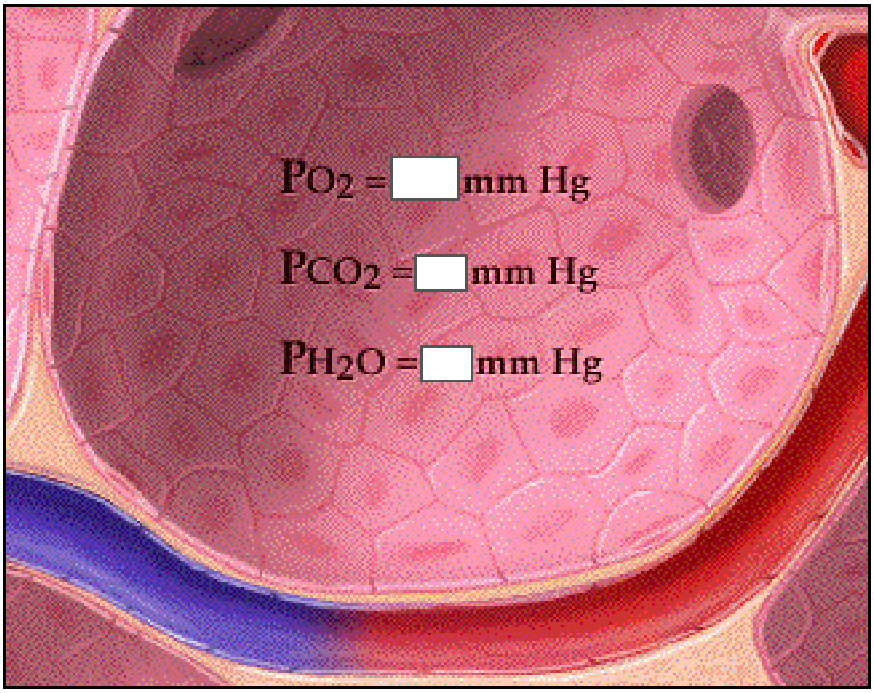
- **External Respiration.**
  - Blood that is low in oxygen is pumped from the right side of the heart, through the pulmonary arteries to the lungs.
  - External respiration occurs within the lungs, as carbon dioxide diffuses from the pulmonary capillaries into the alveoli, and oxygen diffuses from the alveoli into the pulmonary capillaries.
  - Oxygen-rich blood leaves the lungs and is transported through the pulmonary veins to the left side of the heart.
- **Internal Respiration.**
  - From there it is pumped through the systemic circuit to tissues throughout the body.
  - Internal respiration occurs within tissues, as oxygen diffuses from the systemic capillaries into the cells, and carbon dioxide diffuses from the cells into the systemic capillaries.

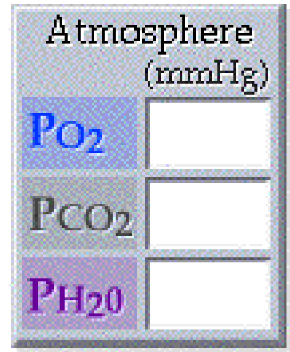
### Page 7. Factors Influencing External Respiration

- Efficient external respiration depends on three main factors:
  1. The surface area and structure of the respiratory membrane. The 300 million alveoli, covered with a dense network of pulmonary capillaries, provide an enormous surface area for efficient gas exchange. In addition, the thinness of the respiratory membrane increases efficiency.
  2. The partial pressure gradients between the alveoli and capillaries.
  3. Efficient gas exchange requires matching alveolar airflow to pulmonary capillary blood flow.

### Page 8. External Respiration: Partial Pressures

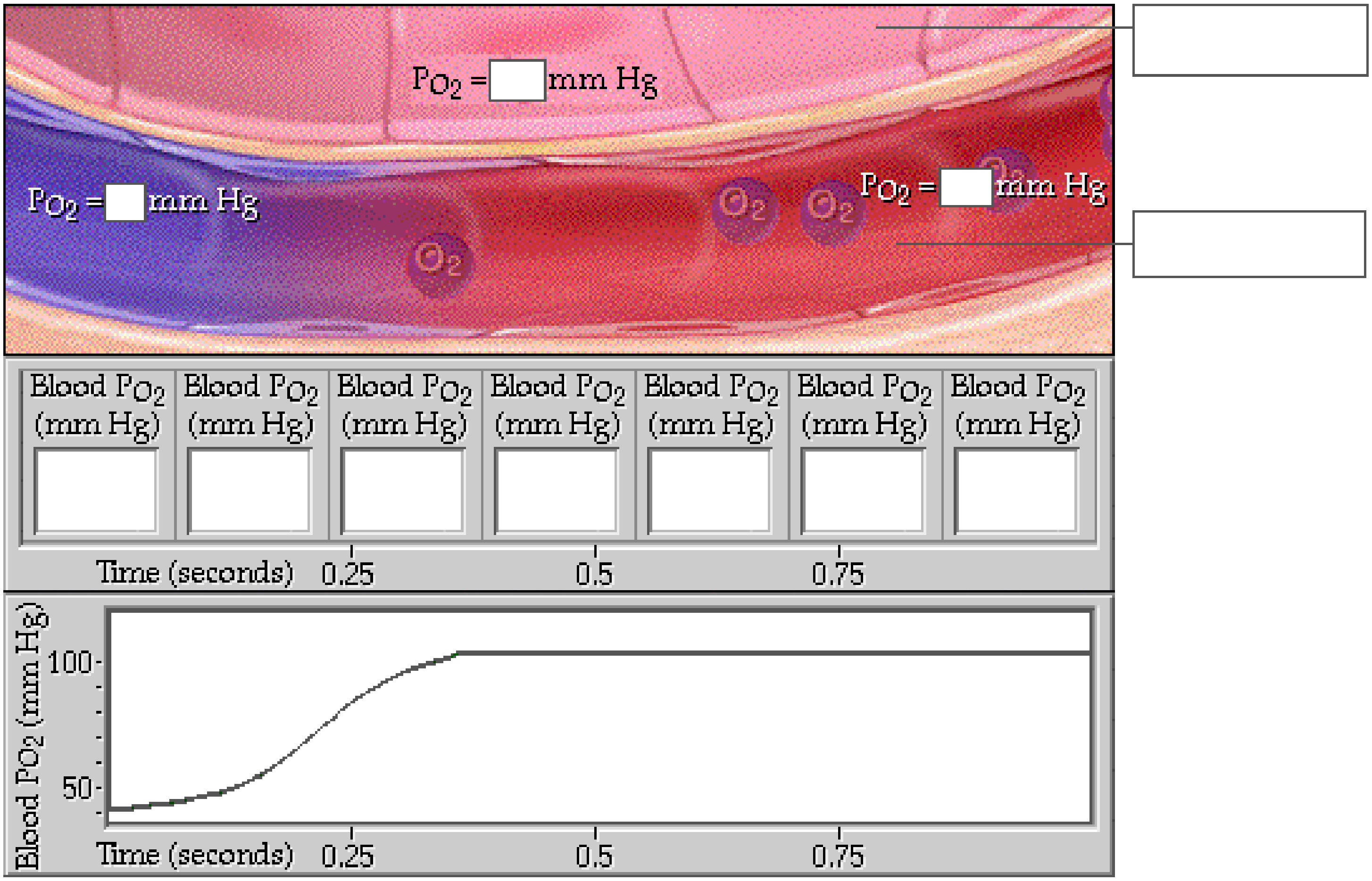
- Let's see how partial pressure gradients affect gas exchange between the alveoli and the pulmonary capillaries.
- Notice that the partial pressures in the alveoli differ from those in the atmosphere. This difference is caused by a combination of several factors:
  1. Humidification of inhaled air. As it travels through the respiratory passageways to the alveoli, air is humidified, picking up water molecules. This greatly increases the partial pressure of water.
  2. Gas exchange between the alveoli and pulmonary capillaries. A continuous exchange of oxygen and carbon dioxide occurs between the alveoli and pulmonary capillaries, changing the partial pressures of both gases. Oxygen diffuses out of the alveoli into the pulmonary capillaries and carbon dioxide diffuses from the pulmonary capillaries into the alveoli.
  3. Mixing of new and old air. Since the alveoli do not completely empty between breaths, the air in the alveoli is a mixture of new air and air remaining from previous breaths.
- Label this diagram:



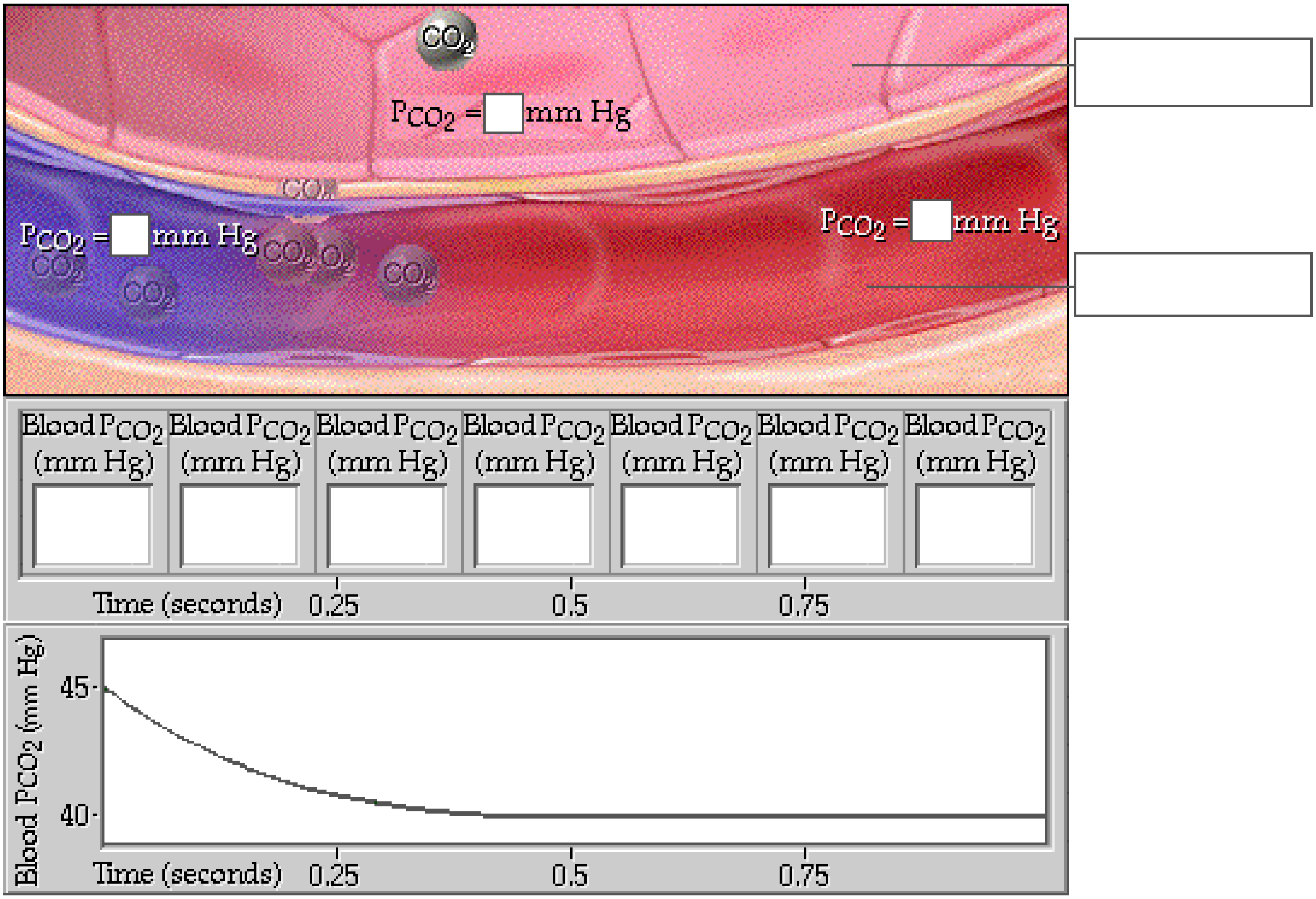

**Page 9. External Respiration: Loading $O_2$**

- Let's first look at the loading of oxygen into the blood. Each alveolus is surrounded by a network of capillaries. This diagram shows just one alveolus and one capillary.
- The $P_{O_2}$ of the alveolar air is 104 mm Hg. At rest, the oxygen-poor blood entering the pulmonary capillaries has a $P_{O_2}$ of 40 mm Hg.
- As blood flows past the alveolus, the $P_{O_2}$ increases.
- Notice that there is a net diffusion of oxygen along its partial pressure gradient, from the alveolus into the blood, until equilibrium is reached. The $P_{O_2}$ of the oxygen-rich blood has increased to 104 mm Hg.
- As indicated in the graph, equilibrium is reached rapidly, within the first third of the pulmonary capillary.
- Label this diagram:




**Page 10. External Respiration: Unloading $CO_2$**

- Now let's look at the unloading of carbon dioxide from the blood into the alveolus.
- The $P_{CO_2}$ of the alveolar air is 40 millimeters of mercury. At rest, the $P_{CO_2}$ of the blood entering the pulmonary capillaries is 45 millimeters of mercury.
- As blood flows past the alveolus, the $P_{CO_2}$ decreases. Carbon dioxide diffuses along its partial pressure gradient, from the blood into the alveolus, until equilibrium is reached. The $P_{CO_2}$ of the blood has decreases to 40 millimeters of mercury.
- Equilibrium is reached rapidly, within the first four tenths of the pulmonary capillary.
- Label this diagram:




**Page 11. External Respiration $O_2$ and $CO_2$ Exchange**

- Loading oxygen and unloading carbon dioxide occur simultaneously. As you inhale, you replenish oxygen, and as you exhale, you eliminate carbon dioxide.
- Notice how much smaller carbon dioxide's partial pressure gradient is than oxygen's. As Henry's law states, the number of molecules which dissolve in a liquid is proportional to both the partial pressure and the gas solubility. Since carbon dioxide is very soluble in blood, a large number of molecules diffuse along this small partial pressure gradient. Oxygen, which is less soluble, requires a much larger concentration gradient to provide adequate oxygen to the body.

**Page 12. Ventilation-Perfusion Coupling: Effect of $P_{O_2}$**

- The third factor in external respiration is ventilation-perfusion coupling, which facilitates efficient gas exchange. It does this by maintaining alveolar airflow that is proportional to the pulmonary capillary blood flow.
- When airflow through a bronchiole is restricted, as when blocked by mucus, the resulting low $P_{O_2}$ causes the local arterioles to vasoconstrict. This response redirects the blood to other alveoli which have a higher airflow, and therefore have more oxygen available to be picked up by the blood.
- In regions with high airflow compared to their blood supply, the resulting high $P_{O_2}$ causes the local arterioles to vasodilate. This brings more blood to the alveoli, allowing the blood to pick up the abundant oxygen.

## Page 13. Ventilation-Perfusion Coupling: Effect of $P_{CO2}$

- We've seen that during ventilation-perfusion coupling, the arterioles respond to changes in $P_{O2}$. The bronchioles, on the other hand, respond to changes in $P_{CO2}$.
- When airflow through a bronchiole is lower than normal, the $P_{CO2}$ rises. The bronchioles respond by dilating, thereby eliminating the excess carbon dioxide from the alveoli.
- When airflow through a bronchiole is high compared to its blood supply, the $P_{CO2}$ drops. The bronchioles then constrict, reducing the airflow so it is proportional to the local blood flow.

## Page 14. Predict the Effect of $P_{O2}$ and $P_{CO2}$

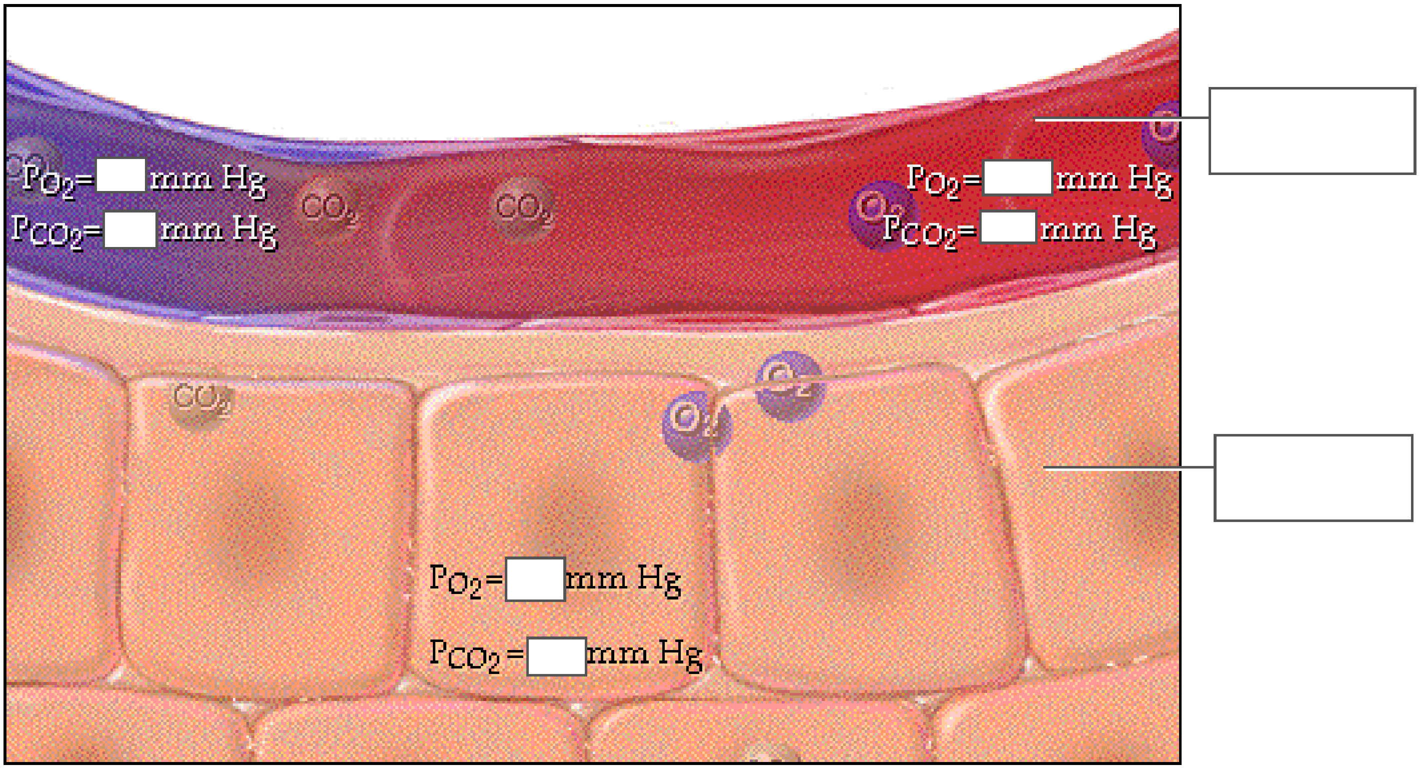
- Assume that ventilation to an alveolar sac is low, due to a small tumor growing in the bronchiole. The $P_{O2}$ decreases because oxygen is not replenished, and the $P_{CO2}$ increases, because the carbon dioxide is not eliminated. See if you can predict the response of the arterioles and bronchioles.
- The low $P_{O2}$ causes the arterioles to constrict, and the high $P_{CO2}$ causes the bronchioles to dilate. The airflow and blood flow are now in the proper proportions for optimum gas exchange. Notice that both the arterioles and bronchioles respond simultaneously.

## Page 15. Internal Respiration

- During internal respiration:
  - Oxygen diffuses from the systemic capillaries into the cells.
  - Carbon dioxide diffuses from the cells into the systemic capillaries.
- Factors affecting the exchange of oxygen and carbon dioxide during internal respiration:
  1. The available surface area, which varies in different tissues throughout the body.
  2. Gases diffuse along their partial pressure gradients.
  3. The rate of blood flow in a specific tissue.
     - Blood flow in a tissue varies for many reasons, including the tissue's metabolic rate. Recall that during metabolism, cells use oxygen and produce carbon dioxide.

