

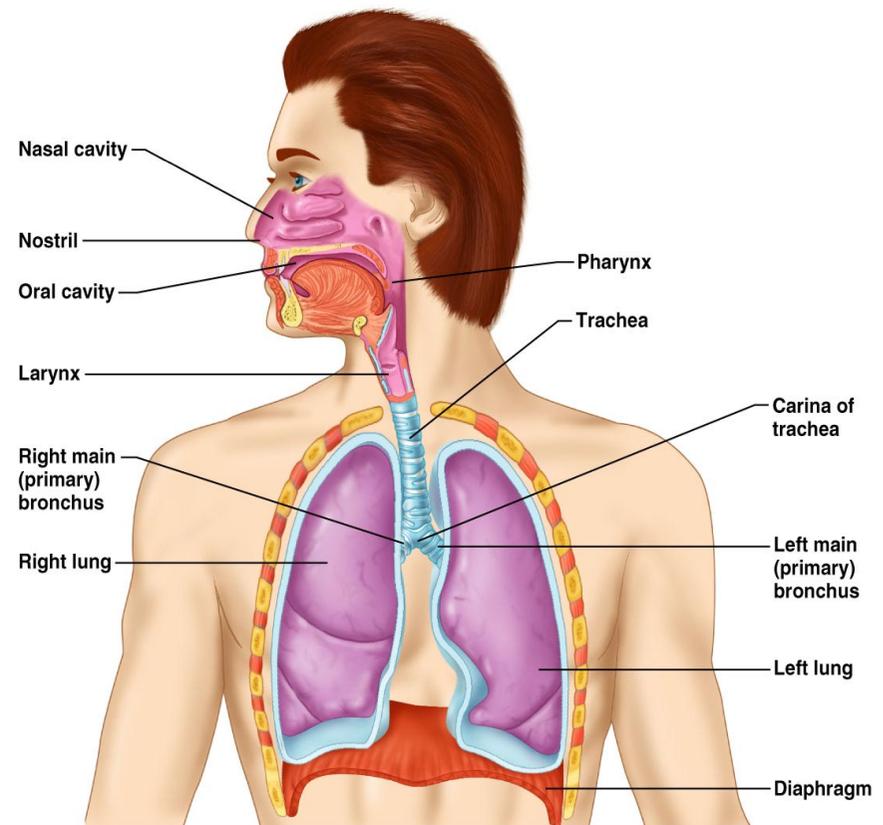
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# Functions of The Respiratory System

- To allow gases from the environment to enter the bronchial tree through inspiration by expanding the thoracic volume.
- To allow gas exchange to occur at the respiratory membrane, so that oxygen diffuses into the blood while carbon dioxide diffuses into the bronchial tree.
- To permit gases in the lungs to be eliminated through expiration by decreasing the thoracic volume.

# General anatomy of The respiratory System

- Consists of a tube that divides into small branching tubes in the lungs: External nares → nasal cavity → nasaopharynx → laryngopharynx → larynx → trachea → primary bronchi → lungs (secondary bronchi → tertiary bronchi → bronchioles → alveolar sacs → alveoli).

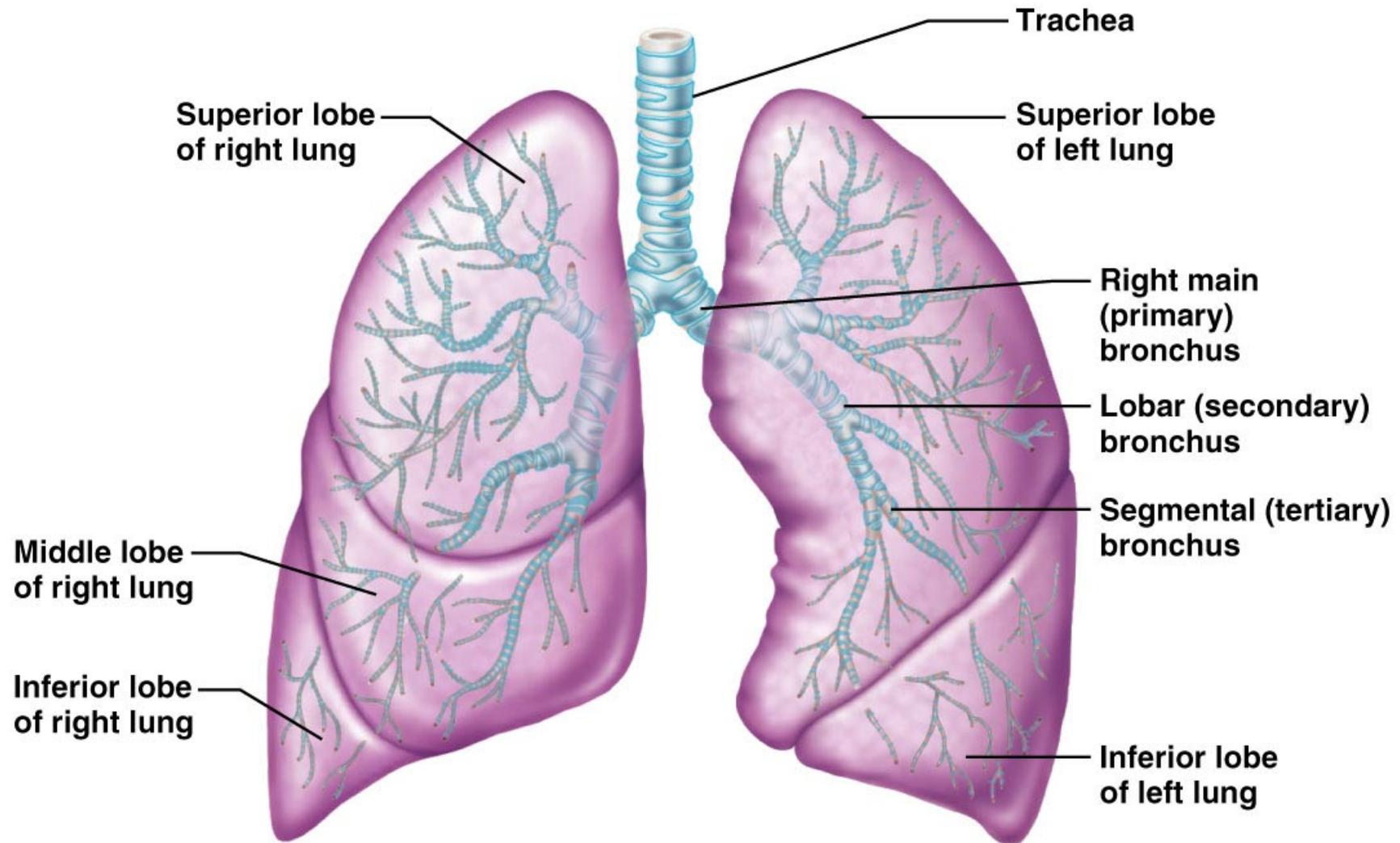


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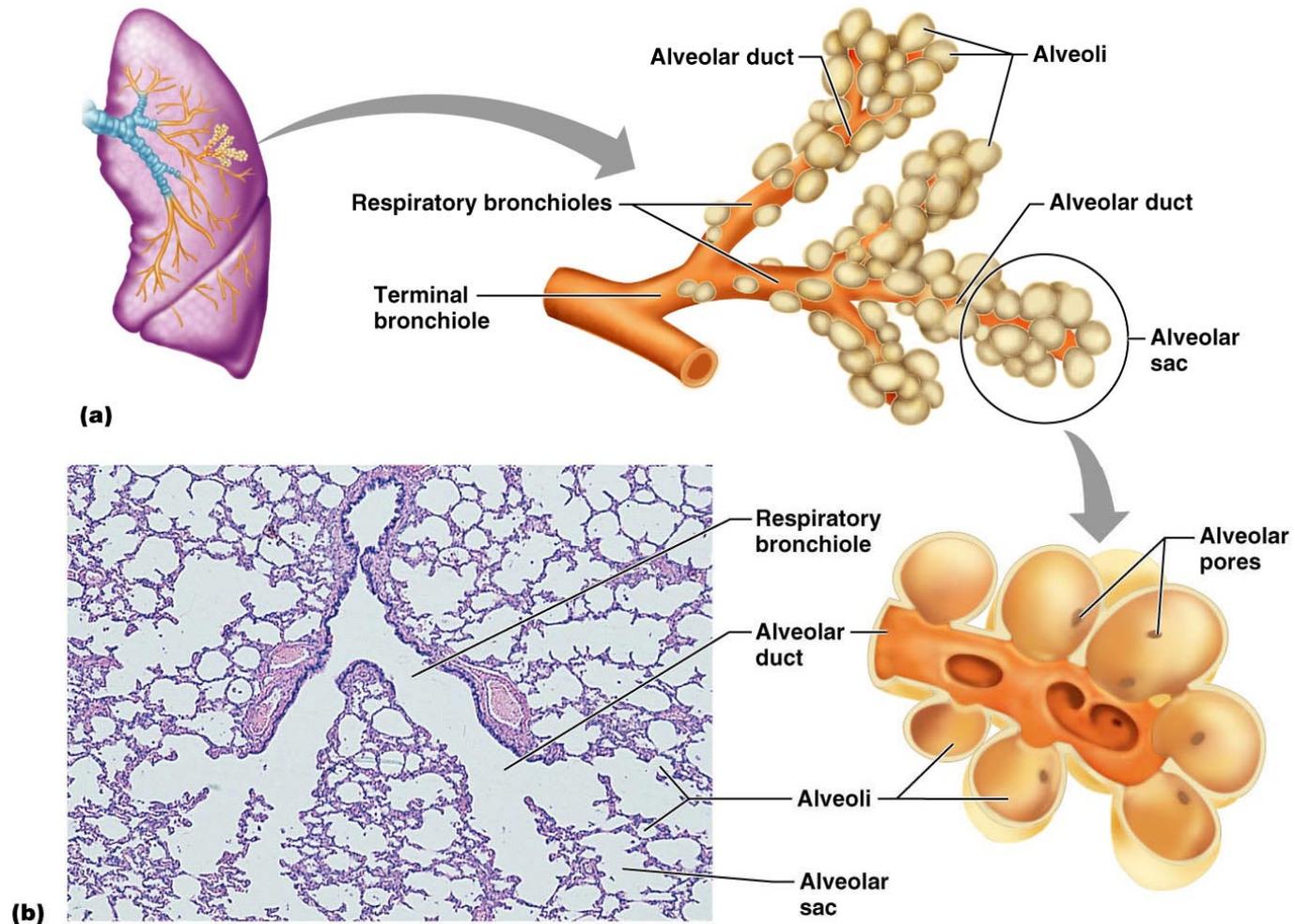
# Lungs

- Cone – shaped organs located in the thoracic cavity.
- Thoracic cavity is lined with a body membrane called **parietal pleura**, while the surface of lungs is covered with **visceral pleura**.
- The thin space between the two pleural membranes is called **pleural cavity** which is filled with a clear fluid called **plural fluid** to minimize friction between the tissues and to provide **surface tension** in the pleural cavity. [water molecules in the pleural fluid allow the two pleural membranes to adhere to one another, to prevent collapsing of the lungs].
- A chemical substance called **surfactant** secreted by the lungs also facilitate the surface tension.

