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# Control of breathing

Respiratory block

PHYSIOLOGY 438 TEAMWORK

- Red: important
- Black: in male / female slides
- Pink: in female slides only
- Blue: in male slides only
- Yellow: notes
- Gray: extra information
- Textbook: Guyton + Linda

Editing file

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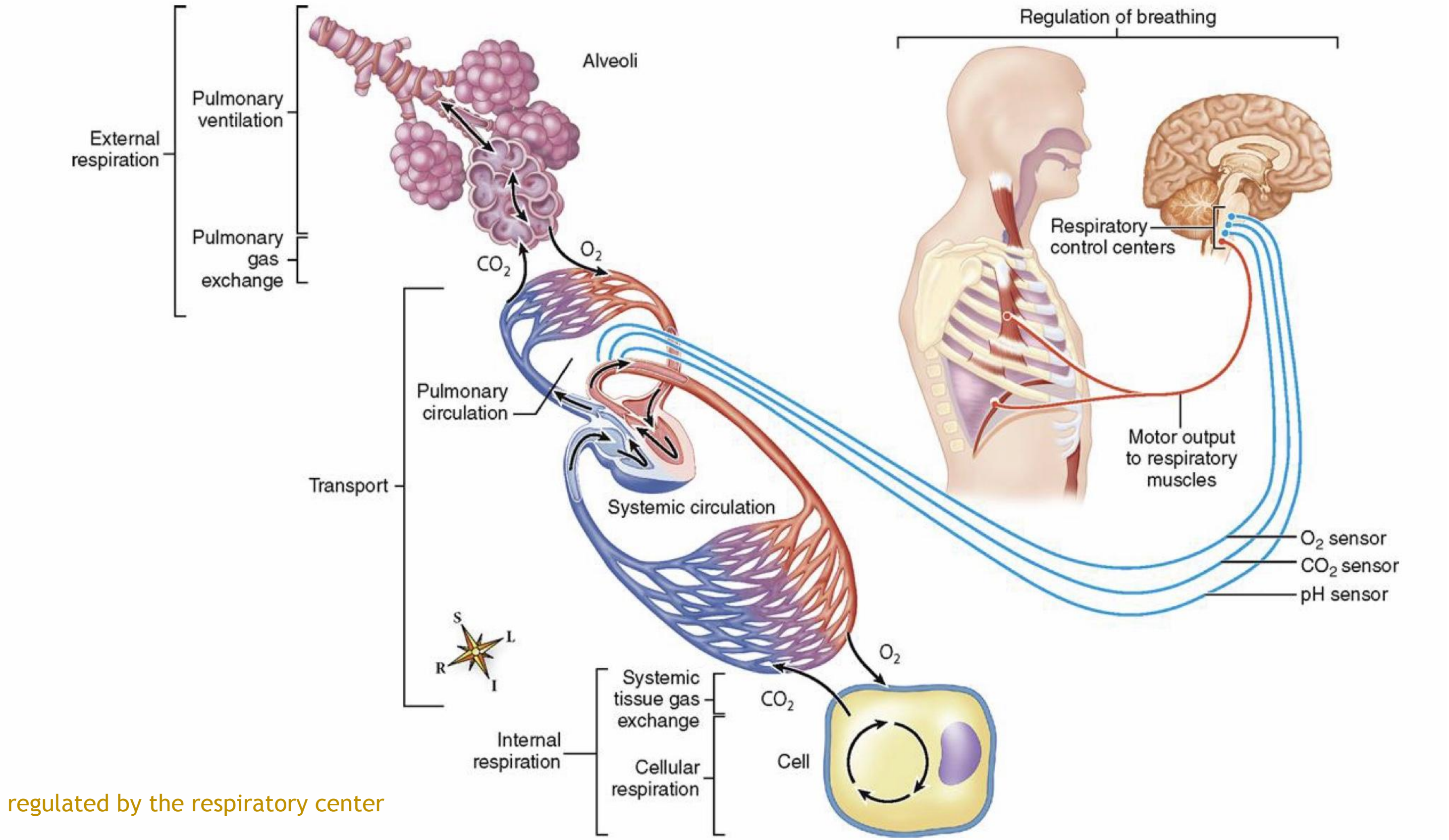
# Objectives

1. Understand the role of the medulla oblongata in determining the basic pattern of respiratory activity.
2. List some factors that can modify the basic breathing pattern like e.g. a- The Hering-Breuer reflexes, b- The proprioreceptor reflexes, c- The protective reflexes, like the irritant, and the J-receptors.
3. Understand the respiratory consequences of changing $PO_2$, $PCO_2$, and PH.
4. Describe the locations and roles of the peripheral and central chemoreceptors.
5. Compare and contrast metabolic and respiratory acidosis and metabolic and respiratory alkalosis.

