Slide 1

Control of Breathing

Objectives

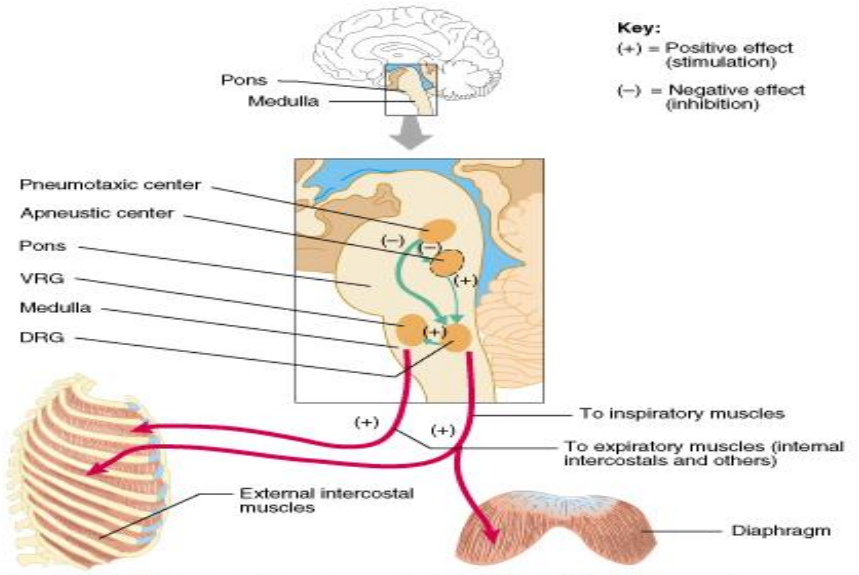
- By the end of this lecture you should be able to: -
- Understand the role of the medulla oblongata in determining the basic pattern of respiratory activity.
- List some factors that can modify the basic breathing pattern like e.g.
- a- The Hering-Breuer reflexes, b- The proprioreceptor reflexes, and 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.

Controls of rate and depth of respiration

- Arterial PO_2
  - When PO_2 is VERY low (Hypoxia), ventilation increases
- Arterial PCO_2
  - The most important regulator of ventilation is PCO_2, small increases in PCO_2, greatly increases ventilation
- Arterial pH
  - As hydrogen ions increase (acidosis), alveolar ventilation increases.

Slide 4

Respiratory Centers



Slide 5

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
  -Inactive during normal quiet breathing
  -Activated by inspiratory area during forceful breathing
  -Causes contraction of internal intercostals and abdominal muscles
- The medullary respiratory center stimulates basic inspiration for about 2 seconds and then basic expiration for about 3 seconds (5sec/ breath = 12breaths/min).

The respiratory center is composed of several groups of neurons located bilaterally in the medulla oblongata and pons of the brain stem, as shown in Figure 41-1 . 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; and (3) thepneumotaxic center, located dorsally in the superior portion of the pons, which mainly controls rate and depth of breathing.

.

Slide 6

Pontine Respiratory centers

- Transition between inhalation and exhalation is controlled by:

Pneumotaxic area

Inhibits inspiratory area of medulla to stop inhalation.

Breathing is more rapid when pneumotaxic area is active.

Apneustic area

Stimulates inspiratory area of medulla to prolong inhalation.

A Pneumotaxic Center Limits the Duration of Inspiration and Increases the Respiratory Rate

A pneumotaxic center, located dorsally in the nucleus parabrachialis of the upper pons, transmits signals to the inspiratory area. The primary effect of this center is to control the "switch-off" point of the inspiratory ramp, thus controlling the duration of the filling phase of the lung cycle. When the pneumotaxic signal is strong, inspiration might last for as little as 0.5 second, thus filling the lungs only slightly; when the pneumotaxic signal is weak, inspiration might continue for 5 or more seconds, thus filling the lungs with a great excess of air.

The function of the pneumotaxic center is primarily to limit inspiration. This has a secondary effect of increasing the rate of breathing because limitation of inspiration also shortens expiration and the entire period of each respiration. A strong pneumotaxic signal can increase the rate of breathing to 30 to 40 breaths per minute, whereas a weak pneumotaxic signal may reduce

the rate to only 3 to 5 breaths per minute.