## Page 16. Internal Respiration $O_2$ and $CO_2$ Exchange

- Label this diagram as you go through this page:




- The exchange of oxygen and carbon dioxide during internal respiration:
- In relatively inactive organs, the tissue cells have a $P_{O_2}$ of 40 millimeters of mercury, and a $P_{CO_2}$ of 45 millimeters of mercury.
- As the blood enters the systemic capillaries, it has a $P_{O_2}$ of 100 millimeters of mercury, and a $P_{CO_2}$ of 40 millimeters of mercury.
- Notice that the $P_{O_2}$ of blood entering the systemic capillaries is lower than the alveolar $P_{O_2}$ of 104 millimeters of mercury. This small decrease is due primarily to imperfect ventilation-perfusion coupling in the lungs.
- Gas exchange continues until equilibrium is reached. At equilibrium, the blood in the systemic capillaries has a $P_{O_2}$ of 40 millimeters of mercury, and a $P_{CO_2}$ of 45 millimeters of mercury.
- The oxygen-poor blood now returns, through the systemic veins, to the right side of the heart.

**Page 17. Summary**

- Gas laws show the relationship between partial pressure, solubility, and concentration of gases.
- Gases diffuse along their partial pressure gradients, from regions of high partial pressure to regions of low partial pressure.
- During external respiration, oxygen loads from alveoli into pulmonary capillaries and carbon dioxide unloads from pulmonary capillaries into alveoli.
- During internal respiration, oxygen unloads from systemic capillaries into cells and carbon dioxide loads from cells into systemic capillaries.
- Efficient gas exchange depends on several factors including surface area, partial pressure gradients, blood flow and airflow.

- During external respiration, ventilation-perfusion coupling maintains airflow and blood flow in proper proportions for efficient gas exchange.

** Now is a good time to go to quiz questions 4-8:
- Click the Quiz button on the left side of the screen.
- Click on the scrolling page list at the top of the screen and choose "4. External Respiration".
- Work through quiz questions 4-8.

## Notes on Quiz Questions:

### Quiz Question #1a:

- This question asks you to calculate the partial pressure of oxygen gas in an atmosphere in a fictitious situation.

### Quiz Question #1b:

- This question asks you to determine the relative amount of carbon dioxide and oxygen dissolved in the blood in a fictitious situation.

### Quiz Question #2a:

- This question asks you to determine gas solubility differences.

### Quiz Question #2b:

- This question asks you to find ways to increase the solubility of nitrogen in the blood.

### Quiz Question #3:

- This question asks you to predict what happens to the concentration of nitrogen gas in the blood of divers who are under pressure.

### Quiz Question #4:

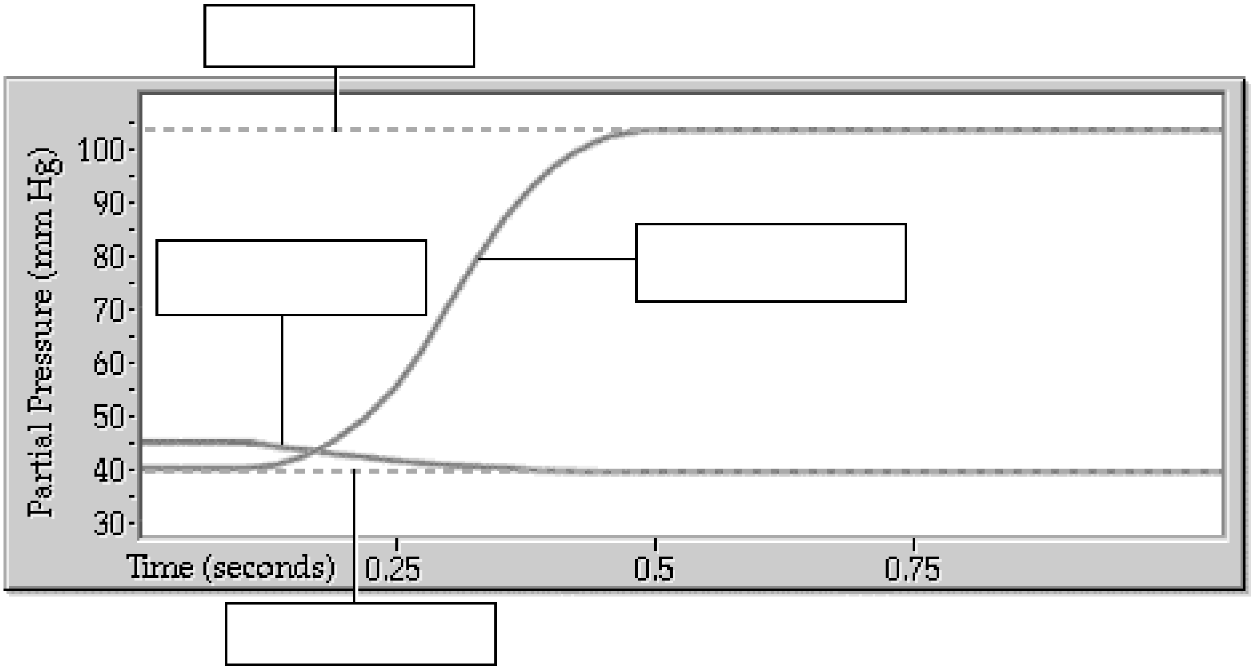
- This question asks you to recall the partial pressures of carbon dioxide and oxygen gas during external respiration.

### Quiz Question #5:

- This question asks you to recall the partial pressures of carbon dioxide and oxygen gas during internal respiration.

### Quiz Question #6:

- This question asks you to label a graph of partial pressures vs. time during external respiration.




**Quiz Question #7:**

- This question asks you to identify the factors that could increase the partial pressure of oxygen in the pulmonary capillaries.

**Quiz Question #8:**

- This question asks you to predict what happens during an asthma attack.

**Study Questions on Gas Exchange:**

1. (Page 1.) What four gases are found in the atmosphere?

2. (Page 1.) Each of these gases exerts a pressure, what is the total pressure of all the gases in the atmosphere called?

3. (Page 1.) What is a typical atmospheric pressure at sea level in millimeters of Hg?

4. (Page 1.) What is Dalton's Law of Partial Pressures?

5. (Page 2.) As altitude increases, what happens to the atmospheric pressure?

6. (Page 2.) Oxygen gas makes up 20.9% of the atmosphere at sea level where the atmospheric pressure is 760 mm Hg. a. What percentage of oxygen gas is there at a high altitude, where the atmospheric pressure is 440 mm Hg? b. Explain what happens to the partial pressure of oxygen gas at the high altitude.

7. (Page 3.) Henry's Law states that the amount of gas which dissolves in a liquid is proportional to what two factors?

8. (Page 4.) In a container containing water and oxygen gas, some of the oxygen dissolves in the water. When equilibrium is reached, the pressure of the oxygen gas above the water ____________ the pressure of oxygen in the liquid.

a. is greater than b. is less than c. is equal to

9. (Page 4.) In a container containing water and oxygen gas, some of the oxygen dissolves in the water. When equilibrium is reached, the rate of oxygen gas diffusing into the water ____________ the rate of oxygen gas diffusing out of the water.
a. is greater than b. is less than c. is equal to

10. (Page 4.) In a container containing water and oxygen gas, if you increase the pressure in the container ______ oxygen molecules dissolves in the liquid, moving from a region of _________ pressure.
a. more, low to high b. less, low to high
c. more, high to low d. less high to low

11. (Page 4.) If you have two closed containers of water and gas at the same pressure and one container contains oxygen gas and the other contains carbon dioxide gas, which of these statements is true?
a. Both gases dissolve equally in the water.
b. The carbon dioxide gas dissolves in the water to a greater extent than the oxygen gas.
c. The oxygen gas dissolves in the water to a greater extent than the carbon dioxide gas.

12. (Page 4.) Which is more soluble in water, carbon dioxide or oxygen?

13. (Page 6.) a. Where do both internal and external respiration occur? b. What happens to oxygen and carbon dioxide during both internal and external respiration?

14. (Page 7.) Efficient external respiration depends on what three main factors?

15. (Page 7.) What two factors account for the surface area and structure of the respiratory membrane allowing for efficient external respiration?

16. (Page 8.) What three factors account for the differences in the partial pressures in the alveoli from those in the atmosphere?

17. (Page 8.) As air travels through the respiratory passageways to the alveoli it is humidified, picking up water molecules. What effect does this have on the partial pressure of water?

18. (Page 8.) As gases are exchanged between the alveoli and pulmonary capillaries, what happens to the partial pressures of both gases?

19. (Page 8.) Do the alveoli completely empty between breaths?

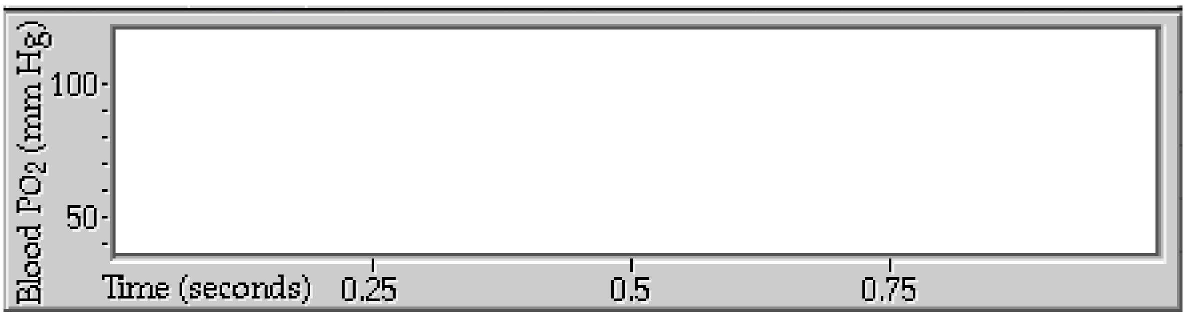
20. (Page 9.) The $P_{O_2}$ of the alveolar air is 104 mm Hg. At rest, the oxygen-poor blood entering the pulmonary capillaries has a $P_{O_2}$ of 40 mm Hg. As blood flows past the alveolus, the $P_{O_2}$ ___________.
a. increases b. decreases

21. (Page 9.) The $P_{O_2}$ of the alveolar air is 104 mm Hg. At rest, the oxygen-poor blood entering the pulmonary capillaries has a $P_{O_2}$ of 40 mm Hg. During external respiration there is a net diffusion of oxygen along its partial pressure gradient, from the alveolus into the blood, until equilibrium is reached. As this occurs, the $P_{O_2}$ of the blood _____________.

a. increases to 104 mm Hg b. decreases to 40 mm Hg

22. (Page 9.) During external respiration, oxygen equilibrium is reached ______________ of the pulmonary capillary.
a. at the end b. within the first half c. within the first third

23. (Page 9.) Fill out this graph to show what happens to the partial pressure of oxygen in the pulmonary arteries during external respiration:

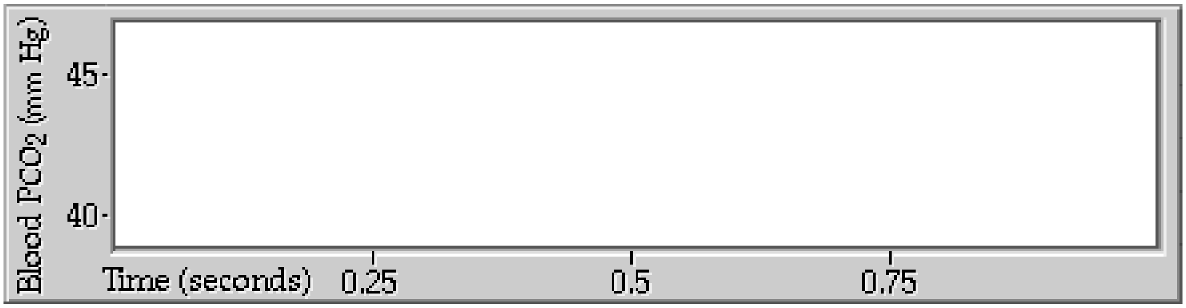



24. (Page 10.) The $P_{CO_2}$ of the alveolar air is 40 millimeters of mercury. At rest, the $P_{CO_2}$ of the blood entering the pulmonary capillaries is 45 millimeters of mercury. As blood flows past the alveolus, the $P_{CO_2}$ ____________.
a. increases b. decreases

25. (Page 10.) The $P_{CO_2}$ of the alveolar air is 40 millimeters of mercury. At rest, the $P_{CO_2}$ of the blood entering the pulmonary capillaries is 45 millimeters of mercury. During external respiration carbon dioxide diffuses along its partial pressure gradient, from the blood into the alveolus, until equilibrium is reached. As blood flows past the alveolus, the $P_{CO_2}$ ____________.
a. increases to 45 mm Hg b. decreases to 40 mm Hg

26. (Page 10.) During external respiration, carbon dioxide equilibrium is reached ______________ of the pulmonary capillary.
a. at the end b. within the last half c. within the first four-tenths

27. (Page 10.) Fill out this graph to show what happens to the partial pressure of carbon dioxide in the pulmonary arteries during external respiration:




28. (Page 11.) Why does carbon dioxide have a smaller partial pressure gradient than oxygen?

29. (Page 12.) Explain how ventilation-perfusion coupling facilitates efficient gas exchange.

30. (Page 12.) What factor causes vasoconstriction and vasodilation associated with ventilation-perfusion coupling?

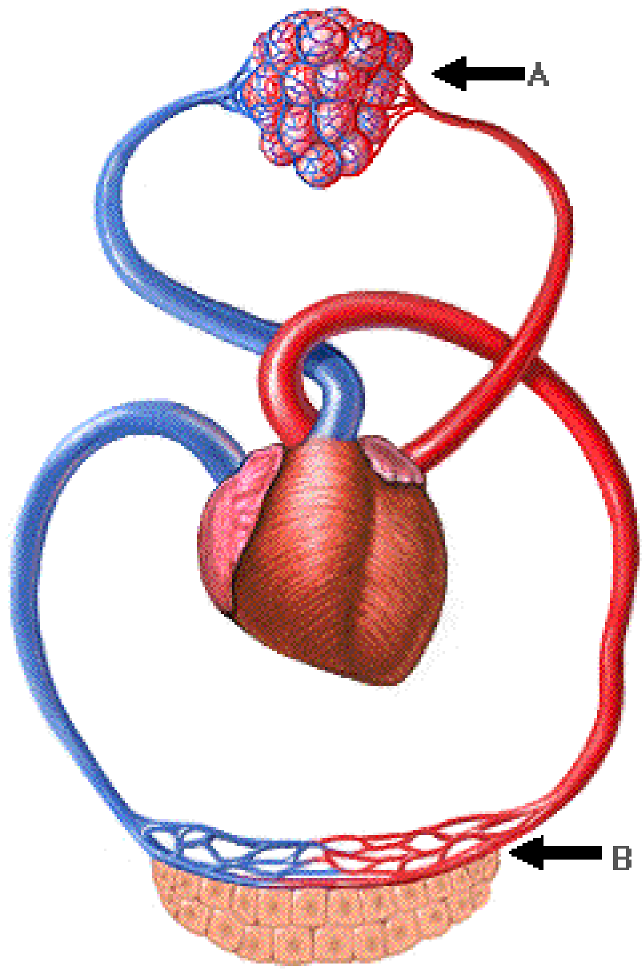
31. (Page 13.) How do bronchioles respond to levels of blood gases?

32. (Page 13.) What would cause the $P_{CO_2}$ in the bronchioles to rise?

33. (Page 13.) During ventilation-perfusion coupling, the arterioles respond to changes in _________ and the bronchioles respond to changes in _____________ .
a. $P_{O_2}$ b. $P_{CO_2}$

34. (Page 14.) Match the following:

| | |
|---|---|
| a. Arterioles constrict | Low $P_{CO_2}$ |
| b. Arterioles dilate | Low $P_{O_2}$ |
| c. Bronchioles constrict | High $P_{CO_2}$ |
| d. Bronchioles dilate | High $P_{O_2}$ |




35. (Page 15.) On this diagram, indicate where both internal and external respiration occurs.

36. (Page 15.) On this diagram, indicate where there would be a net movement of oxygen into the blood and carbon dioxide out of the blood.

37. (Page 15.) On this diagram, indicate where there would be a net movement of oxygen out of the blood and carbon dioxide into the blood.

38. (Page 15.) What three factors affect the exchange of oxygen and carbon dioxide during internal respiration?

39. (Page 16.) Why would the rate of blood flow vary within a tissue?

40. (Page 16.) As gases are exchanged between the tissues and systemic capillaries, what happens to the partial pressures of both gases?

41. (Page 16.) The $P_{O_2}$ of the blood entering the systemic capillaries is 100 mm Hg. As blood flows through the systemic capillaries, the $P_{O_2}$ __________.
 a. increases b. decreases

42. (Page 16.) The $P_{CO_2}$ of the blood entering the systemic capillaries is 40 mm Hg. As blood flows through the systemic capillaries, the $P_{CO_2}$ __________.
 a. increases b. decreases

43. (Page 16.) The $P_{O_2}$ of the blood entering the systemic capillaries is 100 mm Hg. During internal respiration there is a net diffusion of oxygen along its partial pressure gradient, from the blood into the tissues, until equilibrium is reached. As this occurs, the $P_{O_2}$ of the blood ____________.
 a. increases to 104 mm Hg b. decreases to about 40 mm Hg

44. (Page 16.) The $P_{CO_2}$ of the blood entering the systemic capillaries is about 40 millimeters of mercury. At rest, the $P_{CO_2}$ of the blood leaving the systemic capillaries is about 45 millimeters of mercury. As blood flow through the systemic capillaries, the $P_{CO_2}$ ____________.

a. increases b. decreases

45. (Page 16.) During internal respiration carbon dioxide diffuses along its partial pressure gradient until equilibrium is reached. As blood flows through the systemic capillaries, the $P_{CO_2}$ ____________.

a. increases to about 45 mm Hg b. decreases to about 40 mm Hg

# Gas Transport



**Page 1. Introduction**

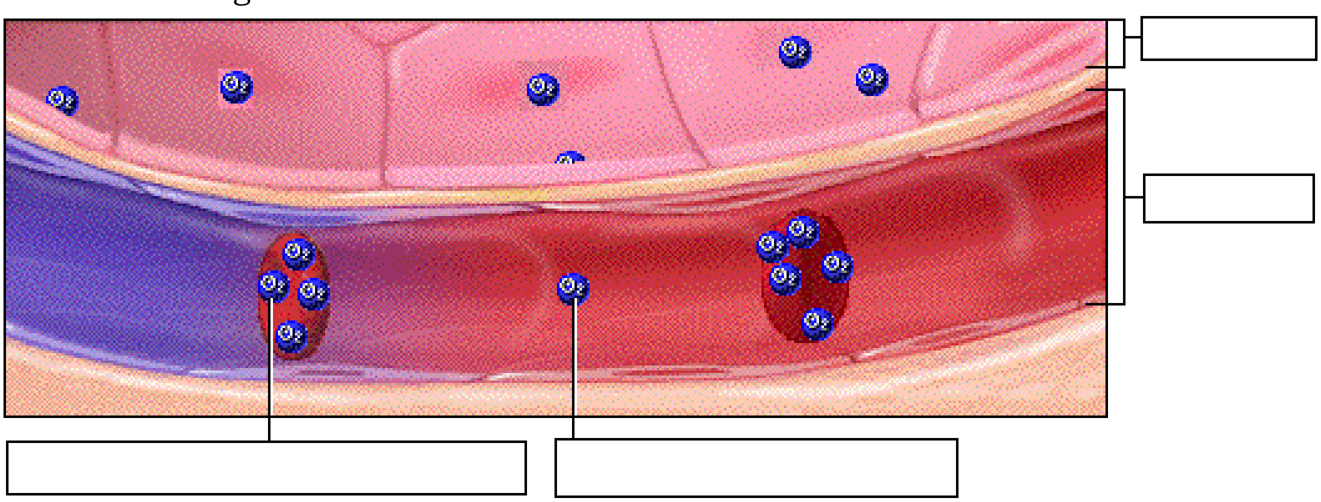
- The blood transports oxygen and carbon dioxide between the lungs and other tissues throughout the body.
- These gases are carried in several different forms:
  1. dissolved in the plasma
  2. chemically combined with hemoglobin
  3. converted into a different molecule

**Page 2. Goals**

- To explore how oxygen is transported in the blood.
- To explore how carbon dioxide is transported in the blood.
- To understand the effect of variables, such as $P_{O_2}$ and $P_{CO_2}$, on oxygen and carbon dioxide transport.