# The overall processes of External Respiration




★ All this process is regulated by the respiratory center

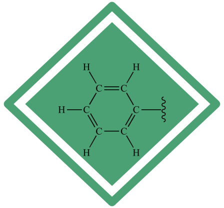
# Controls of rate and depth of respiration

O=O

## Arterial $PO_2$

When $PO_2$ is VERY low (Hypoxia), ventilation increases. (it will stimulate respiration, but it's not a major player)

"Less sensitive, only major changes in $PO_2$ will cause increase ventilation"



## Arterial pH

As hydrogen ions increase (acidosis), alveolar ventilation increases.

Concentration of $H^+$↑> (acidosis)

Concentration of $H^+$↓> (alkalosis)

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

carbonic acid — bicarbonate

Acid/base metabolism in the body is regulated by this chemical equation.

O=C=O

## Arterial $PCO_2$

The most important regulator of ventilation is $PCO_2$ (very strong stimulus), small increases in $PCO_2$, greatly increases ventilation. (even a slight increase in $co_2$ means that there's a problem)

➔ Recall from the 5th lecture

$CO_2$ 20 time more soluble than $O_2$

The Most important center controlling respiration, because it is the origin of the basic rhythm of inspiration (area that initiate inspiration)

# Respiratory centers

Helpful video

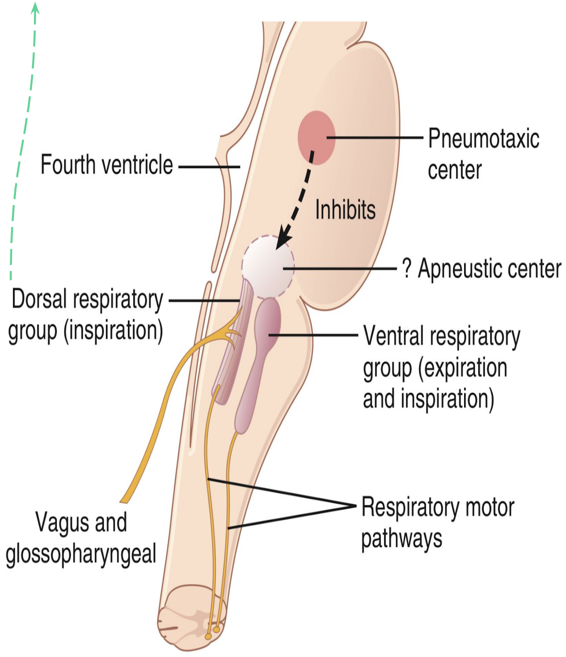



**Figure 42-1.** Organization of the respiratory center.

## Medullary Respiratory centers

**Inspiratory area (Dorsal Respiratory Group) DRG:**

- Determines basic rhythm of breathing.
- Causes contraction of diaphragm and external intercostals.

**Expiratory area (Ventral Respiratory Group) VRG:**

- Although it contains both inspiratory and expiratory neurons.
  It is inactive during normal quiet breathing.
- Activated by inspiratory area during forceful breathing.
- Causes contraction of the internal intercostals and abdominal muscles.

From Guyton

The respiratory center is composed of several groups of neurons located bilaterally in the medulla oblongata and pons of the brain stem. It is divided into three major collections of neurons:
(1) a dorsal respiratory group, located in the dorsal portion of the medulla, which mainly causes inspiration.
(2) a ventral respiratory group, located in the ventrolateral part of the medulla, which mainly causes expiration.
(3) the pneumotaxic center, located dorsally in the superior portion of the pons, which mainly controls rate and depth of breathing.

The medullary respiratory center stimulates basic inspiration for about 2 seconds and then basic expiration for about 3 seconds (5 sec/ breath = 12 breaths/min).

# Respiratory centers

Pontine (bridge) Respiratory centers

Transition between inhalation and exhalation is controlled by:

## Pneumotaxic area:

- Inhibits inspiratory area of medulla to stop inhalation.

