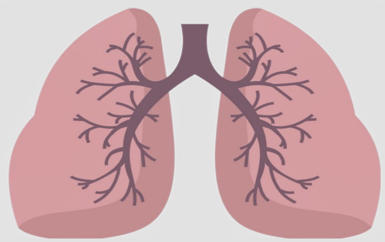
Revised & Approved by: Shayma Abdullah Alghanoum, Faisal Alotaibi

MED439

Control of Breathing



Respiratory Block

Physiology 439 team work

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

Editing file

@Physiology_439

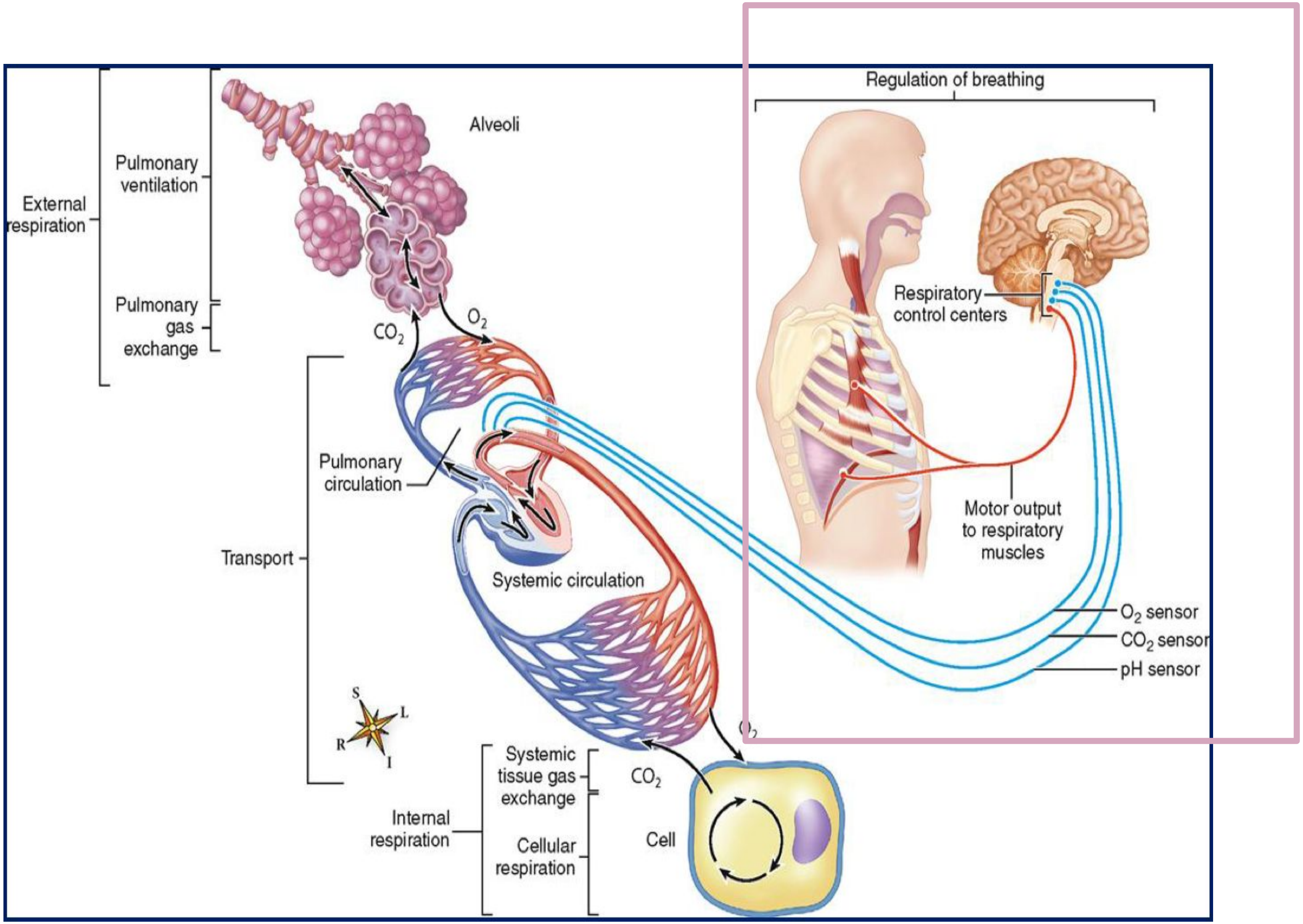
Objectives :

01 Understand the role of the medulla oblongata in determining the basic pattern of respiratory activity.

02 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.

03 Compare and contrast metabolic and respiratory acidosis , PCO central chemoreceptors. and metabolic and respiratory alkalosis.