**Page 3. Oxygen Transport**

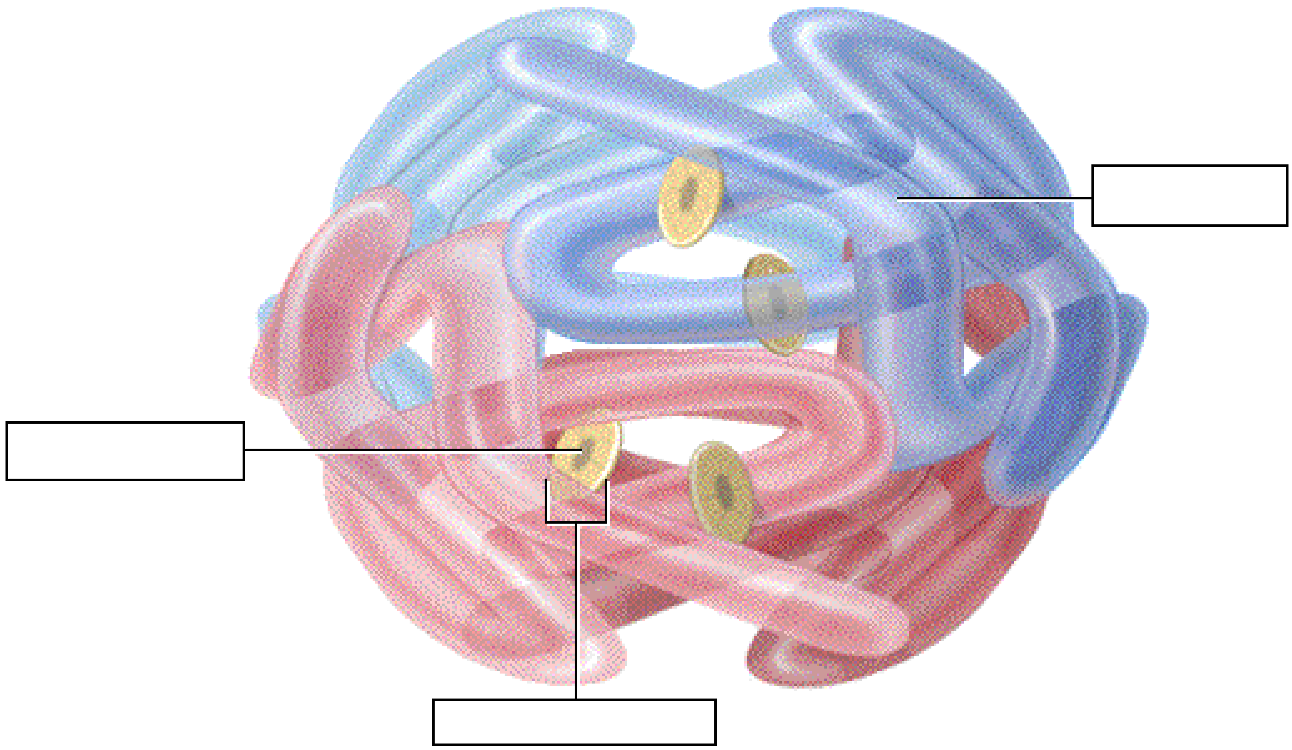
- Transport of oxygen during external respiration**:**
  - With its low solubility, only approximately 1.5% of the oxygen is transported dissolved in plasma.
- The remaining 98.5% diffuses into red blood cells and chemically combines with hemoglobin.
- Label this diagram:



**Page 4. Hemoglobin**

- Within each red blood cell, there are approximately 250 million hemoglobin molecules.
- Each hemoglobin molecule consists of:
  1. A globin portion composed of 4 polypeptide chains.
  2. Four iron-containing pigments called heme groups.
- Each hemoglobin molecule can transport up to 4 oxygen molecules because each iron atom can bind one oxygen molecule.
- When 4 oxygen molecules are bound to hemoglobin, it is 100% saturated; when there are fewer, it is partially saturated.

- Oxygen binding occurs in response to the high partial pressure of oxygen in the lungs.
- When hemoglobin binds with oxygen, it is called oxyhemoglobin.
- When one oxygen binds to hemoglobin, the other oxygen molecules bind more readily. This is called cooperative binding. Hemoglobin's affinity for oxygen increases as its saturation increases.
- Label this diagram:



**Page 5. Oxyhemoglobin and Deoxyhemoglobin**

- The formation of oxyhemoglobin occurs as a reversible reaction, and is written as in this chemical equation:

$$\underset{\substack{\text{Deoxyhemoglobin}\\\text{(reduced hemoglobin)}}}{Hb} + \underset{\text{Oxygen}}{O_2} \underset{\text{tissues}}{\overset{\text{lungs}}{\rightleftharpoons}} \underset{\text{Oxyhemoglobin}}{HbO_2}$$

- In reversible reactions, the direction depends on the quantity of products and reactants present.
- In the lungs, where the partial pressure of oxygen is high, the reaction proceeds to the right, forming oxyhemoglobin.

$$\underset{\substack{\text{Deoxyhemoglobin}\\\text{(reduced hemoglobin)}}}{Hb} + \underset{\text{Oxygen}}{O_2} \underset{\text{tissues}}{\overset{\text{lungs}}{\rightleftharpoons}} \underset{\text{Oxyhemoglobin}}{HbO_2}$$

- In organs throughout the body where the partial pressure of oxygen is low, the reaction reverses, proceeding to the left. Oxyhemoglobin releases oxygen, forming deoxyhemoglobin, which is also called reduced hemoglobin.

$$Hb + O_2 \underset{tissues}{\overset{lungs}{\rightleftharpoons}} HbO_2$$

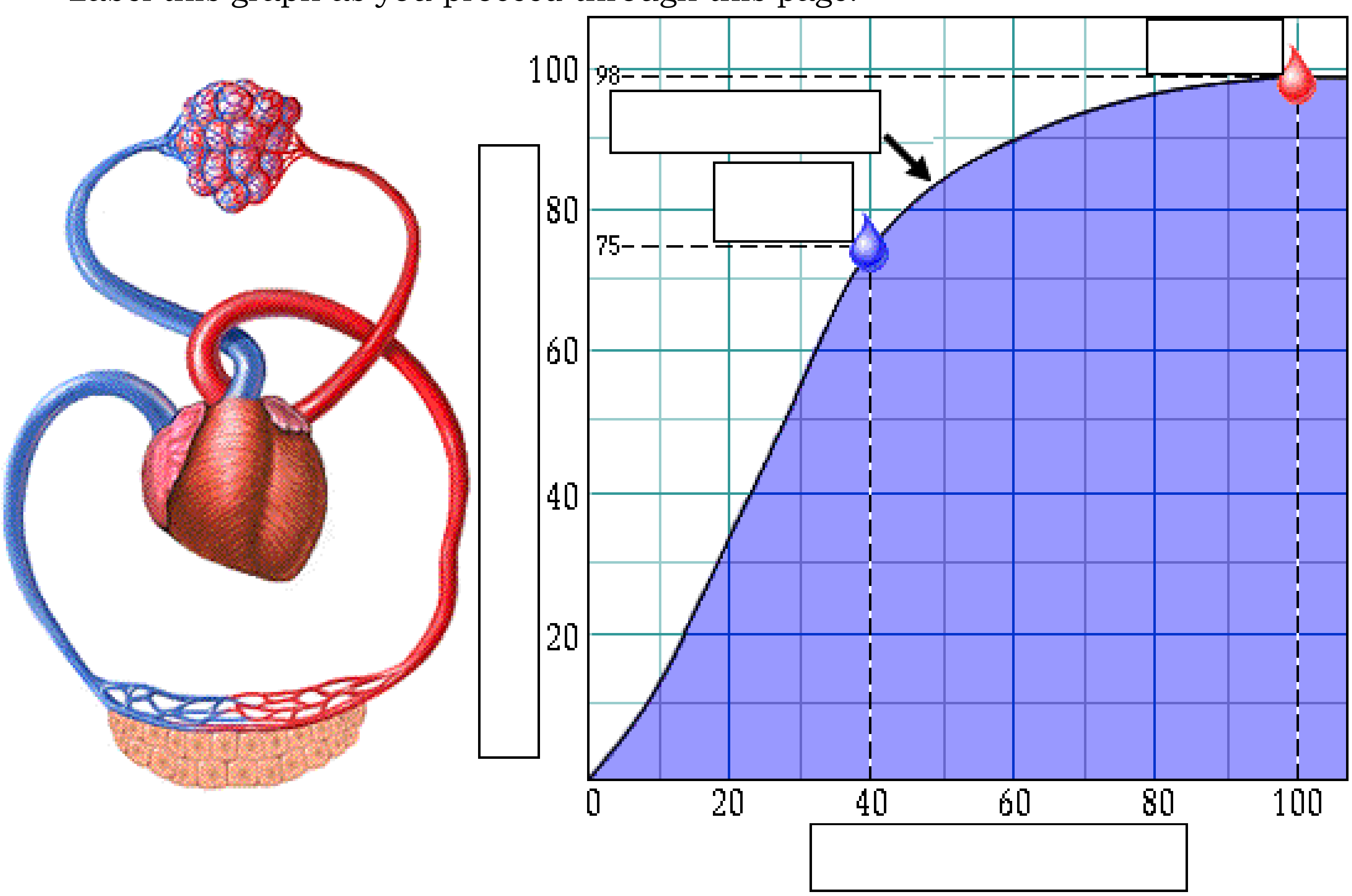
Hb: Deoxyhemoglobin (reduced hemoglobin) | $O_2$: Oxygen | $HbO_2$: Oxyhemoglobin

- Notice that the affinity of hemoglobin for oxygen decreases as its saturation decreases.

**Page 6. Oxygen-Hemoglobin Dissociation Curve**

- The degree of hemoglobin saturation is determined by the partial pressure of oxygen, which varies in different organs throughout the body.
- When these values are graphed, they produce the oxygen-hemoglobin dissociation curve. Notice that the axes on the graph are: partial pressure of oxygen and percent saturation of hemoglobin.
- In the lungs, the partial pressure of oxygen is approximately 100 millimeters of mercury. At this partial pressure, hemoglobin has a high affinity for oxygen, and is 98% saturated.
- In the tissues of other organs, a typical partial pressure of oxygen is 40 millimeters of mercury. Here, hemoglobin has a lower affinity for oxygen and releases some but not all of its oxygen to the tissues. When hemoglobin leaves the tissues it is still 75% saturated.

- Label this graph as you proceed through this page:




- Notice that the oxygen-hemoglobin dissociation curve is an S-shaped curve, with a nearly flat slope at high $P_{O_2}$'s and a steep slope at low $P_{O_2}$'s.

## Page 7. Hemoglobin Saturation at High $P_{O_2}$'s

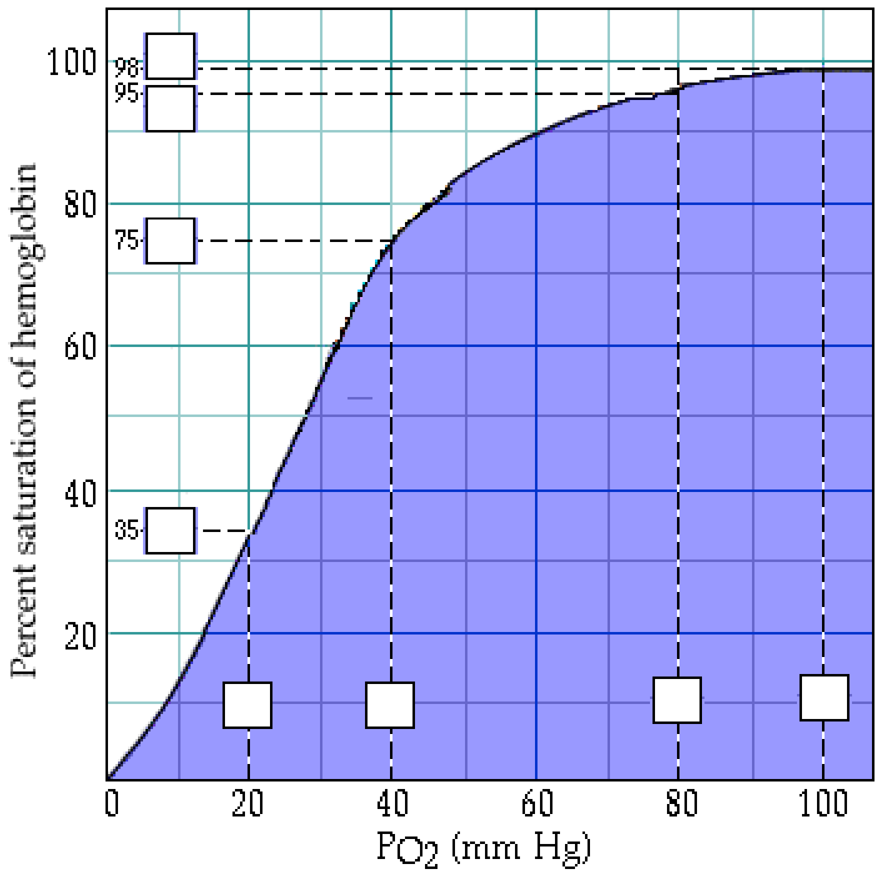
- A closer look at the flat region of the oxygen-hemoglobin dissociation curve between 80 and 100 millimeters of mercury:
  - In the lungs at sea level, a typical $P_{O_2}$ is 100 millimeters of mercury. At this $P_{O_2}$, hemoglobin is 98% saturated.
  - In the lungs of a hiker at higher elevations or a person with particular cardiopulmonary diseases, the $P_{O_2}$ may be 80 millimeters of mercury. At this $P_{O_2}$, hemoglobin is 95% saturated.
  - Notice that even though the $P_{O_2}$ differs by 20 millimeters of mercury there is almost no difference in hemoglobin saturation. This means that although the $P_{O_2}$ in the lungs may decline below typical sea level values, hemoglobin still has a high affinity for oxygen and remains almost fully saturated.

## Page 8. Hemoglobin Saturation at Low $P_{O_2}$'s

- A closer look at the steep region of the graph between 20 and 40 millimeters of mercury.
  - A $P_{O_2}$ of 40 millimeters of mercury is typical in resting organs.
  - At 40 millimeters of mercury, hemoglobin has a lower affinity for oxygen and is 75% saturated.
- In vigorously contracting muscles, would you expect the $P_{O_2}$ is lower than in resting muscle because an actively contracting muscle uses more oxygen, so it has a lower $P_{O_2}$ than a resting muscle, typically 20 millimeters of mercury. At this $P_{O_2}$, hemoglobin is only 35% saturated.
- As the $P_{O_2}$ decreases, hemoglobin releases much more oxygen to the tissues. This allows the body to closely match oxygen unloading by hemoglobin to oxygen utilization by the tissues.

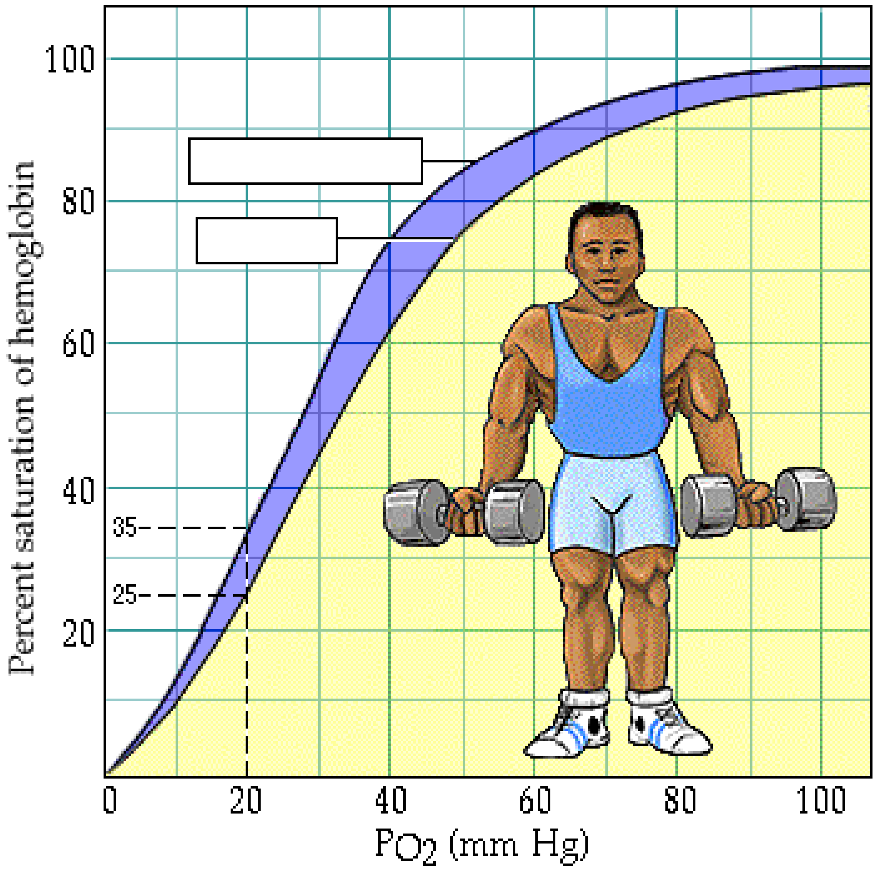
- Fill in the blanks on the graph with the appropriate letters below:

  a. Corresponds to the partial pressure of oxygen in the lungs at a high altitude.
  b. Corresponds to the partial pressure of oxygen in the tissues at rest.
  c. Corresponds to the partial pressure of oxygen in the lungs at a low altitude.
  d. Corresponds to the partial pressure of oxygen in active tissues.
  e. Corresponds to the percent saturation of hemoglobin in the lungs at a high altitude.
  f. Corresponds to the percent saturation of hemoglobin in the tissues at rest.
  g. Corresponds to the percent saturation of hemoglobin in the lungs at a low altitude.
  h. Corresponds to the percent saturation of hemoglobin in active tissues.