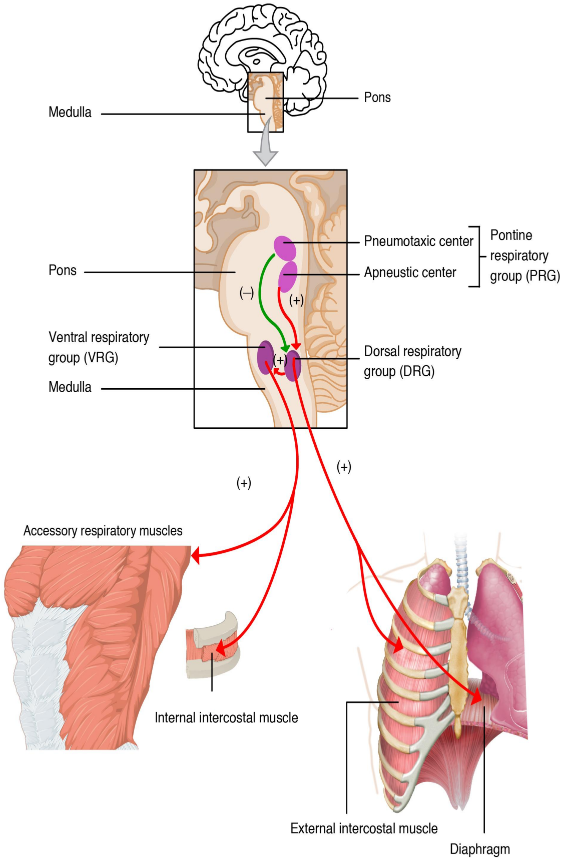
➔ Therefore, breathing is more rapid when pneumotaxic area is active.

limits the period of inspiration.

## Apneustic area:

- Stimulates inspiratory area of medulla to prolong inhalation.

➔ Therefore slow respiration and prolonged respiratory cycles will result if it is stimulated.

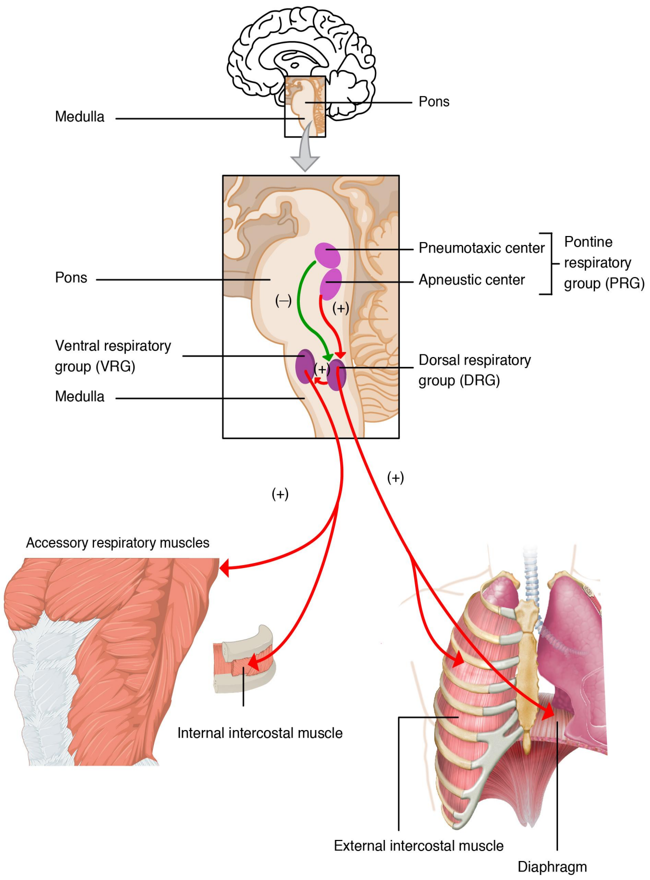



If the pneumotaxic became active it will lead to 1-1.5 sec of inspiration (normal=2) and the rate of expiration will increase (faster).

While Apneustic tries to prolong the inspiration more than normal 2.5-3 sec thus the rate of expiration will be reduced.

# Hering-Breuer inflation reflex

- When the lung becomes overstretched (tidal volume is about 1-1.5L), stretch receptors located in the wall of bronchi and bronchioles transmit signals through vagus nerve to DRG producing effect similar to pneumotaxic center stimulation (because they are overstimulated)
- Switches off inspiratory signals and thus stops further inspiration .
- This reflex also increases the rate of respiration as does the pneumotaxic center.
- This reflex appears to be mainly a protective mechanism for preventing excess lung inflation.



