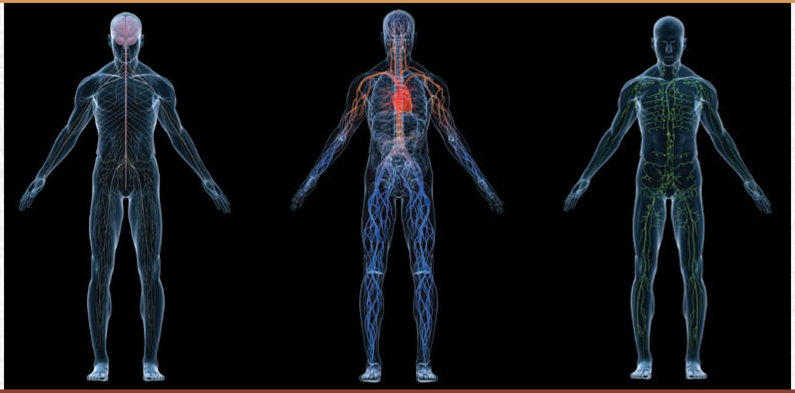
UNIT VII

GUYTON AND HALL Textbook of Medical Physiology

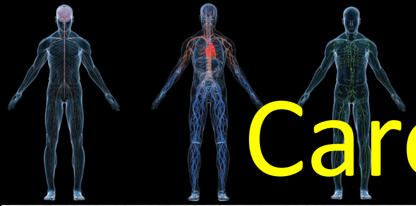
TWELFTH EDITION



Chapter 41:

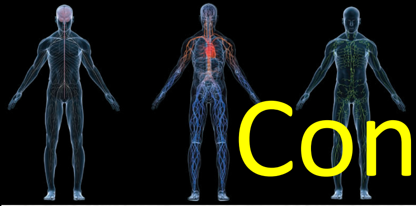
Regulation of Respiration

Slides by Robert L. Hester, PhD



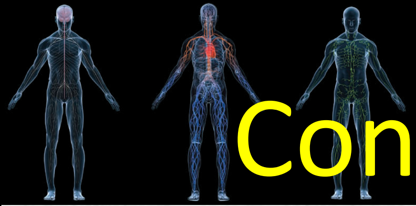
Carotid blood flow (ml/g/min)

Tissue	Blood flow (ml/g/min)	A-V difference (Vol %)	Flow ml/min	O_2 consumption ml/min
Heart	0.8	11	250	27
Brain	0.5	6.2 (25-30% Extraction)	750-900	
Skeletal Muscle	0.03	6	1200	70
Liver	0.6	3.4 Reconditioner organ		
SKIN	0.1			
Kidney	4.2	1.4	1250	18
Carotid bodies	20	0.5	0.6	



Control of Breathing….Introduction

- Q: What the controller system is going to do?
- A: Homeostasis of O_2, CO_2, H^+…Normal ABGs
- Q: How? What are the tools?
- A: by: ↑ventilation or ↓ventilation
- Q: What is the feedback system…nature of the receptor?
- A: ↓ $PaCO_2$, ↑$PaCO_2$, ↓ PaO_2 (below 60 mmHg), ↓ H+, and finally ↑H+
- **Note: ↑PaO_2 has almost no effect on the controller system**

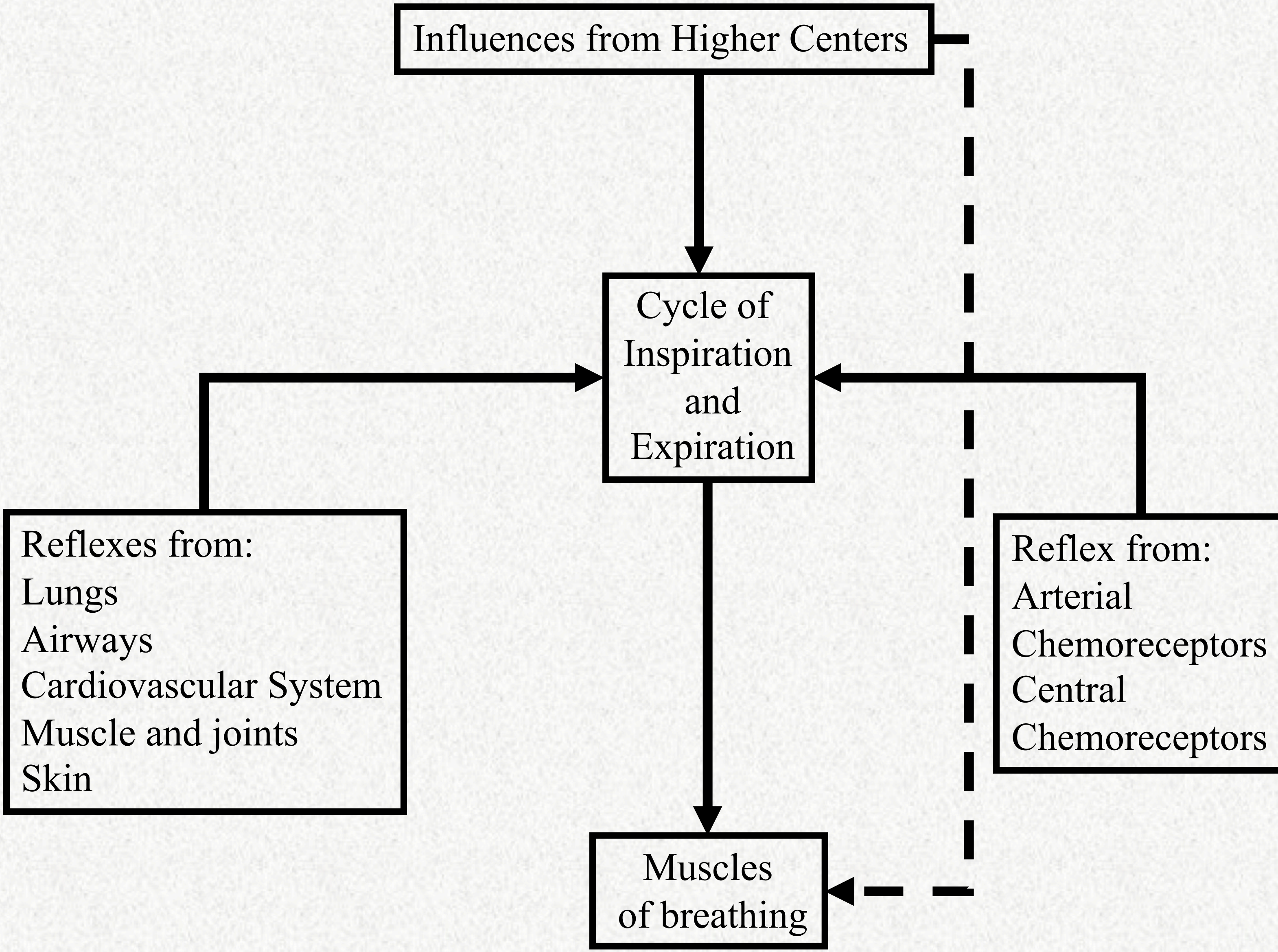


Control Of Breathing ….Introduction

- Again: The main goal of the respiratory system is to maintain normal ABGs: O_2, CO_2, and pH
- The controller center receives feedback response from O_2, CO_2, and pH
- What are the tools: Manipulating ventilation
- Sensor and response: Peripheral and central nervous system

Regulation of Respiration ….Introduction

- Sensors…receptor… afferent pathway
  - gather information regarding CO_2, O_2, and pH
- Central controller
  - integrate signals…translation…output orders…the efferent pathway.
- Effectors
  - Respiratory muscles…receive the output from the respiratory center and produce a response that change the controlled condition.


Influences from Higher Centers
Cycle of Inspiration and Expiration
Reflexes from:
Lungs
Airways
Cardiovascular System
Muscle and joints
Skin
Reflex from:
Arterial Chemoreceptors
Central Chemoreceptors
Muscles of breathing

How alveolar ventilation V_A affects P_AO_2 and P_ACO_2

P_AO_2 depends on :

1. O_2 delivery to alveoli (Alveolar Ventilation V_A).
2. Rate of O_2 absorption to blood (O_2 Consumption VO_2)

$$P_AO_2 \propto (V_A/VO_2)$$

HYPERVENTILATION is when alveolar ventilation is more than CO_2 production $\rightarrow$ decrease P_aCO_2

HYPOVENTILATION is when alveolar ventilation is LESS than CO_2 production $\rightarrow$ increase P_aCO_2

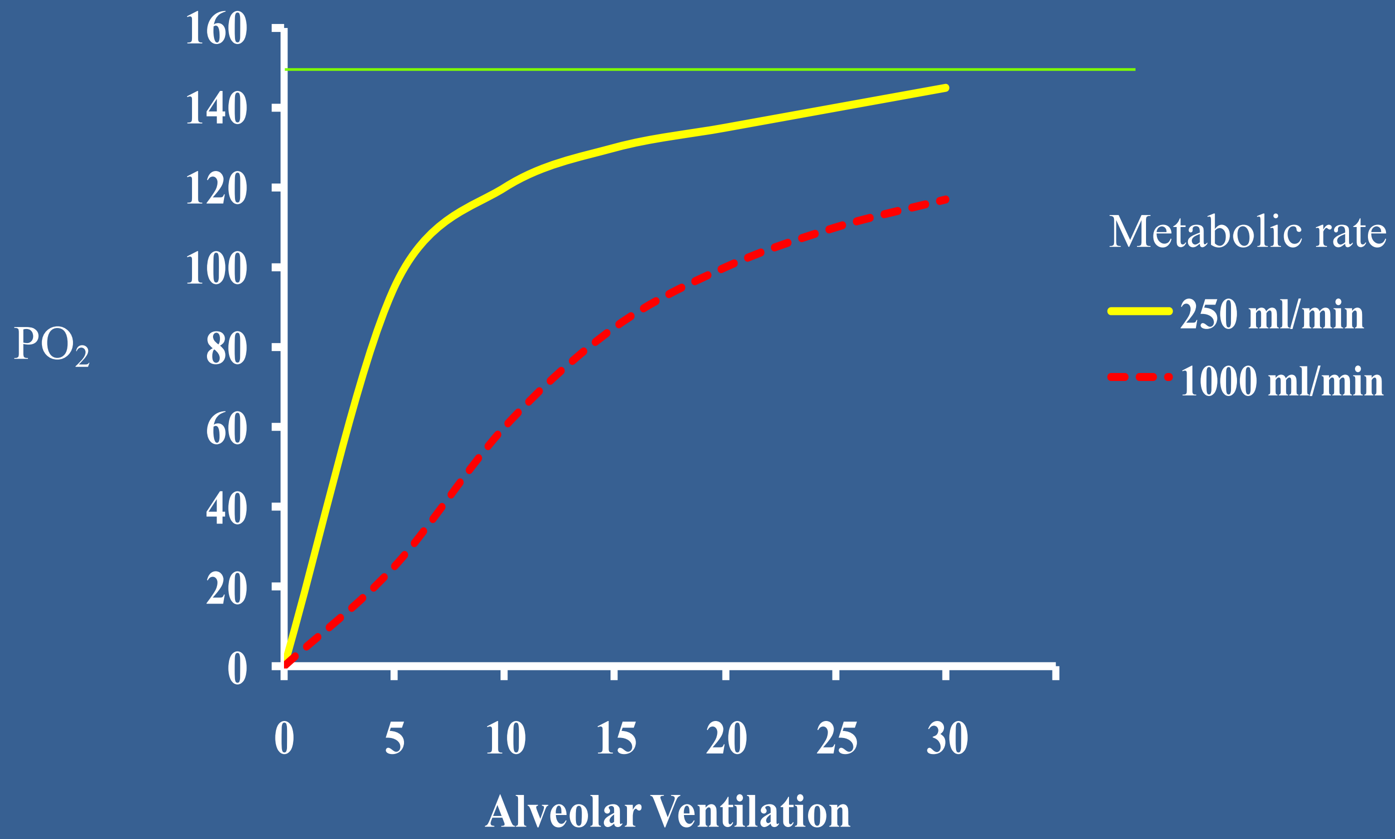
$$P_ACO_2 = (VCO_2/V_A)^* K$$

K”= constant (= 0.863 mmHg. lit/ml).