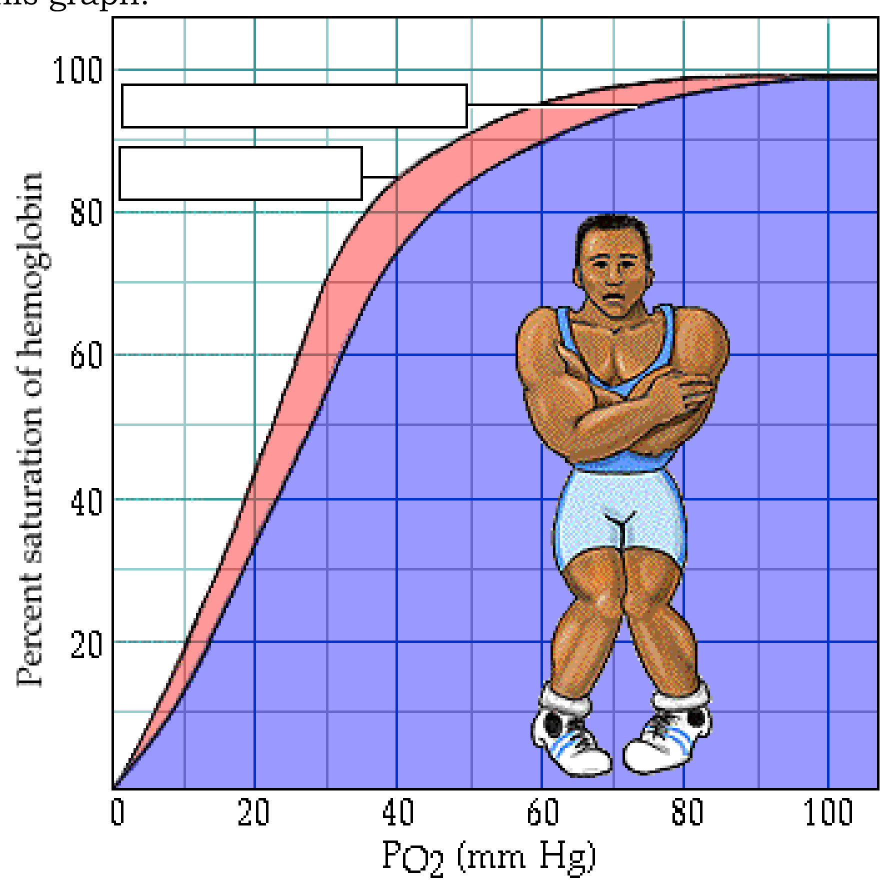

**Page 9. Factors Altering Hemoglobin Saturation**

- Factors which alter hemoglobin saturation:
  1. pH
  2. temperature
  3. $P_{CO_2}$
  4. BPG (2,3-biphosphoglycerate)
- All of these factors, together or individually, play a role during exercise.
- During vigorous exercise, contracting muscles produce more metabolic acids, such as lactic acid, which lower the pH, more heat, and more carbon dioxide. In addition, higher temperature and lower $P_{O_2}$ increase the production of BPG by the red blood cells.
- These conditions decrease hemoglobin's affinity for oxygen, releasing more oxygen to the active muscle cells.
- Let's look at a typical $P_{O_2}$ of active muscle, 20 millimeters of mercury. At a normal blood pH, hemoglobin releases 65% of its oxygen to the muscle cells, and remains 35% saturated. However, as the muscle cells release lactic acid, the pH decreases and hemoglobin releases 75% of its oxygen, leaving it 25% saturated.
- When pH decreases, the curve shifts to the right. This represents increased oxygen unloading compared to normal blood pH.  A similar shift to the right occurs in response to increased temperature, $P_{CO_2}$, or BPG.
- Label this graph:




**Page 10. Predict the Effect of Decreased Temperature**

- Label this graph:

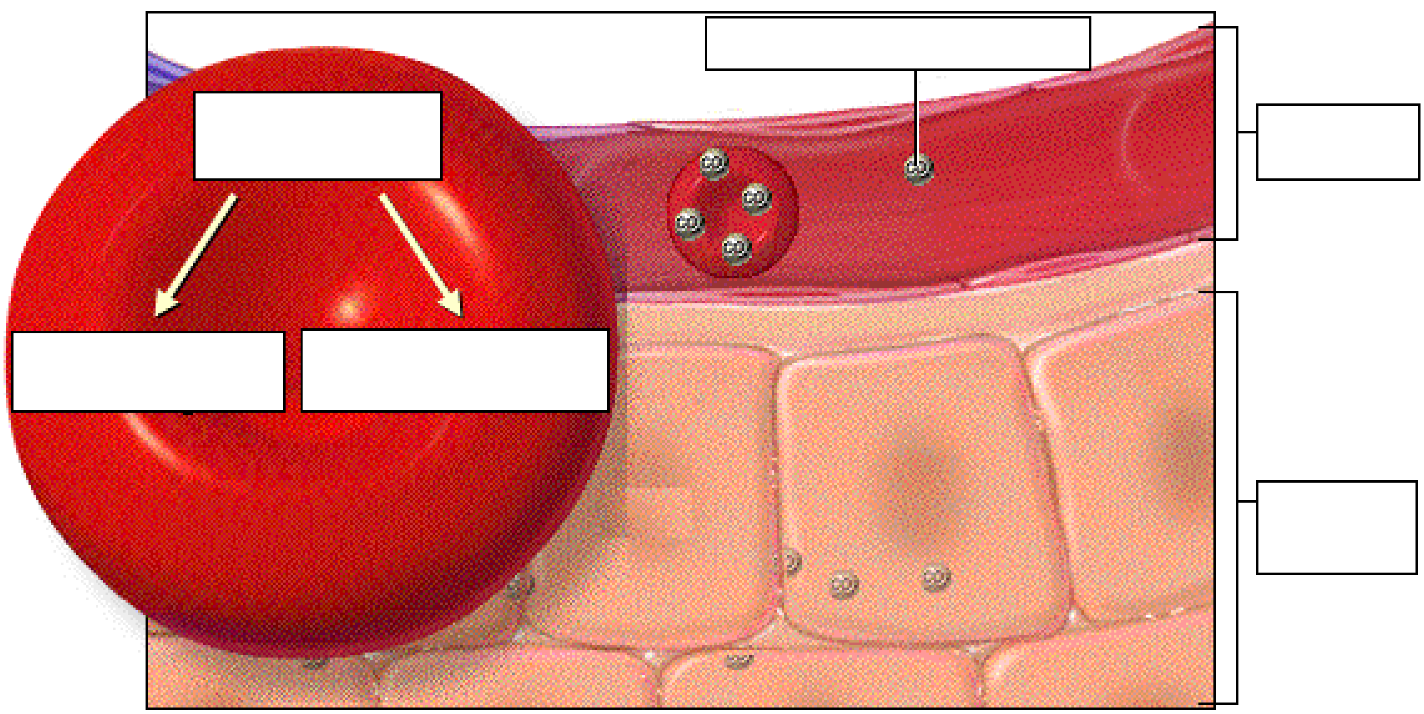


- If body tissues are chilled, their hemoglobin saturation changes.
- At decreased temperatures, hemoglobin's affinity for oxygen is higher, so hemoglobin releases less oxygen to less active tissues. Represented graphically, the curve shifts to the left.
- A similar shift to the left occurs in response to increased pH, decreased $P_{CO_2}$, and decreased BPG.

** Now is a good time to go to quiz questions 1-4:
- Click the Quiz button on the left side of the screen.
- Work through questions 1-4.
- After answering question 4, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "11. $CO_2$ Transport".

**Page 11. $CO_2$ Transport**

- Carbon dioxide transport:
  - Carbon dioxide is produced by cells throughout the body.
  - It diffuses out of the cells and into the systemic capillaries, where approximately 7% is transported dissolved in plasma.
  - The remaining carbon dioxide diffuses into the red blood cells. Within the red blood cells, approximately 23% chemically combines with hemoglobin, and 70% is converted to bicarbonate ions, which are then transported in the plasma.
- Fill in this diagram:



**Page 12. $CO_2$ Transport: Carbaminohemoglobin (Tissues)**

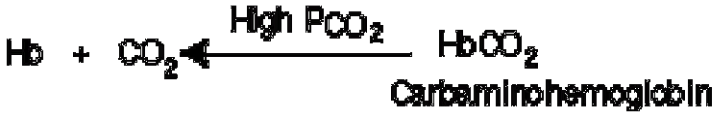
- Of the total carbon dioxide in the blood, 23% binds to the globin portion of the hemoglobin molecule to form carbaminohemoglobin, as written in this equation:

$$\mathrm{Hb} + CO_2 \xleftarrow{\text{Low } P_{CO_2}} \underset{\text{Carbaminohemoglobin}}{\mathrm{HbCO_2}}$$

- Carbaminohemoglobin forms in regions of high $P_{CO_2}$, as blood flows through the systemic capillaries in the tissues.

**Page 13. $CO_2$ Transport: Carbaminohemoglobin (Lungs)**

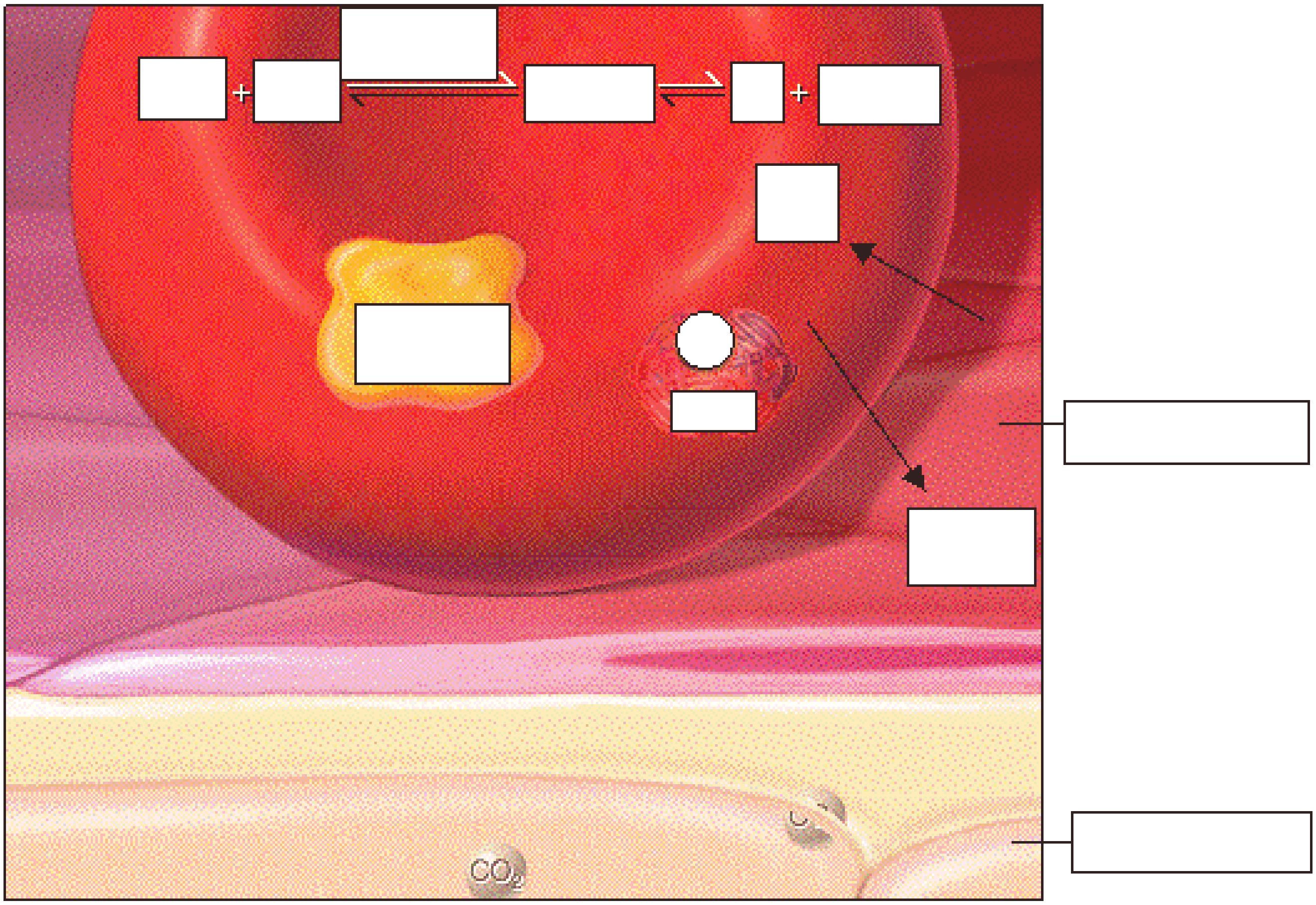
- The formation of carbaminohemoglobin is reversible.




- In the lungs, which have a lower $P_{CO_2}$, carbon dioxide dissociates from carbaminohemoglobin, diffuses into the alveoli, and is exhaled.

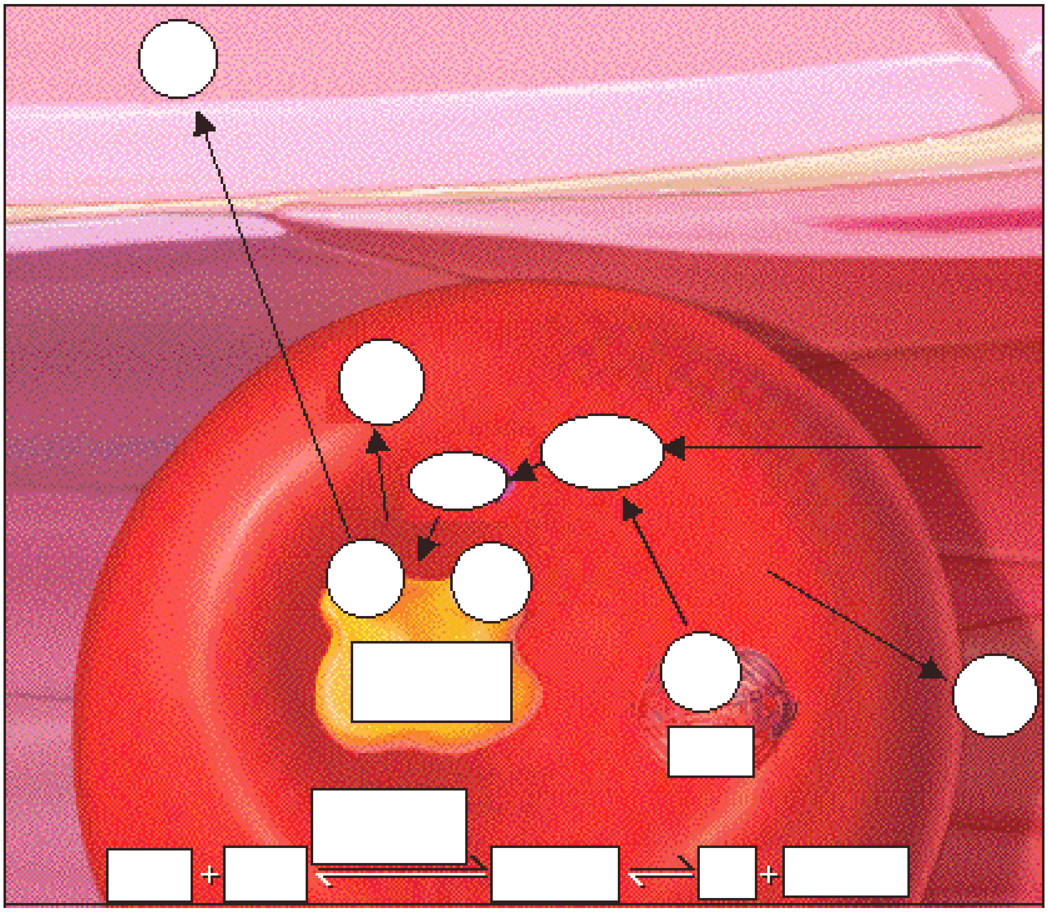
**Page 14. $CO_2$ Transport: Bicarbonate Ions (Tissues)**

- Of the total carbon dioxide in the blood, 70% is converted into bicarbonate ions within the red blood cells, in a sequence of reversible reactions. The bicarbonate ions then enter the plasma.
- In regions with high $P_{CO_2}$, carbon dioxide enters the red blood cell and combines with water to form carbonic acid. This reaction is catalyzed by the enzyme carbonic anhydrase. The same reaction occurs in the plasma, but without the enzyme it is very slow.
- Carbonic acid dissociates into hydrogen ions and bicarbonate ions. The hydrogen ions produced in this reaction are buffered by binding to hemoglobin. This is written as HHb.
- In order to maintain electrical neutrality, bicarbonate ions diffuse out of the red blood cell and chloride ions diffuse in. This is called the chloride shift.
- Within the plasma, bicarbonate ions act as a buffer and play an important role in blood pH control.
- Label this diagram to show what happens at the tissues:




**Page 15. $CO_2$ Transport: Bicarbonate Ions (Lungs)**

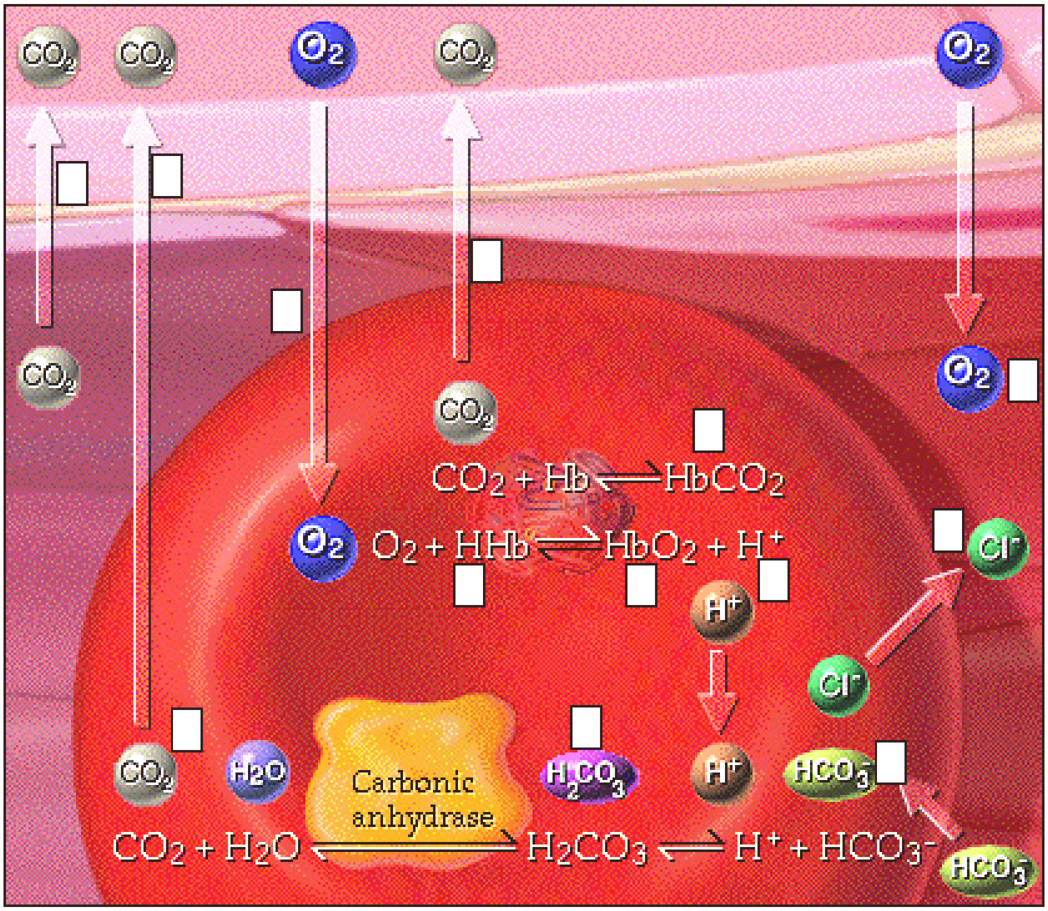
- In the lungs, carbon dioxide diffuses out of the plasma and into the alveoli. This lowers the $P_{CO_2}$ in the blood, causing the chemical reactions to reverse and proceed to the left.
- In the lungs, the bicarbonate ions diffuse back into the red blood cell, and the chloride ions diffuse out of the red blood cell. Recall that this is called the chloride shift.
- The hydrogen ions are released from hemoglobin, and combine with the bicarbonate ion to form carbonic acid.
- Carbonic acid breaks down into carbon dioxide and water. This reverse reaction is also catalyzed by the enzyme carbonic anhydrase.
- Label this diagram:



**Page 16. Summary: $O_2$ Loading and $CO_2$ Unloading in the Lungs**

- Summary of external respiration in the lungs.
- Although we will look at the processes step by step, they actually occur simultaneously.
- Remember, gases always follow their partial pressure gradients.
- As you go through the steps, place the numbers that correspond with the steps in the blanks on this diagram:
  - During external respiration, a small amount of oxygen (1) remains dissolved in the plasma. However, the majority of the oxygen (2) continues into the red blood cells, where it combines with deoxyhemoglobin (3) to form oxyhemoglobin (4), releasing a hydrogen ion (5).
  - When hemoglobin is saturated with oxygen, its affinity for carbon dioxide decreases. Any carbon dioxide combined with hemoglobin (6) dissociates and diffuses out of the red blood cell (7), through the plasma and into the alveoli. In other words, oxygen loading facilitates carbon dioxide unloading from hemoglobin. This interaction is called the Haldane effect.
  - The hydrogen ion released from hemoglobin combines with a bicarbonate ion (8), which diffuses into the red blood cell from the plasma in exchange for a chloride ion (9). Recall that this exchange is the chloride shift. The reaction between hydrogen and bicarbonate ions forms carbonic acid (10).
  - Carbonic acid then breaks down into water and carbon dioxide (11), catalyzed by the enzyme carbonic anhydrase. The water produced by this reaction may leave the red blood cell, or remain as part of the cytoplasm. The carbon dioxide

diffuses out of the red blood cell (12) into the plasma and then into the alveoli. The small amount of carbon dioxide transported in the plasma diffuses into the alveoli (13).