# The respiratory Tract – Bronchial Tree

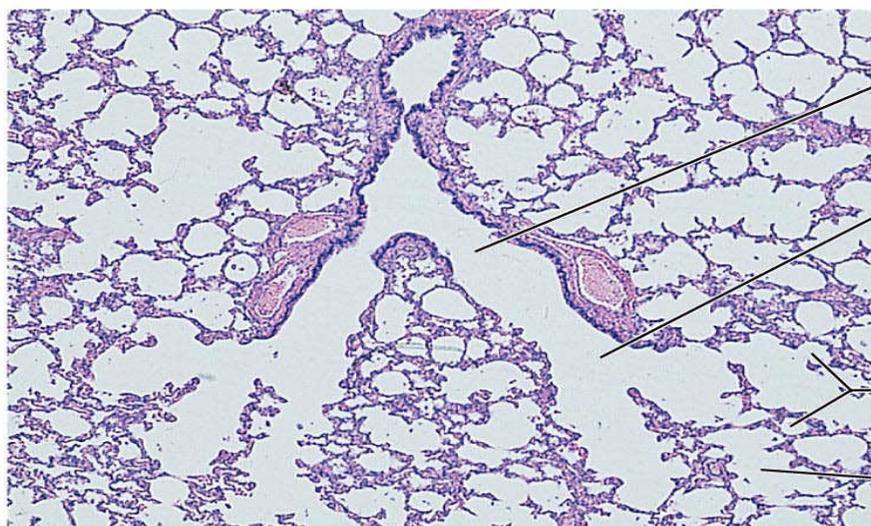


# The Respiratory Tract

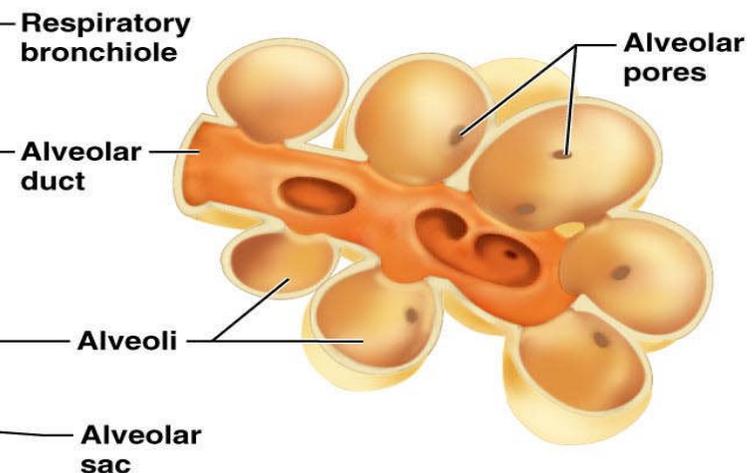


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- The histology along the respiratory tract changes – from the trachea to the tertiary bronchi, the tract is lined with **ciliated pseudostratified columnar epithelium**, **smooth muscle** and **cartilage rings**; the bronchioles are lined with **cuboidal epithelium**; and from the alveolar ducts to the alveoli, the tract is lined with **simple squamous epithelium**.
- Inferior to the lungs is a sheet of skeletal muscle under involuntary control, called **diaphragm**, to facilitate the control of thoracic volume.



(b)



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# The Bronchial tree

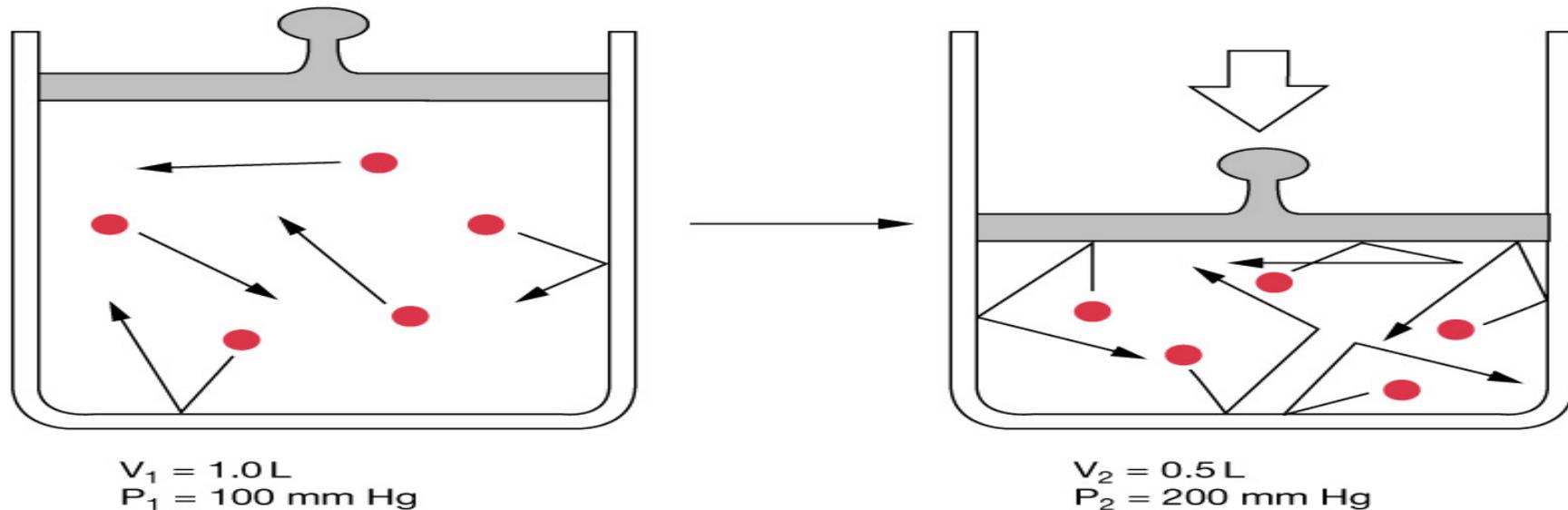
- tree – like branching tubes extended from the trachea. Only the **primary bronchi** are external to the lungs, while the rest of the bronchial tree is embedded in lung tissues.
- diameters of the tubes from primary bronchi to tertiary bronchi are large, so that support with cartilage rings is necessary.
- diameter at the bronchioles is down to 1 mm where the tubes do not need cartilage rings for support. This structure is composed of cuboidal cells where diffusion is also not possible.
- from the alveolar duct to the alveoli, the lining tissue becomes simple squamous epithelium where **gas exchange** is possible. Since there is a much larger surface area at the alveoli, almost all gas exchange occurs at the alveoli [300 million alveoli provide a total surface area similar to a tennis court!].

# Breathing Mechanisms – physical laws

- The **Gas law** states that gas molecules always diffuse from a higher pressure area to a lower pressure area.
- The **Boyle's law** states that **pressure** and **volume** are inversely related (with the temperature remains constant), where pressure will increase in a smaller volume of gases, and pressure decreases in a larger volume of gases

$$\text{Boyle's Law: } P_1V_1 = P_2V_2$$

Decreasing volume increases collisions and increases pressure.



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## Inspiration (Inhalation)

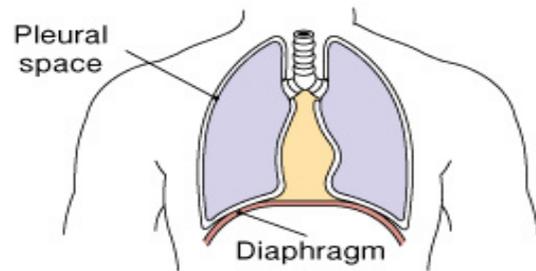
- An active process where nerve impulses from medulla oblongata cause the contraction of **diaphragm** and **external intercostals muscles**.
- As these muscles contract, thoracic **volume increases** which **decreases the pressure** within the lung (**intraalveolar pressure**) due to the boyle's law.
- When intraalveolar pressure falls below the **atmospheric pressure** (758 mmHg versus 760 mmHg, respectively), the gas law dictates that now gases move from the environment into lungs.

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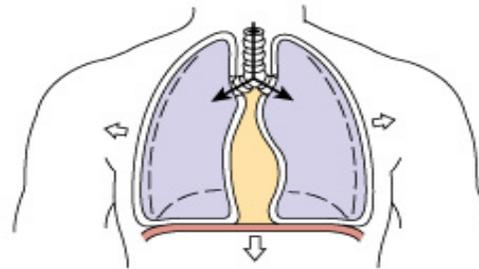
## Expiration (exhalation)

- a passive process where elastic tissues of the lungs and diaphragm recoil to their original position.
- as the diaphragm and external intercostals muscles relax and recoil, thoracic volume decreases which raises the intra alveolar pressure (again due to the boyle's law).
- when intraalveolar pressure is risen above the atmospheric pressure (762 mmHg versus 760 mmHg, respectively), gases move from the lungs into the environment (again due to the gas law).

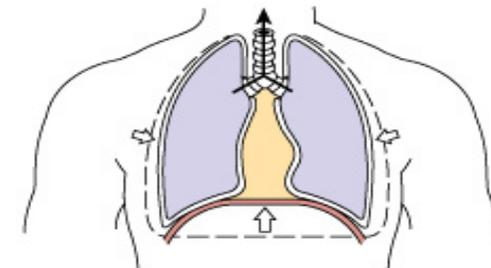
# Inspiration vs. Expiration



**(a)** At rest, diaphragm is relaxed.



**(b)** Diaphragm contracts, thoracic volume increases.



**(c)** Diaphragm relaxes, thoracic volume decreases.

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# Pulmonary Ventilation - Inspiration

- Pulmonary ventilation is the mechanism by which air is exchanged between the atmosphere and the alveoli.
- Air is exchanged due to the expansion and contraction of the lungs.
- Contraction of the diaphragm pulls down, enlarging the intrapleural cavity.
- Elevation of the ribs also expands the intrapleural cavity.
- These factors **decrease** the intrapleural cavity pressure: thus, air flows into the lungs (**inspiration**).

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# Pulmonary ventilation - Expiration

- During expiration the diaphragm relaxes, the ribs are pulled down.
- This **increases** the intrapleural cavity pressure.
- This results in the movement of air out of the lungs.
- Normal quiet breathing is accomplished entirely by the movement of the diaphragm.
- In the "normal sized" person, about **6** liters of gas per minute move in and out of the lungs.
- Ventilation can increase up to almost **100** liters per minute during maximal exercise.

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# Lung Capacities

- Lung capacities (air volumes contained in the lungs) can be measured by a **Spirometer**, and provide invaluable information regarding the normal function of the respiratory system.
- **Tidal volume (TV)**
  - Amount of air moving in and out of the lungs during normal breathing.
  - Average value is about 500 ml.
- **Inspiratory reserve volume (IRV)**
  - Amount of air that can be inhaled after normal inspiration.
  - Average value is about 3,000 ml.
  - Can be calculated by:  $IRV = IC - TV$  where IC represents inspiratory capacity.

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- **Expiratory reserve volume (ERV)**

- Amount of air that can be exhaled after normal expiration. Average value is about 1,100 ml.

- **inspiratory capacity (IC)**

- Total amount of air that can be inhaled.
- Average value is about 4,000 ml. can be calculated by:  $IC = VC - ERV$  where VC represents vital capacity.

- **Vital capacity (VC)**

- Total amount of air that can be exhaled. Average value is about 5,000 ml. Can be calculated by:  $VC = TV + IRV + ERV$ .
- Can also be determined by predicted VC values on a chart based on a person's age and height.

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- **Residual volume (RV)**

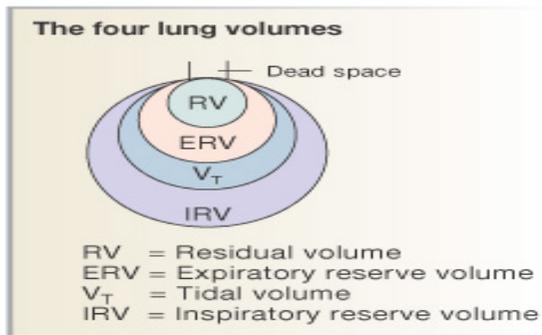
- Amount of air that is always left in the lungs after expiration. Average value is about 1,200 ml.