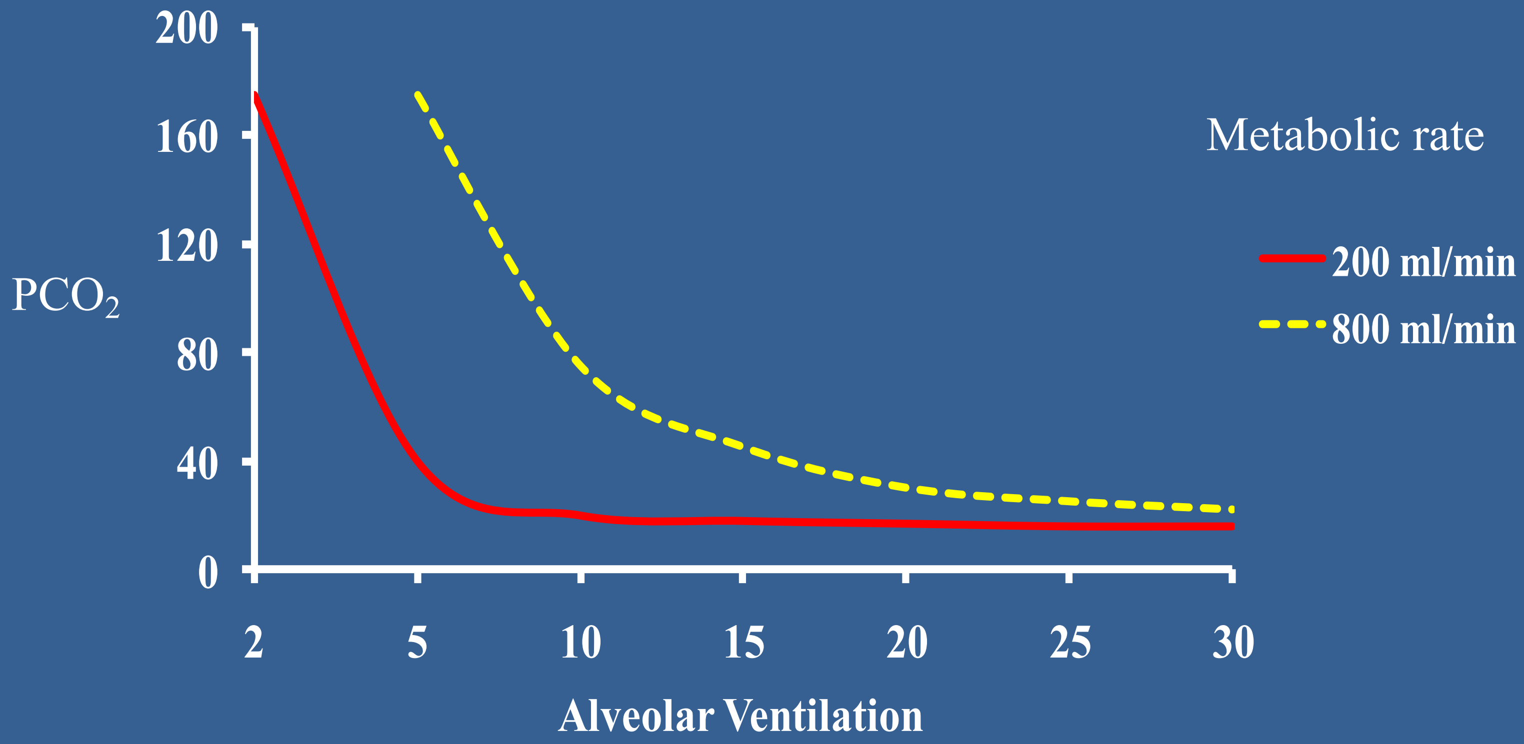
If ventilation is doubled then P_ACO_2 decreases to ½

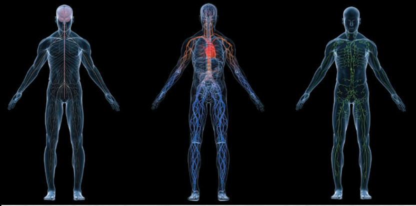
If ventilation is halved then PCO_2 is doubled…keeping CO_2 production constant.....*See the two graphs in the next two slide.*

Partial pressure of oxygen in alveoli



Partial pressure of CO_2 in alveoli





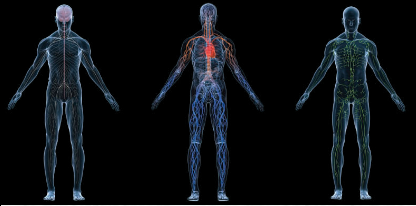
Question

Metabolic rate is doubled but alveolar ventilation is not changed. What happens to systemic arterial PCO_2?

A. Increases

B. Decreases

C. no change



Question

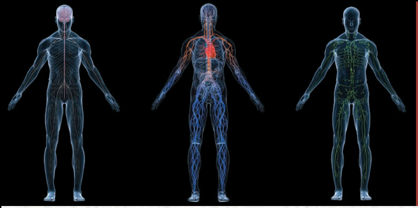
In which of the following conditions is alveolar PO_2 increased and alveolar PCO_2 decreased

A. Breathing air with 19% PO_2

B. Increased alveolar ventilation and unchanged metabolism

C. Decreased alveolar ventilation and unchanged metabolism

D .Increased metabolism and unchanged alveolar ventilation



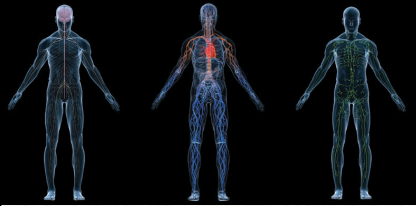
Question

What is the effect of anemia on ventilation?

A. decrease ventilation

B. increase ventilation

C. no change in ventilation.



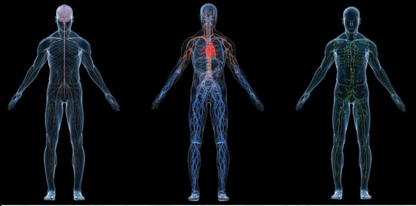
Question

Breathing CO acutely will __?__ respiration?

A. increase

B. decrease

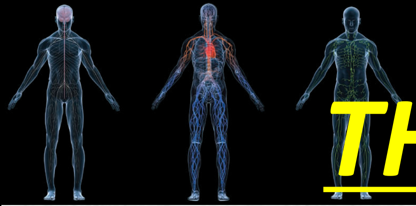
C. not change



Answer

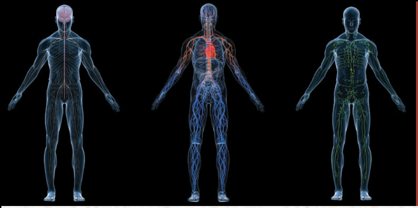
Breathing CO will not change respiration?

Arterial PO_2 does not change, PCO_2 does not change



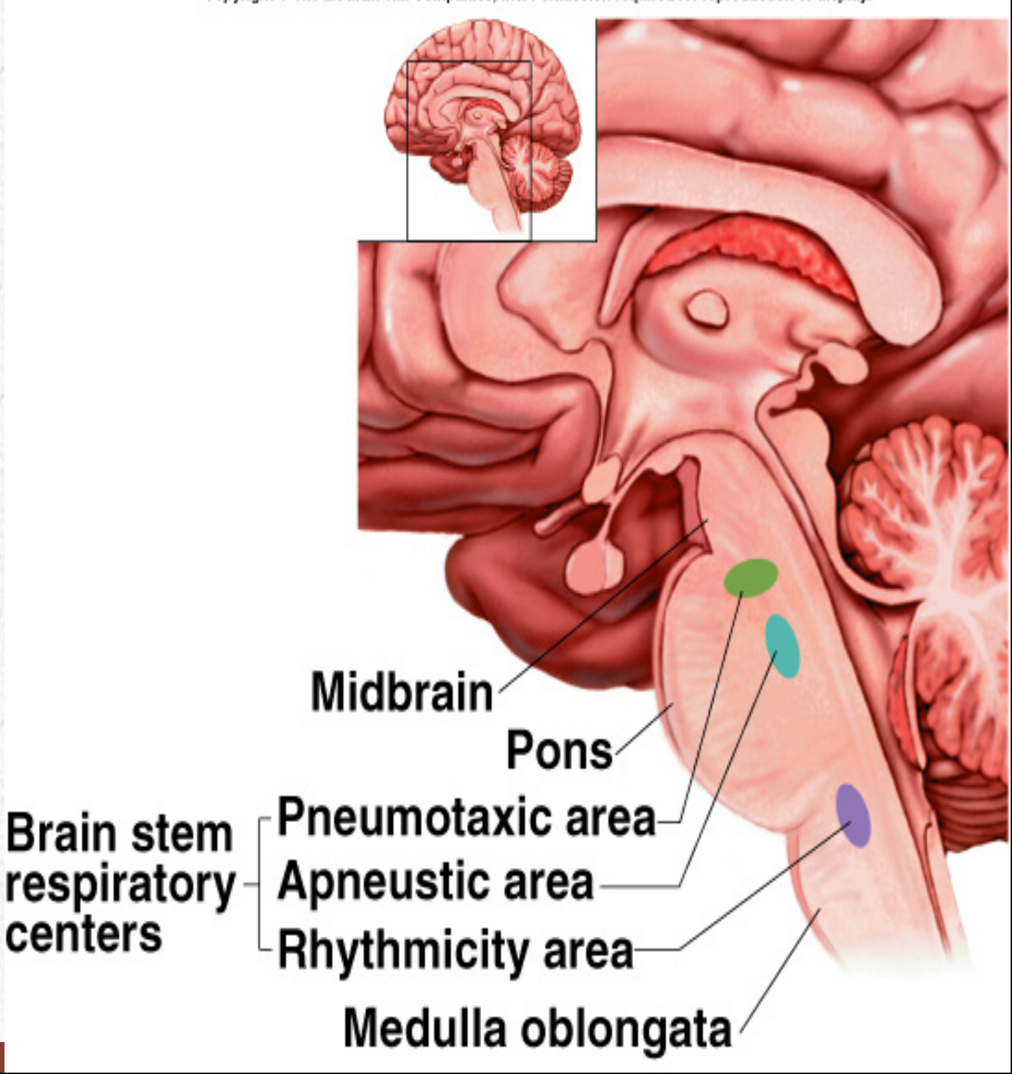
THE RESPIRATORY CENTER

- It is a loose collection of inspiratory and expiratory neurons situated in the medulla oblongata of the brain stem. Is not a discrete identifiable center in the strict anatomical sense. When inspiratory neurons are active, expiratory neurons are inhibited and vise versa.