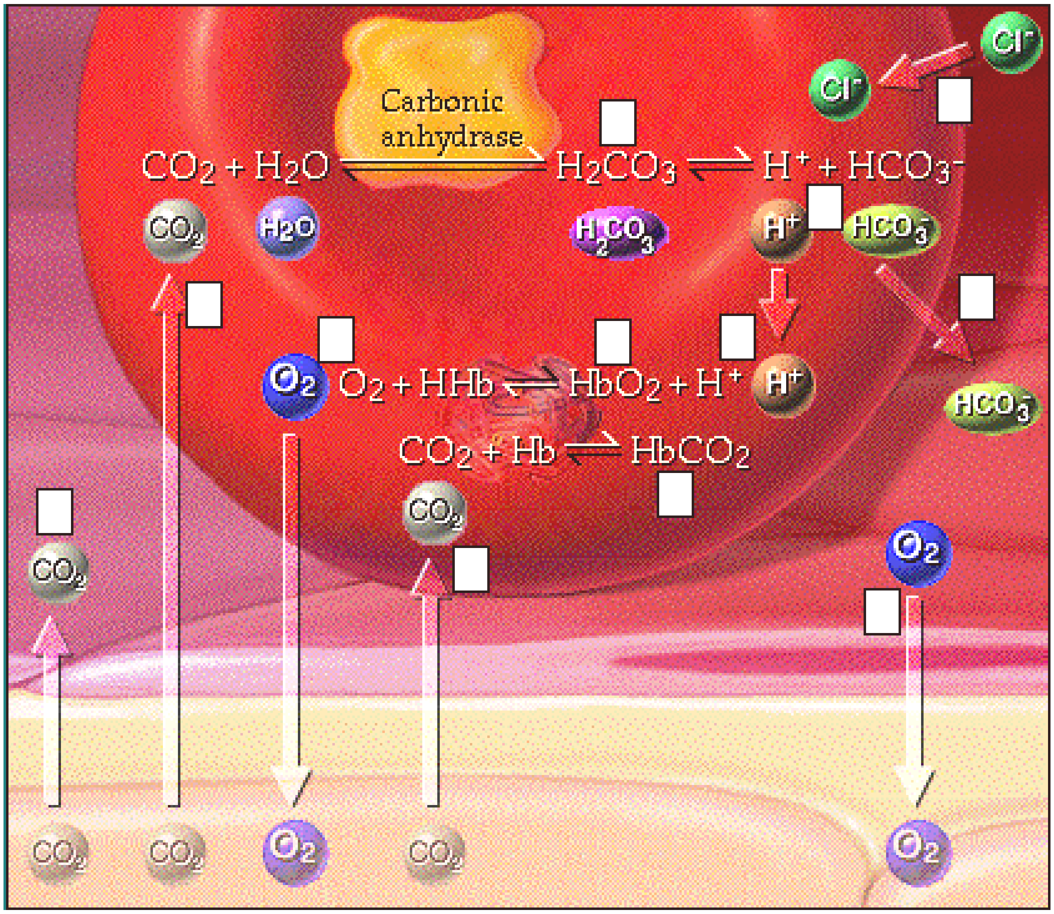



**Page 17. Summary: $O_2$ Unloading and $CO_2$ Loading in the Tissues**

Summary of internal respiration in the tissues.

- As you go through the steps, place the numbers that correspond with the steps in the blanks on this diagram:
  - During internal respiration, a small amount of carbon dioxide (1) remains dissolved in the plasma, but most of the carbon dioxide (2) continues into the red blood cells where much of it combines with water to form carbonic acid (3) or combines with hemoglobin to form carbaminohemoglobin (11). This reaction is catalyzed by carbonic anhydrase. The carbonic acid then dissociates into hydrogen and bicarbonate ions (4).
  - During the chloride shift, bicarbonate ions (5) diffuse out of the red blood cell in exchange for chloride ions (6). Bicarbonate ions act as buffers within the plasma, controlling blood pH.
  - Within the red blood cell, hydrogen ions (7) are buffered by hemoglobin (8). When hemoglobin binds hydrogen ions, it has a lower affinity for oxygen. As a result, oxygen (9) dissociates from hemoglobin, diffuses out of the red blood cell and into the tissues. The interaction between hemoglobin's affinity for oxygen and its affinity for hydrogen ions is called the Bohr effect. By forming hydrogen ions, carbon dioxide loading facilitates oxygen unloading.

- The small amount of oxygen transported in the dissolved state (10) also diffuses out of the plasma and into the tissue cells.




**Page 18 Summary**

- Oxygen is transported in two ways:
  - dissolved in plasma, and
  - bound to hemoglobin as oxyhemoglobin
- The oxygen saturation of hemoglobin is affected by:
  - $P_{O_2}$
  - pH
  - temperature
  - $P_{CO_2}$, and
  - BPG
- Carbon dioxide is transported in three ways:
  - dissolved in plasma
  - bound to hemoglobin as carbaminohemoglobin, and
  - converted to bicarbonate ions
- Oxygen loading facilitates carbon dioxide unloading from hemoglobin. This is known as the Haldane effect.
- When the pH decreases, carbon dioxide loading facilitates oxygen unloading. The interaction between hemoglobin's affinity for oxygen and its affinity for hydrogen ions is called the Bohr effect.

** Now is a good time to go to quiz questions 5-10.

- Click the Quiz button on the left side of the screen.
- Click on the scrolling page list at the top of the screen and choose "5. Bicarbonate Ion Equation".
- Work through quiz questions 5-10.

## Notes on Quiz Questions:

### Quiz Question #1: Oxygen and Hemoglobin

- This question asks you to watch an animation of oxygen binding to hemoglobin and determine where in the body the process occurs.

### Quiz Question #2: Oxygen-Hemoglobin Dissociation Curve

- This question asks you to label the oxygen-hemoglobin dissociation curve.

### Quiz Question #3: Shifted Oxygen-Hemoglobin Dissociation Curve

- This question asks you to choose the shift in the oxygen-hemoglobin dissociation curve that occurs when there is a high temperature.

### Quiz Question #4a: Fetal Hemoglobin

- This question asks you to choose the curve that has the higher oxygen saturation.

### Quiz Question #4b: Fetal Hemoglobin

- This question asks you to choose which graph represents fetal hemoglobin as opposed to maternal hemoglobin.
- Fetal hemoglobin has a higher affinity for oxygen than maternal hemoglobin; therefore as the mother's blood enters the placenta, oxygen is transferred from her blood into the fetus's blood. Thus at the same $P_{O2}$, the fetal hemoglobin has a higher percent oxygen saturation than the mother's blood.

### Quiz Question #5: Bicarbonate Ion Equation

- This question asks you to put together the reaction by which carbon dioxide and water form bicarbonate.

### Quiz Question #6: Carbon Dioxide and Hemoglobin

- This question shows you an animation, then asks you to predict if the process occurs in areas of high or low $P_{CO2}$.

### Quiz Question #7: Name That Reaction

- This question asks you to watch an animation, then determine if it is the Haldane effect, Bohr effect, or Chloride shift.

### Quiz Question #8: Gas Transport: Lungs

- This question asks you to determine which direction reactions go in the lungs.

### Quiz Question #9: Gas Transport: Tissues

- This question asks you to determine which direction reactions go in the tissues.

### Quiz Question #10: Lungs or Tissues

- This question asks you to determine if a number of different processes occur in the lungs or the tissues.

**Study Questions on Gas Transport:**

1. (Page 3.) When oxygen diffuses into the blood during external respiration, what two places within the blood does it end up? What percentage of oxygen ends up in each of these two places?

2. (Page 3.) Why does so little oxygen dissolve in the plasma?

3. (Page 3.) Label the diagram on p. 3.

4. (Page 4.) What are the two components of hemoglobin? What is each part made of?

5. (Page 4.) In each hemoglobin molecule:
   a. How many polypeptide chains are there?
   b. How many hemes are there?
   c. How many irons are there?
   d. How many oxygens can bind?

6. (Page 4.) Where, within the hemoglobin, does oxygen bind?

7. (Page 4.) a. When is hemoglobin said to be "saturated"? b. When is hemoglobin said to be "partially saturated"?

8. (Page 4.) What is hemoglobin called when oxygen is attached?

9. (Page 4.) Explain cooperative binding of oxygen to hemoglobin.

10. (Page 4.) Label the diagram of hemoglobin on p. 4.

11. (Page 5.) Give a name to each of these symbols:
    a. Hb b. $HbO_2$

12. (Page 5.) Does this reaction occur at the lungs or at the tissues? $Hb + O_2 \rightarrow HbO_2$

13. (Page 5.) Does this reaction occur at the lungs or at the tissues? $Hb + O_2 \leftarrow HbO_2$

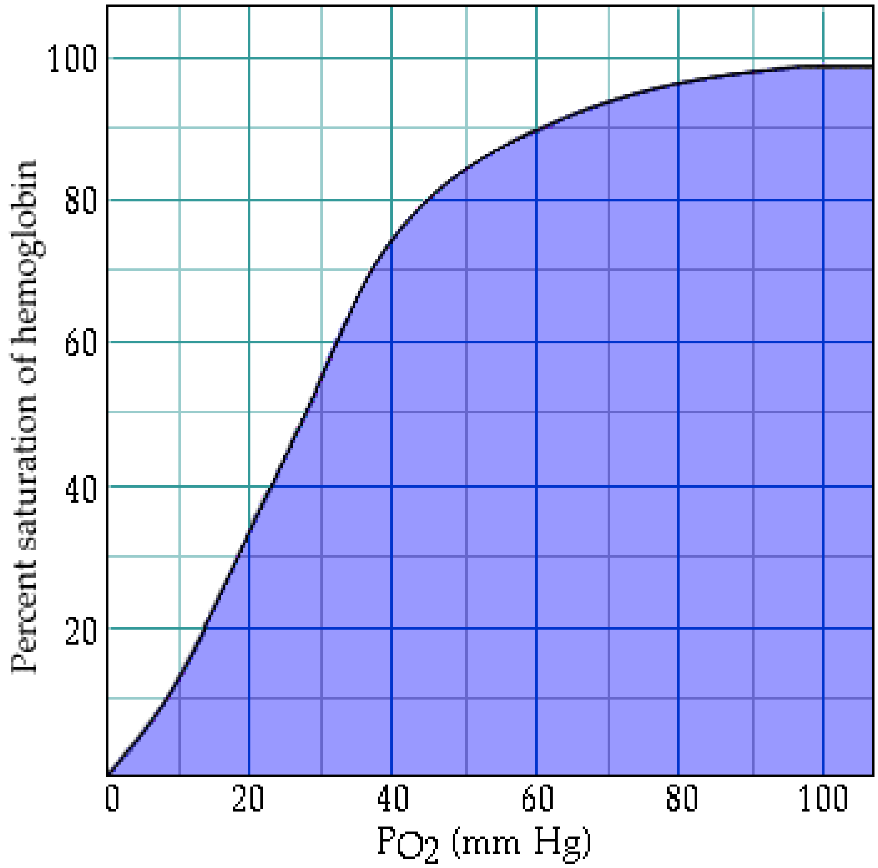
14. (Page 5.) The affinity of hemoglobin for oxygen __________ as its saturation decreases.
    a. increases b. decreases

15. (Page 6.) What determines the degree of hemoglobin saturation?

16. (Page 6.) Label the graph on page 6.

17. (Page 6.) a. What is the approximate partial pressure of oxygen in the lungs? b. What is the percent saturation of hemoglobin in the lungs?

18. (Page 6.) a. What is the approximate partial pressure of oxygen in the tissues? b. What is the approximate percent saturation of hemoglobin in the tissues?




19. (Page 6.) What is this graph called?

20. (Page 6.) Use this graph to determine the percent saturation of hemoglobin in the lungs when the $P_{O2}$ is 100 mm Hg.

21. (Page 6.) Use this graph to determine the percent saturation of hemoglobin in the tissues when the $P_{O2}$ is 40 mm Hg.

22. (Page 6.) What does this statement mean: "When hemoglobin leaves the tissues it is still 75% saturated"?

23. (Page 6.) What is the slope of the oxygen-hemoglobin dissociation curve at both high and low $P_{O2}$'s?

24. (Page 7.) Use this graph to determine the percent saturation of hemoglobin in the lungs when the $P_{O2}$ is 80 mm Hg such as at a high elevation.

25. (Page 7.) At sea level the $P_{O2}$ is 100 mm Hg and the hemoglobin is 98% saturated. At a high altitude, the $P_{O2}$ may be 80 mm Hg but the hemoglobin is 95% saturated. What is the significance of the large difference in $P_{O2}$, but almost no difference in hemoglobin saturation?

26. (Page 8.) Do the graph-labeling exercise on p. 8.

27. (Page 8.) At rest the $P_{O2}$ in the tissues is about 40 mm Hg and the hemoglobin is 75% saturated. In vigorously contracting muscles, the $P_{O2}$ in the tissues may be 20

mm Hg and the hemoglobin is 25% saturated. What is the significance of the large difference in hemoglobin saturation?

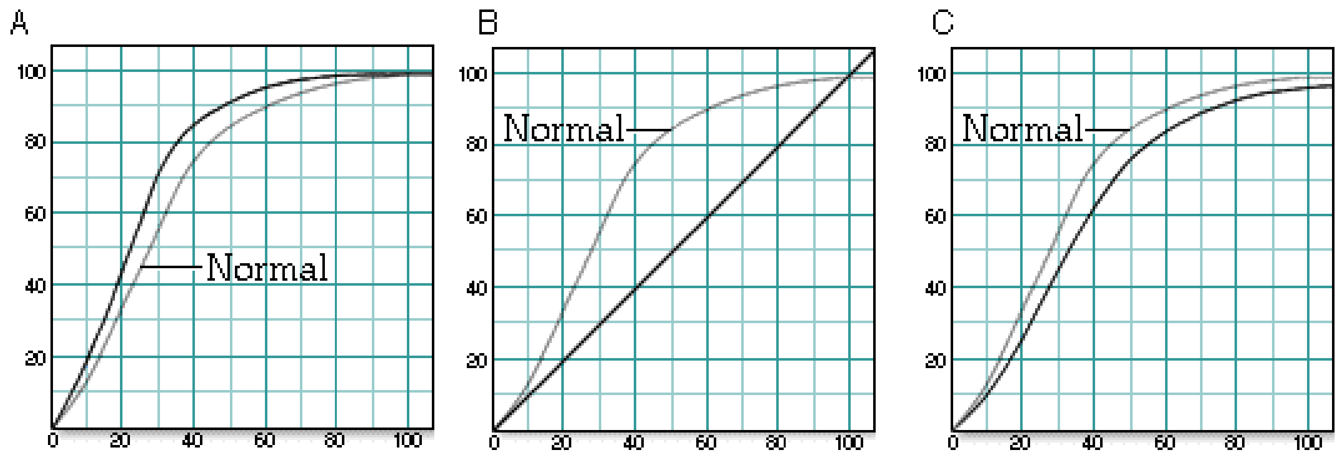
28. (Page 9.) List four factors which alter hemoglobin saturation.

29. (Page 9.) Why do pH, temperature, $P_{CO_2}$, and BPG all change during exercise.

30. (Page 9.) What is the effect of the changing pH, temperature, $P_{CO_2}$, and BPG during exercise on hemoglobin's affinity for oxygen.

31. (Page 9,10.) Which of these graphs of percent saturation of hemoglobin vs. partial pressure of oxygen corresponds to these situations:

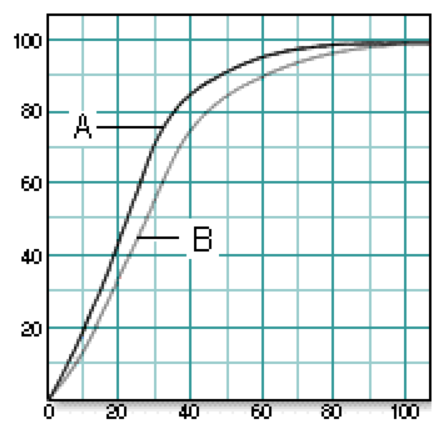
1. decreased muscle pH
2. decreased muscle temperature
3. increased $P_{CO_2}$ in muscle
4. increased muscle pH
5. increased muscle temperature
6. decreased $P_{CO_2}$ in muscle




32. (Page 10.) At decreased temperatures, does hemoglobin's affinity for oxygen increase or decrease?

33. (Page 10.) Which of these curves has the higher oxygen saturation?

34. (Page 10.) Which of these curves represents a situation where there is less affinity of oxygen for hemoglobin?




35. (Page 11.) Label the diagram on page 11.

36. (Page 12.) 23% of the total carbon dioxide in the blood binds to the globin portion of the hemoglobin molecule. What is the name and symbol for the molecule formed?

37. (Page 13.) Does carbaminohemoglobin form in areas of high or low $P_{CO_2}$?

38. (Page 13.) Which of these occurs in the lungs? Which occurs in the tissues?
a. $Hb + CO_2 \rightarrow HbCO_2$ b. $Hb + CO_2 \leftarrow HbCO_2$

39. (Page 14.) Label the diagram on p. 14.

40. (Page 14.) What is the name of the enzyme that catalyzes the reaction of carbon dioxide and water to form carbonic acid?

41. (Page14.) What happens to the hydrogen ions that are generated when carbonic acid dissociates into bicarbonate inside red blood cells?

42. (Page 14.) Explain the chloride shift at the tissues.

43. (Page 14.) Explain the chloride shift at the lungs.

44. (Page 15.) Label the diagram on p. 15.

45. (Page 15.) What happens to the hydrogen ions that are released from hemoglobin at the lungs?

46. (Page 16.) Number the diagram on page 16 to go along with the numbers in the description to illustrate processes that occur at the lungs.

47. (Page 16.) What is the Haldane effect? Where does it occur?