The overall process of external respiration



The last mechanism of External Breathing will be Discussed in this lecture

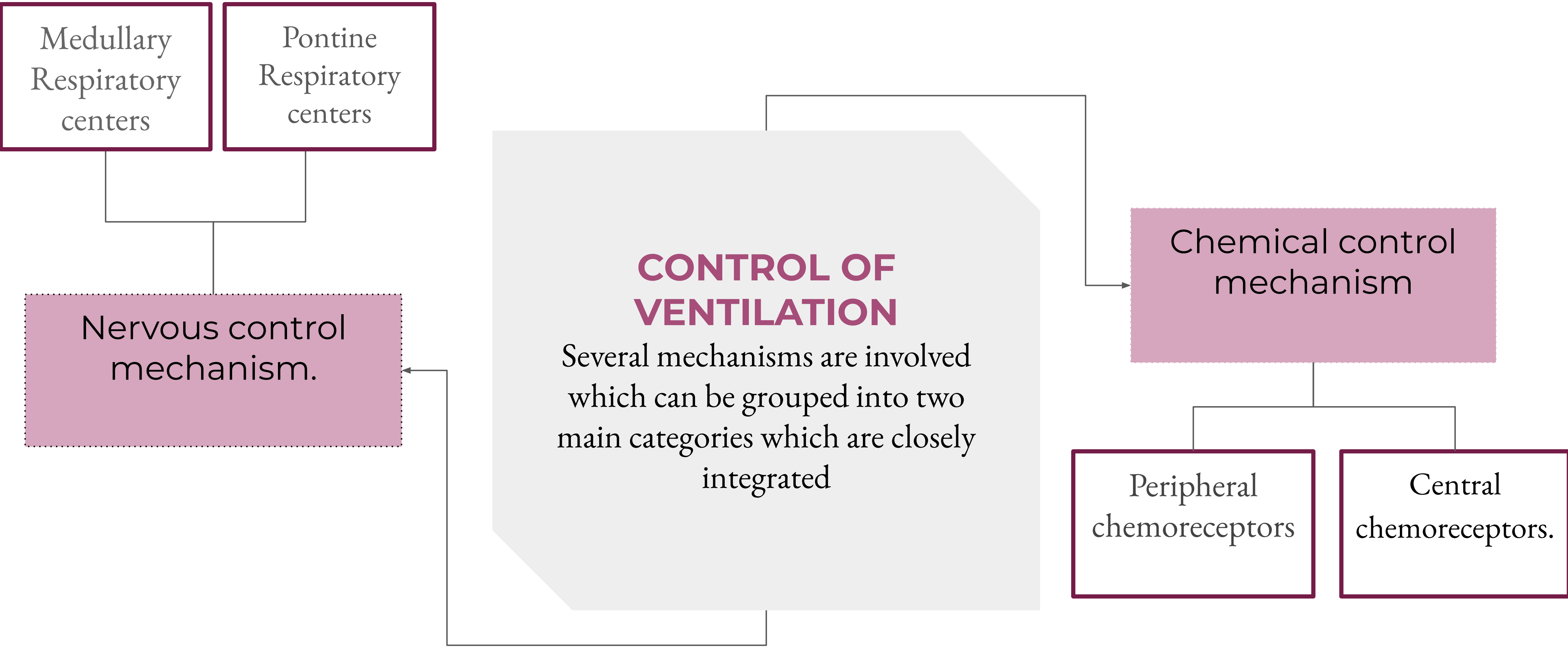
[Take an idea about the lecture with this helpful video]

* A small increase in PCO2 will greatly increase ventilation

لان أي زيادة حتى لو بسيطه في الPco2 راح يأثر في الPH ف لازم نتفادى هذا الشي

Control of rate and depth of respiration

- **Arterial PO2:** → When PO2 is VERY low (Hypoxia) → ventilation increases
- **Arterial PCO2:** → The most important regulator of ventilation is PCO2* → ventilation increases
- **Arterial pH:** → As hydrogen ions increase (acidosis) → ventilation increases



Medullary Respiratory centers
Pontine Respiratory centers
Nervous control mechanism.
CONTROL OF VENTILATION
Several mechanisms are involved which can be grouped into two main categories which are closely integrated
Chemical control mechanism
Peripheral chemoreceptors
Central chemoreceptors.

Nervous control mechanism.

RESPIRATORY NEURONAL CENTER

1-Composed of several groups of neurons.
2-Located in the entire length of the medulla and pons.

Can be divided into four major groups of neurons:

- 1-Dorsal respiratory group
- 2-The pneumotaxic center.
- 3-Ventral respiratory group.
- 4-The apneustic center.

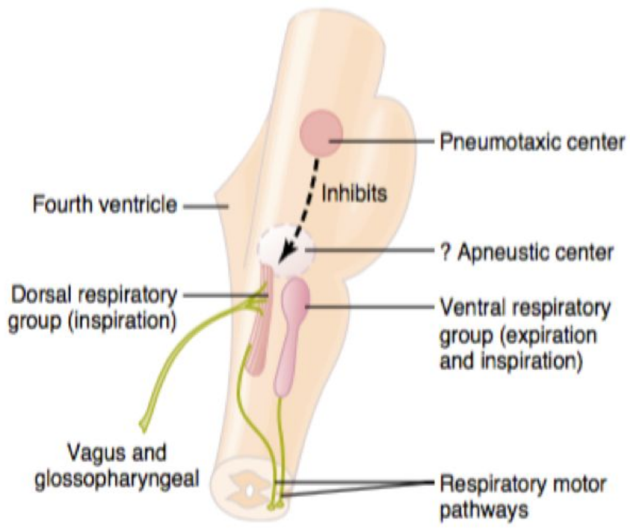


Figure 41–1

Organization of the respiratory center.

