

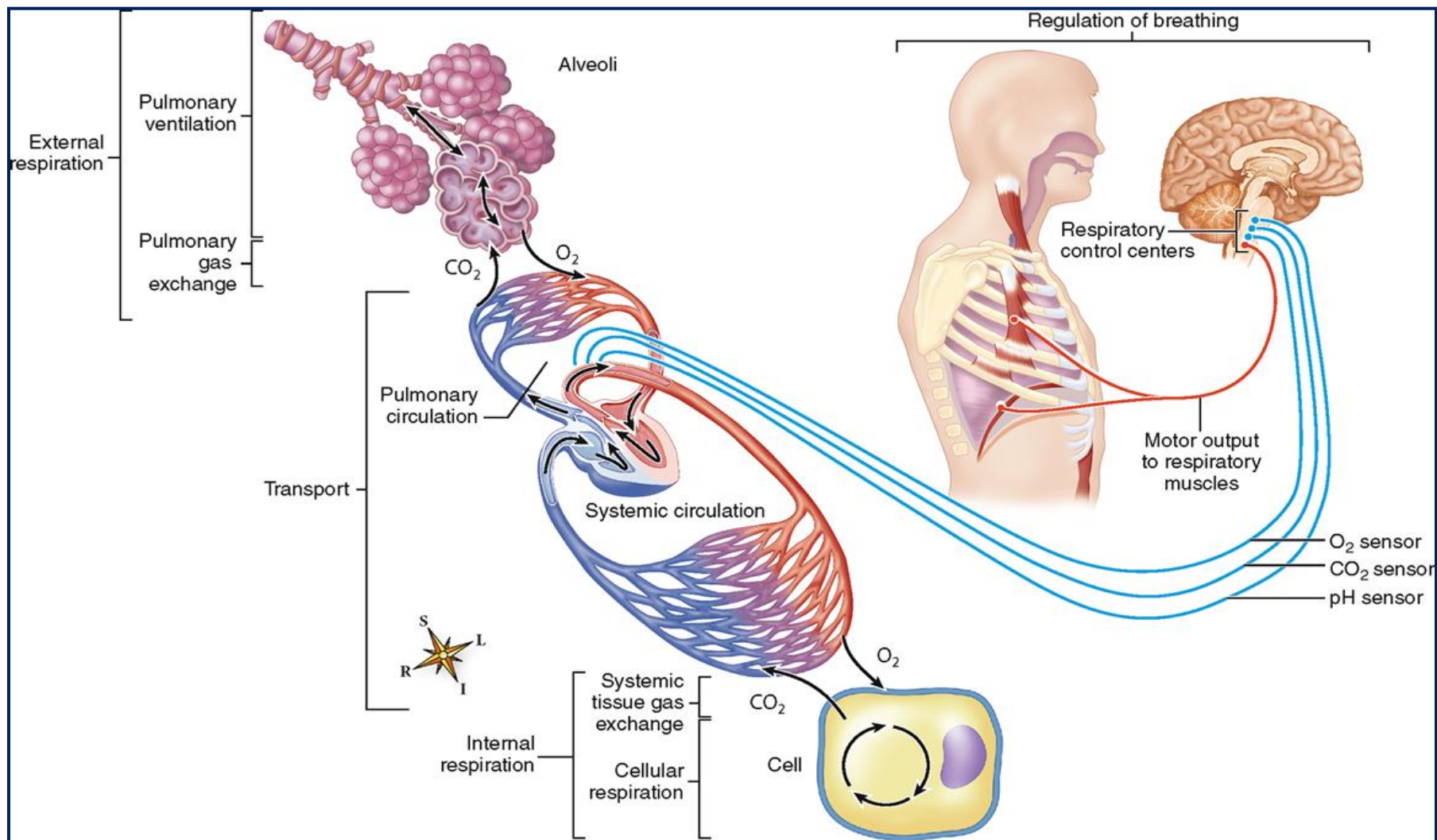
# Control of Breathing

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# Objectives

- **By the end of this lecture you should be able to: -**
- Understand the role of the **medulla oblongata** in determining the basic pattern of respiratory activity.
- List some **factors that can modify the basic breathing pattern** like e.g.
- A- The Hering-Breuer reflexes, B- The proprioceptor reflexes, C- the protective reflexes, like the irritant, and the J-receptors.
- Understand the **respiratory consequences of changing  $PO_2$ ,  $PCO_2$ , and PH.**
- Describe the locations and roles of the **peripheral and central chemoreceptors.**
- Compare and contrast **metabolic and respiratory acidosis and metabolic and respiratory alkalosis.**

# The overall processes of External Respiration



# Control of rate and depth of respiration

- Arterial PO<sub>2</sub>:

When PO<sub>2</sub> is VERY low (Hypoxia): ventilation increases.

- Arterial PCO<sub>2</sub>:

The most important regulator of ventilation is PCO<sub>2</sub>, small increases in PCO<sub>2</sub>: greatly increases ventilation.