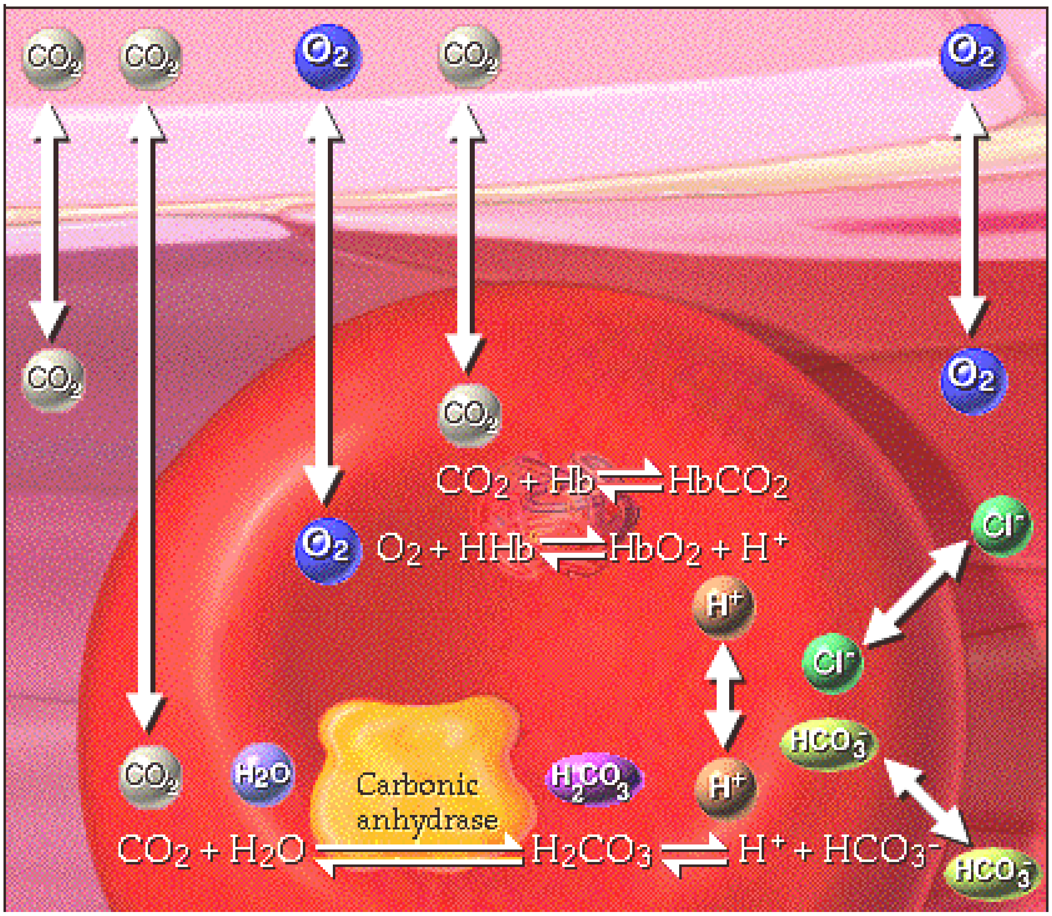
48. (Page 17.) What is the Bohr effect? Where does it occur?

49. (Page 17.) Number the diagram on page 17 to go along with the numbers in the description to illustrate processes that occur at the tissues.

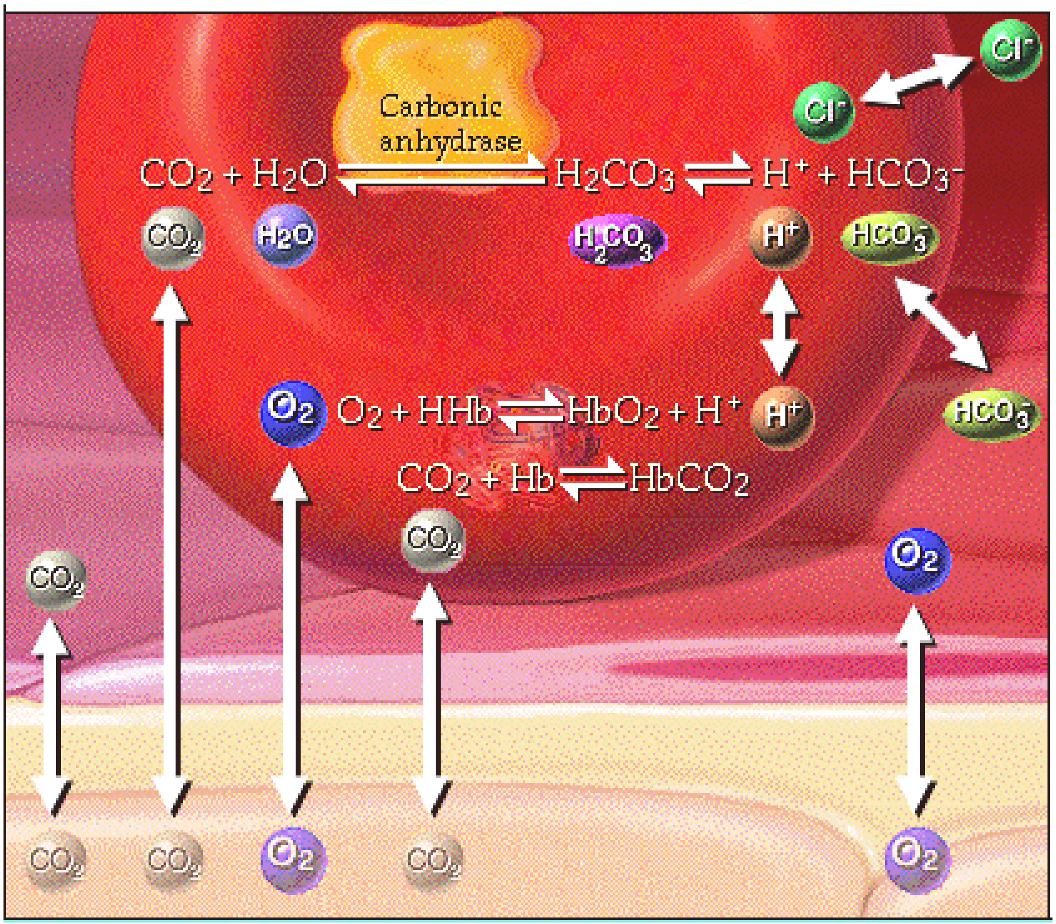
50. (Summary) Do the following processes occur at the lungs or the tissues?
a. $CO_2$ unloading
b. 75% hemoglobin saturation
c. $O_2 + HHb \rightarrow HbO_2 + H^+$
d. $O_2$ loading
e. $H_2CO_3 \leftarrow H+ + HCO_3^-$
f. $CO_2$ loading
g. $H_2CO_3 \rightarrow H+ + HCO_3^-$
h. 98% hemoglobin saturation
i. $CO_2 + H_2O \rightarrow H_2CO_3$
j. $CO_2 + Hb \leftarrow HbCO_3$
k. $CO_2 + Hb \rightarrow HbCO_3$
l. $CO_2 + H_2O \leftarrow H_2CO_3$
m. $O_2$ unloading

n. $O_2$ + HHb $\leftarrow$ $HbO_2$ + $H^+$

51. (Summary) Identify the direction that each of the arrows would take in the lungs:




52. (Summary) Identify the direction that each of the arrows would take in the tissues:



Carbonic anhydrase
CO2 + H2O ⇌ H2CO3 ⇌ H+ + HCO3-
Cl-
Cl-
CO2
H2O
H2CO3
H+
HCO3-
O2
O2 + HHb ⇌ HbO2 + H+
H+
HCO3-
CO2 + Hb ⇌ HbCO2
CO2
O2
CO2
CO2
CO2
O2
CO2
O2

# Control of Respiration

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## Page 1. Introduction

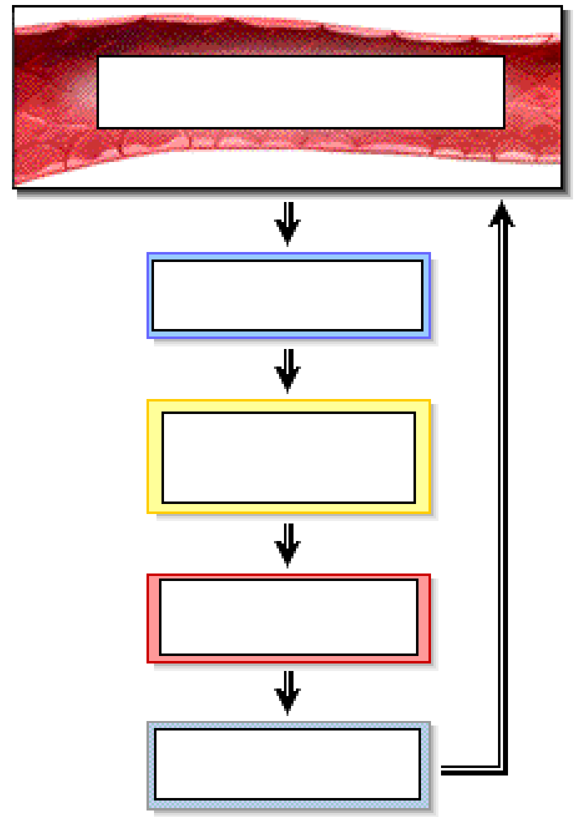
- The basic rhythm of breathing is controlled by respiratory centers located in the brainstem.
- This rhythm is modified in response to input from sensory receptors and from other regions of the brain.

## Page 2. Goals

- To understand how the respiratory centers control breathing to maintain homeostasis.
- To examine how $P_{CO_2}$, pH, $P_{O_2}$, and other factors affect ventilation.
- To understand the relationship between breathing and blood pH.
- To explore the factors which stimulate increased ventilation during exercise.

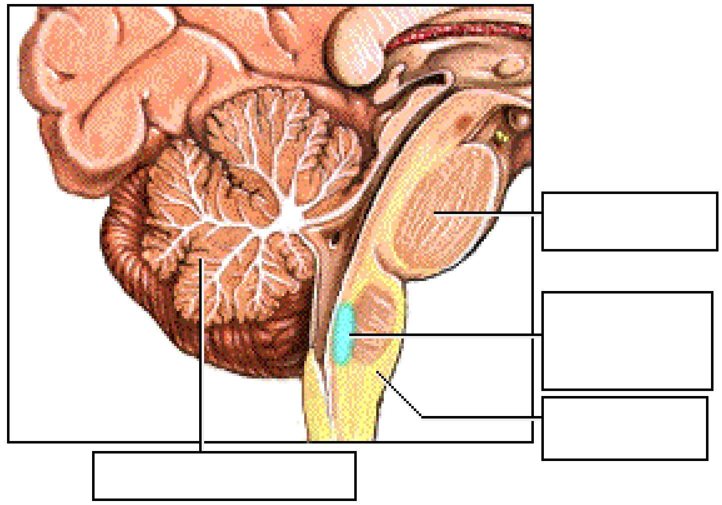
## Page 3. Homeostasis and the Control of Respiration

- Fill out the chart to the right as you proceed through this page.
- The control of respiration is tied to the principle of homeostasis.
- Recall that the body maintains homeostasis through homeostatic control mechanisms, which have three basic components:
    1. receptors
    2. control centers
    3. effectors
- The principal factors which control respiration are chemical factors in the blood.
- Changes in arterial $P_{CO_2}$, $P_{O_2}$ and pH are monitored by sensory receptors called chemoreceptors.
- The chemoreceptors send sensory input to respiratory centers in the brainstem, which determine the appropriate response to the changing variables.
- These centers then send nerve impulses to the effectors, the respiratory muscles, to control the force and frequency of contraction.
- This changes the ventilation, the rate and depth of breathing.
- Ventilation changes restore the arterial blood gases and pH to their normal range.

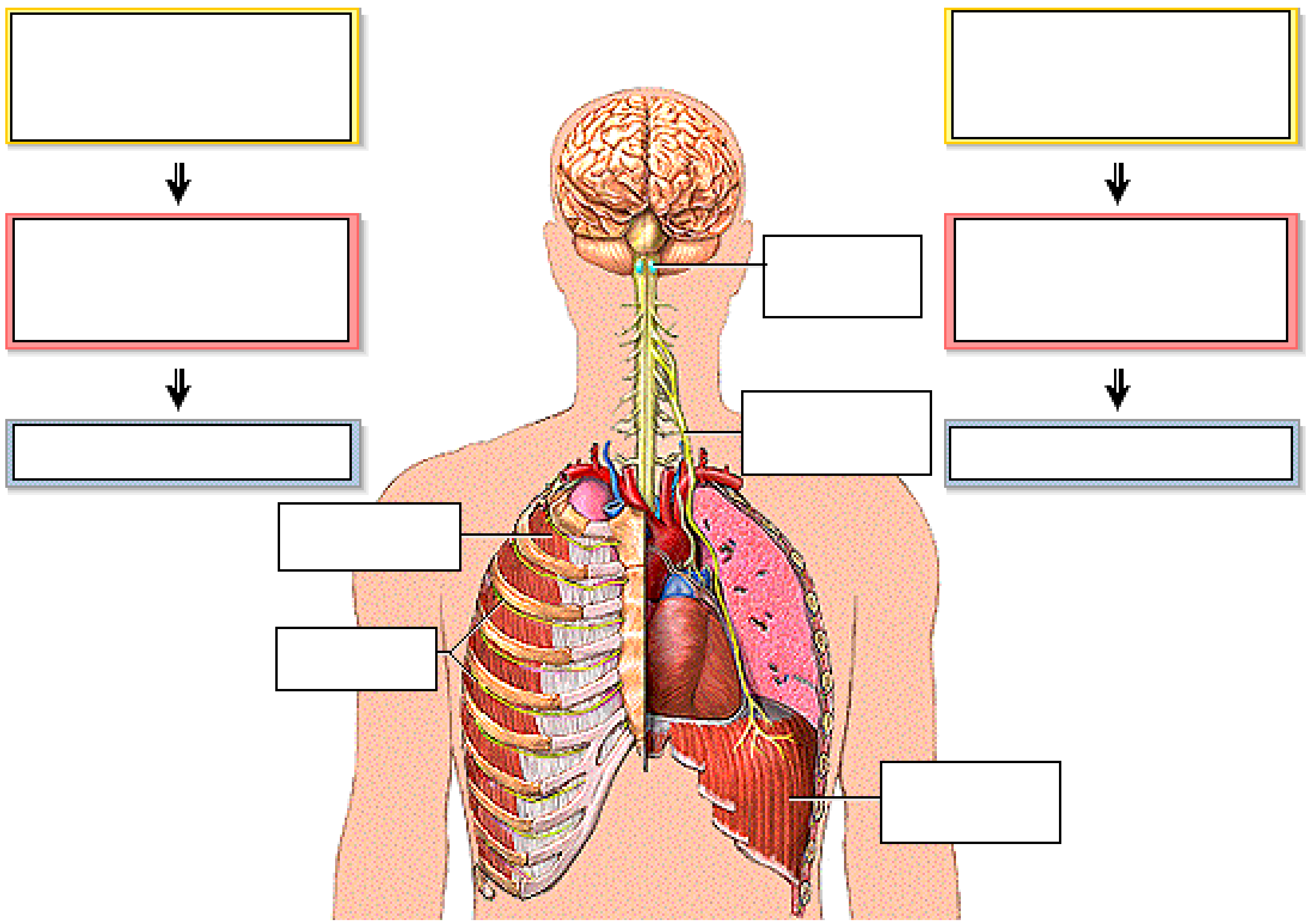


**Page 4. Inspiratory Neurons**

- Label the diagram to the right.
- The basic rhythm of breathing is controlled by respiratory centers located in the medulla and pons of the brainstem.
- Within the medulla, a group of neurons in the ventral respiratory group sets the basic rhythm by automatically initiating inspiration.

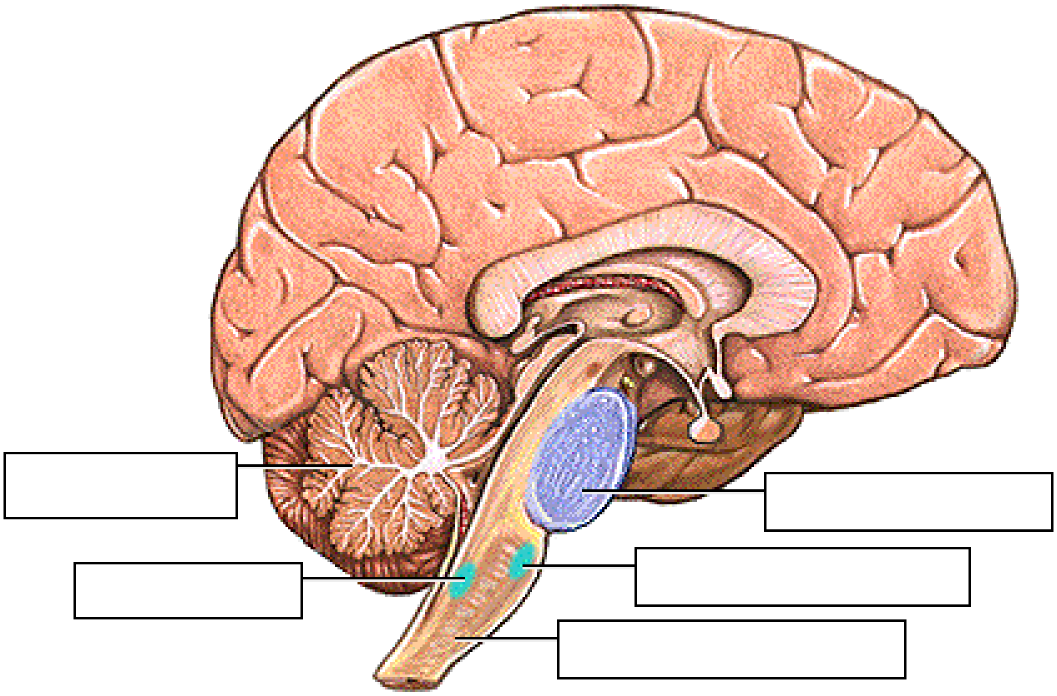


- The inspiratory neurons sends nerve impulses along the phrenic nerve to the diaphragm and along the intercostal nerves to the external intercostal muscles.
- The nerve impulses to the diaphragm and the external intercostal muscles continue for a period of about 2 seconds. This stimulates the inspiratory muscles to contract, initiating inspiration.
- A second group of neurons In the ventral respiratory group now fires, inhibiting the inspiratory neurons for about 3 seconds, which allows the muscles to relax. The elastic recoil of the lungs and chest wall leads to expiration.
- The automatic rhythm generated by these two groups of neurons alternately inhibiting each other produces the normal resting breathing rate, ranging between 12 and 15 breaths per minute.
- Label this diagram:



**Page 5. Other Respiratory Control Centers**

- The dorsal respiratory group, or DRG, acts as an integrating center for peripheral stretch and chemoreceptor inputs, and influences the activity of the neurons in the VRG.
- Both the DRG and the VRG receive inputs from other respiratory centers in the pons, which modify inspiration, and allow for smooth transitions between inspiration and expiration.
- Label the diagram on the next page.

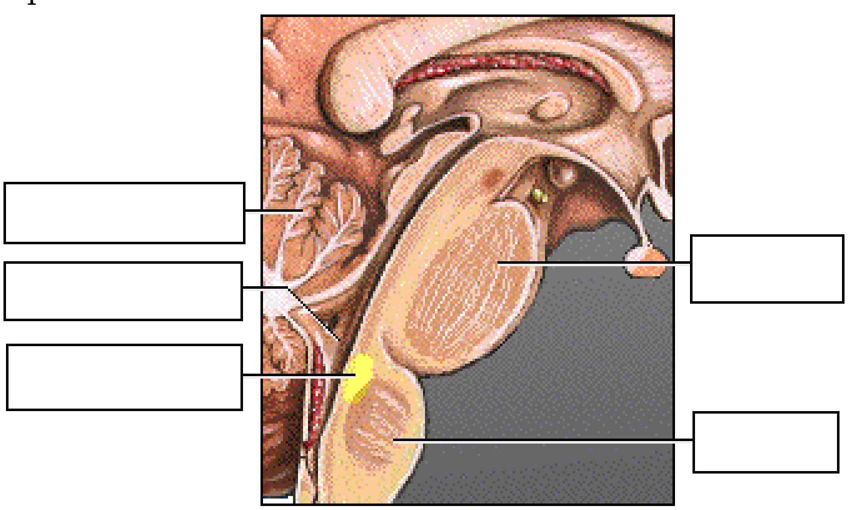


** Now is a good time to go to quiz question 1:

- Click the Quiz button on the left side of the screen.
- After answering question 1, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "6. Location of the Chemoreceptors".