Medullary Respiratory centers

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

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

- Determines basic rhythm of breathing (rhythmicity center)
- The rhythmicity center receives impulses from:
  - 1-Higher brain centers
  - 2-Centers in the brain stem (medulla and pons)
  - 3-Special receptors (respiratory reflexes)
- Causes contraction of diaphragm and external intercostals
- The rhythmicity center sends excitatory impulses via the intercostal and phrenic nerves to the external intercostal muscles and diaphragm

DRG
يحافظ على الـ Rhythm طيب كيف؟
الإشارات تبدا بشكل خفيف بعدين تقوى
اكثر ويصير تقلص ل Diaphragm
بعدين الإشارات توقف ويرجع ال
Diaphragm لوضعه الطبيعي
بمعنى ان الإشارات تبدأ بالتدريج وتوقف

Count:

Medullary Respiratory centers

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).

DRG CONTROL normal (rest) inspiration & expiration
While VRG control forced inspiration & expiration

Pontine Respiratory centers

Transition between inhalation and exhalation is controlled by:

1. Apneustic area:

Stimulates inspiratory area of medulla to prolong inhalation.(so decrease respiratory rate)
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.(so increase respiratory rate)
Therefore, breathing is more rapid when pneumotaxic area is active.

In summary we have 4 centers that control breathing, 2 in the medulla and 2 in the pons
In medulla we have DRG (responsible for basic Rhythm) and VRD(responsible for forced breathing)
DRG is controlled by Apneustic and Pneumotaxic located in the pons which receive input from the Peripheral nervous system about PO2 and Pco2 and respond to it by Apneustic —> prolong breathing and decrease RR
and Pneumotaxic —> inhibit DRG and increases RR

Hering-Breuer inflation reflex

“Protection reflex” By stretching receptors

This reflex appears to be mainly a protective mechanism for preventing excess lung inflation

01

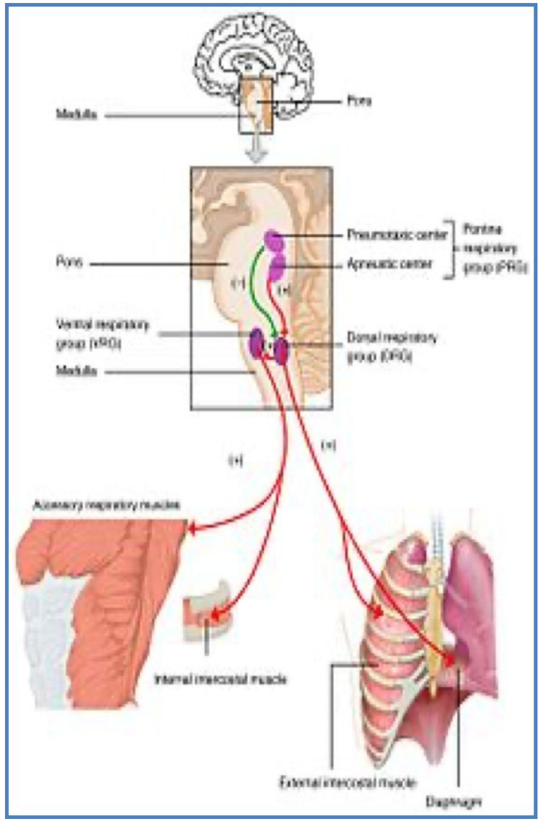
When the lung becomes overstretched (tidal volume is about 1.5 L)stretch receptors located in the wall of bronchi and bronchioles transmit signals through vagus nerve to DRG producing effect similar to pneumotaxic center stimulation.

02

Switches off inspiratory signals and thus stops further inspiration .

03

increases the rate of respiration as does the pneumotaxic center.



Chemical Control Of Ventilation

The rhythmicity center (Dorsal respiratory group) is affected by chemical changes in the blood via

two types of chemoreceptors :

Peripheral chemoreceptors

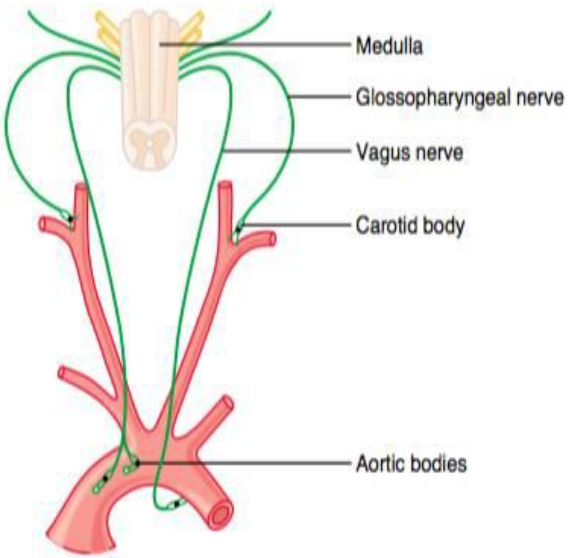


Figure 41–4

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

Central chemoreceptors.