- Arterial pH:

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

# CONTROL OF VENTILATION

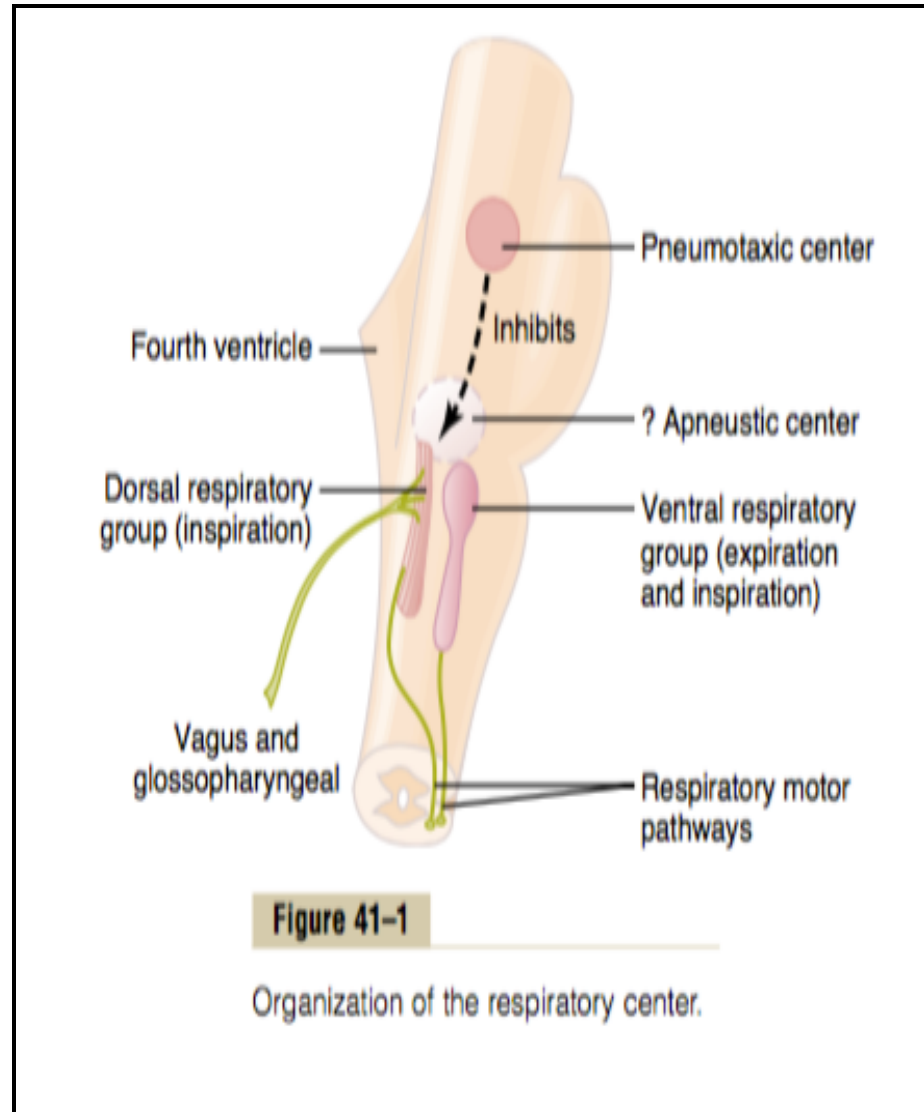
➤ Several mechanisms are involved which can be grouped into two main categories which are closely integrated:-

1- Nervous control mechanism.

2- Chemical control mechanism.

# RESPIRATORY NEURONAL CENTER

- Composed of several groups of neurons.
- Located in the entire length of the medulla and pons.
- Can be divided into four major groups of neurons:-
  - 1-Dorsal respiratory group.
  - 2-Ventral respiratory group.
  - 3-The apneustic center.
  - 4-The pneumotaxic center.



# Medullary Respiratory centers

## 1. Inspiratory area (Dorsal Respiratory Group)-DRG:

- Determines basic rhythm of breathing (rhythmicity center).

- Causes contraction of diaphragm and external intercostals.

- The rhythmicity center received impulses from:

- 1-Higher brain centers

- 2-Centers in the brain stem (medulla and pons)

- 3-Special receptors (respiratory reflexes)

- The rhythmicity center sends excitatory impulses via the intercostal and phrenic nerves to the external intercostal muscles and diaphragm.

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

## 2. 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 ( mainly expiratory).



# Pontine Respiratory centers

- Transition between inhalation and exhalation is controlled by:

## **1. Apneustic area:**

Stimulates inspiratory area of medulla to prolong inhalation. Therefore slow respiration and prolonged respiratory cycles will result if it is stimulated. It receives inhibitory impulses from the sensory vagal fibers and inhibitory impulses from the pneumotaxic center.