Peripheral > faster because they are in the blood,but less powerful.
Central > slower but more powerful.

# Chemical Control of Respiration

## Peripheral and central chemoreceptors

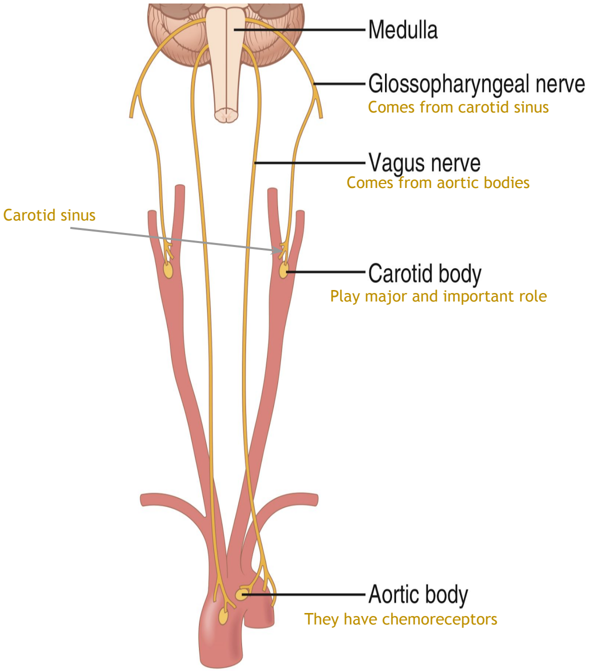



**Figure 42-4.** Respiratory control by peripheral chemoreceptors in the carotid and aortic bodies.

Peripheral chemoreceptors could be stimulated by:
Decrease $PO_2$
Increase $PCO_2$
Change in $H^+$ (acidosis)

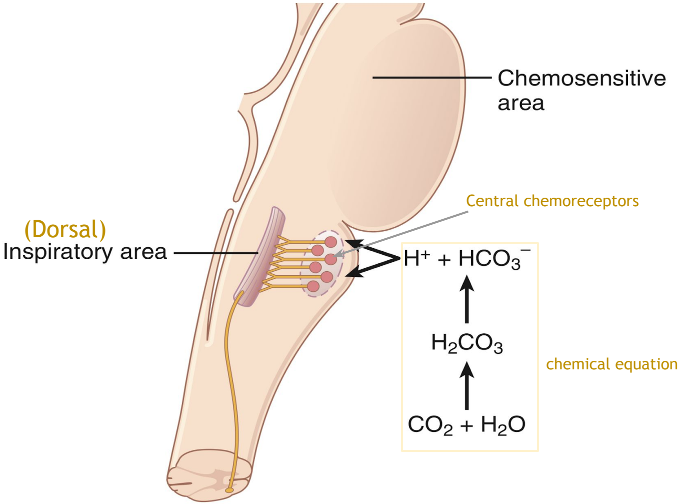
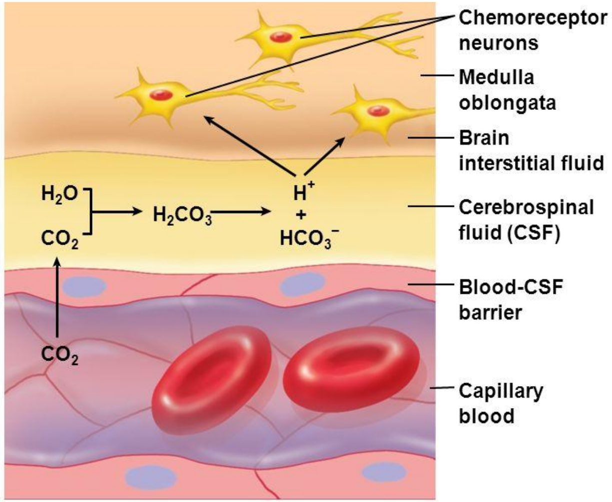