- **Total lung capacity (TLC)**

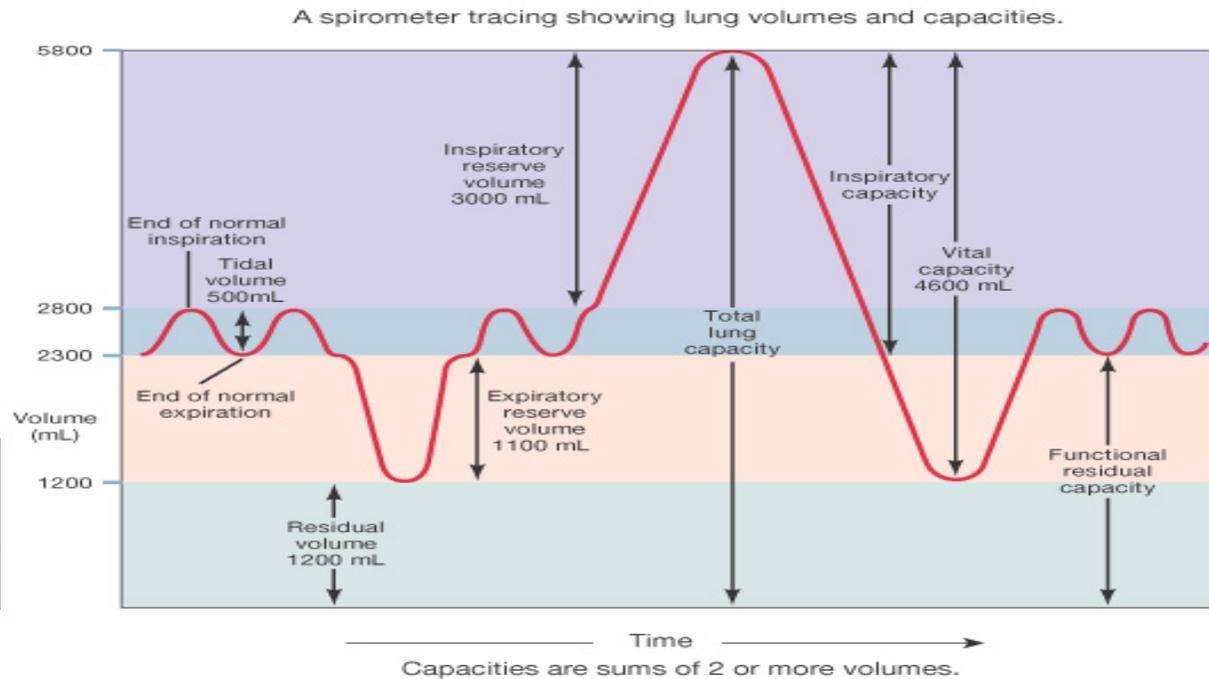
- Total amount of air that the lungs contain, including residual volume. Average value is about 6,000 ml. Can be calculated by:  
 $TLC = VC + RV$ .

- **Anatomic dead space** refers to the amount of air remain in the bronchial tree that is not involved in gas exchange, due to obstruction of air flow or damage in the bronchial tree.

- **Alveolar dead space** refers to the amount of air in the alveolar ducts or alveolar sacs that is not involved in gas exchange, due to poor blood flow or unusually long diffusion distances in gas exchange.
- **Physiologic dead space** refers to the total amount of air in the lungs that is not involved in gas exchange (i.e. anatomic dead space + alveolar dead space).



Pulmonary volumes				
		Males	Females	
Vital capacity	IRV	3000	1900	Inspiratory capacity
	V <sub>T</sub>	500	500	
Residual volume	ERV	1100	700	Functional residual capacity
		1200	1100	
		5800 mL	4200 mL	



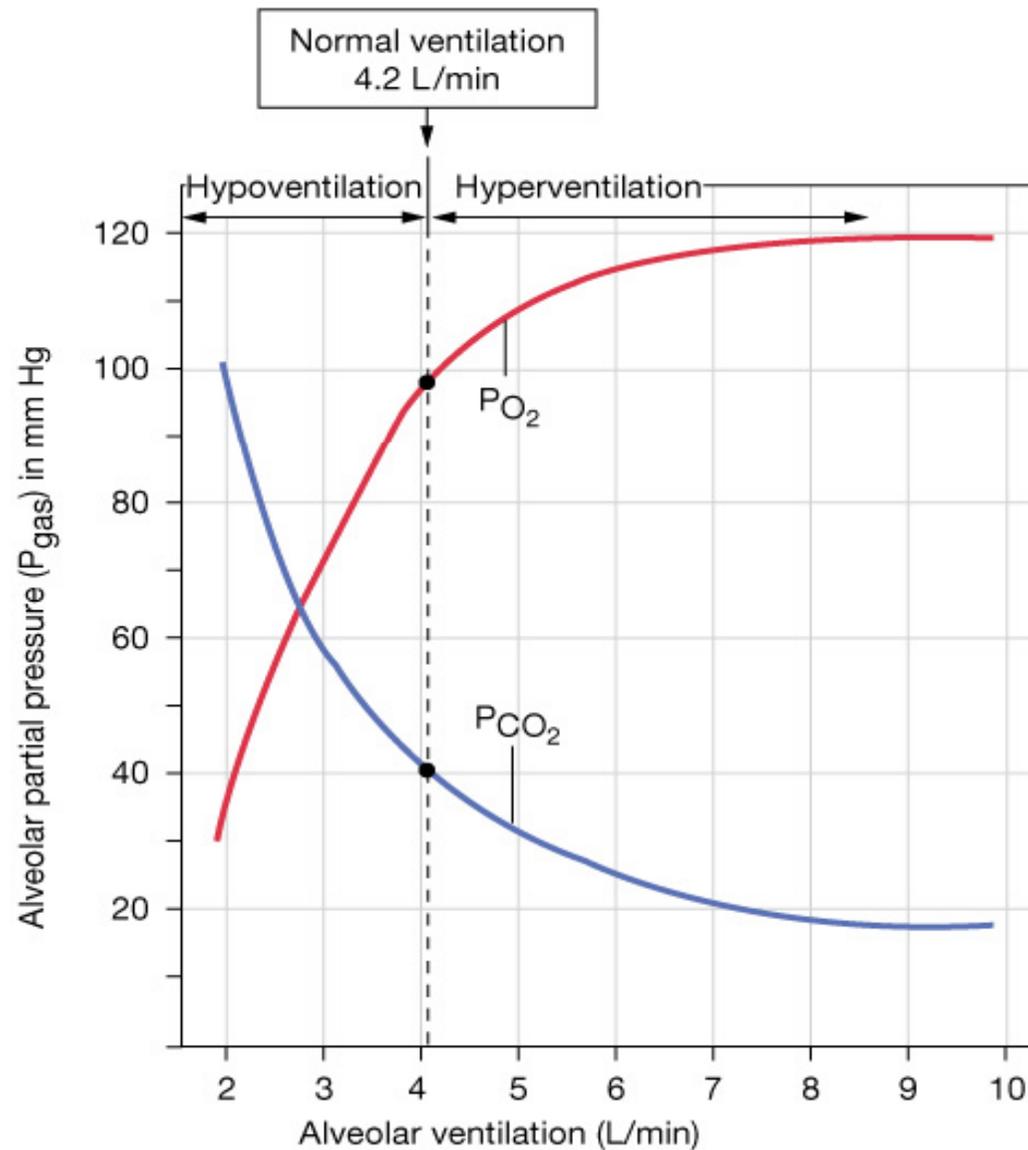
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# Control of breathing

- 1. Four major factors that affect normal breathing:
  - **Stretching** in the lungs and thoracic walls
  - **O<sub>2</sub>** level in the blood
  - **CO<sub>2</sub>** level in the blood
  - **H<sup>+</sup>** level in the blood
- 2. Normal breathing is inhibited by stretching of the lungs and thoracic walls, a rise in O<sub>2</sub> level, and a decrease in CO<sub>2</sub> and H<sup>+</sup> levels; while normal breathing is stimulated by relaxing of the lungs and thoracic walls, a decrease in O<sub>2</sub> level, and a rise in CO<sub>2</sub> and H<sup>+</sup> levels.

- 
- Chemicals, and emotional state also affect breathing.
  - Stretch of tissues: inhibits inspiration by triggering an inflation reflex which reduces the duration of inspiratory movements. This, also prevents overinflation of the lungs during forceful breathing. Hyperventilation decreases carbon dioxide concentration as well.
  - Low blood  $PO_2$ : increase alveolar ventilation (peripheral chemoreceptors in the carotid bodies & aortic bodies detect low  $O_2$  concentrations).
  - High blood  $P_{CO_2}$ : increase alveolar ventilation.
  - High CSF,  $H^+$  ion concentration: increase breathing rate and alveolar ventilation.  $CO_2$  combines with water to form carbonic acid, which in turn, releases  $H^+$  ions in CSF.