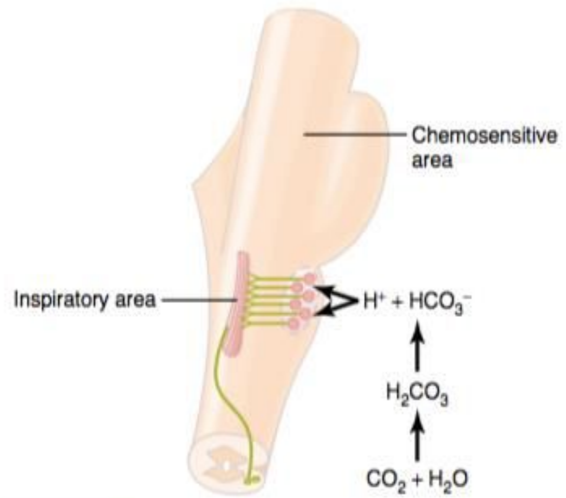


Figure 41–2

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

Peripheral chemoreceptors sends signals which are either excitatory or inhibitory. These signals depend on pH, CO_2, and O_2.

- 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 (حساسيته للO2 اعلى)
- ↓ of PO_2,↑ in PCO_2 and ↓ of pH, stimulate the chemoreceptors to increase ventilation.

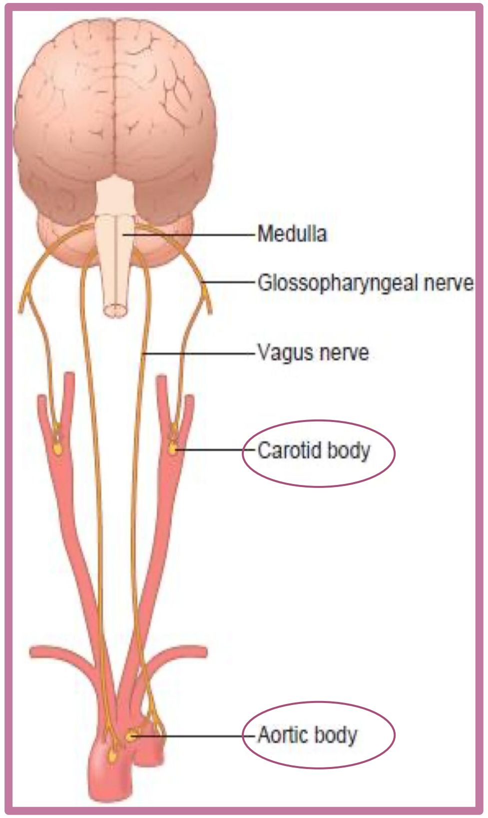
Respiratory control by peripheral chemoreceptors in carotid and aortic bodies

- At Normal PO_2, PCO_2 and pH, low grade of tonic activity in the nerves.(At these circumstances the signals will be at a normally low rate).
- ↓ PCO_2 and ↑pH causes low tonic activity which causes a decrease in ventilation.
- In metabolic acidosis:

↓ pH causes an increase in ventilation to wash out CO_2 and to bring pH to normal.

- In metabolic alkalosis:

↑ pH(due to low amount of CO_2) causes decrease ventilation, the CO_2 is kept in the blood to compensate the drop in CO_2 levels.



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 Po2 in the range of 60 down to 30 mm Hg.

Under these conditions, low arterial Po2 obviously drives the ventilatory process quite strongly.