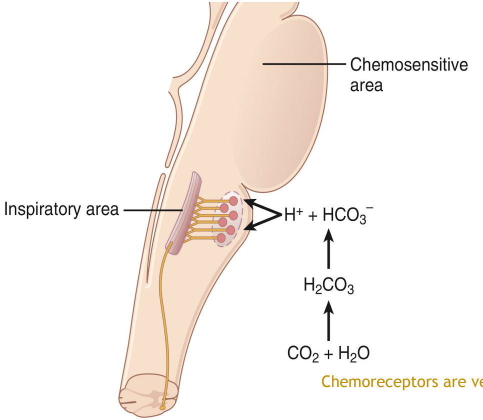

**Figure 42-2.** Stimulation of the *brain stem inspiratory* area by signals from the *chemosensitive area* located bilaterally in the medulla, lying only a fraction of a millimeter beneath the ventral medullary surface. Note also that hydrogen ions stimulate the chemosensitive area, but carbon dioxide in the fluid gives rise to most of the hydrogen ions.

$O_2$ and $CO_2$ can crosse the BBB and but $H^+$ cannot.
why only the peripheral chemoreceptors are detecting hypoxia?
Due to the position of the peripheral chemoreceptors which are located inside the big blood vessels and their blood supply is 20 times greater than its volume. And It means that the saturation of oxygen inside it is like the arterial blood ($PO_2$=95 mmHg). Which enables them to detect any decrease in oxygen saturation in arterial blood.
On the other hand, the central chemoreceptors are surrounded by the interstitial fluid of the brain . And Like any other interstitial fluid in the body, the $PO_2$ in it is only 40 mmHg. So for this reason, it is unable to detect the changes in the arterial blood $PO_2$.

# Effect of blood CO2 level on central chemoreceptors

- Although carbon dioxide (can cross BBB) has little direct effect in stimulating the neurons in the chemosensitive area, it does have a potent indirect effect. It does this by reacting with the water of the tissues to form carbonic acid, which dissociates into hydrogen and bicarbonate ions; the hydrogen ions then have a potent direct stimulatory effect on respiration.




Chemoreceptors are very sensitive to hydrogen ion.

**Figure 42-2.** Stimulation of the *brain stem inspiratory* area by signals from the *chemosensitive area* located bilaterally in the medulla, lying only a fraction of a millimeter beneath the ventral medullary surface. Note also that hydrogen ions stimulate the chemosensitive area, but carbon dioxide in the fluid gives rise to most of the hydrogen ions.

# Why does blood carbon dioxide have a more potent effect in stimulating the chemosensitive neurons than do blood hydrogen ions?

The blood - brain barrier is nearly impermeable to $H^+$ ions

When the blood $PCO_2$ increases, so does the PCO2 of both the *interstitial fluid of the medulla and the CSF*.
($CO_2$ passes this barrier very easily)
In these fluids, the $CO_2$ reacts with the water to form new $H^+$ ions.

Thus, more $H^+$ ions are released into the respiratory chemosensitive sensory area of the medulla when the blood $CO_2$ concentration increases than when the blood $H^+$ ion increases. For this reason, respiratory center activity is increased very strongly by changes in blood $CO_2$, a fact that we subsequently discuss quantitatively.

comparing between ↑$CO_2$ and↑ hydrogen, who's affecting more? The $CO_2$
why? ↑CO2 in the blood will cause more↑ventilation than increase in blood H+ and that's will NOT affect the CNS (medullary response center) since it does not cross the BBB. On the other hand, CO2 can cross the BBB and it indirectly gives off H+ there from its reaction with H2O (acid/base equation). So, the Cerebrospinal fluid and the interstitial fluid of the medulla the hydrogen ion will stimulate the chemoreceptors directly.

From Guyton
The figure shows quantitatively the approximate effects of blood $PCO_2$ and blood pH (which is an inverse logarithmic measure of hydrogen ion concentration) on alveolar ventilation. Note especially the marked increase in ventilation caused by an increase in $PCO_2$ in the normal range between 35 and 75 mm Hg, which demonstrates the tremendous effect that $CO_2$ changes have in controlling respiration. By contrast, the change in respiration in the normal blood pH range, which is between 7.3 and 7.5, is less than one tenth as great.

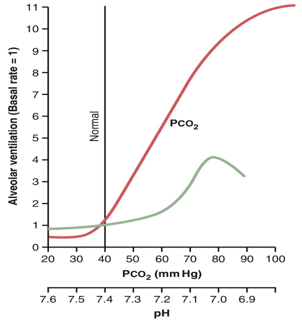



**Figure 42-3.** Effects of increased arterial blood $PCO_2$ and decreased arterial pH (increased hydrogen ion concentration) on the rate of alveolar ventilation.