Brain Stem Respiratory Centers

- Neurons in the reticular formation of the medulla oblongata form the rhythmicity center:
  - Controls automatic breathing.
  - Consists of interacting neurons that fire either during inspiration (I neurons) or expiration (E neurons).



Respiratory Center

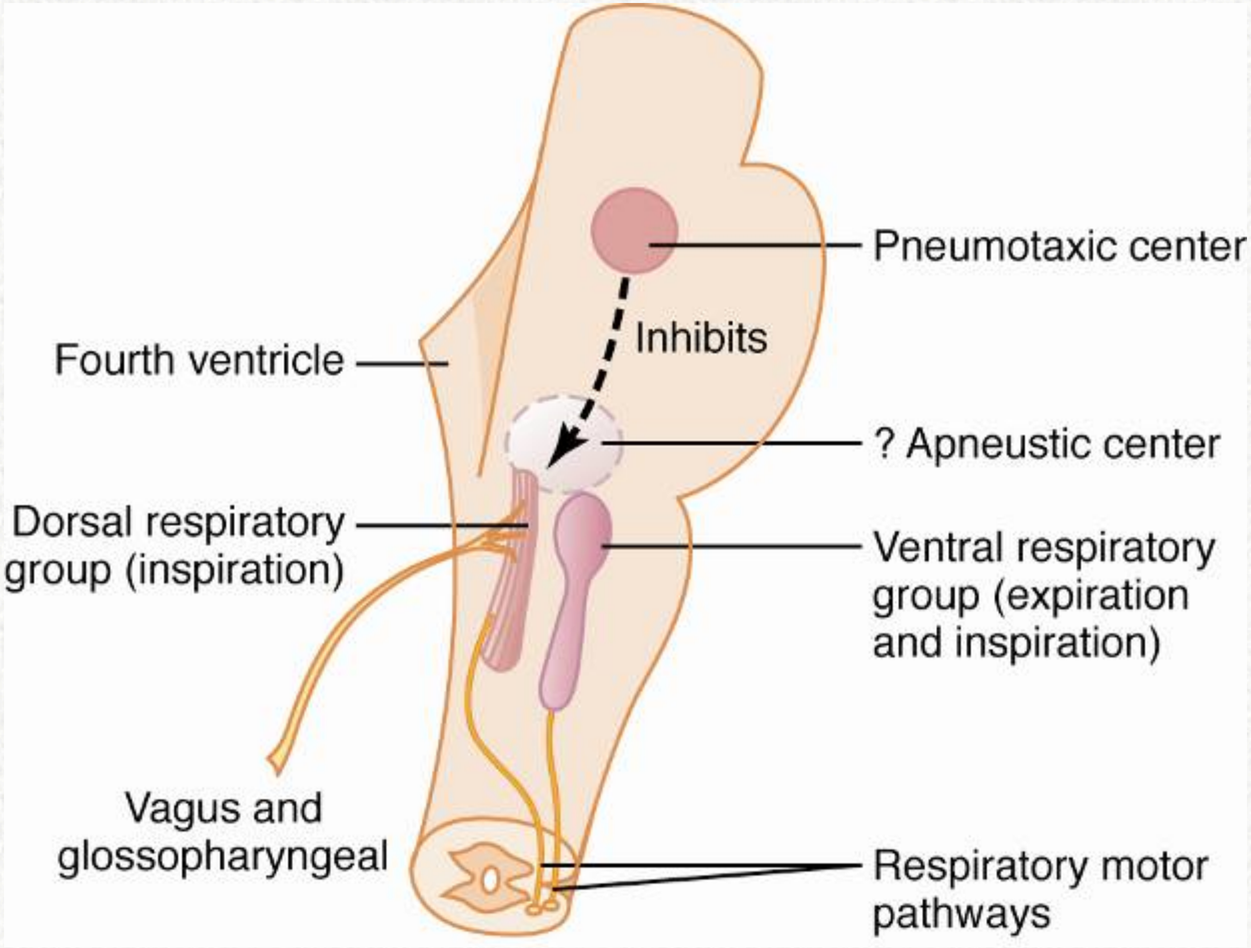
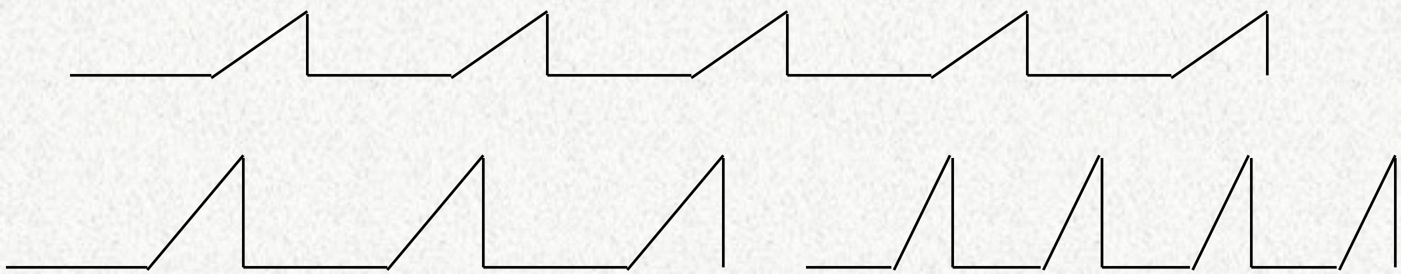


Figure 41-1

Medullary Respiratory Center

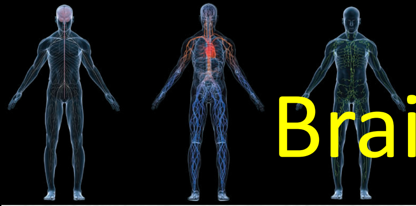
Dorsal respiratory group

- inspiration,   intrinsic nerve activity



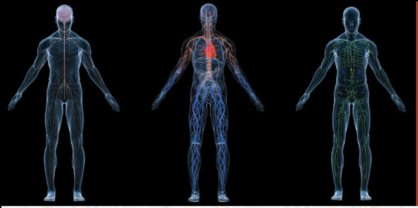
Respiratory Center

- Ventral Respiratory Group
  - Inactive during quiet respiration
  - Active respiration
  - Projections from the Dorsal Respiratory Group



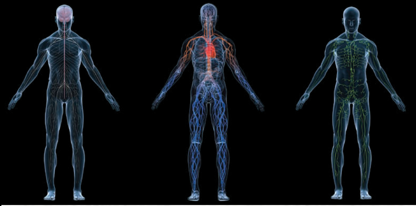
Brain Stem Respiratory Centers (continued)

- "I" neurons project to, and stimulate spinal motor neurons that innervate respiratory muscles.
- Expiration is a passive process that occurs when the I neurons are inhibited.
- Activity varies in a reciprocal way.



Rhythmicity Center

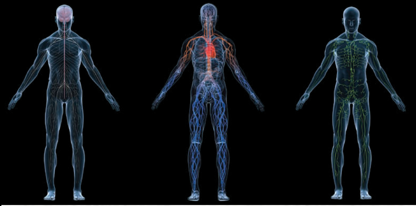
- "I" neurons located primarily in dorsal respiratory group (DRG):
  - Regulate activity of phrenic nerve.
    - Project to and stimulate spinal interneurons that innervate respiratory muscles.
- "E" neurons located in ventral respiratory group (VRG):
  - Passive process.
    - Controls motor neurons to the internal intercostal muscles.
- Activity of E neurons inhibit I neurons.
  - Rhythmicity of I and E neurons may be due to pacemaker neurons located in the upper part of the VRG.



Pons Respiratory Centers

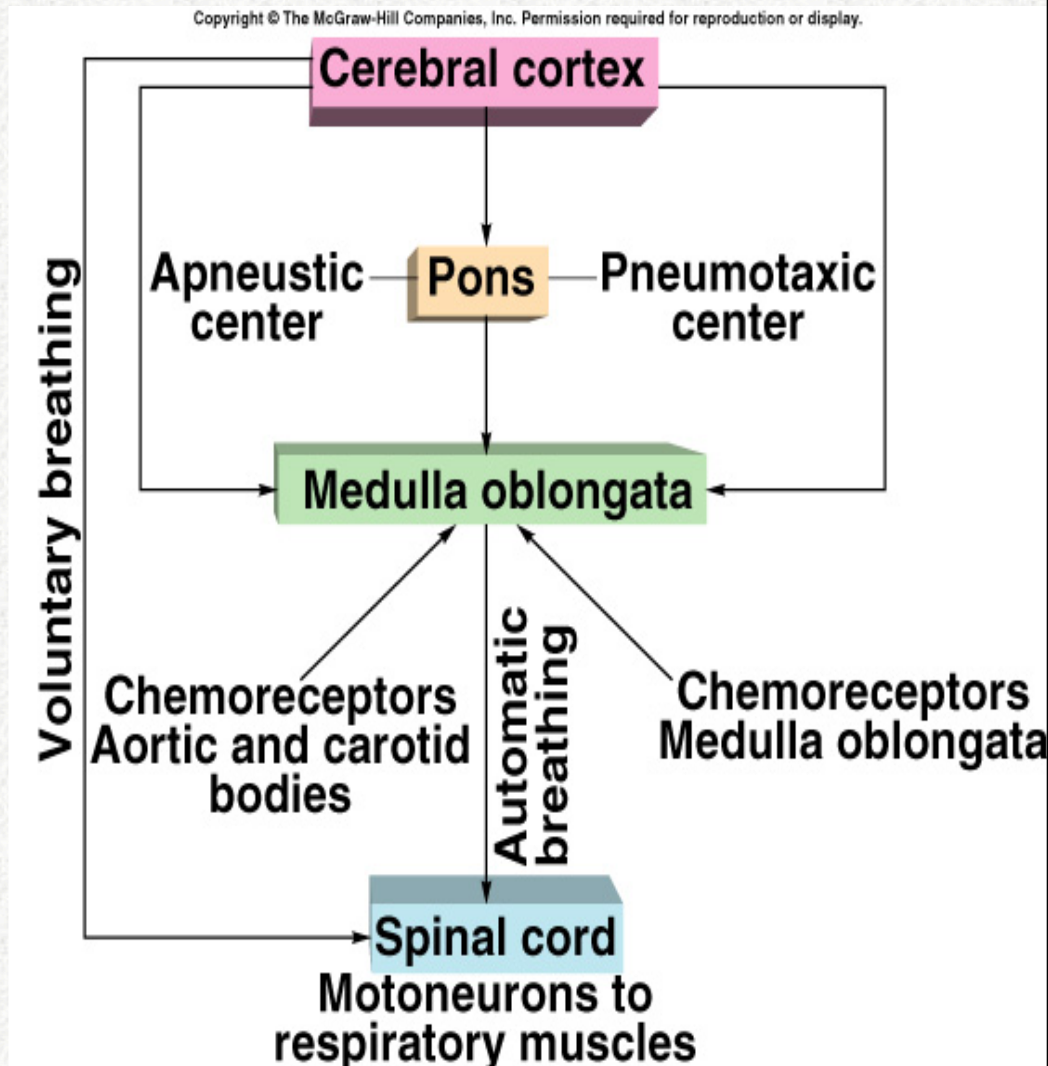
- Activities of medullary rhythmicity center is influenced by pons.
- Apneustic center:
  - Promotes inspiration by stimulating the I neurons in the medulla.
- Pneumotaxic center:
  - Antagonizes the apneustic center.
  - Inhibits inspiration and thus increase RR.