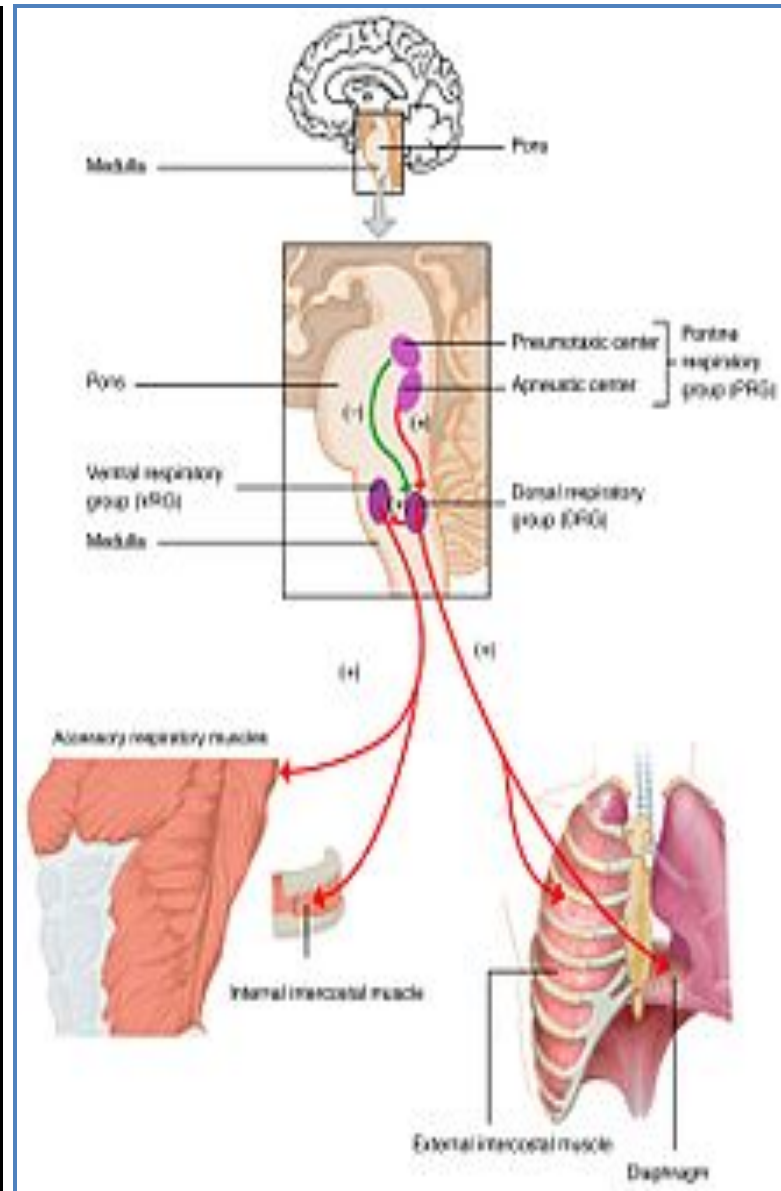
## **2. Pneumotaxic area:**

It transmits inhibitory impulses to the apneustic center and to the inspiratory area to switch off inspiration.

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

# Hering-Breuer inflation reflex

- When the lung becomes overstretched (tidal volume is about 1.5 L), stretch receptors located in the wall of bronchi and bronchioles transmit signals through vagus nerve to DRG producing effect similar to pneumotaxic center stimulation.
- 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



# CHEMICAL CONTROL OF VENTILATION

The rhythmicity center is affected by chemical changes in the blood via two types of chemoreceptors:-

1-Peripheral chemoreceptors.

2-Central chemoreceptors.

# Chemical Control of Respiration

## Peripheral and central chemoreceptors

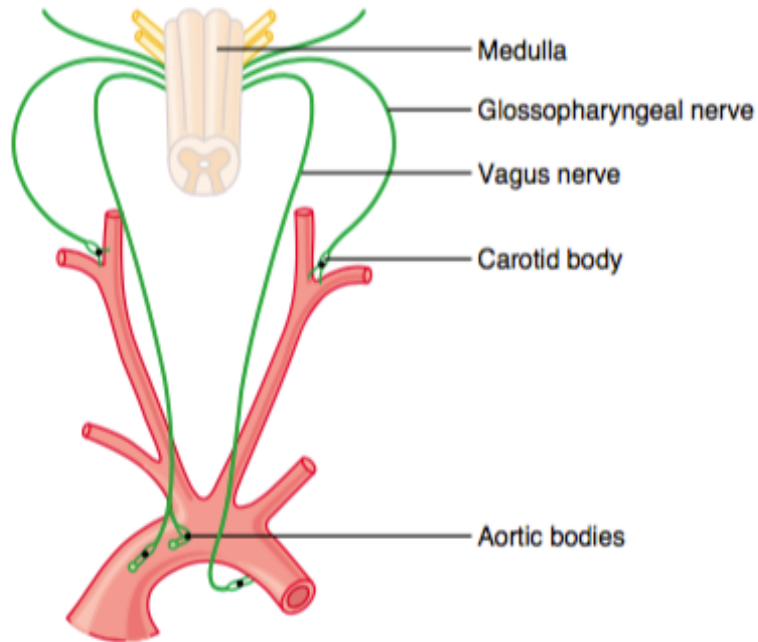


Figure 41-4

Respiratory control by peripheral chemoreceptors in the carotid and aortic bodies.

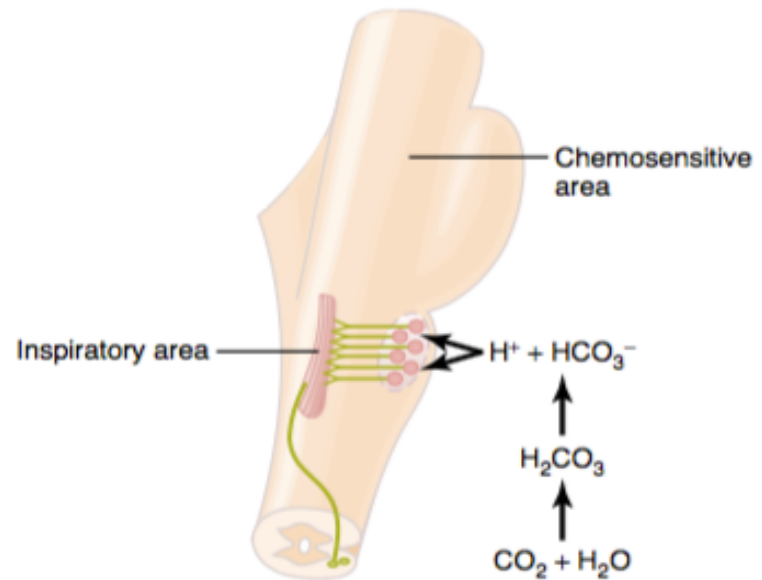


Figure 41-2

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.