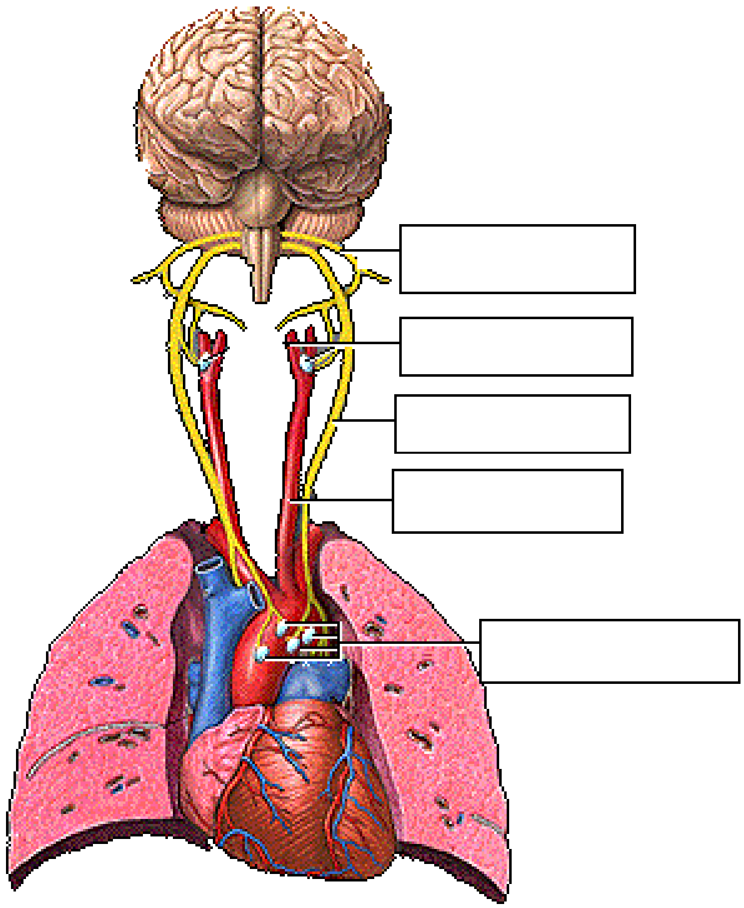
**Page 6. Location of the Chemoreceptors**

- Although the basic rhythm of breathing is established by the respiratory centers, it is modified by input from the central and peripheral chemoreceptors.
- They respond to changes in the $P_{CO_2}$, pH, and $P_{O_2}$ of arterial blood, which are the most important factors that alter ventilation.

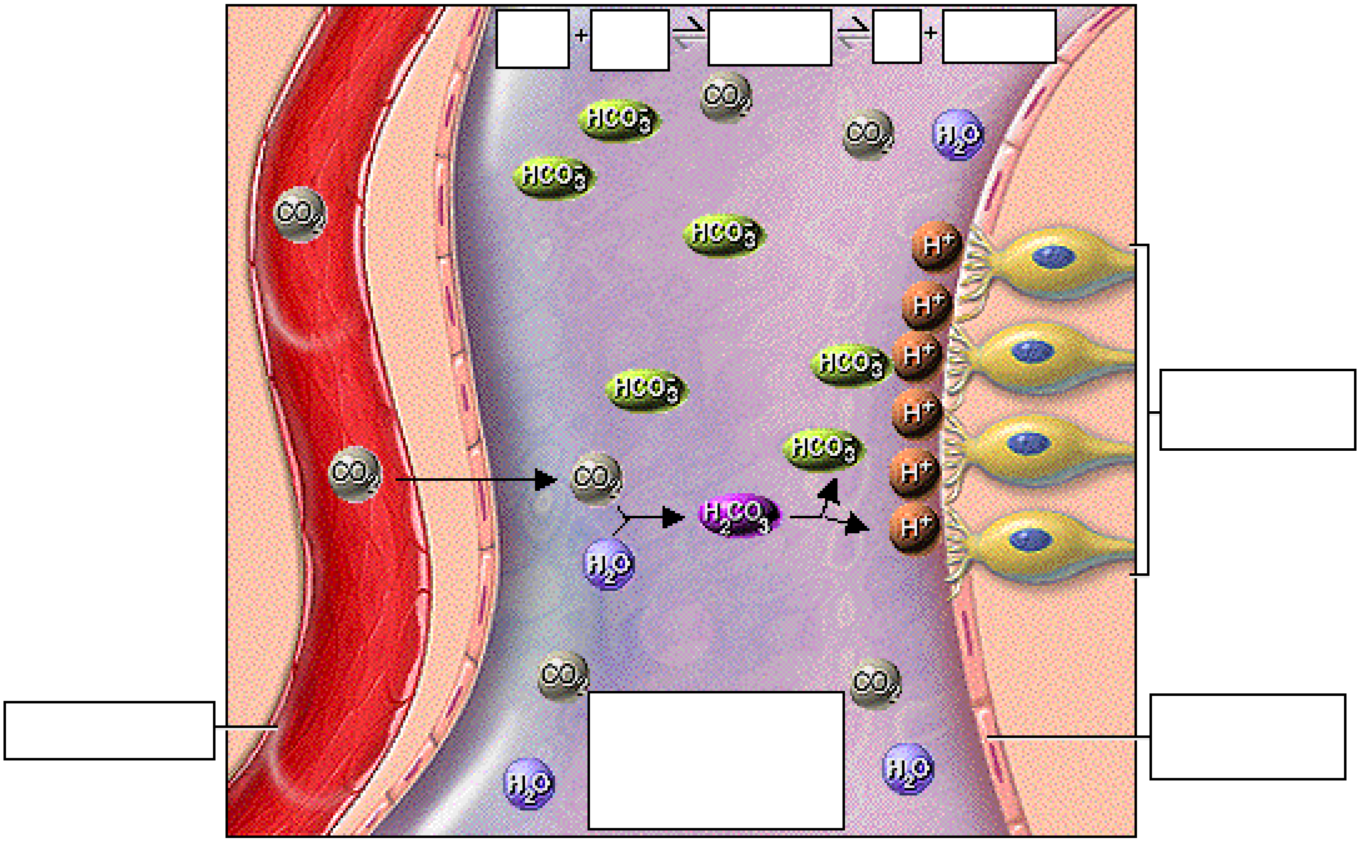


- The central chemoreceptors in the medulla monitor the pH associated with $CO_2$ levels within the brain. The chemoreceptors synapse directly with the respiratory centers.
- The peripheral chemoreceptors are found in two locations:
  1. the aortic bodies within the aortic arch
  2. the carotid bodies at the bifurcation of the common carotid arteries

- The peripheral chemoreceptors monitor the $P_{CO_2}$, pH and $P_{O_2}$ of arterial blood. This information travels to the respiratory centers via the vagus and glossopharyngeal nerves.



**Page 7. Central Chemoreceptors: Effect of $P_{CO_2}$**




• The most important factor controlling the rate and depth of breathing is the effect of carbon dioxide on the central chemoreceptors.

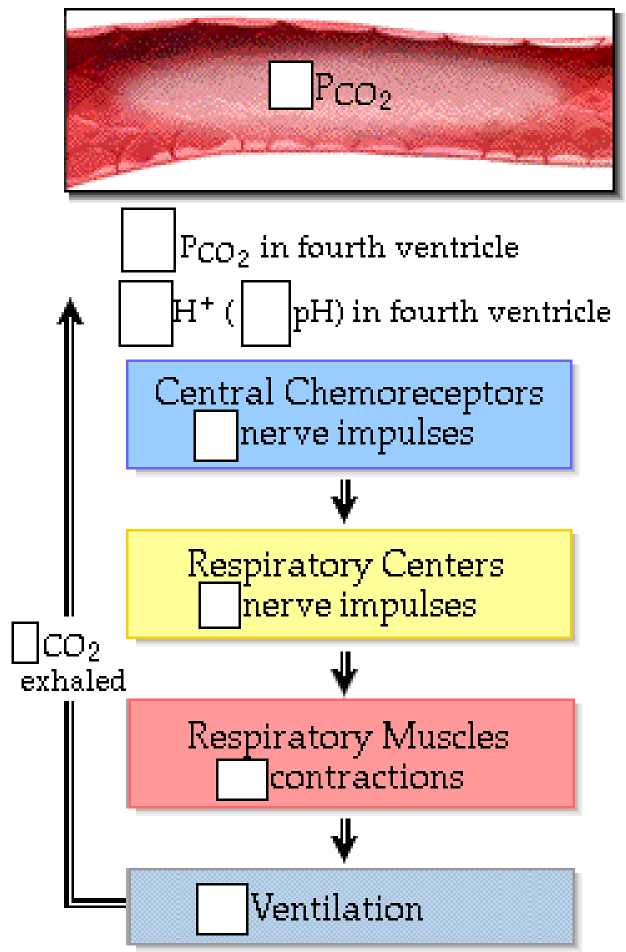
• Carbon dioxide readily diffuses from the blood into the brain. Here, carbon dioxide combines with water to form carbonic acid, which dissociates into hydrogen ions and bicarbonate ions.

• The hydrogen ions stimulate the central chemoreceptors, which send nerve impulses to the respiratory centers in the medulla.

• As carbon dioxide increases, so does the number of hydrogen ions, which in turn lowers the pH. The central chemoreceptors actually respond to this pH change caused by the blood $P_{CO_2}$.

**Page 8. Predict the Effect of Increased $P_{CO_2}$**

- Fill in the diagram to the right:
- What will happen to the breathing rate and depth if the arterial $P_{CO_2}$ increases?
- An increase in the $P_{CO_2}$ in the blood leads to an increase in hydrogen ions in the brain, decreasing the pH.
- The central chemoreceptors fire more frequently, sending more nerve impulses to the respiratory centers, which in turn send more nerve impulses to the respiratory muscles.
- This results in an increased breathing rate and depth, allowing more carbon dioxide to be exhaled, returning the blood $P_{CO_2}$ to normal levels.

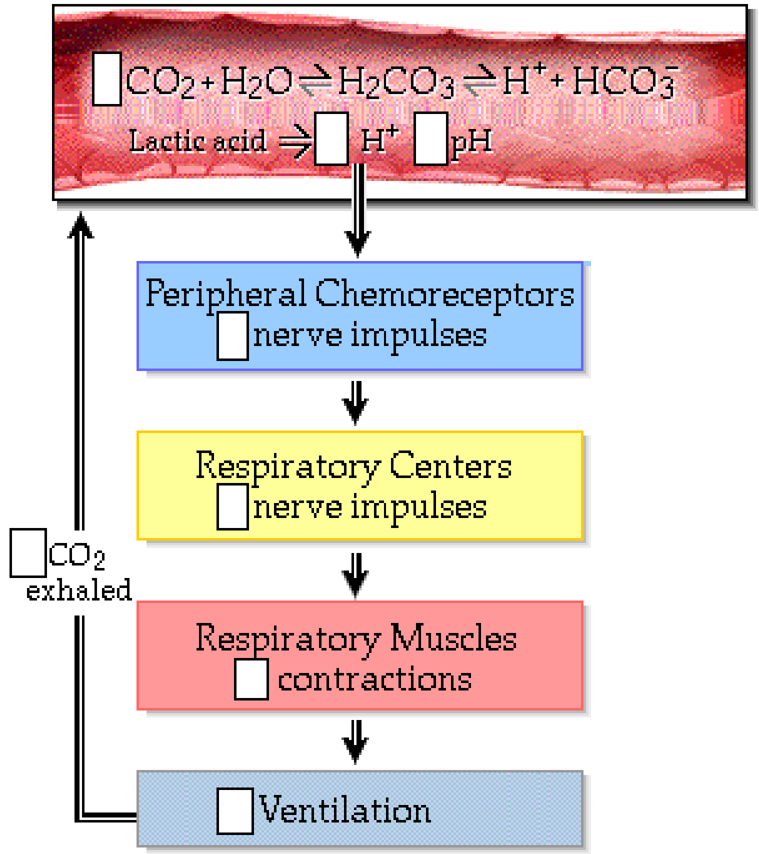



** Now is a good time to go to quiz question 2:
- Click the Quiz button on the left side of the screen.
- Click on the scrolling page list at the top of the screen and choose "2: Central Chemoreceptors".
- After answering question 2, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "9. Peripheral Chemoreceptors: Effect of pH Changes".

## Page 9. Peripheral Chemoreceptors: Effect of pH Changes

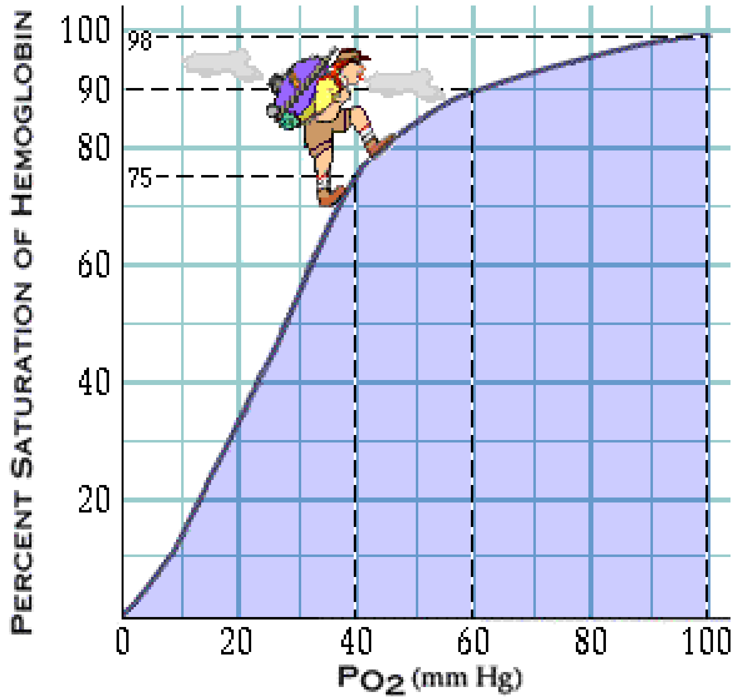
- The peripheral chemoreceptors also respond to pH changes caused by $P_{CO2}$ changes, however they directly monitor changes in the arterial blood, not the cerebrospinal fluid as the central chemoreceptors do.
- The role of the peripheral chemoreceptors:
  - Increased carbon dioxide levels in the arterial blood result in decreased blood pH, which stimulates the peripheral chemoreceptors.
  - They respond by sending more nerve impulses to the respiratory centers, which stimulate the respiratory muscles, causing faster and deeper breathing.
  - More carbon dioxide is exhaled, which drives the chemical reaction to the left and returns the $P_{CO_2}$ and pH to normal levels.

- Fill in the diagram to the right:
- The peripheral chemoreceptors also respond to acids such as lactic acid, which is produced during strenuous exercise:
  - Active muscles produce lactic acid, which enters the blood, releases hydrogen ions, and lowers the pH.
  - The decreased pH stimulates the peripheral chemoreceptors to send more nerve impulses to the respiratory centers, which stimulate the respiratory muscles to increase the breathing rate and depth.
  - More carbon dioxide is exhaled, lowering the $P_{CO_2}$ in blood, driving the chemical reaction to the left, and lowering hydrogen ion levels.

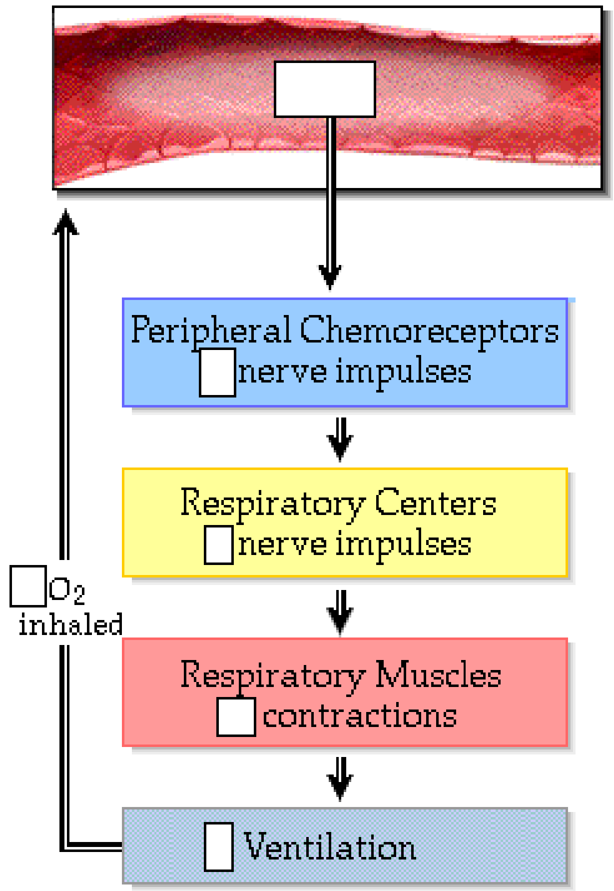



**Page 10. Peripheral Chemoreceptors: Effect of $P_{O_2}$**

- The peripheral chemoreceptors also monitor arterial $P_{O_2}$, however, the arterial $P_{O_2}$ must drop below 60 millimeters of mercury before the chemoreceptors respond.
- The normal alveolar $P_{O_2}$ of about 100 millimeters of mercury results in 98% hemoglobin saturation in the blood.
- If the $P_{O_2}$ drops to 60 millimeters of mercury, hemoglobin is still 90% saturated.
- Any increased ventilation in this range of $P_{O_2}$'s results in only a small increase in the amount of oxygen loaded into the blood.
- However, at very high altitudes, the alveolar $P_{O_2}$ may fall to 40 millimeters of mercury and hemoglobin will be only 75% saturated. At this point, increased ventilation will make a dramatic difference in the amount of oxygen loaded into the blood.



• The low $P_{O_2}$ in the blood stimulates the peripheral chemoreceptors to send nerve impulses to the respiratory centers which stimulate the respiratory muscles, increasing ventilation. More oxygen is inhaled, and the arterial $P_{O_2}$ returns to normal levels.




** Now is a good time to go to quiz questions 3 and 4:

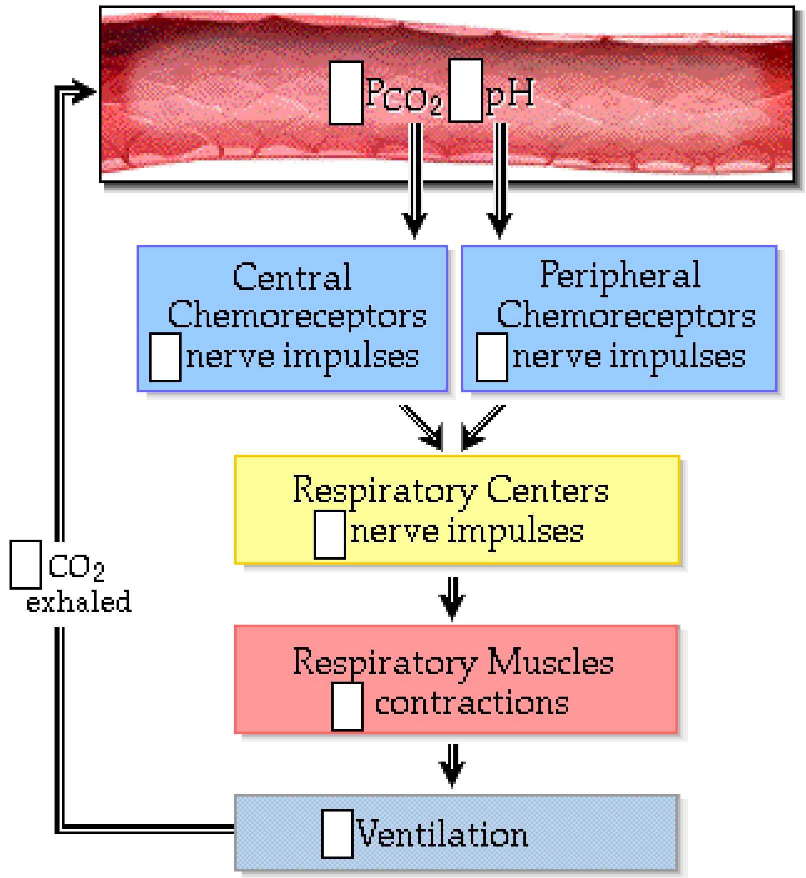
- Click the Quiz button on the left side of the screen.
- Click on the scrolling page list at the top of the screen and choose "3. Peripheral Chemoreceptors: $O_2$".
- After answering question 4b, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "11. Hyperventilation".