# A change in blood $CO_2$ concentration has a potent *acute effect* on controlling respiratory drive but only a weak *chronic effect* after a few days' adaptation.

Excitation of the respiratory center by $CO_2$ is great after the blood $CO_2$ first increases, but it gradually declines over the next 1 to 2 days.

**1**

Part of this decline results from renal readjustment of the $H^+$ ion concentration in the circulating blood back toward normal after the $CO_2$ first increases.

**2**

The kidneys increasing the blood $HCO_3$, which binds with $H^+$ ions in the blood and CSF to reduce their concentrations.

**3**

the $HCO_3$ ions slowly diffuse through the BBB– CSF barriers and combine directly with the $H^+$ ions adjacent to the respiratory neurons as well, thus reducing the $H^+$ ions back to near normal.

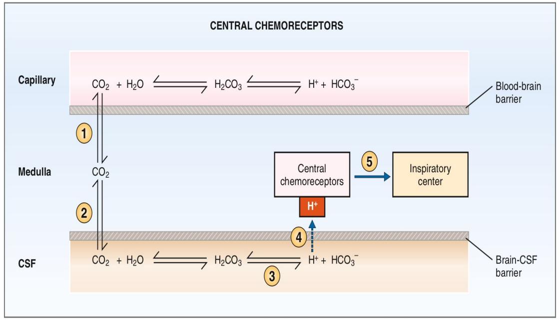



**Figure 5-32** **Response of central chemoreceptors to pH.** The circled numbers correspond to the numbered steps discussed in the text. CSF, Cerebrospinal fluid.

**From Linda**

Commands from the cerebral cortex can temporarily override the automatic brain stem centers. For example, a person can voluntarily hyperventilate (i.e., increase breathing frequency and volume). The consequence of hyperventilation is a decrease in $PaCO_2$, which causes arterial pH to increase. Hyperventilation is self-limiting, however, because the decrease in $PaCO_2$ will produce unconsciousness and the person will revert to a normal breathing pattern. Although more difficult, a person may voluntarily hypoventilate (i.e., breath-holding). Hypoventilation causes a decrease in PaO2 and an increase in PaCO2, both of which are strong drives for ventilation. A period of prior hyperventilation can prolong the duration of breath-holding.

# Peripheral Chemoreceptor System Activity—Role of Oxygen in Respiratory Control

Most of the chemoreceptors are in the carotid bodies. However, a few are also in the aortic bodies.

When the oxygen concentration in the arterial blood falls below normal, the chemoreceptors become strongly stimulated.

The impulse rate is particularly sensitive to changes in arterial $PO_2$ in the range of 60 down to 30 mm Hg.

Under these conditions, low arterial $PO_2$ obviously drives the ventilatory process quite strongly.

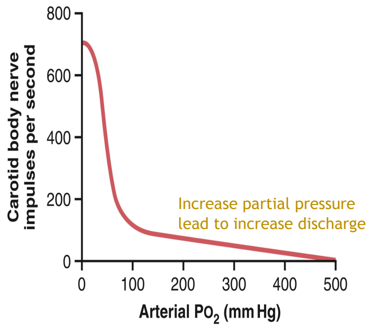



**Figure 42-5.** Effect of arterial $Po_2$ on impulse rate from the carotid body.

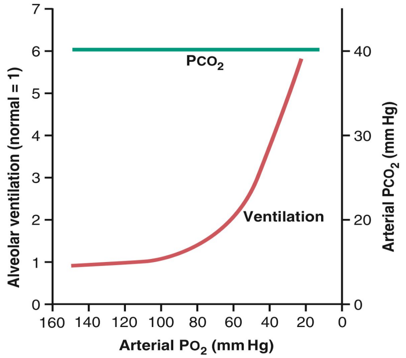



**Figure 42-7.** The lower curve demonstrates the effect of different levels of arterial $Po_2$ on alveolar ventilation, showing a sixfold increase in ventilation as the $Po_2$ decreases from the normal level of 100 mm Hg to 20 mm Hg. The upper line shows that the arterial $Pco_2$ was kept at a constant level during the measurements of this study; pH also was kept constant.