Peripheral chemoreceptors

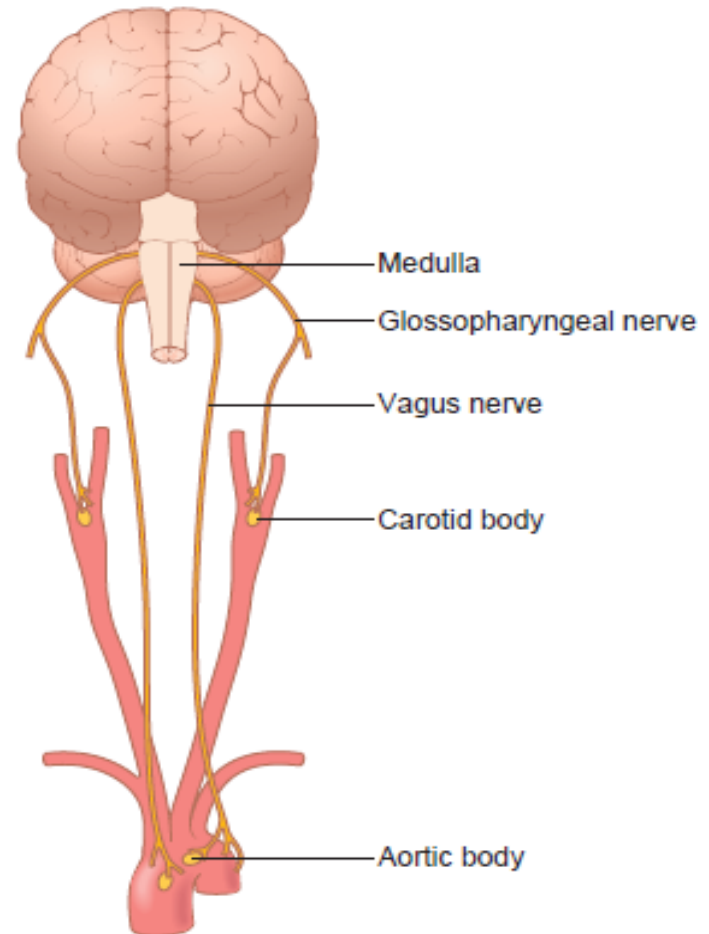
Central chemoreceptors

# Peripheral chemoreceptors:

- Located mainly in the carotid and aortic bodies, but may be found anywhere in the circulatory system.
- When stimulated, send excitatory impulses to the rhythmicity center (via glossopharyngeal and vagus nerves).
- Highly sensitive to changes in arterial  $PO_2$  and to a lesser extent to  $PCO_2$  and pH.
- Fall of  $PO_2$ , rise in  $PCO_2$  and fall of pH, stimulate the chemoreceptors to increase ventilation.

# Respiratory control by peripheral chemoreceptors in carotid and aortic bodies

- Normal  $PO_2$ ,  $PCO_2$  and pH, low grade of tonic activity in the nerves.
- $\downarrow PCO_2$  and  $\uparrow pH$  causes low tonic activity which cause decrease ventilation
- In metabolic acidosis:  
 $\downarrow pH$  causes increase in ventilation to wash out  $CO_2$  and to bring pH to normal.
- In metabolic alkalosis:  
 $\uparrow pH$  causes decrease ventilation,  $CO_2$  retained in the blood to compensate.



# 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 oxygen concentration in the arterial blood falls below normal, the chemoreceptors become strongly stimulated.
- Impulse rate is particularly sensitive to changes in arterial  $P_{O_2}$  in the range of 60 down to 30 mm Hg.
- Under these conditions, low arterial  $P_{O_2}$  obviously drives the ventilatory process quite strongly.

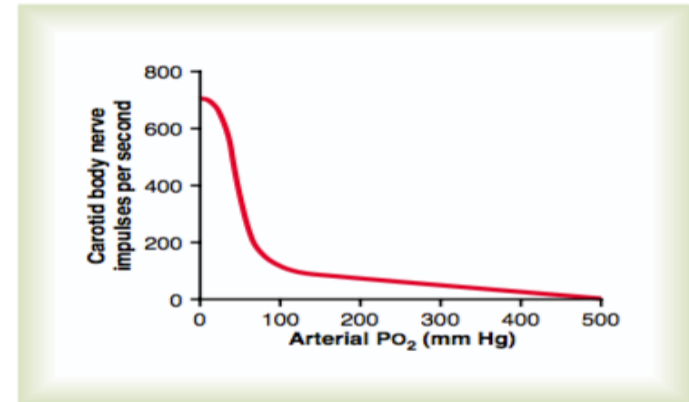


Figure 41-5

Effect of arterial  $P_{O_2}$  on impulse rate from the carotid body of a cat.