**Page 11. Hyperventilation**

- What changes will occur if a person hyperventilates, that is, breathes deeper and faster than necessary for normal gas exchange?
- During hyperventilation, carbon dioxide is exhaled, lowering the $P_{CO_2}$.
- This drives the chemical reaction to the left, decreasing the hydrogen ion concentration, and increasing pH:

$CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow H^+ + HCO_3^-$

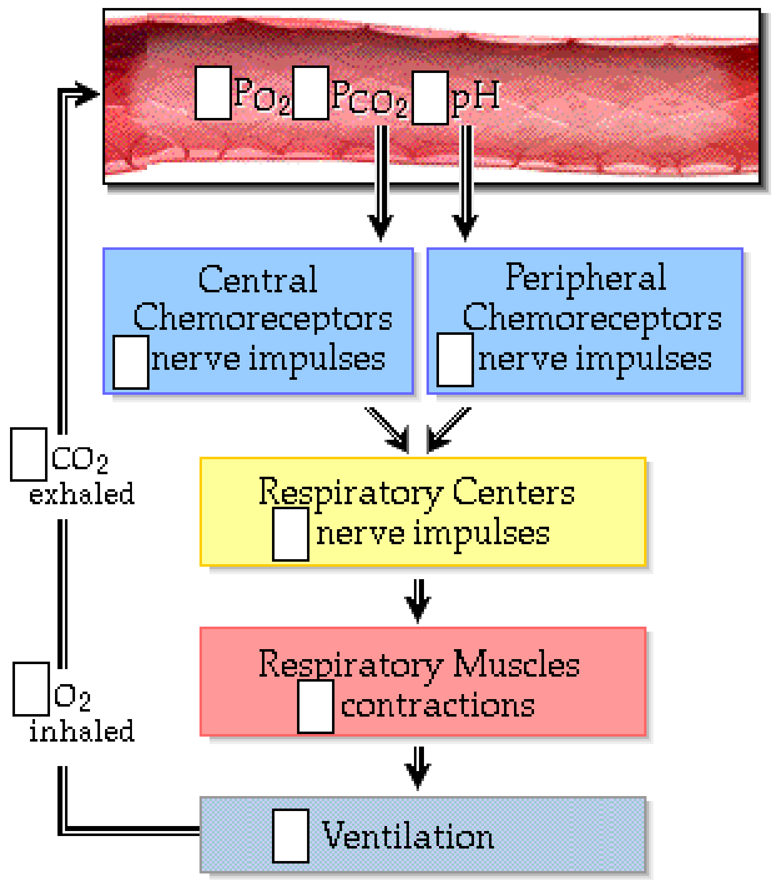
- Since the $P_{CO_2}$ is low, the central chemoreceptors send fewer impulses to the respiratory centers.
- Since the pH is high, the peripheral chemoreceptors also send fewer impulses to the respiratory centers, which send fewer nerve impulses to the respiratory muscles, thereby further decreasing breathing rate and depth and returning the arterial gases and pH to normal levels.




- Hyperventilation does not normally cause an increase in the oxygen levels in the blood, because oxygen is poorly soluble in blood and normally hemoglobin in arterial blood is saturated with oxygen already.

**Page 12. Hypoventilation**

- Now predict what changes will occur if a person hypoventilates.
- Hypoventilation occurs when the breathing rate and depth is too low to maintain normal blood gas levels.
- During hypoventilation, not enough oxygen is inhaled, so the $P_{O_2}$ decreases. In addition, carbon dioxide builds up in the blood, increasing the $P_{CO_2}$. This drives the chemical reaction to the right, increasing the $H^+$ concentration and decreasing pH.
- The $P_{O_2}$ drops, but not enough to stimulate the peripheral chemoreceptors.
- The high $P_{CO_2}$ stimulates the central chemoreceptors to send more impulses to the respiratory centers.
- A decrease in pH stimulates the peripheral chemoreceptors, which also send more nerve impulses to the respiratory centers, which stimulate the respiratory muscles, increasing the breathing rate and depth.
- This allows oxygen to be inhaled, carbon dioxide to be exhaled, and drives the chemical reaction to the left, returning the arterial gases and pH to normal levels.

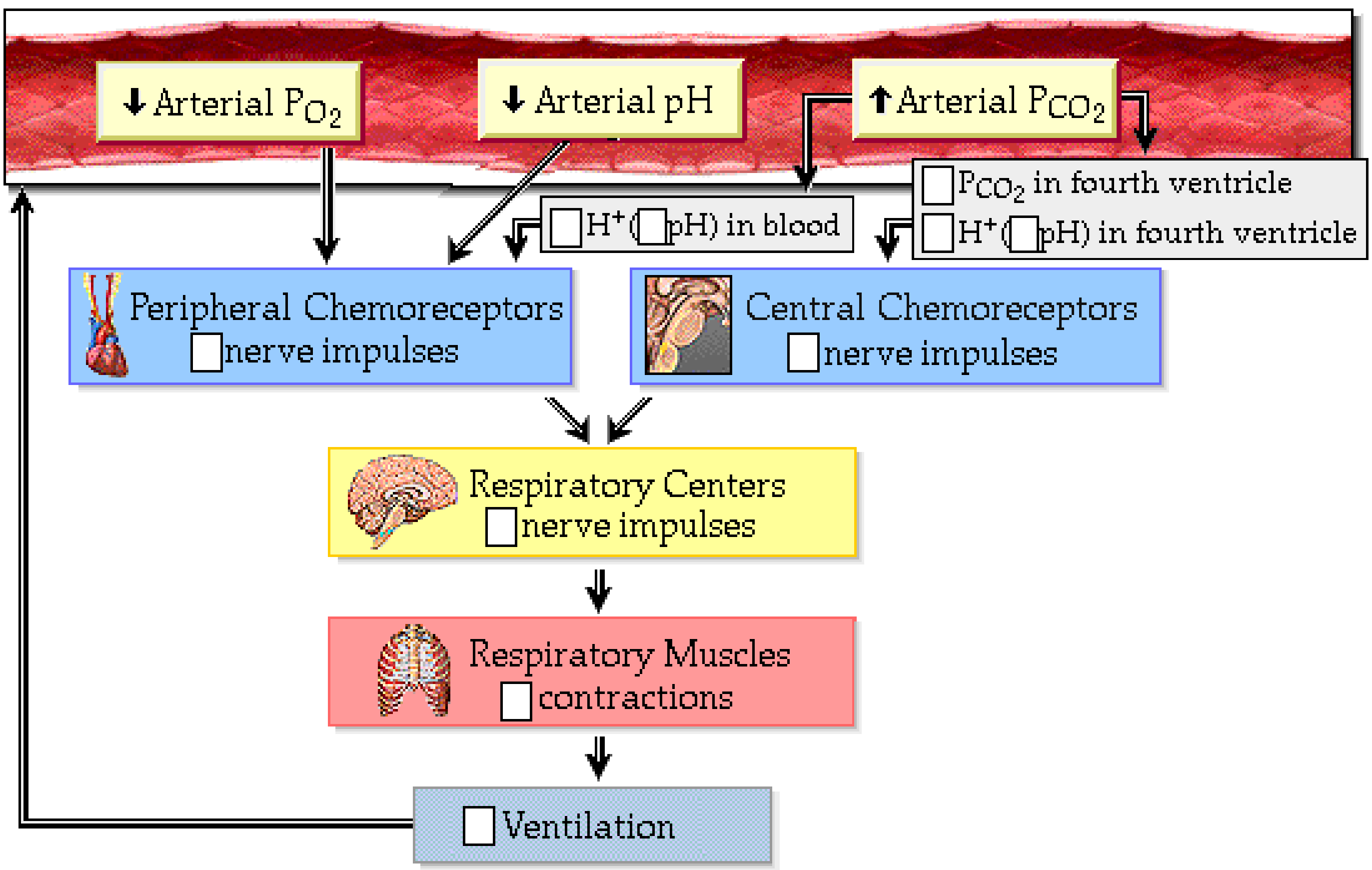



**Page 13. Summary: Effects of $P_{O_2}$, pH, and $P_{CO_2}$**

- This chart summarizes how the three major chemical factors - $P_{O_2}$, pH, and $P_{CO_2}$ - modify breathing rate and depth.
- When the $P_{O_2}$ drops below 60 millimeters of mercury, the peripheral chemoreceptors send nerve impulses to the respiratory centers. The respiratory

centers send nerve impulses to the respiratory muscles, increasing ventilation. More oxygen is inhaled, returning the $P_{O_2}$ to normal levels.

- When cells release acids into the blood, the acids release hydrogen ions, which lower the pH. This stimulates the peripheral chemoreceptors to send more nerve impulses to the respiratory centers. They, in turn, send more nerve impulses to the respiratory muscles, increasing ventilation. More carbon dioxide is exhaled, which returns the pH to normal levels.
- An increase in $P_{CO_2}$ leads to a decreased pH in the blood, which stimulates the peripheral chemoreceptors to send more nerve impulses to the respiratory centers. In addition, the increased $P_{CO_2}$ leads to a decreased pH within the brain. This stimulates the central chemoreceptors to send more nerve impulses to the respiratory centers. The respiratory centers send more nerve impulses to the respiratory muscles, which increase breathing rate and depth. More carbon dioxide is exhaled, returning the $P_{CO_2}$ and pH to normal levels.




**Page 14. Other Factors Which Influence Ventilation**

Several other factors influence ventilation. These factors include:

1. Voluntary control.
    - By sending signals from the cerebral cortex to the respiratory muscles, we can voluntarily change our breathing rate and depth when holding our breath, speaking, or singing.

- However, chemoreceptor input to the respiratory centers will eventually override conscious control and force you to breathe.

2. Pain and emotions.
   - Pain and strong emotions, such as fear and anxiety, act by way of the hypothalamus to stimulate or inhibit the respiratory centers.
   - Laughing and crying also significantly alter ventilation.
3. Pulmonary irritants.
   - Dust, smoke, noxious fumes, excess mucus and other irritants stimulate receptors in the airways.
   - This initiates protective reflexes, such as coughing and sneezing, which forcibly remove the irritants from the airway.
4. Lung hyperinflation.
   - Stretch receptors in the visceral pleura and large airways send inhibitory signals to the inspiratory neurons during very deep inspirations, protecting against excessive stretching of the lungs. This is known as the inflation, or Hering-Breuer, reflex.

## Page 15. Exercise and Ventilation

- Changes in ventilation during exercise:
  - Ventilation increases during strenuous exercise, with the depth increasing more than the rate.
  - It appears that changes in $P_{CO_2}$ and $P_{O_2}$ do not play a significant role in stimulating this increased ventilation.
- Although the precise factors which stimulate increased ventilation during exercise are not fully understood, they probably include:
  1. Learned responses.
     - Ventilation increases within seconds of the beginning of exercise, probably in anticipation of exercise, a learned response.
  2. Neural input from the motor cortex.
     - The motor areas of the cerebral cortex which stimulate the muscles also stimulate the respiratory centers.
  3. Receptors in muscles and joints.
     Proprioceptors in moving muscles and joints stimulate the respiratory centers.
  4. Increased body temperature.
     - An increase in body temperature stimulates the respiratory centers.
  5. Circulating epinephrine and norepinephrine.
     - Circulating epinephrine and norepinephrine secreted by the adrenal medulla stimulates the respiratory centers.
  6. pH changes due to lactic acid
     - Lactic acid, produced by exercising muscles, is another stimulus.

## Page 16. Summary

- The basic rhythm of breathing is set by the ventral respiratory group, located in the medulla. Other respiratory centers, located in the medulla and pons, also control breathing.
- Chemoreceptors monitor the $P_{CO_2}$, pH, and $P_{O_2}$ of arterial blood and alter the basic rhythm of breathing.

- Carbon dioxide, reflected by changes in pH, is the most important stimulus controlling ventilation.
- pH changes due to metabolic acids also alter ventilation.
- Oxygen stimulates ventilation only when the blood $P_{O_2}$ is very low.

• Other factors, such as voluntary control, pain and emotions, pulmonary irritants, and lung hyperinflation, also play roles in controlling ventilation.

• The control of ventilation during exercise, while complex and not fully understood, involves multiple inputs including chemical and neural factors.

** Now is a good time to go to quiz questions 5 and 6:

- Click the Quiz button on the left side of the screen.
- Click on the scrolling page list at the top of the screen and choose "5.Change in Breathing Rate and Depth".
- Work through quiz questions 5 and 6.

**<u>Notes on Quiz Questions:</u>**

**Quiz Question #1a,b: Respiratory Centers**

• This question asks you to identify the parts of the brain which are responsible for setting the basic rhythm of breathing, forceful expiration, and allowing for smooth transitions between inspiration and expiration.

**Quiz Question #2a,b: Central Chemoreceptors**

• This question asks you to chose the substances that stimulates the central chemoreceptors.

**Quiz Question #3: Peripheral Chemoreceptors: $CO_2$**

• This question asks you to list the sequence of events that occurs when there is an increase in blood levels of carbon dioxide.

**Quiz Question #4a,b: Peripheral Chemoreceptors: $O_2$**

• This question asks you to predict when peripheral chemoreceptors will be stimulated due to lack of oxygen and how they respond

**Quiz Question #5: Change in Breathing Rate and Depth**

• This question asks you to determine the factors that will increase the rate of respiration.

**Quiz Question #6a,b: Breath Holding**

• This question asks you to predict what happens when you hold your breath.

**<u>Study Questions on Control of Respiration:</u>**

1. (Page 1.) What controls the basic rhythm of breathing?

2. (Page 3.) What are the three components of a homeostatic control mechanisms?

3. (Page 3.) What are the principal factors which control respiration?

4. (Page 3.) What monitors changes in arterial $P_{CO_2}$, $P_{O_2}$ and pH?

5. (Page 3.) Where do the chemoreceptors send sensory input to?

6. (Page 3.) Where do the respiratory centers send impulses to?

7. (Page 3.) How is homeostasis of $P_{CO_2}$, $P_{O_2}$ and pH maintained?

8. (Page 4.) Label the first diagram on p. 4.

9. (Page 4.) Where, within the brainstem, is the respiratory center that controls the basic rhythm of breathing?

10. (Page 4.) Where, within the brainstem, are the inspiratory neurons?

11. (Page 4.) Label the anatomy on the second diagram on p. 4.

12. (Page 4.) Explain how the inspiratory neurons initiate inspiration.

13. (Page 4.) Explain how the inspiratory neurons initiate expiration.

14. (Page 4.) What is a normal respiratory rate?

15. (Page 5.) Label the diagram on page 5.

16. (Page 5.) What is the function of the dorsal respiratory group?

17. (Page 5.) Where are the respiratory centers that are responsible for smooth transitions between inspiration and expiration?

18. (Page 6.) Label the first diagram on page 6.

19. (Page 6.) Label the second diagram on page 6.

20. (Page 6.) What are the two general categories of chemoreceptors involved in respiration?

21. (Page 6.) Where are the central chemoreceptors located?

22. (Page 6.) Where are the peripheral chemoreceptors located?

23. (Page 6.) What do the central chemoreceptors monitor?

24. (Page 6.) What do the peripheral chemoreceptors monitor?

25. (Page 6.) How does information get from the chemoreceptors to the respiratory centers?

26. (Page 7.) What is the most important factor controlling the rate and depth of breathing?

27. (Page 7.) Does the carbon dioxide stimulate the central chemoreceptors directly?

28. (Page 7.) What is the relationship between hydrogen ions and pH?

29. (Page 7.) Label the diagram on page 7.

30. (Page 8.) In each of these blanks, put "increase(s)" or "decrease(s)": If the arterial $P_{CO_2}$ increases, there is a(an) a. _______ in the $P_{CO_2}$ in the fourth ventricle. This causes a(an) b. ________ in hydrogen ions in the cerebrospinal fluid, which c. ___________ the pH of the cerebrospinal fluid. The hydrogen ions stimulate the central chemoreceptors to d. ________ their rate of firing, which e. __________ the nerve impulses to the respiratory centers. This f. _______ the rate of nerve impulses to the respiratory muscles, resulting in a(an) g. ______ in breathing rate and depth. As a result, there is a(an) h. _________ in carbon dioxide exhalation which i. _________ the blood $P_{CO_2}$ to normal levels.

31. (Page 9.) Do peripheral chemoreceptors directly respond to changes in the arterial blood, venous blood, or brain?

32. (Page 9.) What do the peripheral chemoreceptors directly respond to?
33. (Page 9.) In each of these blanks, put "increase(s)" or "decrease(s)": An increase in carbon dioxide levels in the arterial blood result in a(an) a. _______ in blood pH. There is a(an) b. ________ in the rate of firing of the peripheral chemoreceptors, which c, _______ the rate of respiration. As a result there is a(an) d. ______ in carbon dioxide exhalation, which drives the chemical reaction to the left and e. _________ $P_{CO_2}$ and pH returns to normal levels.

34. (Page 9.) In each of these blanks, put "increase(s)" or "decrease(s)": The peripheral chemoreceptors also respond to acids such as lactic acid, which a. ________ during strenuous exercise. The lactic acid enters the blood and b. __________ the concentration of hydrogen ions which c. _________ the pH which d. _______ the firing rate of the peripheral chemoreceptors. There is a(an) e. ________ in nerve impulses to the respiratory centers, which f. _______ the breathing rate and depth. There is a(an) g. _________ in carbon dioxide is exhalation which h. __________ the $P_{CO_2}$ in blood, driving the chemical reaction to the left, and i. ________ hydrogen ion levels.

35. (Page 10.) When are peripheral chemoreceptors stimulated by oxygen?

36. (Page 10.) In each of these blanks, put "increase(s)" or "decrease(s)": When the $P_{O_2}$ of the arterial blood decreases to below 60 mm Hg, there is a(an) a. _______ in the rate of firing in the peripheral chemoreceptors resulting in a(an) b. _________ in nerve impulses to the respiratory centers. As a result there is a(an) c. _________ in

ventilation. As a result, the oxygen level in the blood d. _______ and the arterial $P_{O_2}$ returns to normal levels.

37. (Page 11.) In hyperventilation, which blood gas is affected the most, oxygen or carbon dioxide?

38. (Page 11.) What happens to blood levels of carbon dioxide during hyperventilation?

39. (Page 11.) As a result of hyperventilation, which direction does this reaction go?
a. $CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow H^+ + HCO_3^-$ b. $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$

40. (Page 11.) In each of these blanks, put "increase(s)" or "decrease(s)": During hyperventilation, carbon dioxide levels in the blood a. ________. This causes a(an) b. ______ in the hydrogen ion concentration. pH c. _________. The rate of firing of the peripheral and central chemoreceptors d. __________. There is a(an) e. ________ in impulses to the respiratory centers and the respiratory rate f. ________.

41. (Page 12.) What happens to blood levels of carbon dioxide during hypoventilation?

42. (Page 12.) As a result of hypoventilation, which direction does this reaction go?
a. $CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow H^+ + HCO_3^-$ b. $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$

43. (Page 12.) In each of these blanks, put "increase(s)" or "decrease(s)": During hypoventilation, carbon dioxide levels in the blood a. ________. This causes a(an) b. ______ in the hydrogen ion concentration. pH c. _________. The rate of firing of the peripheral and central chemoreceptors d. __________. There is a(an) e. ________ in impulses to the respiratory centers and the respiratory rate f. ________.
44. (Page 14.) Besides pH, $P_{CO_2}$ and $P_{O_2}$ what other factors influence ventilation?
45. (Page 14.) What is the Hering-Breuer reflex?
46. (Page 15.) Do changes in $P_{CO_2}$ and $P_{O_2}$ play a significant role in stimulating increased ventilation due to exercise?
47. (Page 15.) What are the factors that stimulate increased ventilation during exercise?