– **It is the Switch of** inspiration and modulate respiratory system



Chemoreceptors

- 2 groups of chemo-receptors that monitor changes in blood PCO_2, PO_2, and pH.
- Central:
  - Medulla…chemosensitive area…sensitive to H+
- Peripheral:
  - Carotid and aortic bodies.
    - Control breathing indirectly via sensory nerve fibers to the medulla (X, IX). Sensitive to O2

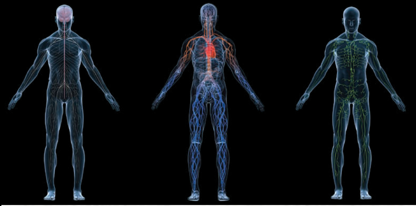


Effects of Blood P_{C0_2} and pH on Ventilation

- Chemoreceptor input modifies the rate and depth of breathing.
  - Oxygen content of blood decreases more slowly because of the large “reservoir” of oxygen attached to hemoglobin. HbO_2 dissociation curve is sigmoidal
  - Central Chemoreceptors are more sensitive to changes in PCO_2 through the H+

- $$H_20 + C0_2 \longleftrightarrow H_2C0_3 \longleftrightarrow H^+ + HC0_3^-$$

- Rate and depth of ventilation adjusted to maintain arterial PCO_2 equals to 40 mm Hg.

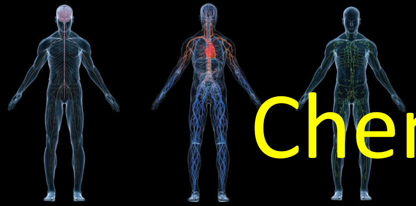


Chemoreceptor Control

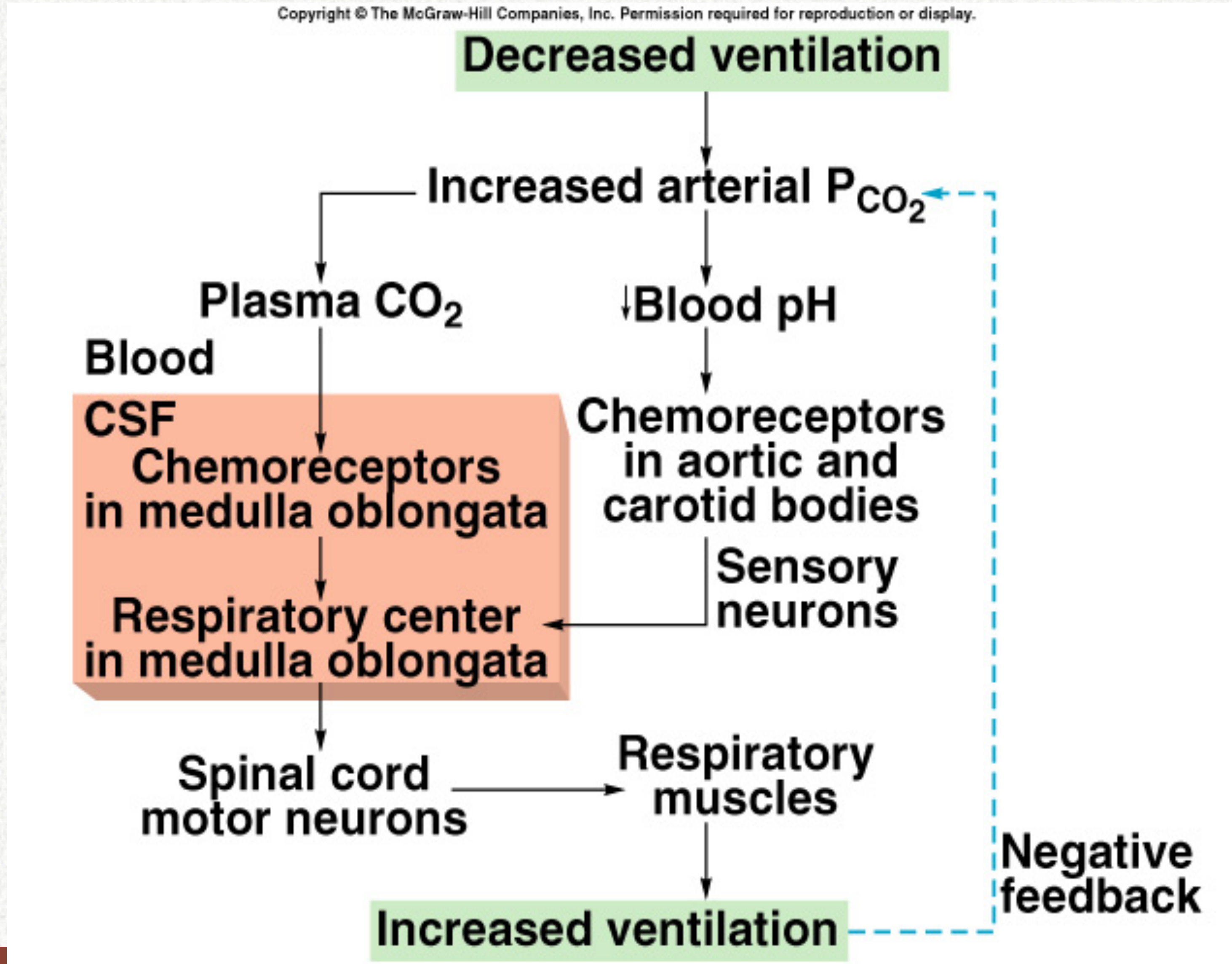
- Central chemoreceptors:

  More sensitive to changes in arterial $PC0_2$ through H+

- **$H_20 + CO_2$ → H_2C0_3 → H^+**
- H^+ cannot cross the blood brain barrier.
- CO_2 can cross the blood brain barrier and will form H_2CO_3.
  - H^+ lowers pH of CSF fasters than it lowers blood pH…no enough buffers in CSF
    - Directly stimulates central chemoreceptors.



Chemoreceptor Control of Breathing

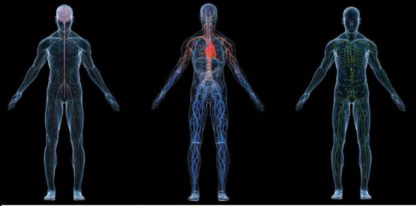


Effects of Blood PO_2 and PCO2 on Ventilation

- **O_2 and CO_2 potentiation effect**
  - Low PO_2 Influences chemoreceptor sensitivity to changes in POC_2….potentiation
  - High PCO_2 enhances sensitivity of carotid bodies to fall in PO_2…..potentiation
- Hypoxic drive:
  - Emphysema blunts the chemoreceptor response to PCO_2…because kidneys correct pH in chronic situation. By making more $HC0_3^-$ which buffers the fall in CSF pH. Therefore, giving the COPD patient pure O_2 to breath will suppress ventilation…since the low PO_2 is the one which drives ventilation in this patient…don't remove the drive!

Effects of Pulmonary Receptors on Ventilation

- Lungs contain receptors that influence the brain stem respiratory control centers via sensory fibers in vagus.
  - Unmyelinated C fibers can be stimulated by:
    - Histamine and bradykinin:
      - Released in response to noxious agents.
  - Irritant receptors are rapidly adaptive receptors.



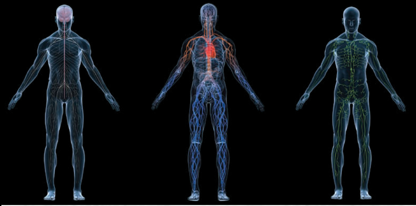
Lung receptors

- **Pulmonary Stretch Receptors**

- Located in smooth muscle of large and small airway and minimize work of breathing by inhibiting large tidal volumes

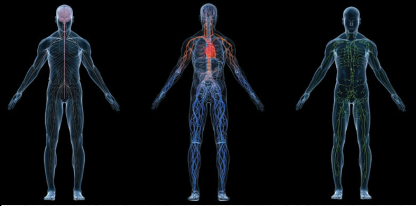
- **Hering-Breuer reflex**” are Pulmonary stretch receptors activated during inspiration.
- Inhibits respiratory centers to prevent undue tension on lungs.
- Hering Breuer inflation reflex can be easily manifested in dogs & cats but not in man (unless $V_T \geq 1.5$ liters). So its function in man is uncertain.   However, in newborn where V_T is small, it may be important.

- Irritant receptors
  - Nasal mucosa, upper airways, possibly alveoli
  - Bronchoconstriction which lead to cough and sneeze
- J receptors
  - Located in the capillary wall, interstitium
  - Lung disease and edema (pulmonary congestion)
  - Rapid shallow breathing (tachypnea)



Other Reflexes

- Arterial Baroreceptors
  - Stimulation by elevated blood pressure results in brief apnea and bronchodilation
- Muscles and Tendons
  - Muscles of respiration as well as skeletal muscles, joints and tendons
  - Adjust ventilation to elevated workloads



Chemical Control of Respiration

- Carbon Dioxide works centrally through H^+
- Oxygen works peripherally at the carotid and aortic bodies.