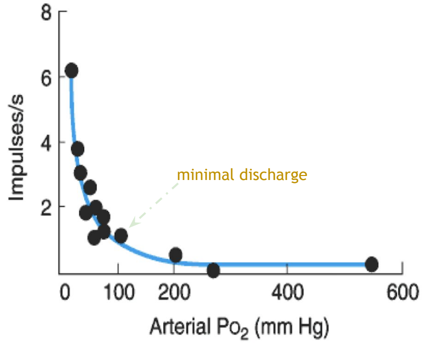
# Effect of Carbon Dioxide and Hydrogen Ion Concentration on Chemoreceptor Activity.

An increase in either carbon dioxide concentration or hydrogen ion concentration also excites the chemoreceptors and, in this way, indirectly increases respiratory activity.

There is one difference between the peripheral and central effects of carbon dioxide: the stimulation by way of the peripheral chemoreceptors occurs as much as five times as rapidly as central stimulation, so that the peripheral chemoreceptors might be especially important in increasing the rapidity of response to carbon dioxide at the onset of exercise.

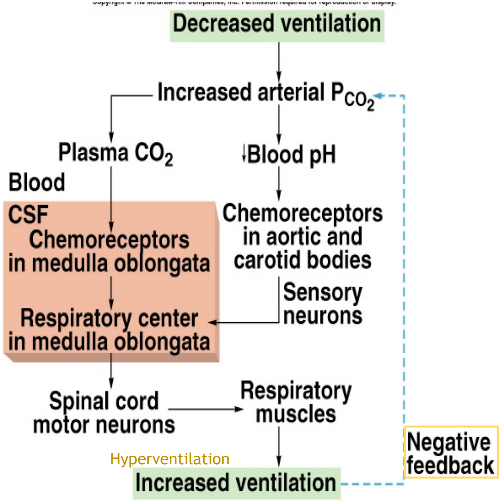
## Summary of Chemoreceptor Control of Breathing

Figure 36–6.






Change in the rate of discharge of a single afferent fiber from the carotid body when arterial $PO_2$ is reduced. (Courtesy of S Sampson.)



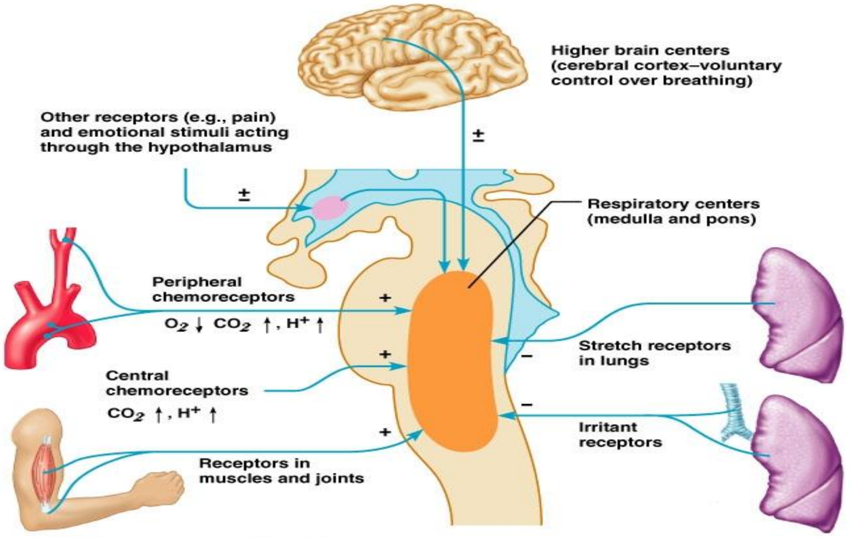
# Other Factors Influencing Respiration

## Effect of irritant receptors in the airways

The epithelium of trachea, bronchi and bronchioles is supplied by irritant receptors that are stimulated by irritants that enter the respiratory airways causing coughing, sneezing and bronchoconstriction in bronchial asthma and emphysema.

## Function of lung J receptors

Few receptors in the wall of the alveoli in juxtaposition to the pulmonary capillaries. They are stimulated especially when pulmonary capillaries become engorged by blood or when pulmonary edema occur e.g in CHF, their excitation cause the person a feeling of dyspnea.