# Effect of changing alveolar ventilation on $P_{O_2}$ & $P_{CO_2}$ in the alveoli

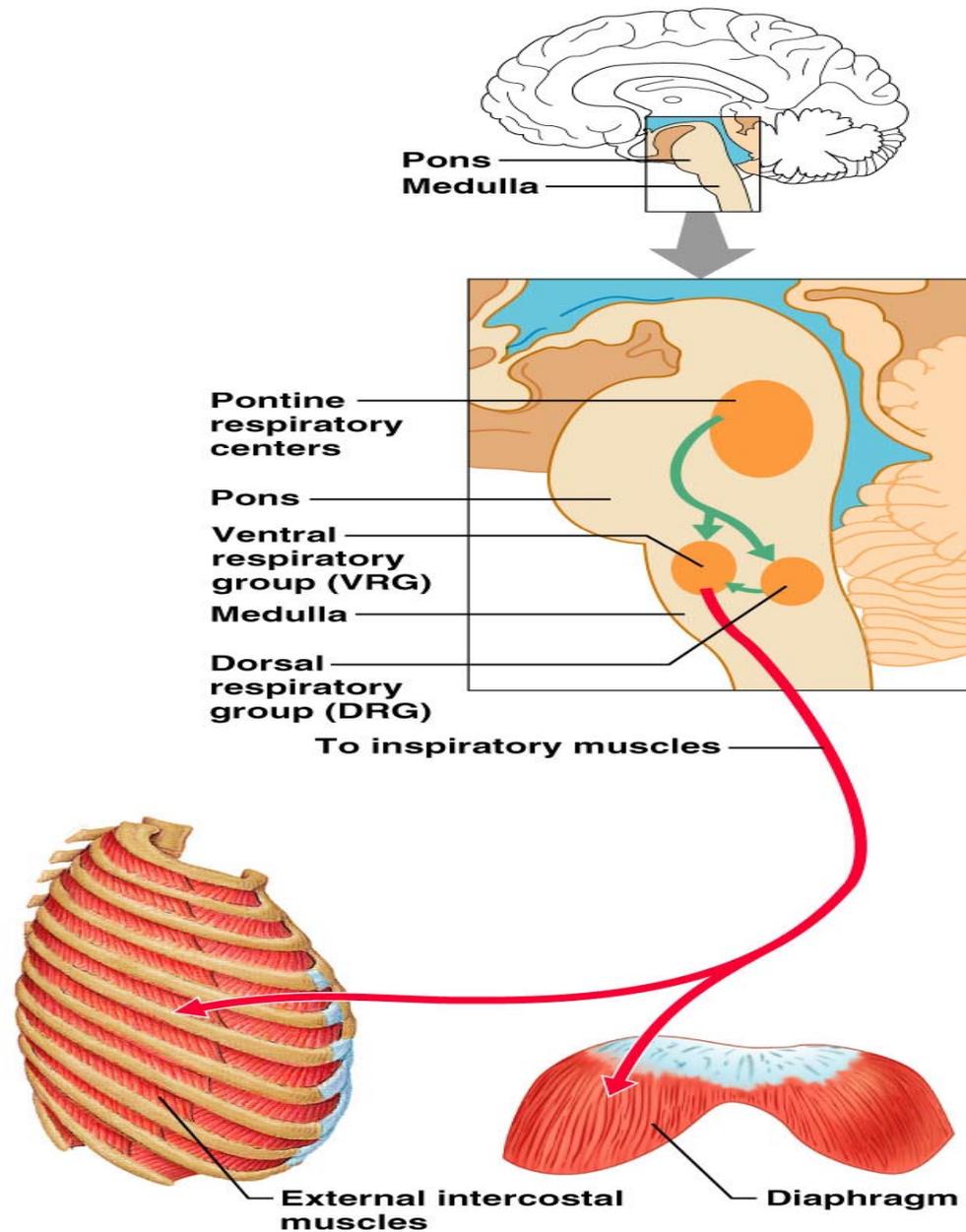


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# Respiratory Centers

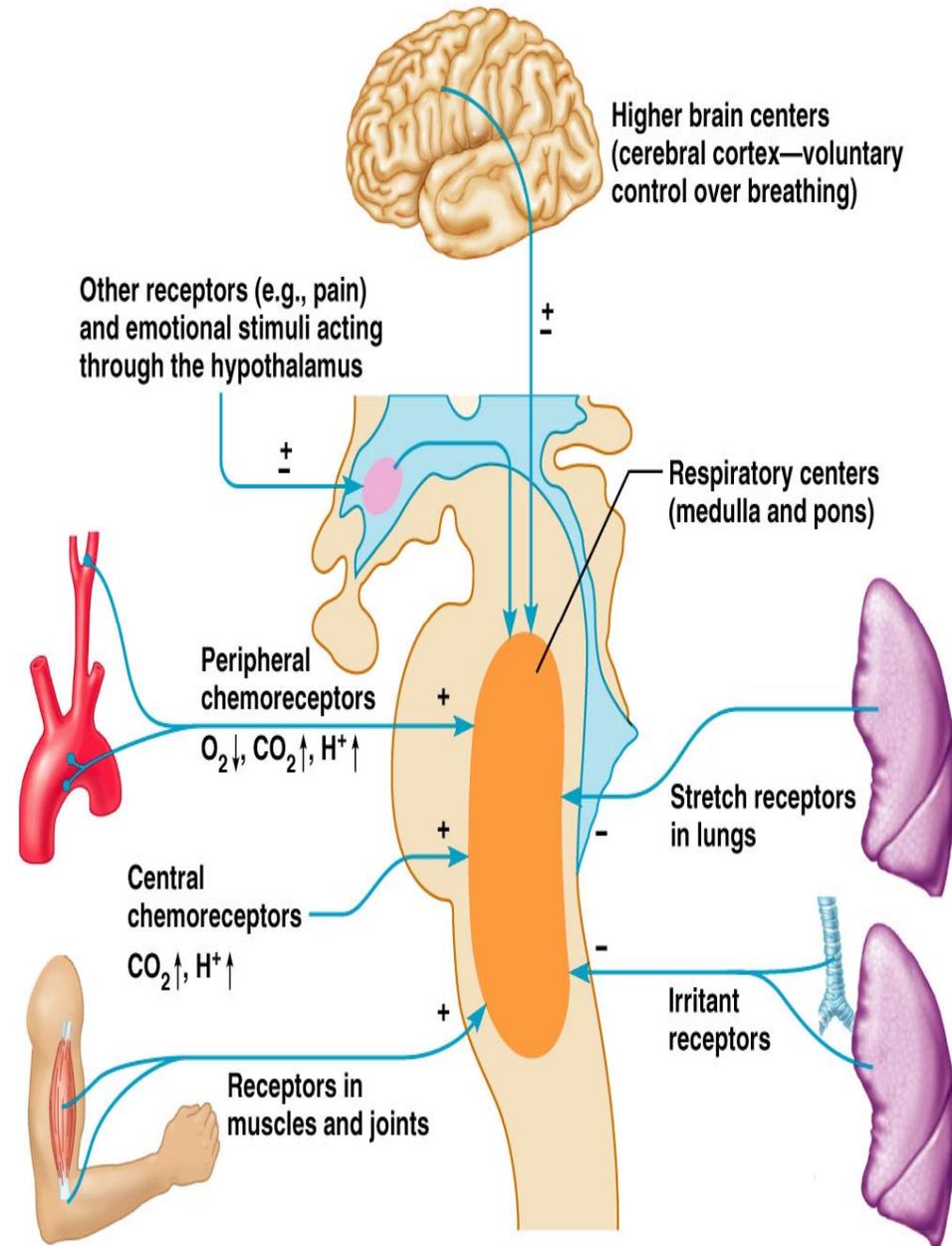
- 3. Normal breathing is a rhythmic, involuntary action regulated by the **respiratory centers** in the pons and medulla oblongata of the brain stem.
- **Rhythmicity area** in the medulla oblongata sets the basic rhythm of inspiration and expiration, and is subdivided into the **dorsal respiratory group** (which controls normal breathing) and the **ventral respiratory group** (which controls forceful, voluntary breathing).
- **Pneumotaxic area** in the pons sets the depth, duration, and rate of breathing by influencing the dorsal respiratory group.

# Respiratory Centers

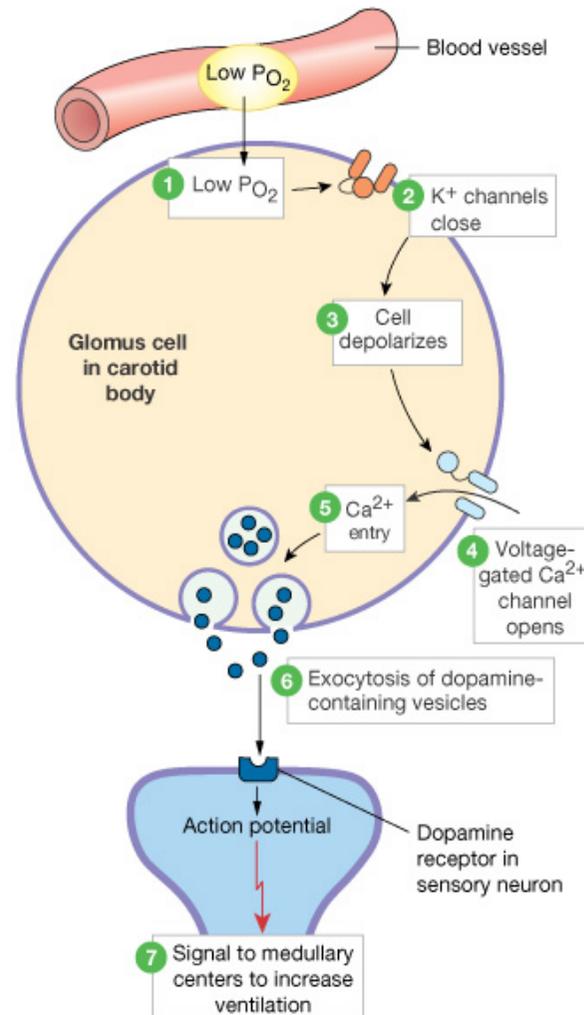


# Chemoreceptors

- **Central Chemoreceptors** are associated with the respiratory centers.  $\text{CO}_2$  combines with water to form carbonic acid, which in turn, releases  $\text{H}^+$  ions in CSF. Stimulation of these areas increases alveolar ventilation.
- **Peripheral Chemoreceptors** are in the carotid bodies & aortic bodies. These chemoreceptors sense low  $\text{O}_2$  concentration. when  $\text{O}_2$  concentration is low, alveolar ventilation increases.