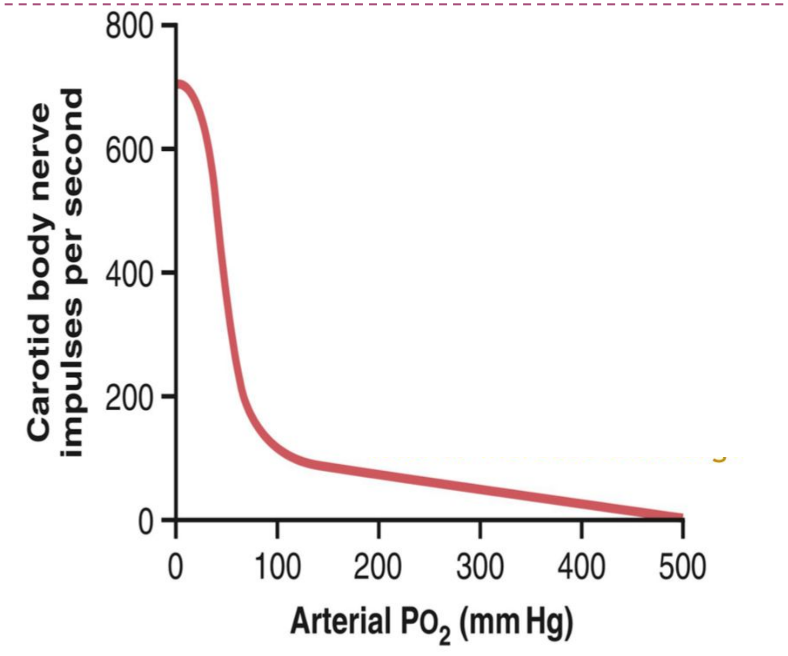


Figure 42-5. Effect of arterial Po_2 on impulse rate from the carotid body.

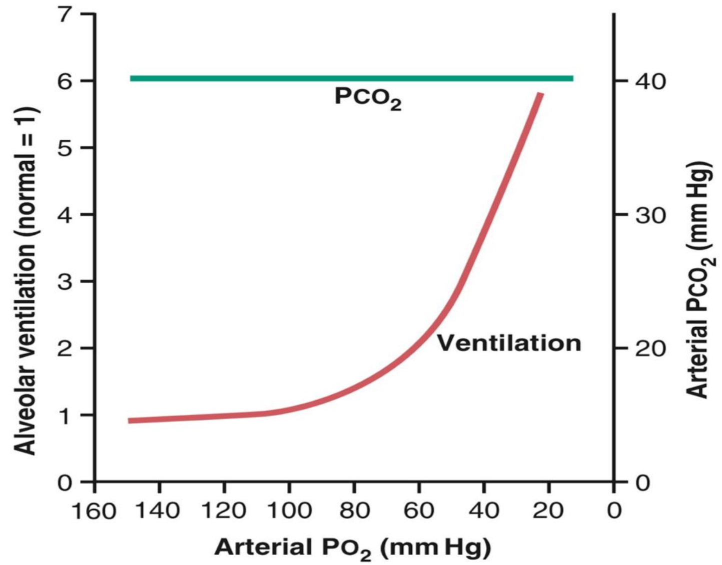


Figure 42-7. The lower curve demonstrates the effect of different levels of arterial Po_2 on alveolar ventilation, showing a sixfold increase in ventilation as the Po_2 decreases from the normal level of 100 mm Hg to 20 mm Hg. The upper line shows that the arterial Pco_2 was kept at a constant level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

Central chemoreceptors

- Most probably located on the ventrolateral surface (الجزء الأمامي الجانبي) of medulla oblongata (which is bathed "surrounded with" cerebrospinal fluid).
- Highly sensitive to the hydrogen ion concentration of the CSF(cerebrospinal fluid).
- Evoked "triggered" by arterial PCO_2 (CO_2 can freely cross the blood brain barrier(BBB) into CSF, while BBB is relatively impermeable to H and HCO^-_3 ions)

Effect of CO2 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.

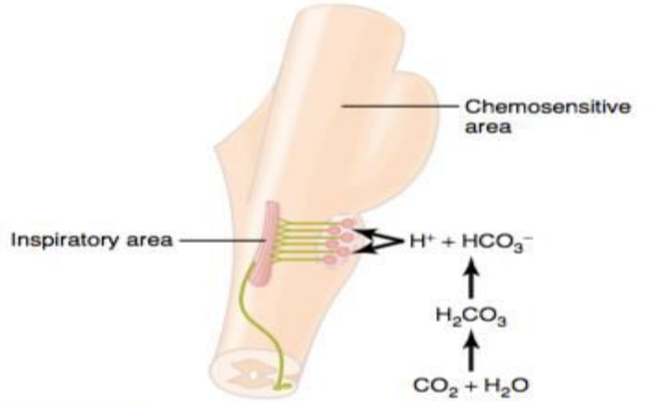


Figure 41–2

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.

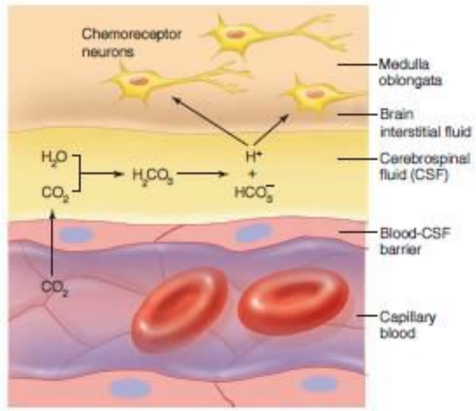


Figure 16.29 How blood CO_2 affects chemoreceptors in the medulla oblongata. An increase in blood CO_2 stimulates breathing indirectly by lowering the pH of blood and cerebrospinal fluid (CSF). This figure illustrates how a rise in blood CO_2 increases the H^+ concentration (lowers the pH) of CSF and thereby stimulates chemoreceptor neurons in the medulla oblongata.