Chemosensitive Area of Respiratory Center

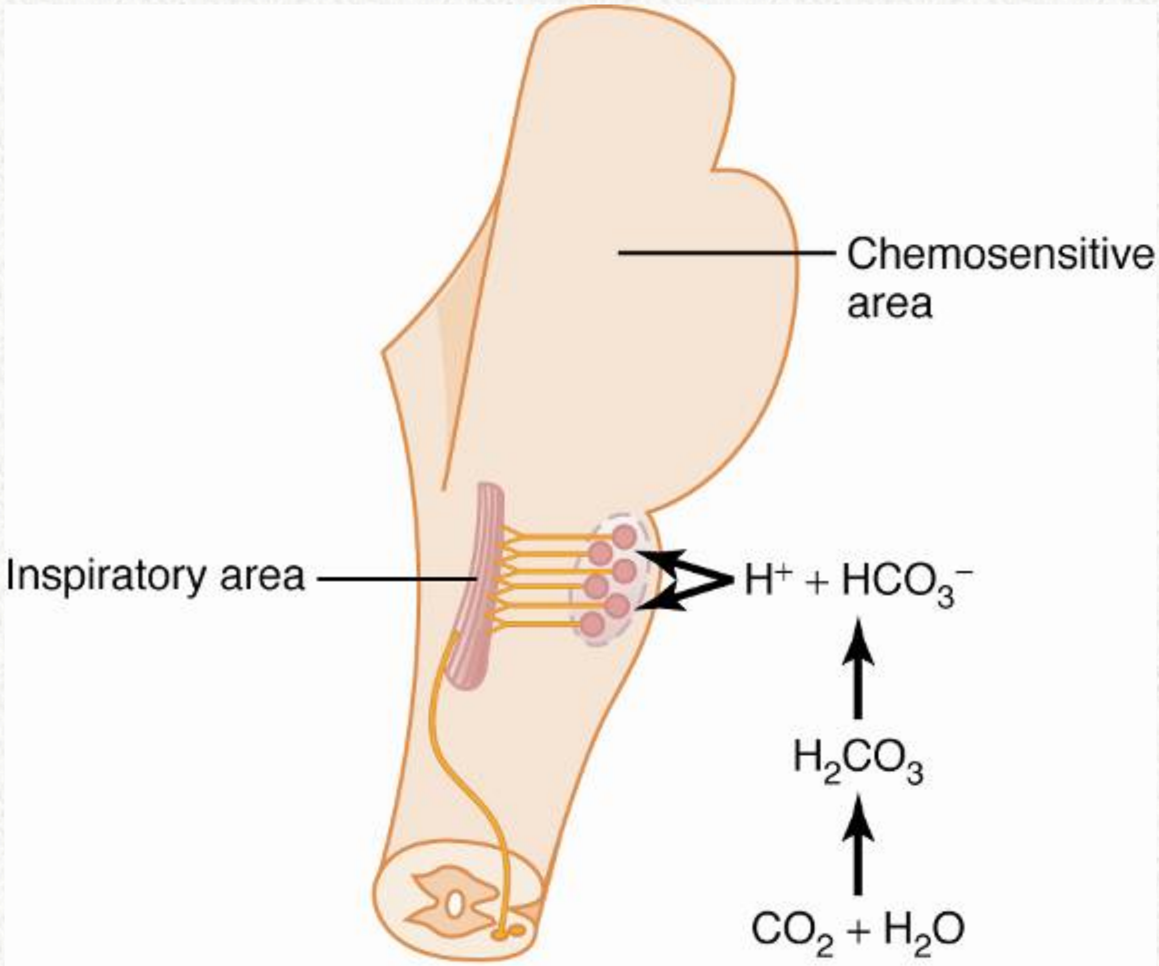
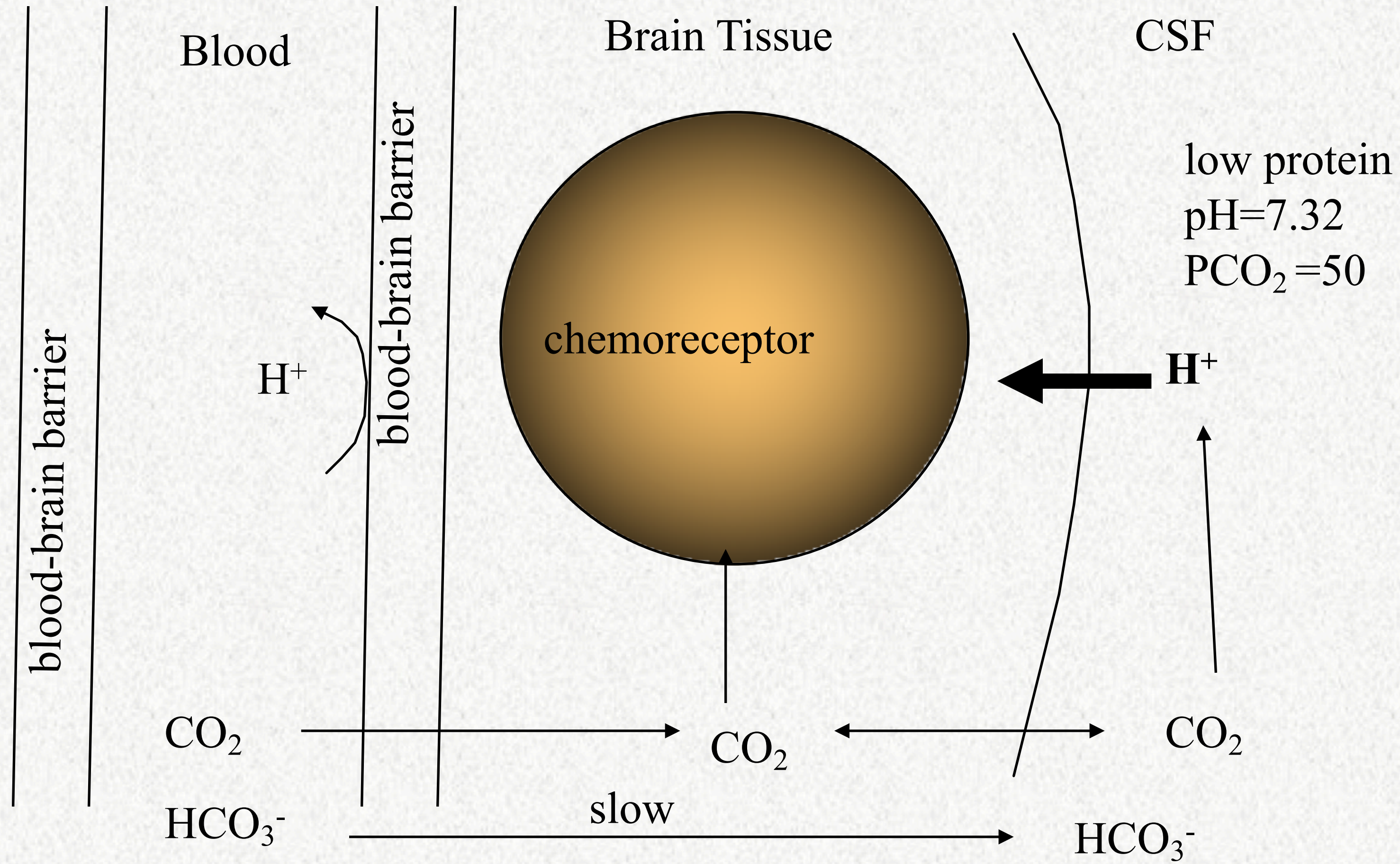


Figure 41-2

Chemosensitive Area of Respiratory Center



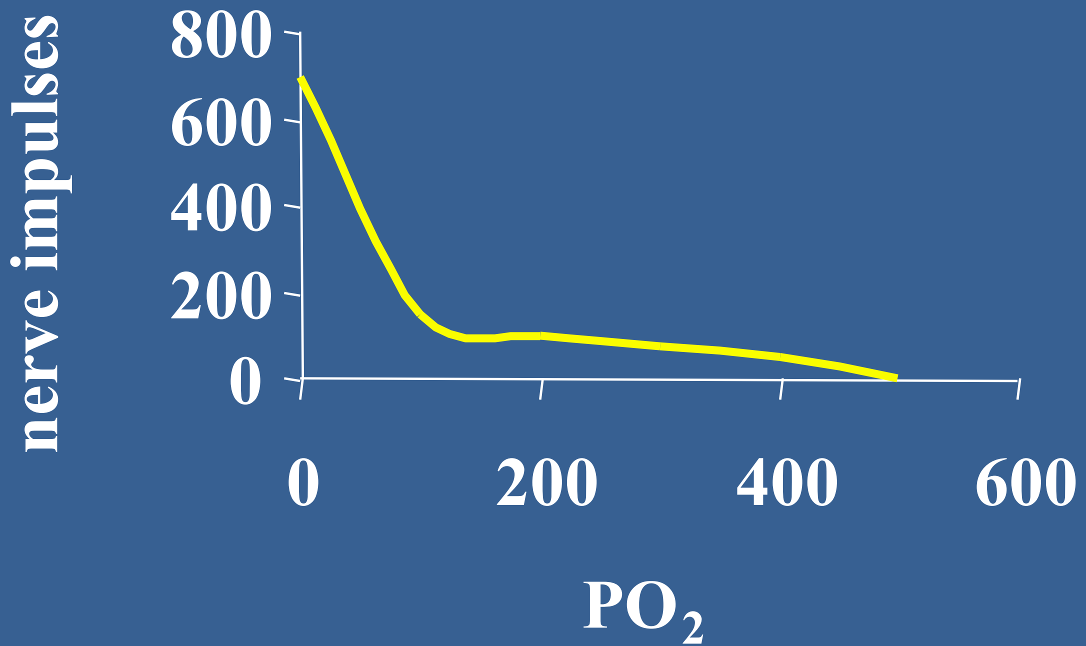
Comparison between Blood and CSF

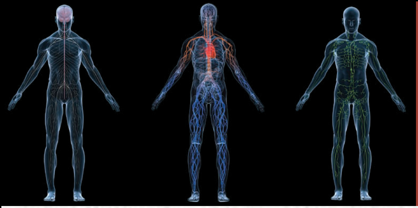
	CSF	***BLOOD***
HCO_3^-	24	28
protein	<45 mg%	6-8 g%
pH	7.32	7.4