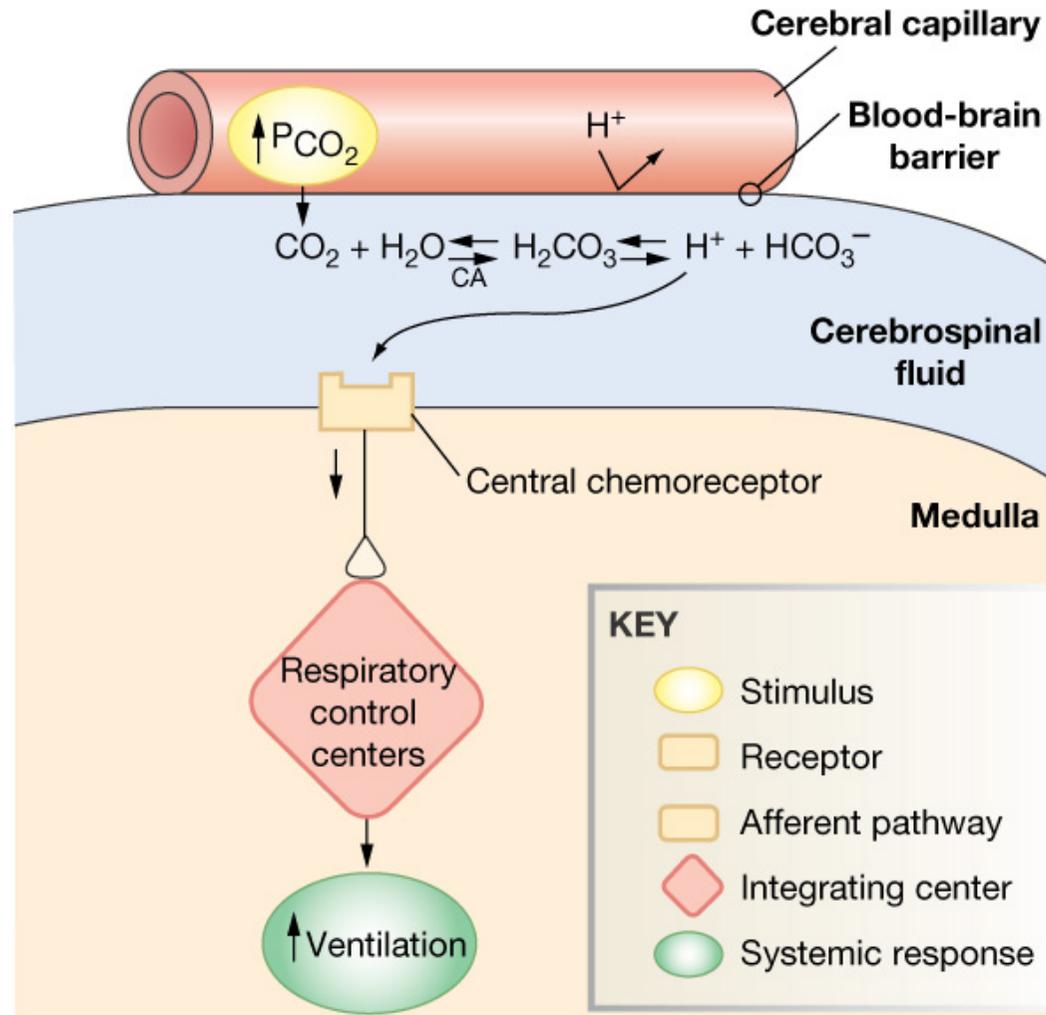


# Peripheral Chemoreceptors



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# Central Chemoreceptors

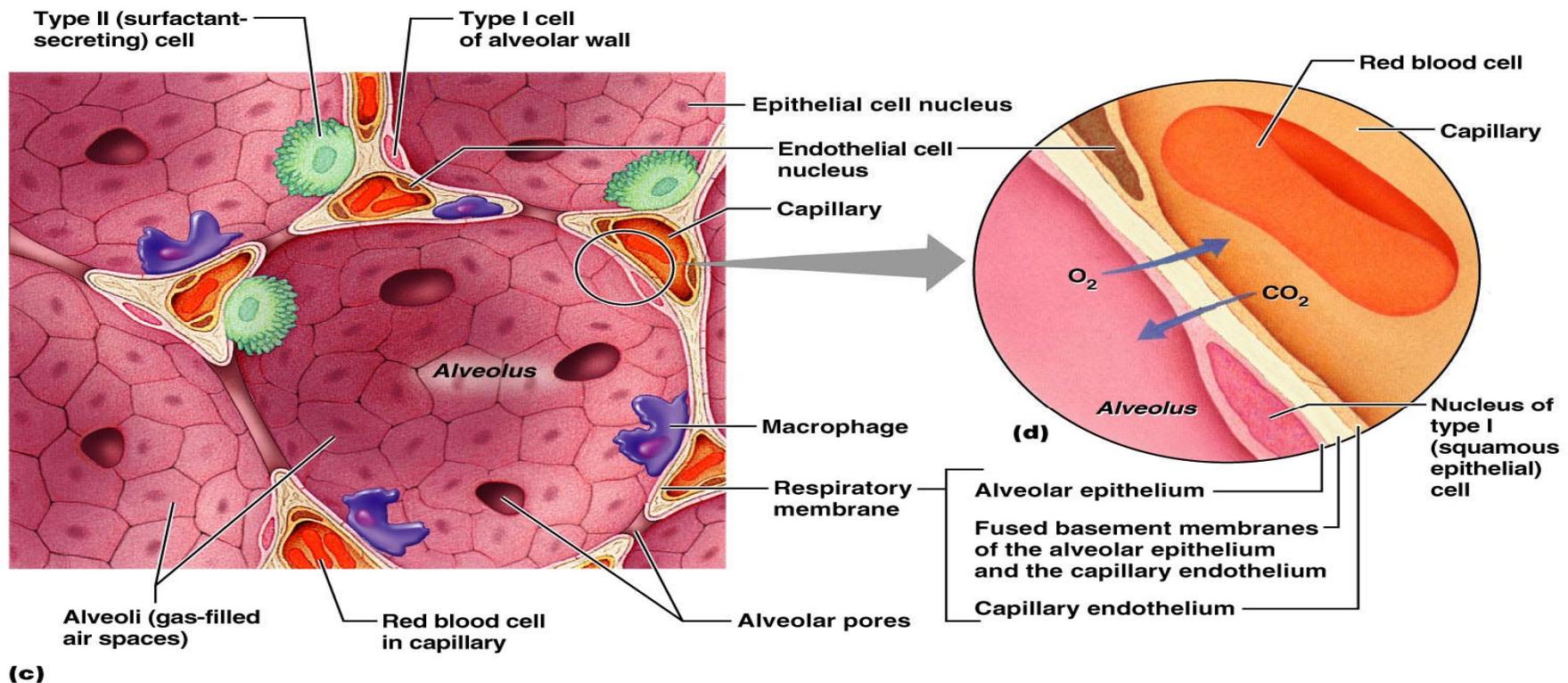


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- **Pco<sub>2</sub>**: Medullary chemoreceptors are sensitive to the PH of CSF. Diffusion of Co<sub>2</sub> from the blood into CSF lowers the PH of CSF by forming carbonic acid. Similarly, the aortic and carotid bodies are stimulated by a fall in blood PH, induced by increases in blood Co<sub>2</sub>.
  - **PH**: peripheral chemoreceptors are stimulated by decreased blood PH independent of the effect of blood Co<sub>2</sub>. Chemoreceptors in the medulla are not affected by changes in blood PH because H<sup>+</sup> cannot cross the blood brain barrier.
  - **Po<sub>2</sub>**: Low blood Po<sub>2</sub> augments the chemoreceptor response to increases in blood Pco<sub>2</sub> and can stimulate ventilation directly when the Po<sub>2</sub> falls below 50 mmHg.
  - **Ventilation**: the amount of air moved in and out of the lungs during each minute is called pulmonary ventilation. Increase in metabolism is accompanied by increases in ventilation (due to increase in plasma Co<sub>2</sub>).

# Gas Exchange

**Respiratory membrane** is formed by the walls of alveoli and capillaries where they are both made of simple squamous epithelium, thin enough to allow diffusion of gases called **gas exchange** to occur.



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## Dalton's Law

- Gases (particularly O<sub>2</sub> and CO<sub>2</sub> for this discussion) always diffuse from high pressure to low pressure. Each gas in a mixture of gases produces its own pressure called **partial pressure (pp or p)**, and the sum of all partial pressure is the total pressure of that gas mixture – a physical law called the **Dalton's law**. Therefore, the directions of diffusion during gas exchange in the lungs and in body tissues are based on the differences in partial pressure of these gases.

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# External & Internal Respiration

- **External Respiration:** occurs in the lungs to oxygenate the blood and remove CO<sub>2</sub> from the deoxygenated blood. O<sub>2</sub> diffuses from the alveoli into capillaries, while CO<sub>2</sub> diffuses from the capillaries into alveoli.
- **Internal respiration** (tissue respiration). occurs in the body tissues to provide O<sub>2</sub> to tissue cells and remove CO<sub>2</sub> from the cells. O<sub>2</sub> is critical in the release of energy molecules (i.e. ATP) , a process called **cellular respiration**, while CO<sub>2</sub> is a byproduct of metabolism which can become harmful to tissue cells in large quantities.
- O<sub>2</sub> diffuses from the capillaries into tissue cells, while CO<sub>2</sub> diffuses from tissue cells into capillaries.

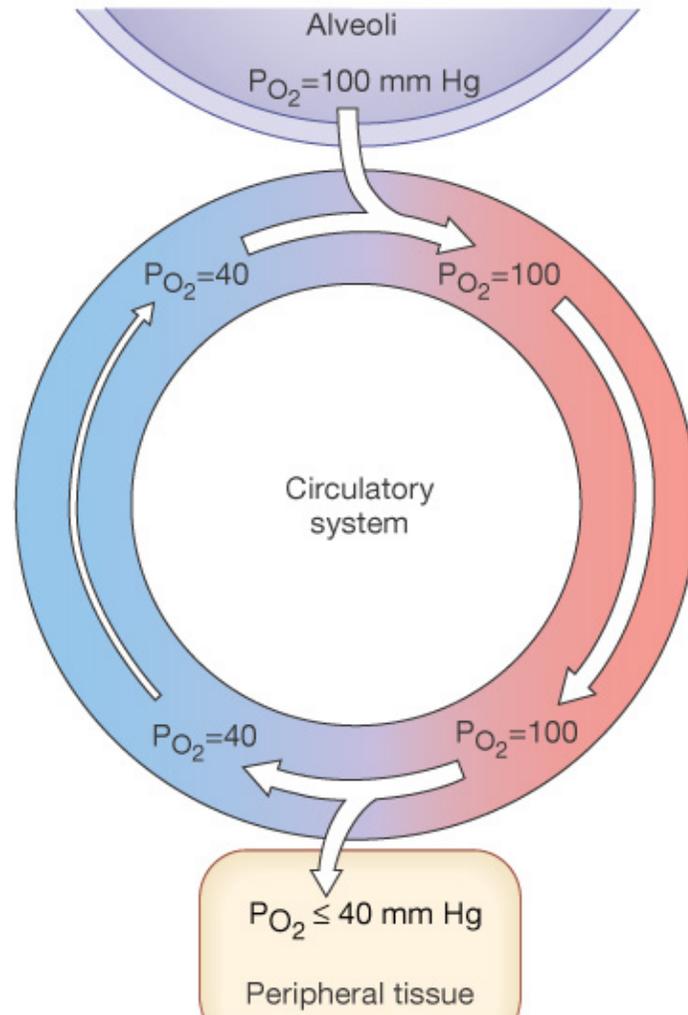
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# Alveolar Gas exchange

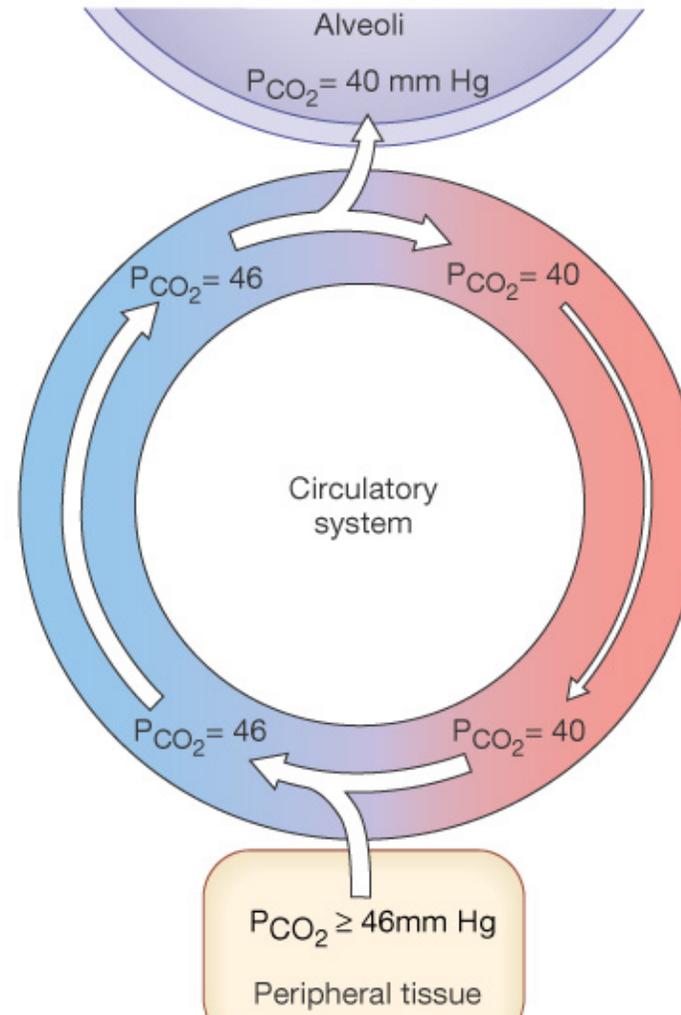
- Gas exchanges between the air and the blood occur within the **alveoli**.
- 1. The alveoli are tiny sacs clustered at the distal ends of alveolar ducts.
- 2. The respiratory membrane consists of the alveolar and capillary walls. Gas exchange takes place through these walls.
- 3. Diffusion through the respiratory membrane.
- $O_2$  diffuses from the alveolar air into the blood;  $CO_2$  diffuses from the blood into the alveolar air.
- Note: the differences in partial pressure determines the diffusion through the respiratory membrane.