Why does CO2 have a more potent effect in stimulating chemosensitive neurons than do blood H ions?

- Blood brain barrier is nearly impermeable to H+ ions, but CO_2 passes this barrier very easily. When the blood PCO_2 increases, so does the PCO_2 of both the interstitial fluid of the medulla and the CSF.

- In these fluids, the CO_2 reacts with the water to form new H+ ions 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.

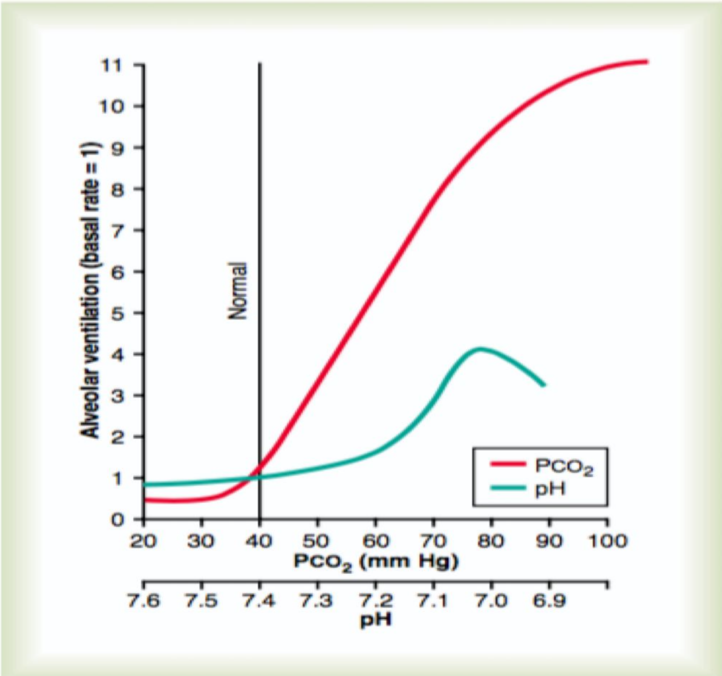


Figure 41–3

Effects of increased arterial blood P_{CO_2} and decreased arterial pH (increased hydrogen ion concentration) on the rate of alveolar ventilation.

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.

From 438 Physiology team

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.

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

This means that:

- 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. (الجسم يتعود عليه)

How does the body adapt to increased CO_2?

• 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.	• The kidneys increasing the blood HCO_3, which binds with H^+ ions in the blood and CSF to reduce their concentrations	• Over a period of hours, 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.

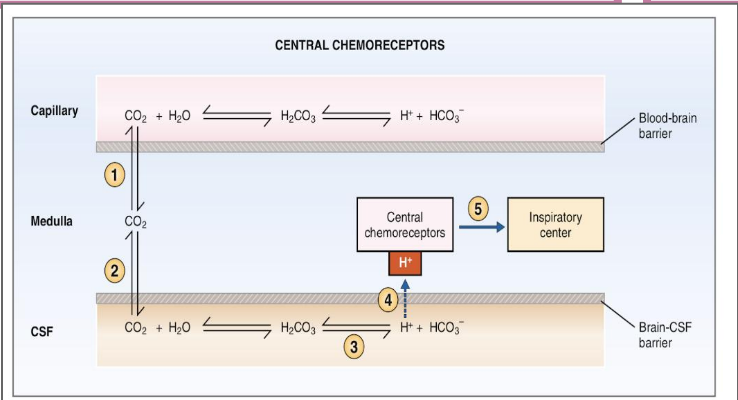


Figure 5-32 **Response of central chemoreceptors to pH.** The circled numbers correspond to the numbered steps discussed in the text. CSF, Cerebrospinal fluid.

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.

Notes:

- If a person has chronic hypercapnia and hypoxia, the body's adaptation to increased CO_2 allows the low O_2 (hypoxia) to be the main drive/stimulus for respiratory regulation.

- PO_2 becomes the main stimulus, not PCO_2.

- If this patient is present to the ER with a respiratory problem, he is immediately given oxygen to correct the hypoxia

- Returning O_2 levels back to normal causes a sharp respiratory rate decline

- This results in shut down or respiratory failure because the hypoxia became the main drive for respiratory regulation.

- For this reason, patients with chronic hypercapnia and hypoxia should be given oxygen, but NOT until it reaches normal levels.