CSF have less buffering capacity…and thus pH is shifted faster

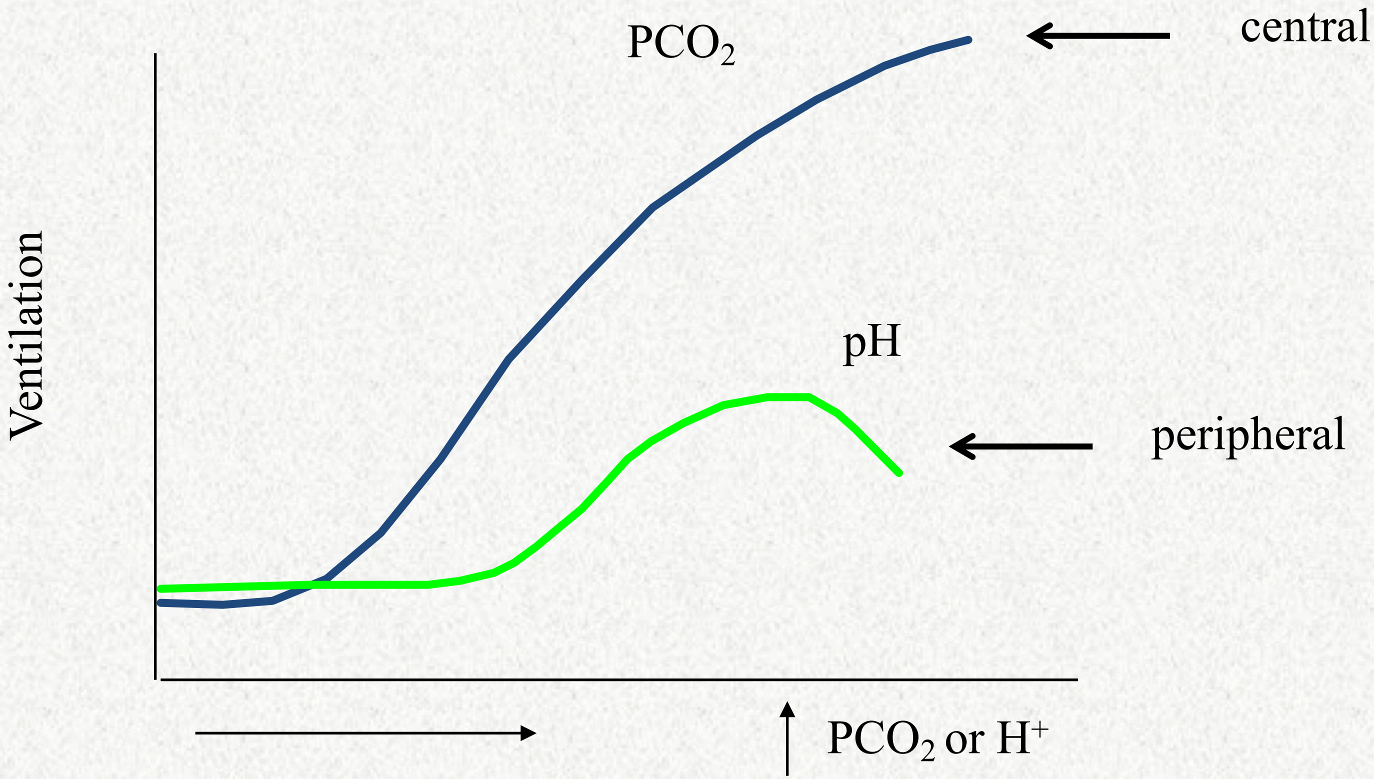
Peripheral Chemoreceptors

- Carotid bodies at the bifurcation of the common carotid artery.
  - –responds mainly (not only) to oxygen (PO_2<60 mmHg)
  - –-responds to carbon dioxide and hydrogen ion…one seventh of the central response but 5 times faster



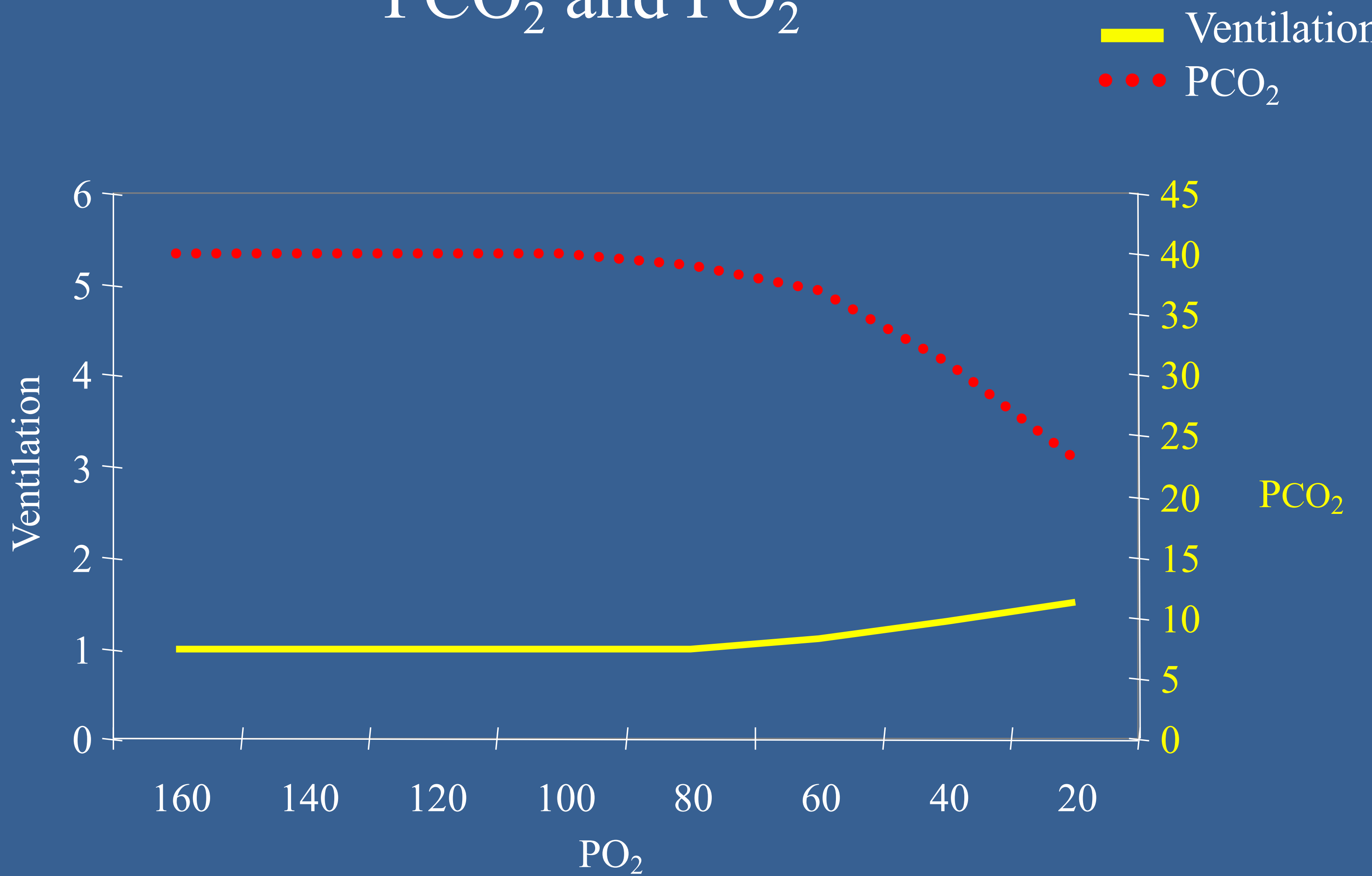


Control of Respiration

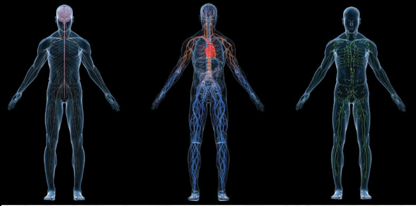


Changes in arterial PCO_2 have greater effect than changes in arterial pH

PCO_2 and PO_2



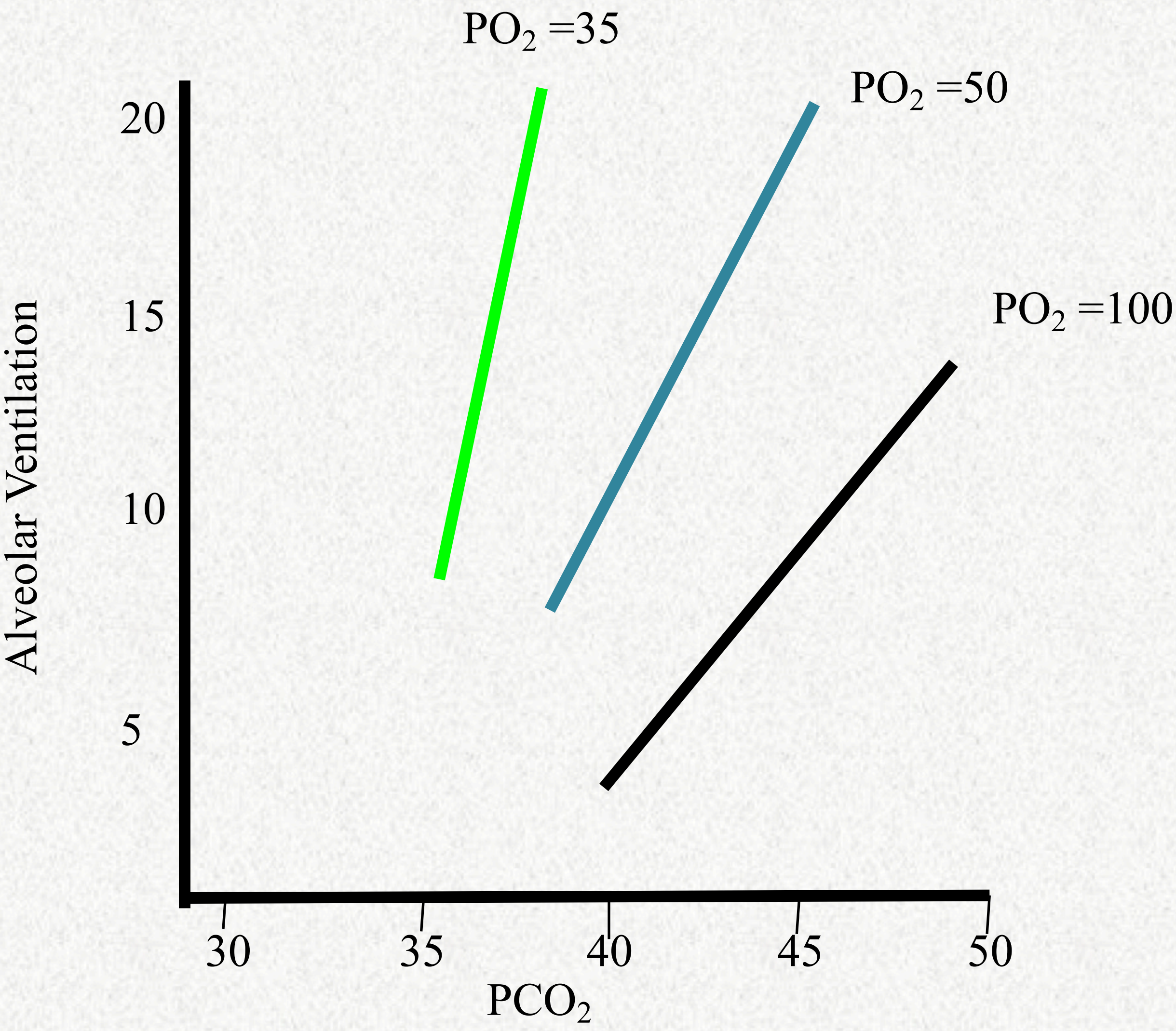
Hypoxic increase in ventilation inhibited by fall in PCO_2

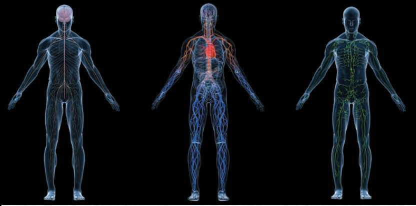


Chemoreceptor Control (continued)