# Gas Exchange at the Alveoli & Cells

(a) Oxygen diffusion



(b) CO<sub>2</sub> diffusion



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# Pulmonary vs. Systemic Capillaries

## **Pulmonary Capillaries:**

- Alveolar  $P_{O_2} = 104$  mmHg
- Pulmonary capillaries  $P_{O_2} = 40$  mmHg

Result:  $O_2$  enters capillaries

- Alveolar  $P_{CO_2} = 40$  mmHg
- Pulmonary capillaries  $P_{CO_2} = 45$  mmHg

Result:  $CO_2$  enters alveoli

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## **Systemic capillaries:**

- Systemic capillaries  $P_{O_2} = 104$  mmHg
- Tissues  $P_{O_2} = >40$  mmHg

Result:  $O_2$  enters tissues

- Systemic capillaries  $P_{CO_2} = 40$  mmHg
- Tissues  $P_{CO_2} = < 45$  mmHg

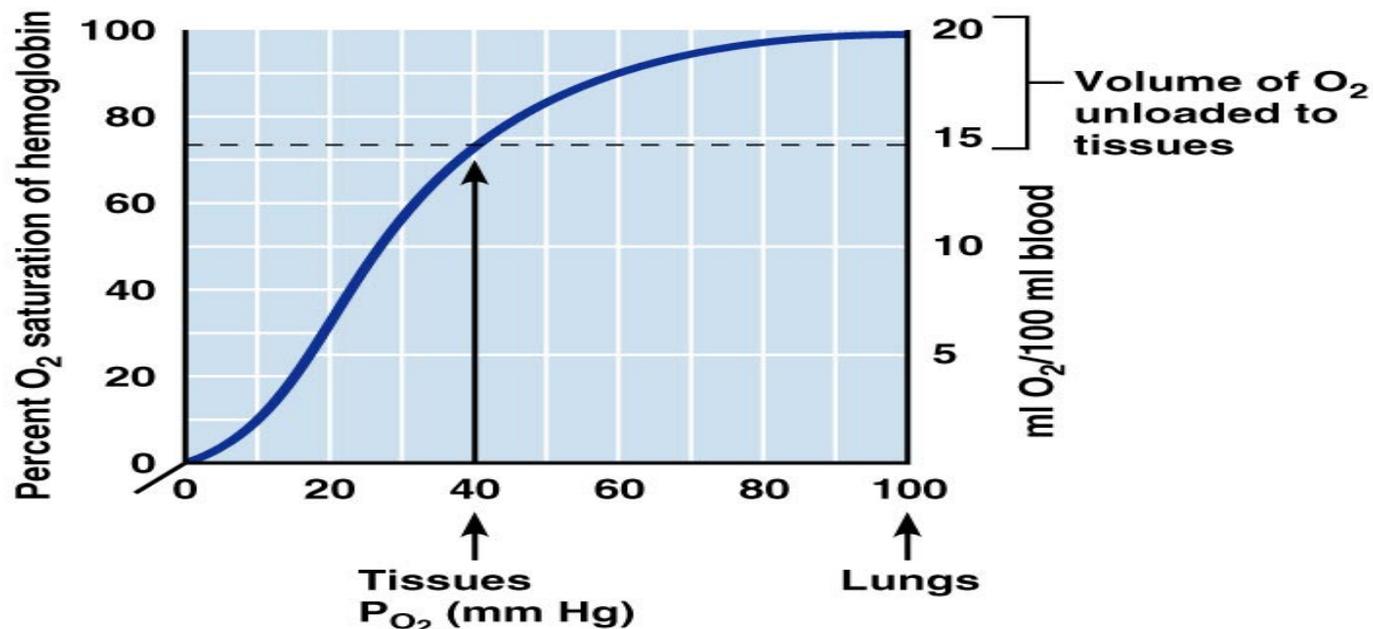
Result:  $CO_2$  enters capillary

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# Gas Transport - Oxygen

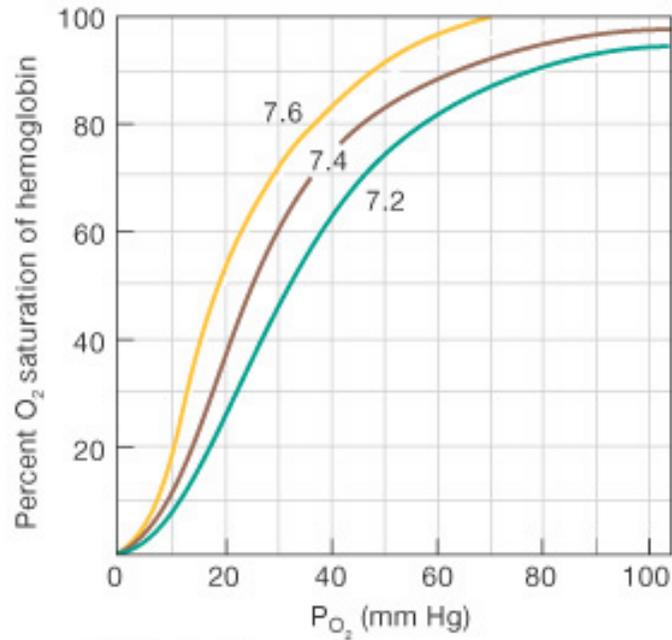
- **98%** of  $O_2$  is transported by binding to **hemoglobin** in erythrocytes [when  $O_2$  binds with hemoglobin (Hb) oxyhemoglobin (oxy-Hb) is formed which shows are a red pigment].
- **2%** of  $O_2$  is dissolved in the blood plasma.
- The resulting oxyhemoglobin is relatively unstable and releases its  $O_2$  in regions where  $P_{O_2}$  is low.
- More  $O_2$  is released as the blood conc. of  $CO_2$  increases, as the blood becomes more **acidic**, and as the blood **Temp.** increases.
- The efficiency of oxy-Hb releasing  $O_2$  to tissue cells during internal respiration is shown on **the  $O_2$ -Hb dissociation curve** which shows a distinctive sigmoid shape.

- On this curve, as  $O_2$  partial pressure increases, the level of Hb saturation increases (each Hb molecule can bind up to four  $O_2$  molecules).
- At about 40 mmHg of  $O_2$ , roughly 75% of Hb is saturated.
- At about 80 mmHg of  $O_2$ , close to 98% of Hb is saturated, and the curve becomes flattened beyond this point where only about 98 - 99% of Hb can be saturated no matter how high the  $O_2$  pressure is.

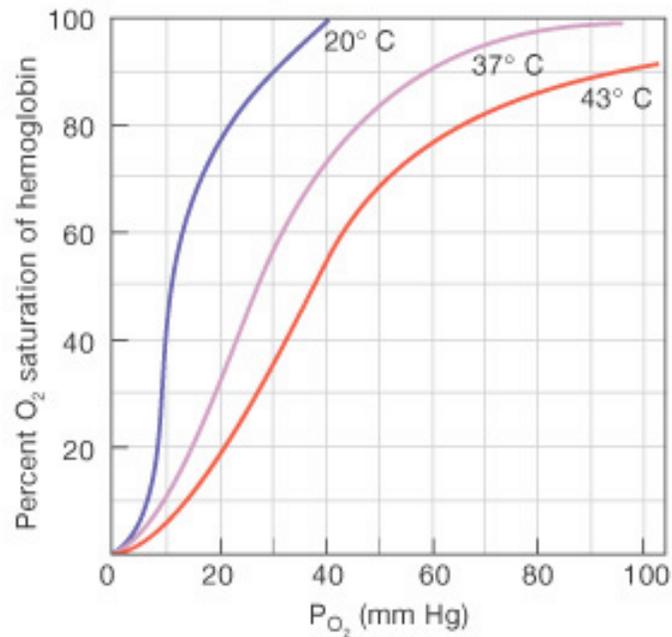


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- 4 main factors that can shift the O<sub>2</sub>-Hb dissociation curve:
    - O<sub>2</sub> pressure – a decrease shifts the curve to the right.
    - CO<sub>2</sub> pressure – an increase shifts the curve to the right.
    - PH of blood – more acidic shifts the curve to the right.
    - Body temperature – an increase shifts the curve to the right.