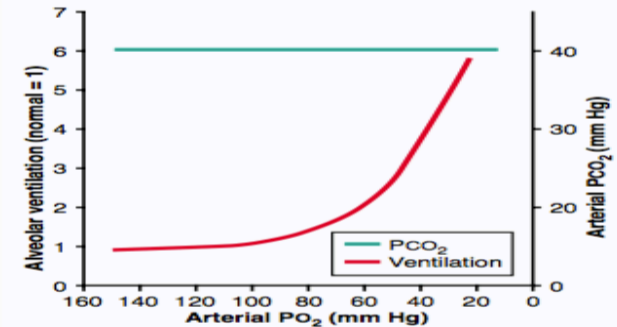


Figure 41-6

The lower curve demonstrates the effect of different levels of arterial  $P_{O_2}$  on alveolar ventilation, showing a sixfold increase in ventilation as the  $P_{O_2}$  decreases from the normal level of 100 mm Hg to 20 mm Hg. The upper line shows that the arterial  $P_{CO_2}$  was kept at a constant level during the measurements of this study; pH also was kept constant.

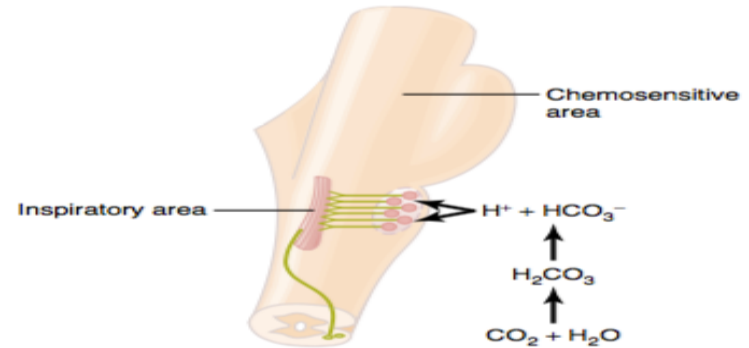
# CENTRAL CHEMORECEPTORS

- Most probably located on the ventrolateral surface of medulla oblongata (which is bathed with cerebrospinal fluid)
- Highly sensitive to the hydrogen ion concentration of the CSF(cerebrospinal fluid).
- evoked by arterial  $\text{PCO}_2$  ( $\text{CO}_2$  can freely cross the blood-brain barrier(BBB) into CSF, while BBB is relatively impermeable to  $\text{H}^+$  and  $\text{HCO}_3^-$  ions)



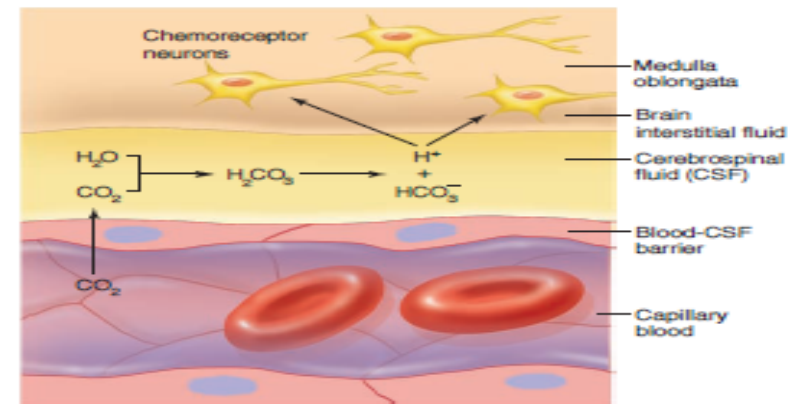
# Effect of CO<sub>2</sub> on central chemoreceptors

Although **carbon dioxide** 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.**



**Figure 41-2**

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.



**Figure 16.29** How blood CO<sub>2</sub> affects chemoreceptors in the medulla oblongata. An increase in blood CO<sub>2</sub> stimulates breathing indirectly by lowering the pH of blood and cerebrospinal fluid (CSF). This figure illustrates how a rise in blood CO<sub>2</sub> increases the H<sup>+</sup> concentration (lowers the pH) of CSF and thereby stimulates chemoreceptor neurons in the medulla oblongata.

# Why does CO<sub>2</sub> have a more potent effect in stimulating chemosensitive neurons than do blood H<sup>+</sup> ions?

Blood-brain barrier is nearly impermeable to H<sup>+</sup> ions, but CO<sub>2</sub> passes this barrier very easily. When the blood PCO<sub>2</sub> increases, so does the PCO<sub>2</sub> of both the interstitial fluid of the medulla and the CSF. In these fluids, the CO<sub>2</sub> reacts with the water to form new H<sup>+</sup> ions. More H<sup>+</sup> ions are released into the respiratory chemosensitive sensory area of the medulla when the blood CO<sub>2</sub> concentration increases than when the blood H<sup>+</sup> ion increases. For this reason, respiratory center activity is increased very strongly by changes in blood CO<sub>2</sub>, a fact that we subsequently discuss quantitatively.