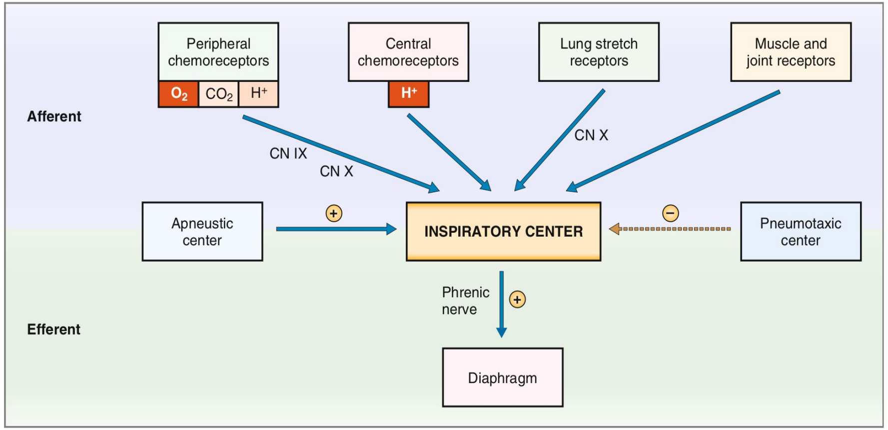




**Figure 5-31** **Brain stem control of breathing.** Afferent (sensory) information reaches the medullary inspiratory center via central and peripheral chemoreceptors and mechanoreceptors. Efferent (motor) information is sent from the inspiratory center to the phrenic nerve, which innervates the diaphragm. CN, Cranial nerve.

| Respiratory Acidosis | Respiratory Alkalosis |
|---|---|
| Hypoventilation | Hyperventilation |
| Accumulation of $CO_2$ in the tissues. | Excessive loss of $CO_2$. |
| ↑ $PCO_2$ | ↓$PCO_2$ ( 35 mmHg). |
| ↓ pH Normal= 7.3 | ↑ pH |

| Metabolic Acidosis | Metabolic Alkalosis |
|---|---|
| Ingestion, infusion or Production of a fixed acid. | excessive loss of fixed acids from the body. |
| ↓renal excretion of hydrogen ion. | Ingestion, infusion or excessive renal reabsorption of bases such as $HCO_3$. |
| Loss of $HCO_3$ or other bases from the EC compartment. | ↑ pH |
| Metabolic disorder as diabetic ketoacidosis Utilize more fat —> the byproduct is acid. | |

Difference between respiratory acidosis VS metabolic acidosis

Respiratory Acidosis: occurs when the lungs fail to remove excess carbon dioxide from the bloodstream during the process of respiration.

Metabolic Acidosis: occurs when the digestive and urinary systems fail to breakdown and maintain the proper level of acids in the blood.

The respiratory system can compensate for metabolic acidosis or alkalosis by altering alveolar ventilation.

# Quiz

You don't understand why we choose this answer?
Click here to read the explanations

1- A stroke that destroys the respiratory area of the medulla would be expected to lead to which of the following?

A. Immediate cessation of breathing
B. Apneustic breathing
C. Rapid breathing (hyperpnea)
D. None of the above (breathing would remain normal)

2-What is the most important pathway for the respiratory response to systemic arterial $CO_2$ ($Pco_2$)?

A. $CO_2$ activation of the carotid bodies
B. Hydrogen ion ($H^+$) activation of the carotid bodies
C. $CO_2$ activation of the chemosensitive area of the medulla
D. $H^+$ activation of the chemosensitive area of the medulla

3-The basic rhythm of respiration is generated by neurons located in the medulla. What limits the duration of inspiration and increases respiratory rate?

A. Apneustic center
B. Dorsal respiratory group
C. Nucleus of the tractus solitarius
D. Pneumotaxic center

4- When the respiratory drive for increased pulmonary ventilation becomes greater than normal, a special set of respiratory neurons that are inactive during normal quiet breathing then becomes active, contributing to the respiratory drive. These neurons are located in which structure?

A. Dorsal respiratory group
B. Ventral respiratory group
C. Pneumotaxic center
D. Nucleus of the tractus solitarius

## SAQ

1- What leads to respiratory acidosis?

2- Why does blood carbon dioxide have a more potent effect in stimulating the chemosensitive neurons than do blood hydrogen ions?

### Answers

1- Hypoventilation which leads to Accumulation of $CO_2$ in the tissues.

↑ $PCO_2$ ———> ↓ pH

2- slide 10

**Key answers:**
1-A 2-D 3-D 4-B

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