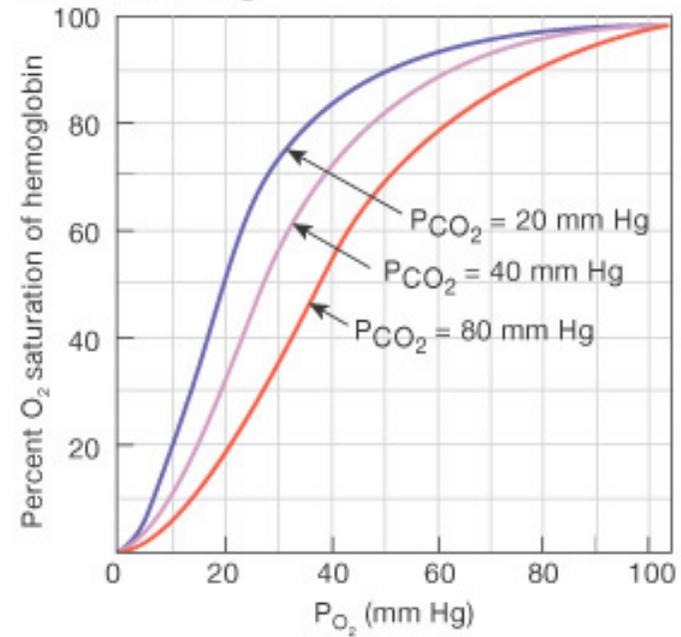
**(a) Effect of pH**



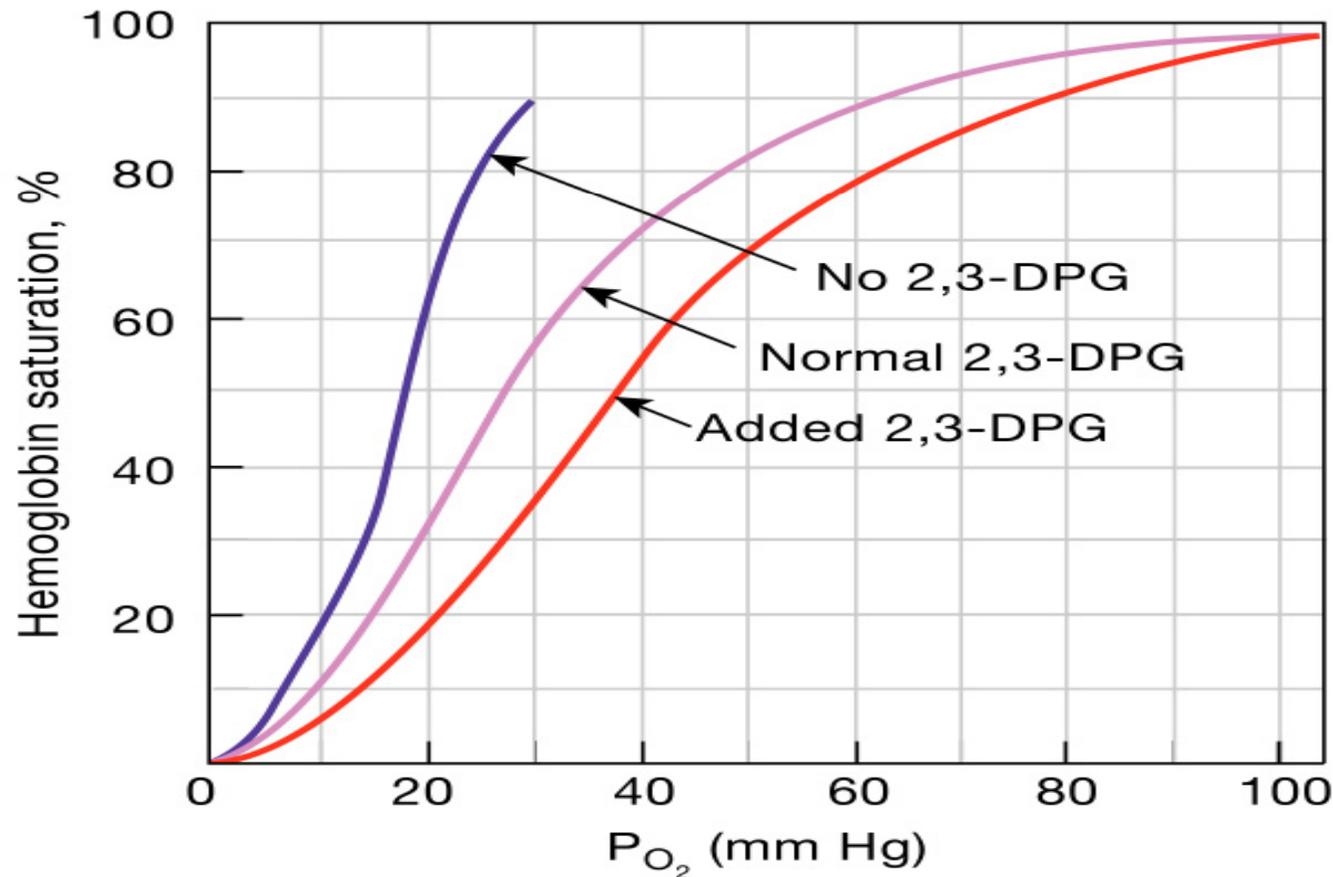
**(b) Effect of temperature**



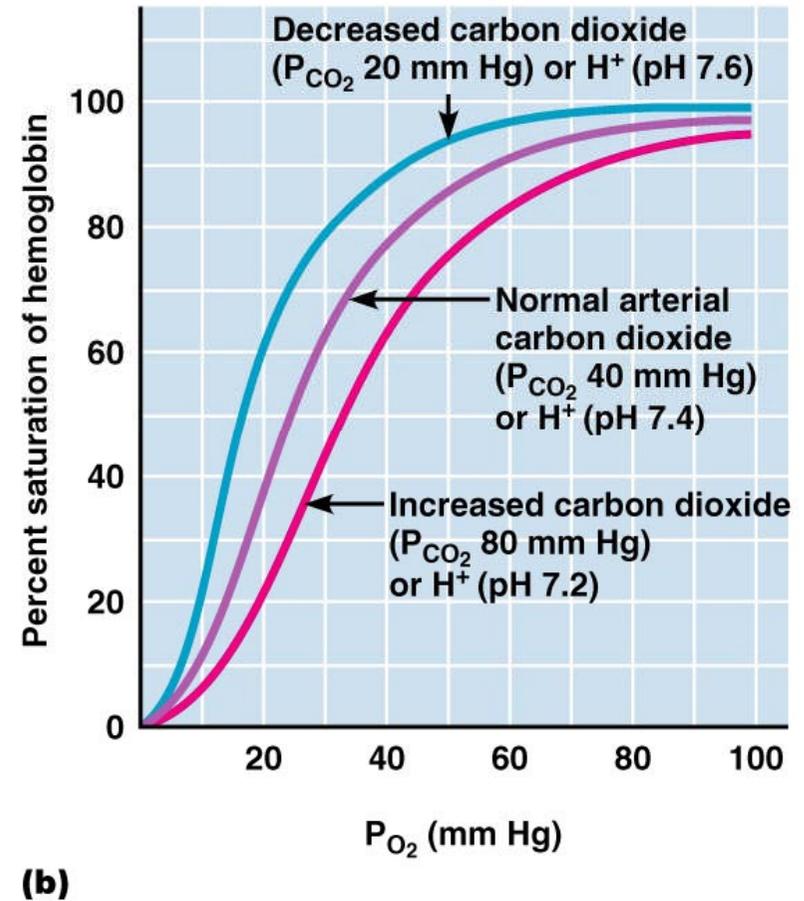
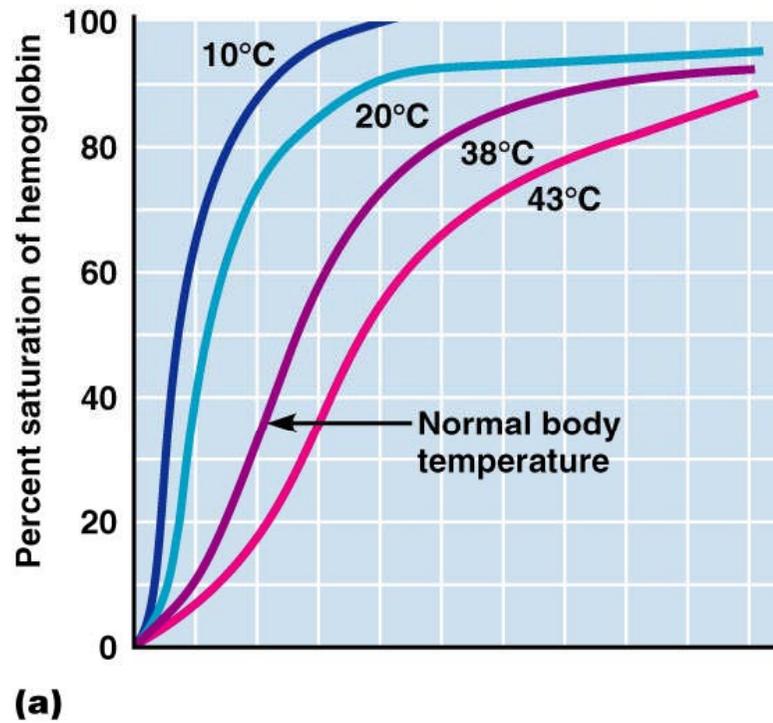
**(c) Effect of  $P_{CO_2}$**



- When this dissociation curve shifts to the right, it is a phenomenon called the **Bohr effect**, where less Hb saturation occurs and more O<sub>2</sub> is being released from oxyhemoglobin. When the dissociation curve shifts to the left (which is less common), it is called the **Haldane effect**, where more Hb saturation occurs and less O<sub>2</sub> release.