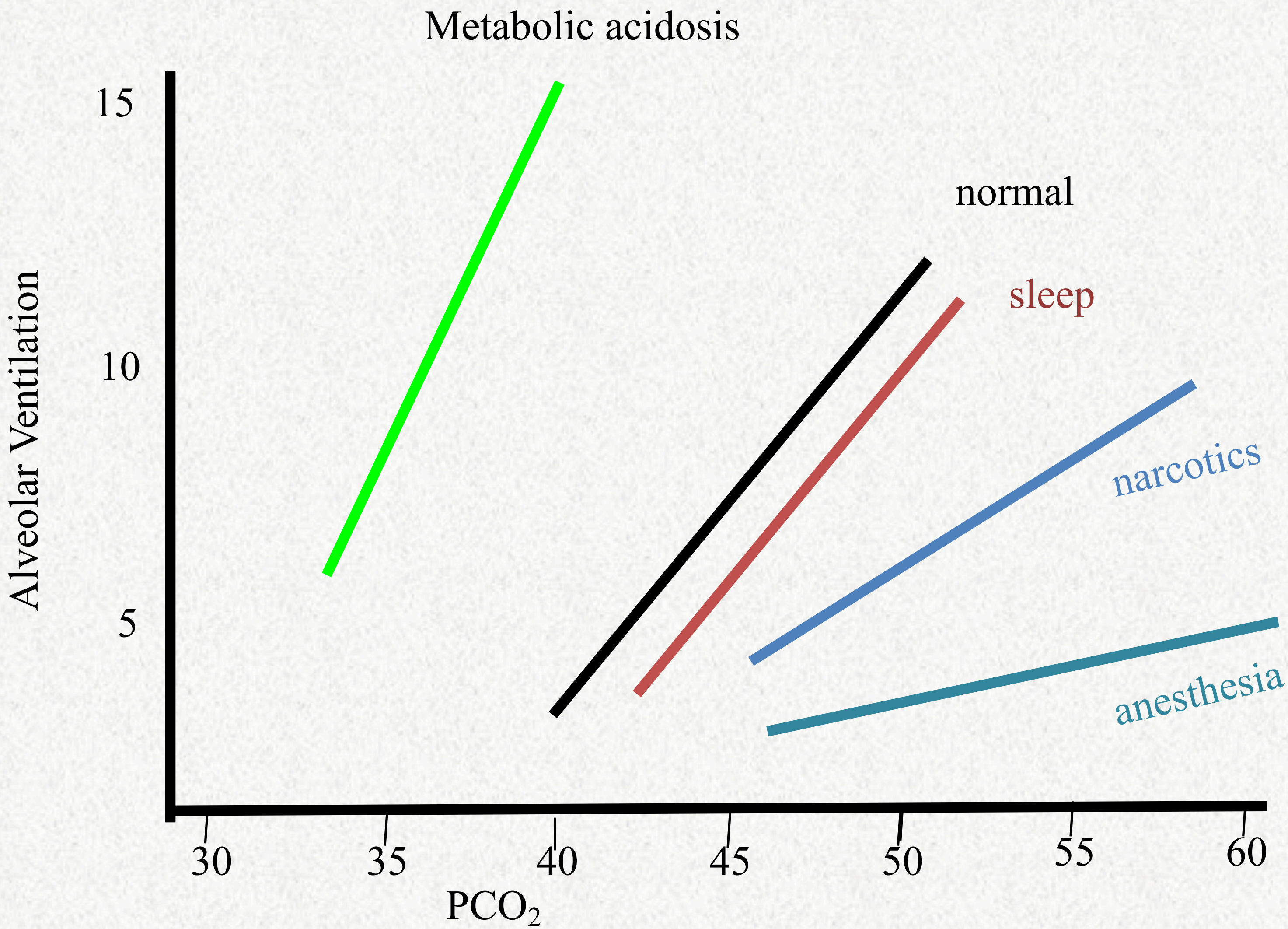
- Peripheral chemoreceptors mainly stimulated by $\downarrow PO_2$
- **$H_20 + C0_2 \rightarrow H_2C0_3 \rightarrow H^+$**
- Stimulated by rise in $[H^+]$ of arterial blood.
  - Increased $[H^+]$ stimulates peripheral chemoreceptors.

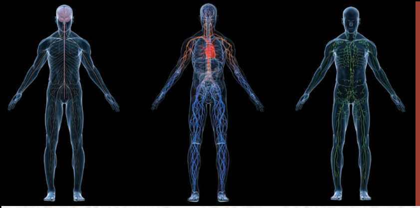
Carbon dioxide response curve at different O2 levels





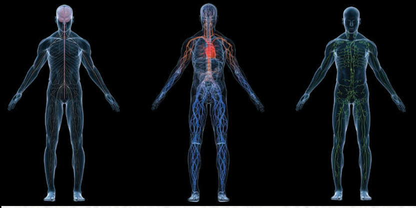
Carbon dioxide response curve under different conditions





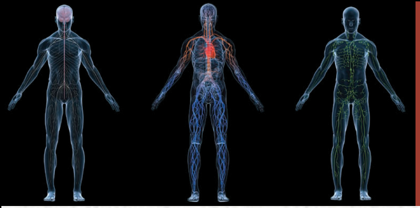
Summary

- Carbon dioxide is major stimulus for increased respiration
- Acts on chemosensitive area through H^+
- Peripheral chemoreceptors are mainly affected by low PO2
- If P_{CO_2} is constant low oxygen can be important
- Questions?
  - Why is oxygen’s effect on respiration blunted?
  - Explain ventilatory drive during severe lung disease…see next slide for answer.

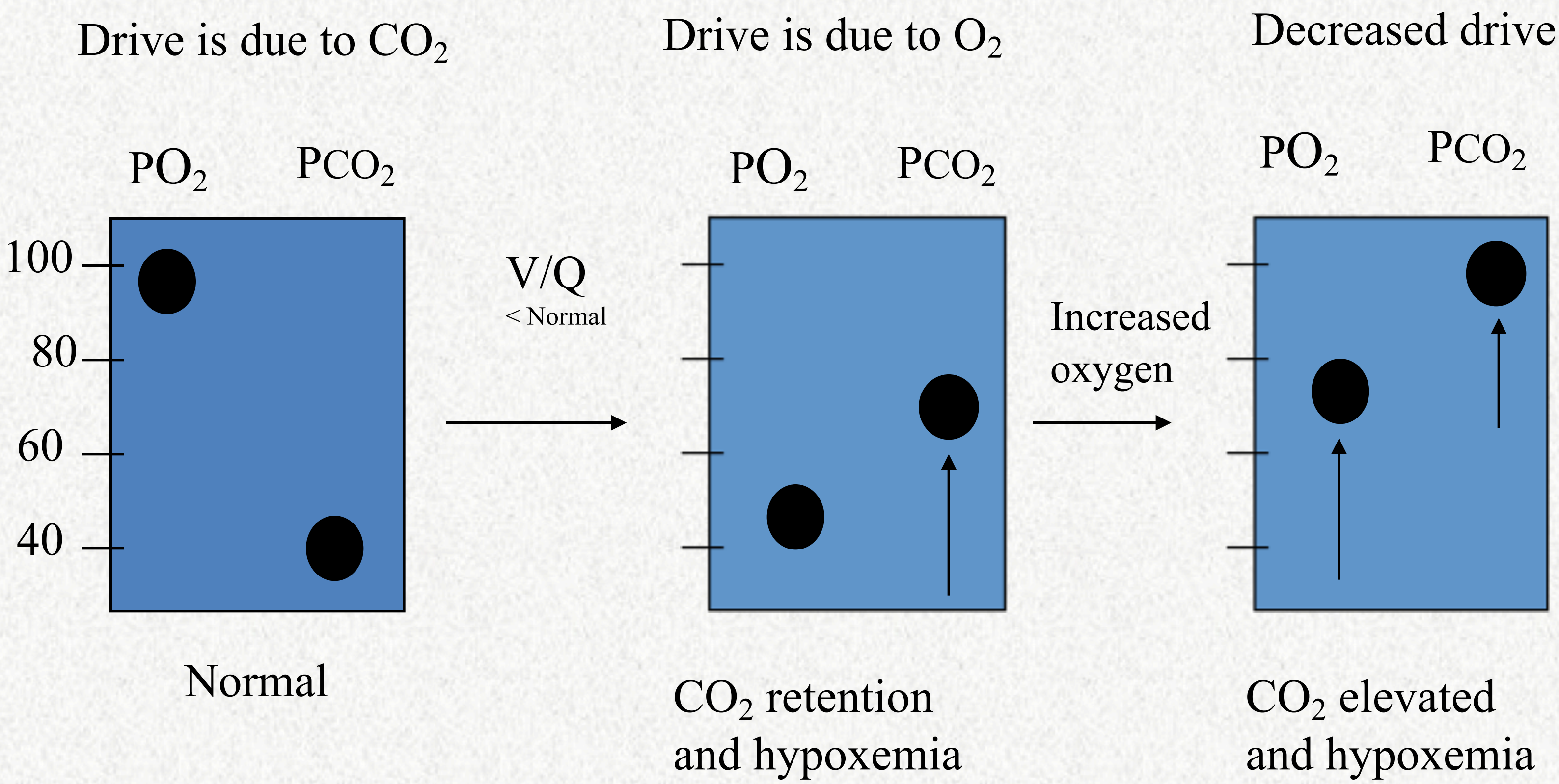


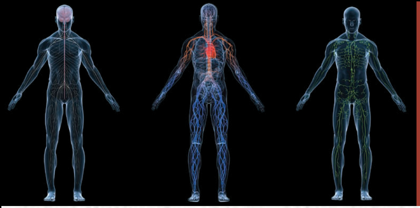
CO_2 Retention

- Severe lung disease, COPD
- Develop hypoxemia and hypercapnia
- Respiratory drive is due to low PO2
- Renal control of acid-base balance
- Treat with hight % oxygen inhibits respiratory drive
- High levels of PCO_2
- Minimal levels of oxygen, monitor blood gases



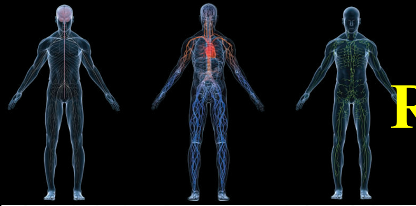
CO_2 Retention





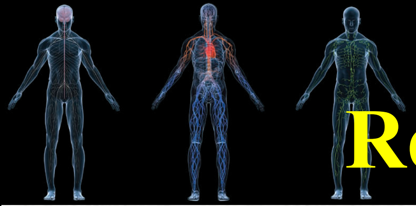
Respiration During Exercise

- Linear increase in ventilation with increasing oxygen consumption. Ventilation increase linearly until it reaches VO_{2max}.
- O_2 consumption at rest is 250 ml/min. In exercise it increases 20 folds (5,000 ml/min).
- arterial PO_2, PCO_2 and pH **do not change** during exercise
- In the contrary, P_aCO_2 may decrease slightly…
- Q: What drives ventilation during Exercise?