Effect of CO2 and H ion concentration on Chemoreceptors Activity

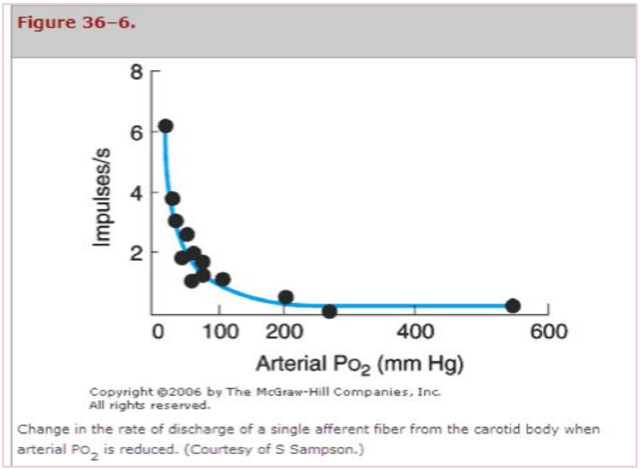
- An increase in either carbon dioxide concentration or hydrogen ion concentration also excites the chemoreceptors and, in this

  way, indirectly increases respiratory activity.

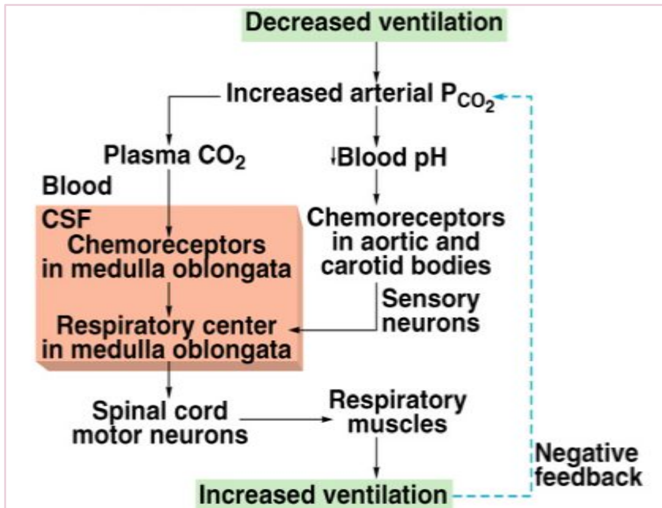
difference between the peripheral and central effects of carbon dioxide:

- 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:



The lower the arterial PO2, the greater the impulse of a nerve from the carotid body to increase respiration and return PO2 levels back to normal.



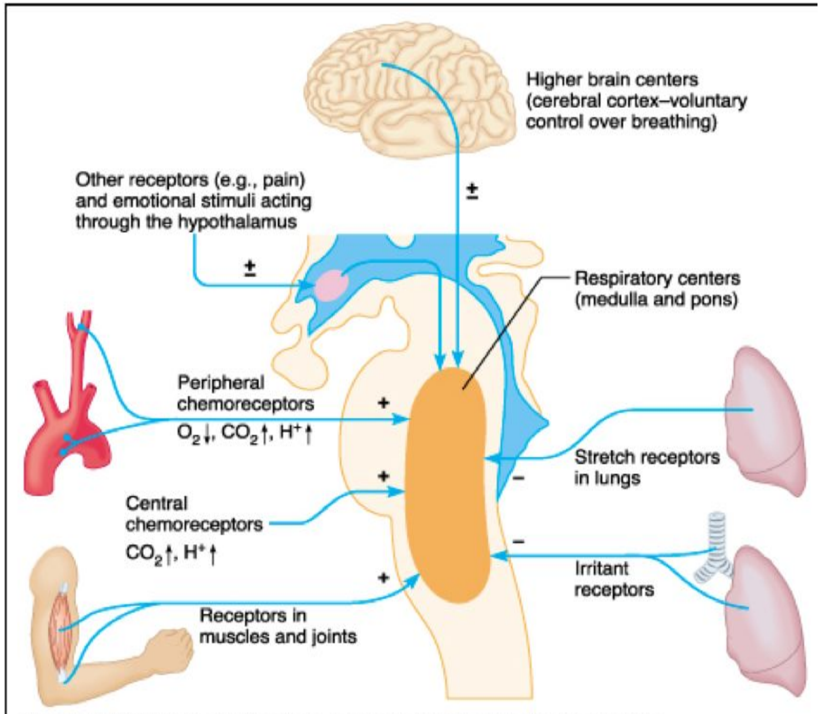
Other factors influencing respiration

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.