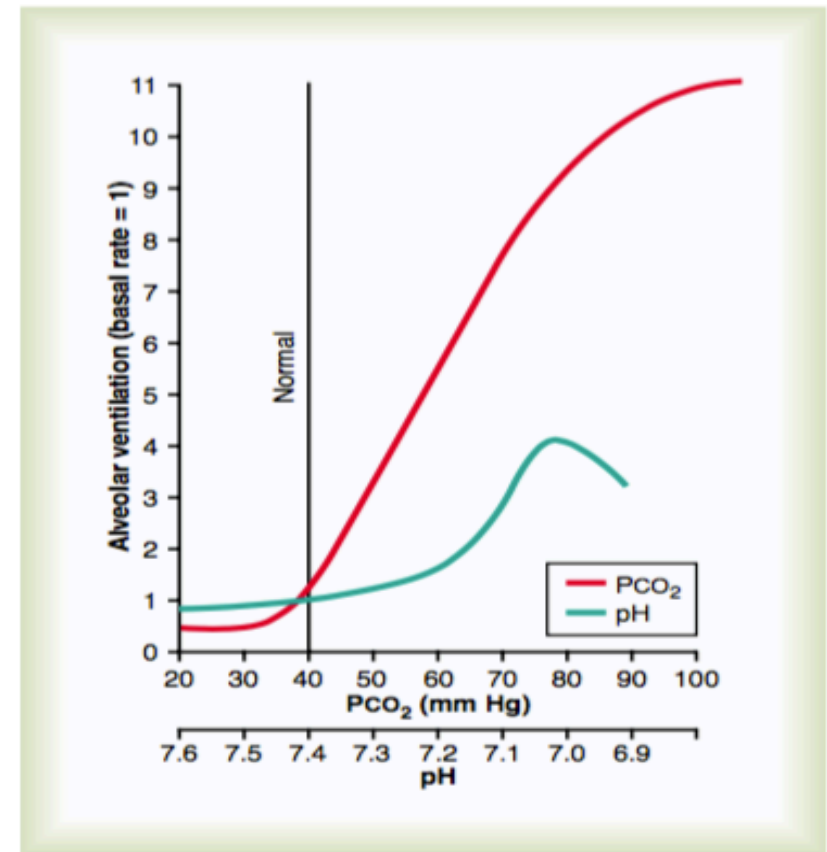


Figure 41-3

Effects of increased arterial blood PCO<sub>2</sub> and decreased arterial pH (increased hydrogen ion concentration) on the rate of alveolar ventilation.

A change in CO<sub>2</sub> concentration has a potent acute effect on controlling respiratory drive but only a weak chronic effect after a few days' adaptation.

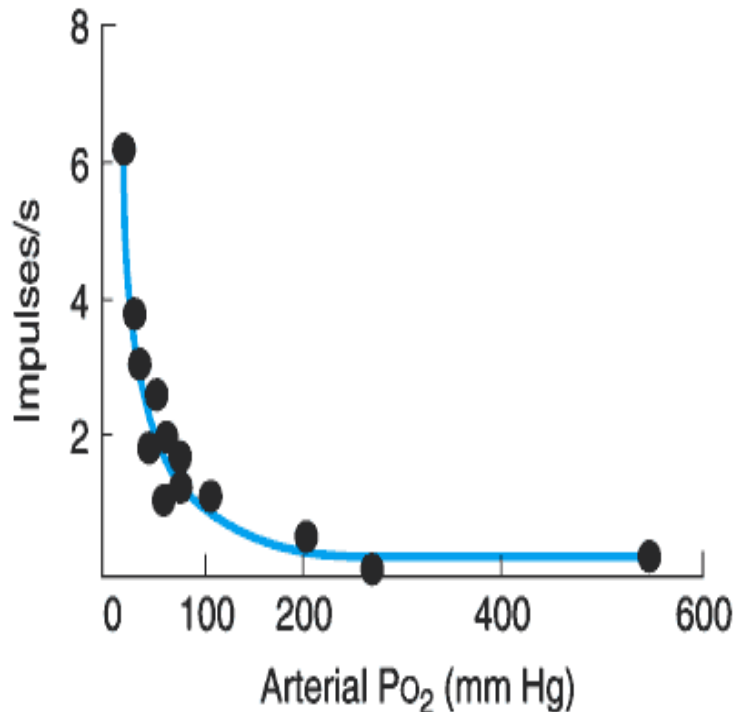
- Excitation of the respiratory center by CO<sub>2</sub> is great after the blood CO<sub>2</sub> first increases, but it gradually declines over the next 1 to 2 days.
- Part of this decline results from renal readjustment of the H<sup>+</sup> ion concentration in the circulating blood back toward normal after the CO<sub>2</sub> first increases.
- The kidneys increase the blood HCO<sub>3</sub><sup>-</sup>, which binds with H<sup>+</sup> ions in the blood and CSF to reduce their concentrations.
- Over a period of hours, the HCO<sub>3</sub><sup>-</sup> ions slowly diffuse through the BBB– CSF barriers and combine directly with the H<sup>+</sup> ions adjacent to the respiratory neurons as well, thus reducing the H<sup>+</sup> ions back to near normal.