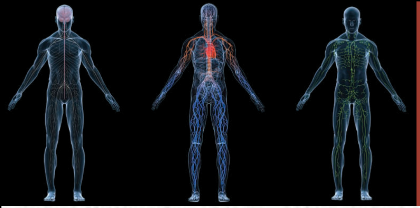
Respiration During Exercise…..Time wise

- Ventilation ↑ immediately (instantaneously) with the onset of exercise, then it gradually ↑ to final value which is determined by the severity of the exercise. The more strenuous the exercise the greater the initial rise at the onset & the higher the final level of ventilation. Following exercise there is an immediate decrease in ventilation followed by a more gradual return to the resting level.
- Because of the initial ↑ in ventilation (before muscle movement) the P_aCO_2 would decrease slightly. And then exercising muscles would produce CO_2 which then returns to normal level which stays at that level until the end of exercise. When muscles stop exercising (end of exercise) ventilation decrease instantly which cause ↑ P_aCO_2, again stimulates the respiratory center which ↑ ventilation slightly and then again decreasing slightly but remains high because of the oxygen debt.



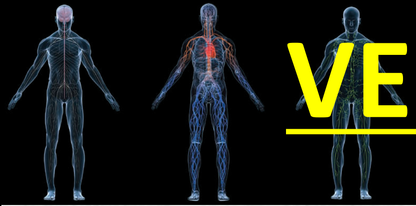
Respiration During Exercise…Drive

- Overflow of signals from cortex
- Body movements
- Increased body temperature
- Designed to control P_{CO_2}
- Learned response
- Conclusion: we are not sure regarding the exact mechanism responsible for increased ventilation during exercise.



Other Factors to Influence Respiration

- Voluntary control
- Activity from vasomotor center
- Body temperature
  - increased production of carbon dioxide
  - direct effect on respiratory center
- Irritants
- Anesthesia



VENTILATION AT HIGH ALTITUDE

		Breathing Air			Breathing Pure O_2	
Height (feet)	Air	Inspired PO_2	P_AO_2	P_ACO_2	P_AO_2	P_ACO_2
0	760	160	100	40		
10,000	523	110	67(77)	36(23)		
20,000	350	73	40(53)	24(10)	262	40
29,029 (8848 m) Mount Everest	226	47	18(30)	24(7)	139	40

**In parenthesis are acclimatized values

PO_2 Responses to High Altitude

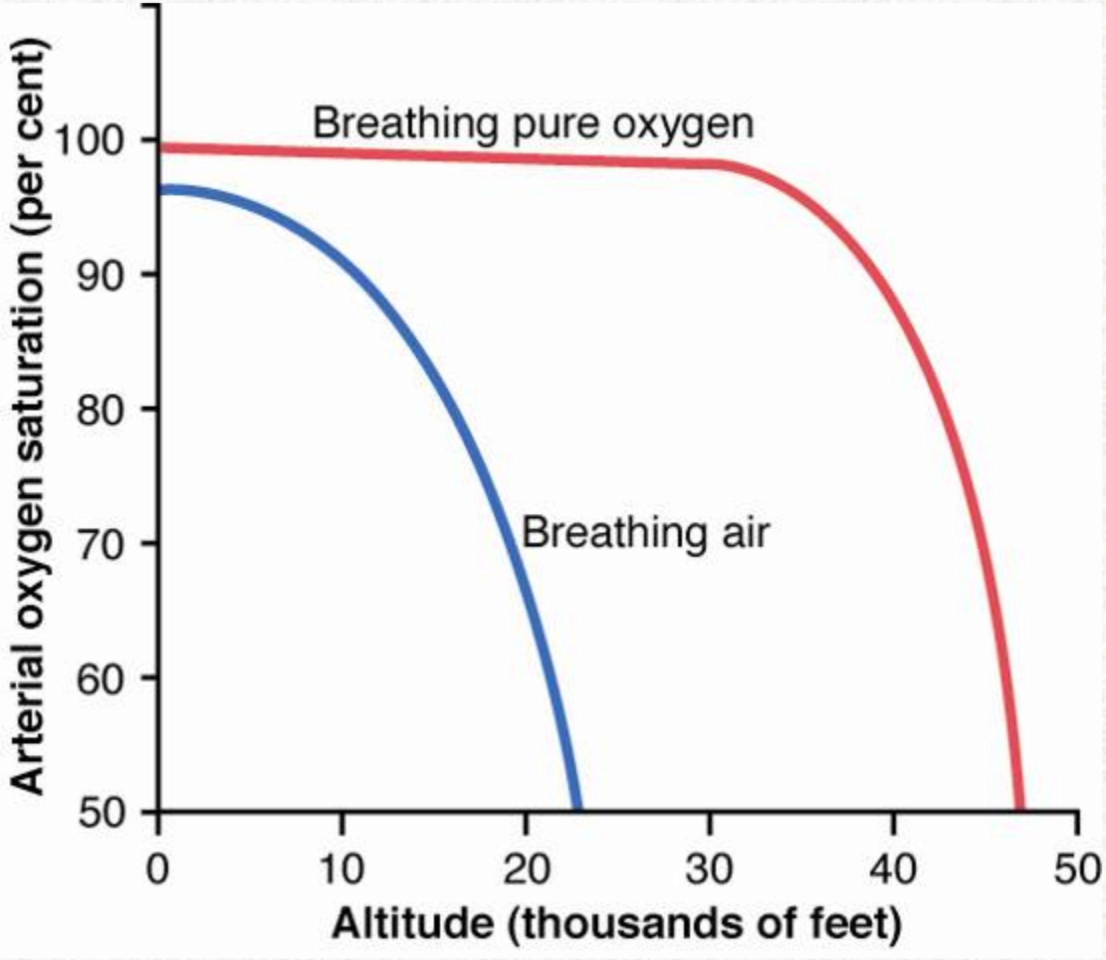
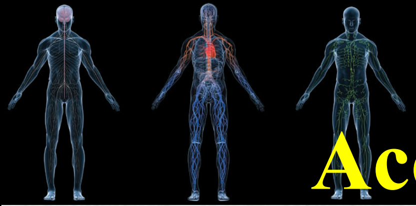
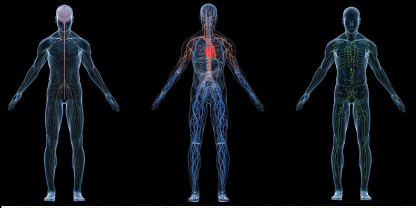


Figure 43-1



Acclimatization….continue

- Increased ventilation
  - due to decreased P_{O_2}
  - increase slowed by decreased P_{CO_2}
  - It increases 70% in the first day and 400-500% in the coming few days.
- Increased hematocrit (content)
- Increased diffusing capacity
- Increased capillarity



Hematocrit Responses during Acclimatization

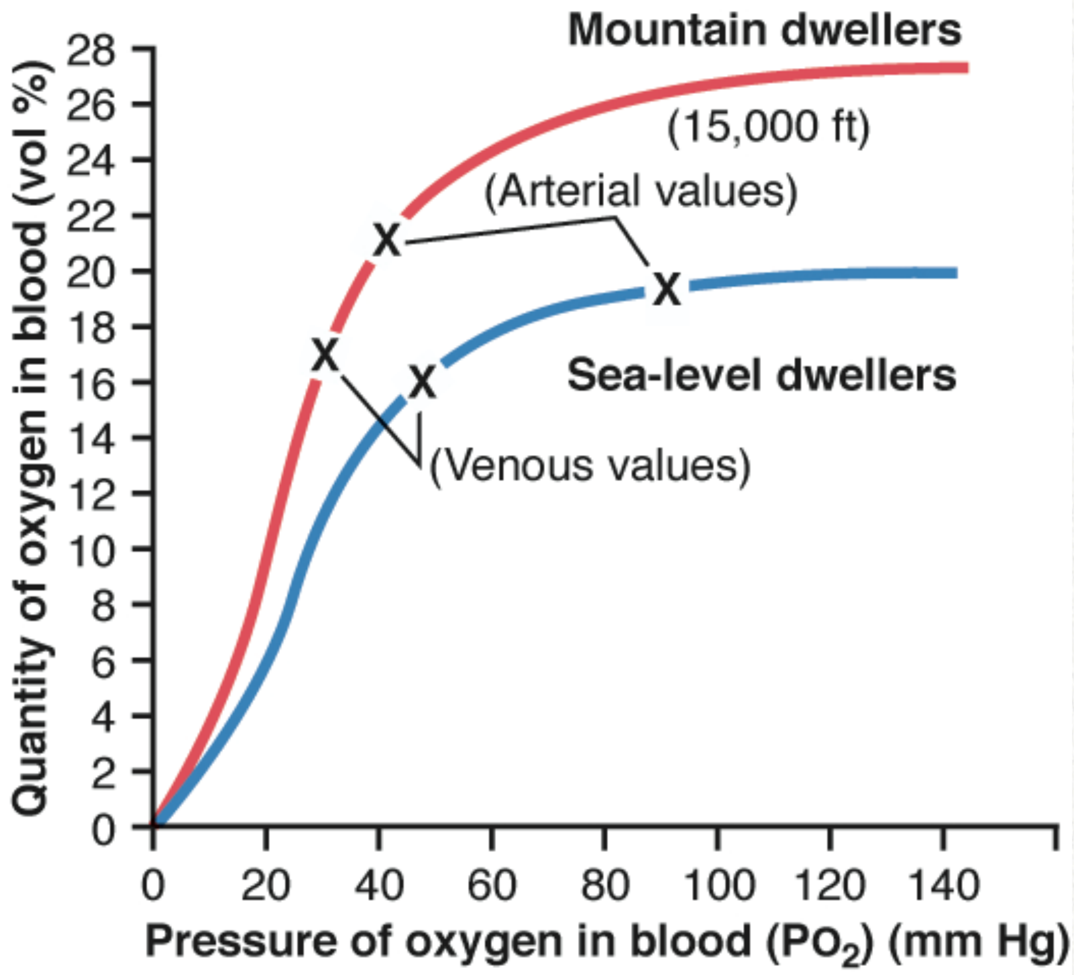
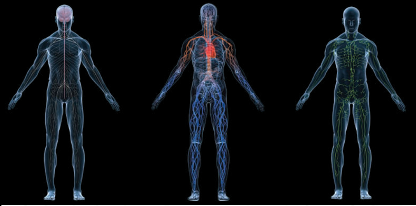


Figure 43-2



Mountain Sickness

- Chronic mountain sickness
  - increase in red cell mass
  - increase in pulmonary arterial pressure
  - enlargement of right heart
- Acute mountain sickness
  - acute cerebral edema
  - acute pulmonary edema

Question

What is atmospheric PO_2 at 10,000 ft (barometric pressure = 508 mmHg)?

Person has normal alveolar ventilation

A. 95 mmHg

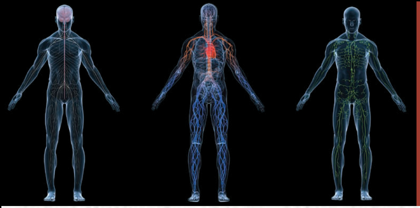
B. 106

C. 149

D. 159

Answer

508*0.21=106



- See you again next semester in renal Physiology…
  - GOOD LUCK