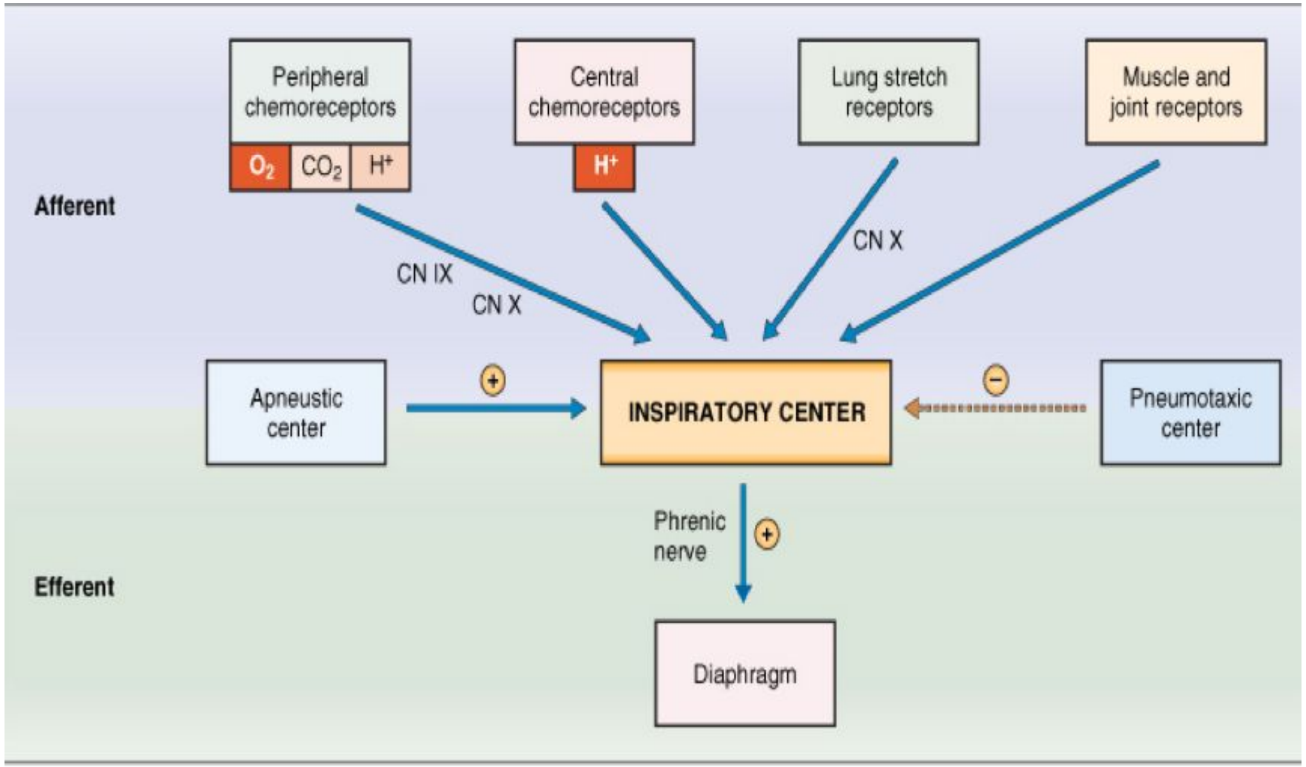
lung J receptors

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.



Helpful summary followed by Quiz

Summary of factors affecting respiration



- Stimulus for <u>peripheral</u> chemoreceptors: ↓O2, ↑CO2, ↓PH, ↑H+
- Stimulus for <u>central</u> chemoreceptors: ↑H+ "direct" ↑Co2" indirect" , why is that? co2 enter the BBB and dissolve in CSF into H+ and bicarbonate than H stimulate the central chemoreceptors which is mean the Co2 itself not the main stimulus

Types of receptors that influence respiration:

- Central chemoreceptors
- Peripheral chemoreceptors
- Lung stretch receptors
- Lung J receptors
- Irritant receptors
- Muscle & joint receptors

Respiratory Acidosis	Respiratory Alkalosis
• Hypoventilation. • Accumulation of CO_2 in the tissues. –PCO_2 increases – pH decreases.	• Hyperventilation. • Excessive loss of CO_2 –PCO_2 decreases (35 mmHg). – pH increases.

Metabolic Acidosis	Metabolic Alkalosis
• 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.	• 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

Another helpful Quiz

Quiz

1.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.DRG
C.VRG
D.Pneumotaxic center

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
E) CO_2 activation of receptors in the lungs

3.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) Apneustic center
B) Dorsal respiratory group
C) Nucleus of the tractus solitarius
D) Pneumotaxic center
E) Ventral respiratory group

4.The afferent (sensory) endings for the Hering-Breuer reflex are mechanoreceptors located in the?

A) Carotid arteries
B) Alveoli
C) External intercostals
D) Bronchi and bronchioles

5.Which of the following is stimulated first during metabolic acidosis?

A) Central chemoreceptors
B) Peripheral chemoreceptors
C) Lung J receptors
D) Lung stretch receptors

1) 2)D 3)E 4)D 5)B

SAQs

1.List the type of receptors that are able to inhibit respiration?

2.Why does CO_2 have a more potent effect in stimulating chemosensitive neurons than do blood H ions?

1.Higher brain centers(cortex),stretch receptors, irritant receptors,receptors in hypothalamus and pneumotaxic center.

2.Since H ions cannot cross the BBB, it needs to be in CO_2 form to cross. That's why Respiratory center activity is increased very strongly by changes in blood CO_2.

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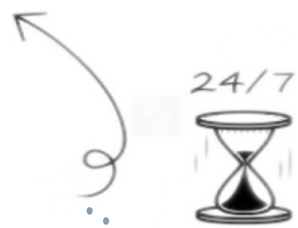
Contact us



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