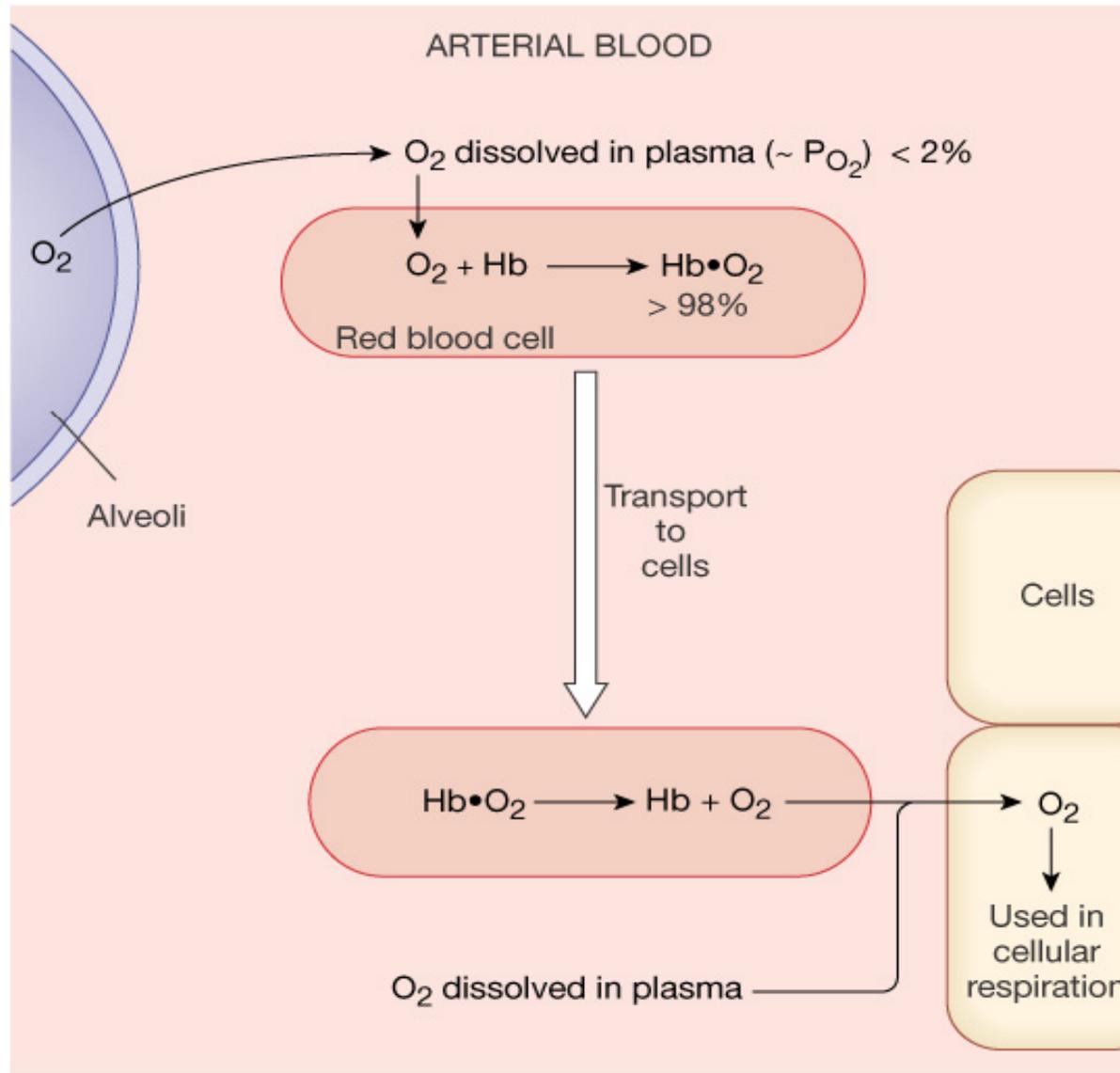


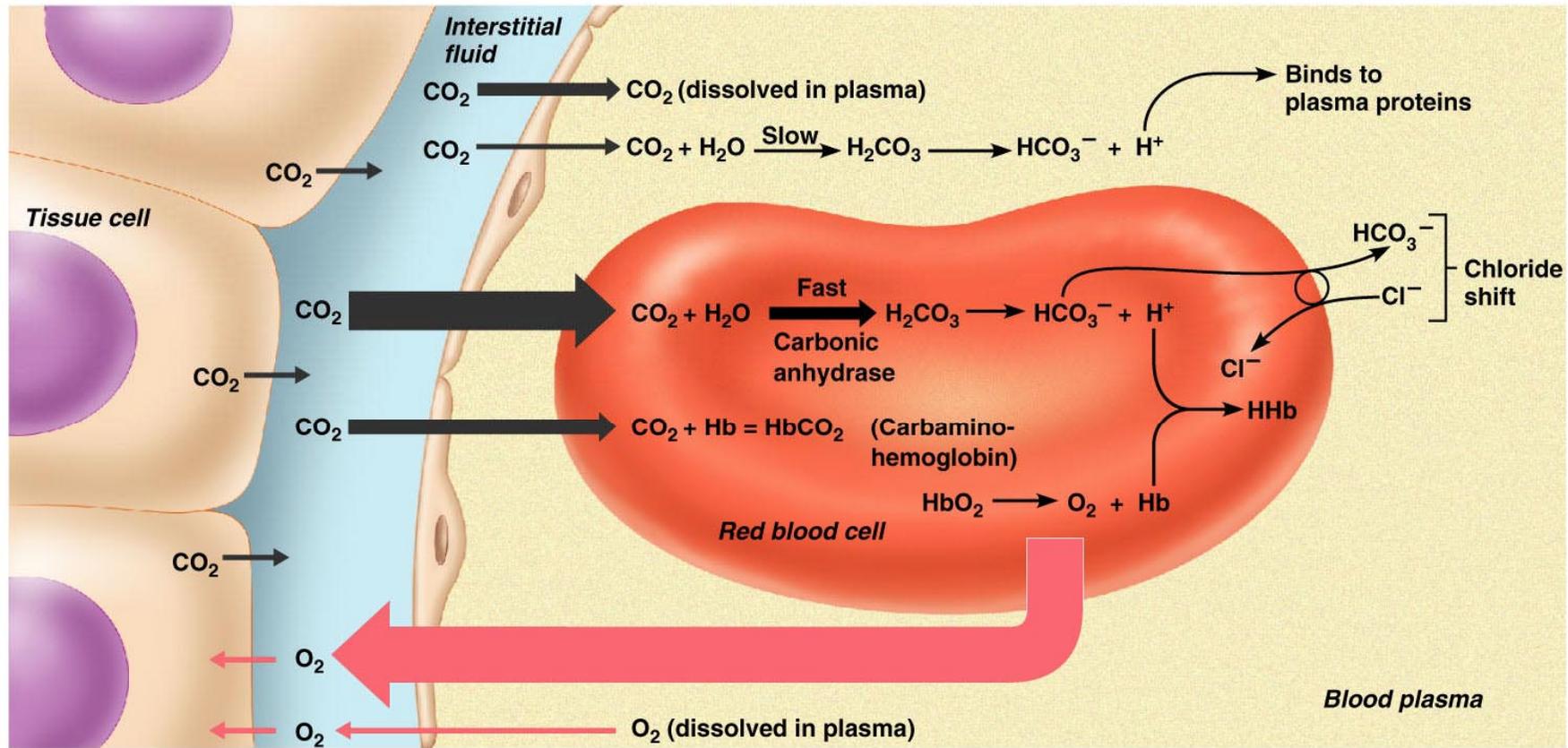
# Oxygen-Hemoglobin dissociation curve



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# Summary of Oxygen transport in the blood





**(a) Oxygen release and carbon dioxide pickup at the tissues**

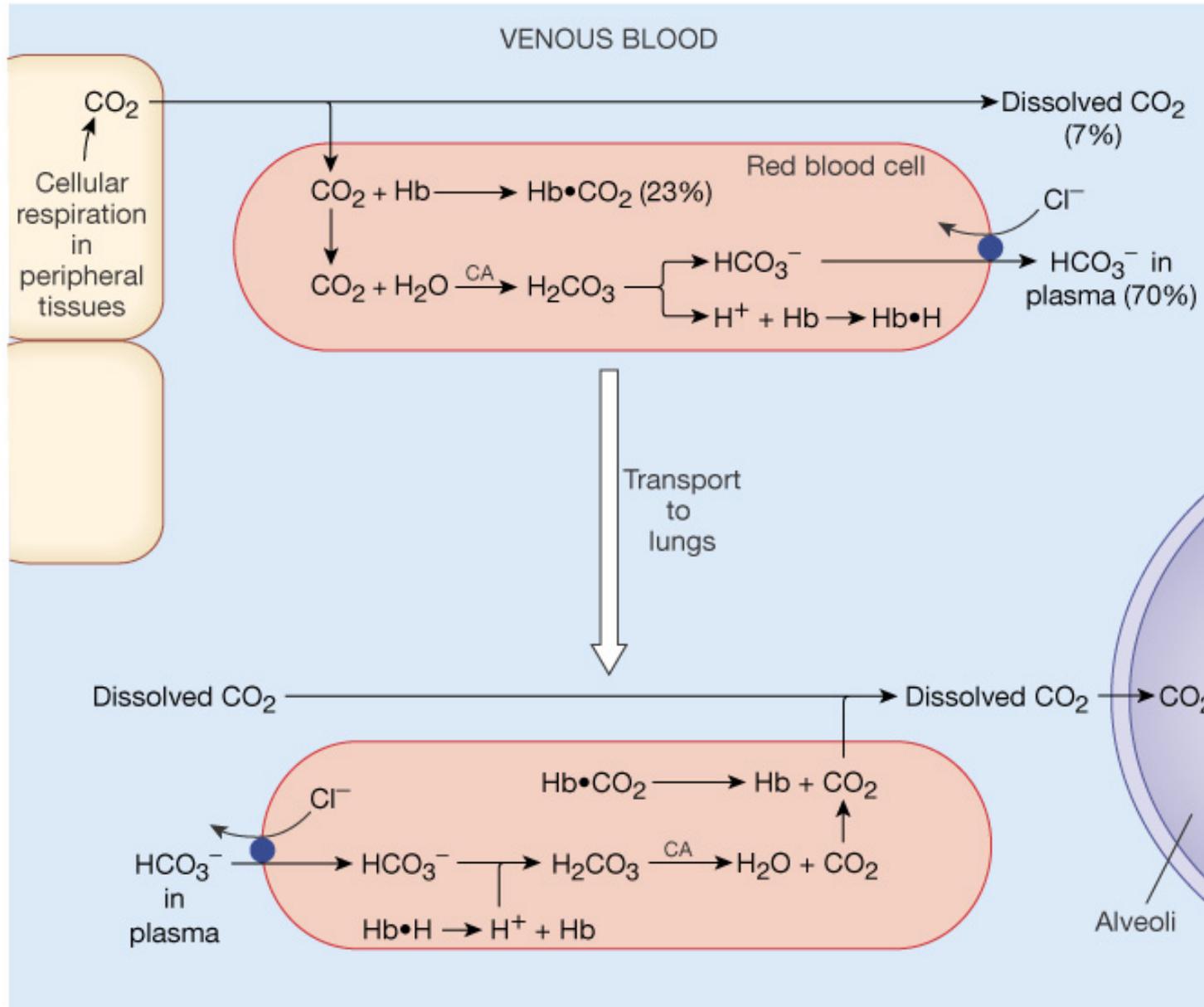
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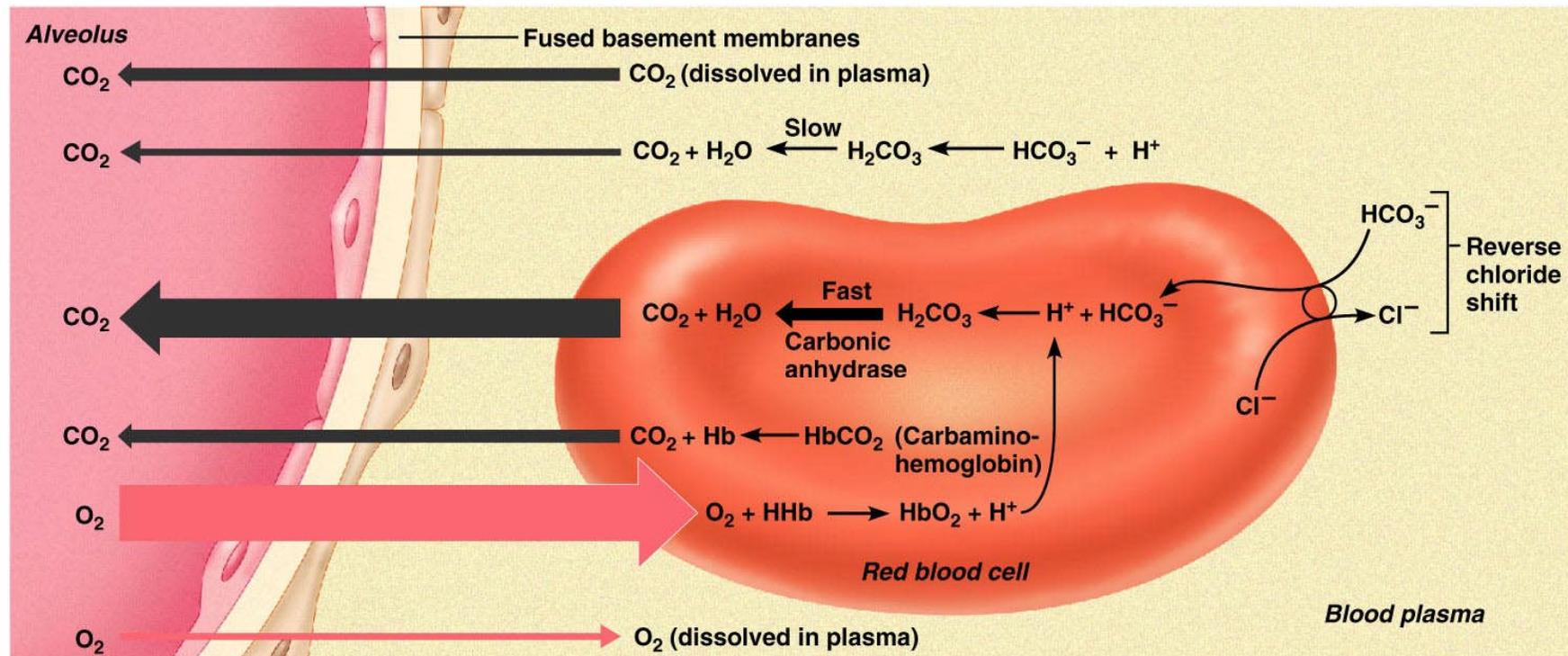
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# Gas Transport – carbon dioxide

- **7%** of CO<sub>2</sub> is dissolved in the blood plasma.
- **23%** of CO<sub>2</sub> binds with hemoglobin in erythrocytes. [when CO<sub>2</sub> binds to Hb, carbaminohemoglobin is formed which shows a bluish pigment].
- **70%** of CO<sub>2</sub> reacts with water and forms carbonic acid in erythrocytes  $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3$
- Carbonic acid is immediately broken down by the enzyme carbonic anhydrase (CA), to become hydrogen ion and bicarbonate ion.
- $\text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^-$
- Where H<sup>+</sup> quickly binds with Hb to prevent it from affecting blood pH too drastically, and HCO<sub>3</sub><sup>-</sup> diffuses into blood plasma and maintains an ionic balance with chloride anion (Cl<sup>-</sup>).

# Carbon dioxide transport in the blood





**(b) Oxygen pickup and carbon dioxide release in the lungs**

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## Gas Transport – carbon monoxide

- **Co** forms as a result of incomplete combustion of fuels.
- It combines with hemoglobin more readily than **O<sub>2</sub>** and forms a stable compound.
- **Co** is **toxic** because the hemoglobin with which it combines is no longer available for **O<sub>2</sub>** transport.

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# Clinical Terms

- **Anoxia**: absence or a deficiency of O<sub>2</sub> within tissues.
- **Asphyxia**: deficiency of O<sub>2</sub> and excess of Co<sub>2</sub> in the blood and tissues.
- **Atelectasis**: collapse of a lung or some portion of it.
- **Bronchitis**: inflammation of the bronchial lining.
- **Cheyne – strokes – respiration**: irregular breathing pattern of a series of shallow breaths that increases in depth and rate, followed by breaths that decrease in depth and rate.
- **Dyspnea**: difficulty in breathing.
- **Hyperoxia**: excess oxygenation of the blood.
- **Hyperpnea**: increase in the depth and rate of breathing.

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# Clinical Terms

- **Hypoxia**: diminished availability of O<sub>2</sub> in the tissues.
- **Pneumothorax**: entrance of air into the space between the pleural membrane, followed by collapse of the lung.
- **Tachypnea**: rapid, shallow breathing.
- **Asthma**: the dyspnea, wheezing and other symptoms of asthma are produced by obstruction of air flow through the bronchioles that occur in episodes or "attacks" (obstruction is due to inflammation).
- **Lung cancer**: 1/3 of cancer death in the U.S. – smoking is the leading cause.