# Effect of CO<sub>2</sub> and H<sup>+</sup> 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

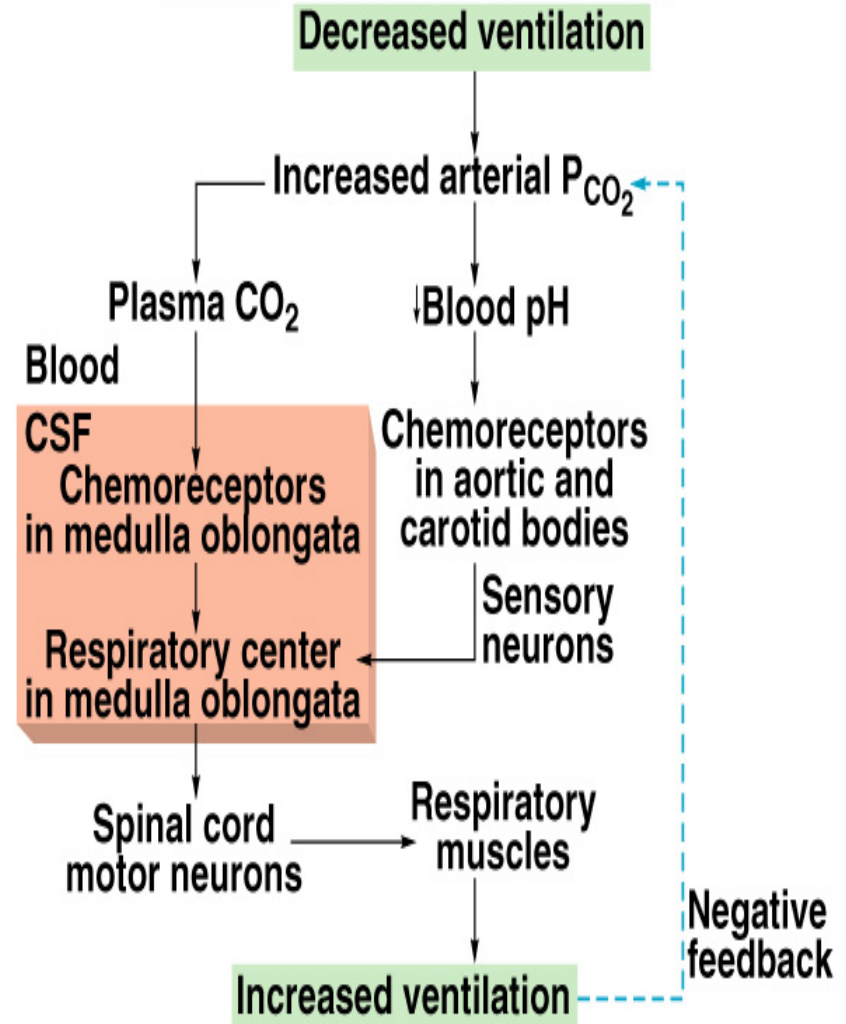
Figure 36-6.



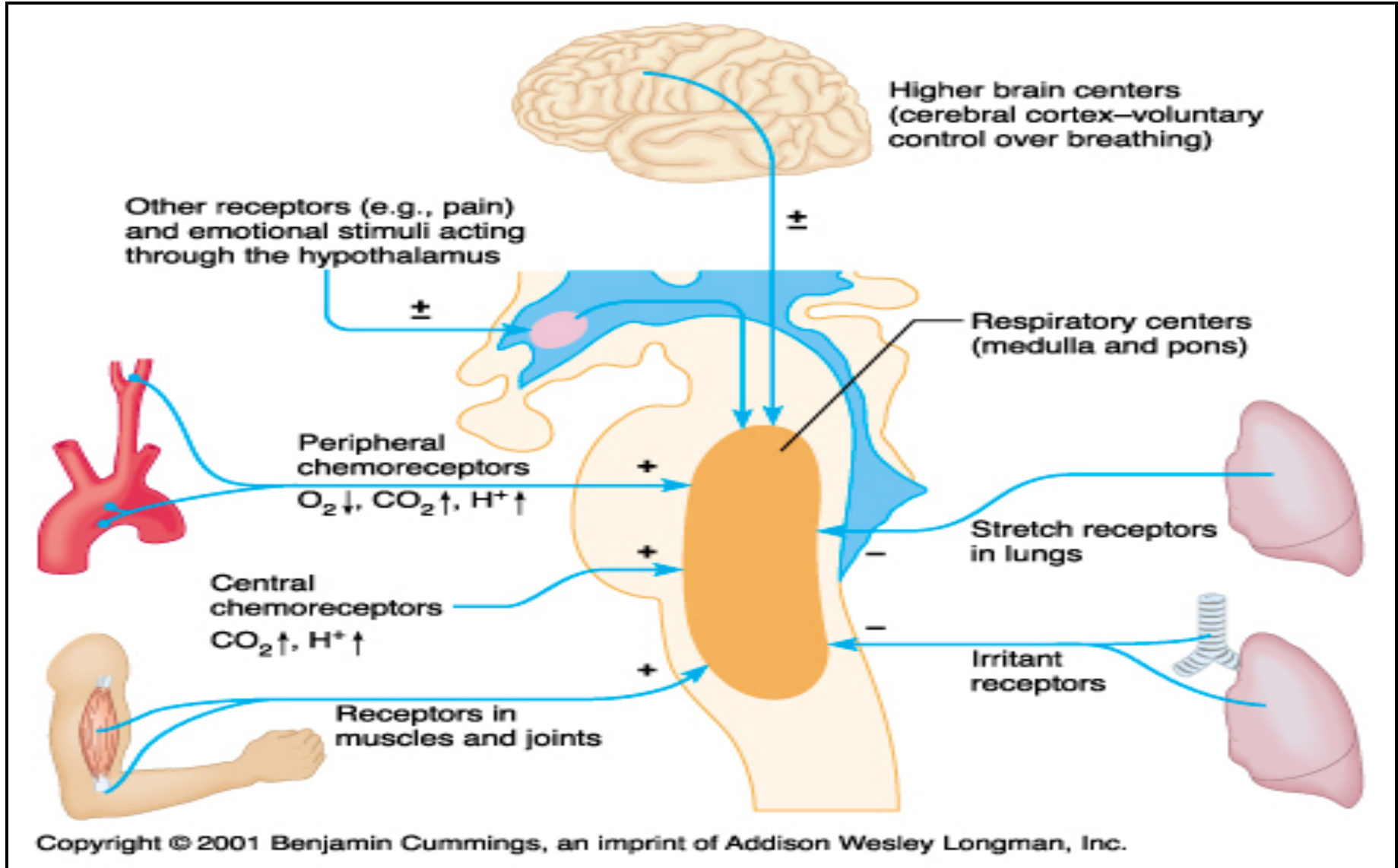
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Change in the rate of discharge of a single afferent fiber from the carotid body when arterial  $P_{O_2}$  is reduced. (Courtesy of S Sampson.)

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# Other Factors Influencing Respiration



# Cont. factors influencing respiration

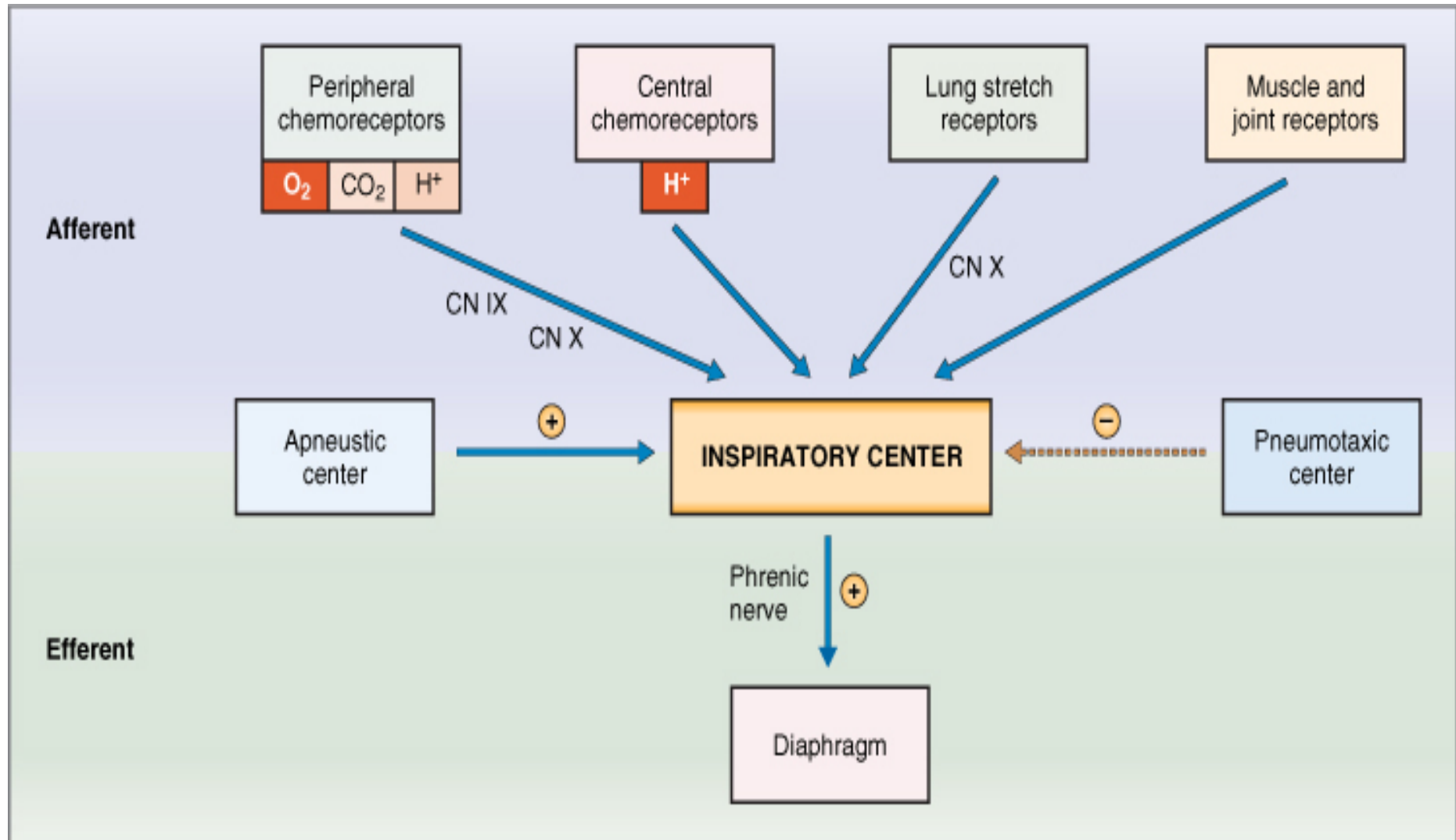
- Effect of irritant receptors in the airways:

The epithelium in the trachea, bronchi, and bronchioles is supplied by irritant receptors that are stimulated by irritants that enters 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 juxta position to the pulmonary capillaries. They are stimulated especially when the pulmonary capillary becomes engorged by blood or when pulmonary edema occurs e.g. in CHF, their stimulation cause the patient feels dyspnea.

# Summary of factors affecting respiration





## Respiratory Acidosis

- Hypoventilation.
- Accumulation of CO<sub>2</sub> in the tissues.
  - P<sub>CO2</sub> increases
  - pH decreases.

## Respiratory Alkalosis

- Hyperventilation.
- Excessive loss of CO<sub>2</sub>.
  - P<sub>CO2</sub> decreases ( 35 mmHg).
  - pH increases.

## Metabolic Acidosis

- Ingestion, infusion, or production of a fixed acid.
- Decreased renal excretion of hydrogen ions.
- Loss of bicarbonate or other bases from the extracellular compartment.
- Metabolic disorders as diabetic ketoacidosis.

## Metabolic Alkalosis

- Excessive loss of fixed acids from the body
- Ingestion, infusion, or excessive renal reabsorption of bases such as bicarbonate
- pH increases.

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