The apneustic center of pons sends signals to the dorsal respiratory center in the medulla to delay the 'switch off' signal of the inspiratory ramp provided by thepneumotaxic center of pons. It controls the intensity of breathing. The apneustic center is inhibited by pulmonary stretch receptors

Slide 7

Most of the chemoreceptors are in the *carotid bodies*. However, a few are also in the *aortic bodies*, and a very few are located elsewhere in association with other arteries of the thoracic and abdominal regions.

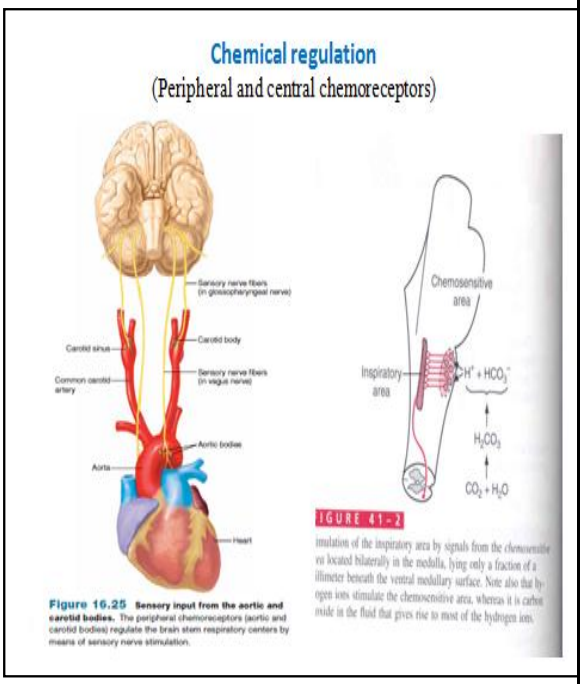


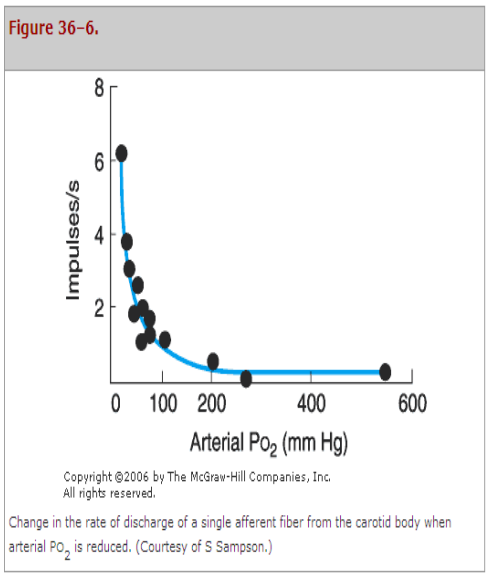
Figure 16.25 **Sensory input from the aortic and carotid bodies.** The peripheral chemoreceptors (aortic and carotid bodies) regulate the brain stem respiratory centers by means of sensory nerve stimulation.

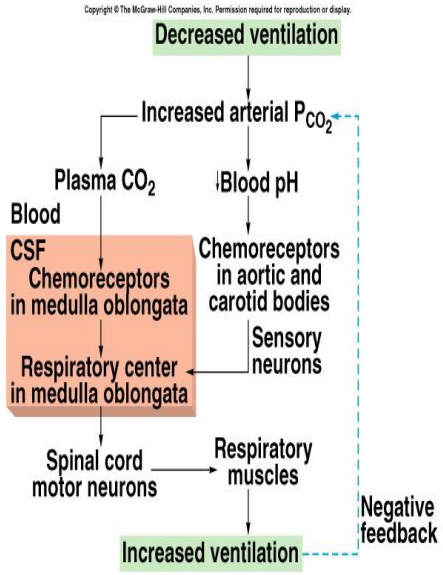
Excess carbon dioxide or excess hydrogen ions in the blood mainly act directly on **the respiratory center** itself, causing greatly increased strength of both the inspiratory and the expiratory motor signals to the respiratory muscles.

In addition to control of respiratory activity by the respiratory center itself, still another mechanism is available for controlling respiration. This is the ***peripheral chemoreceptor system*****,** shown in Figure 41-4. Special nervous chemical receptors, called*chemoreceptors*, are located in several areas outside the brain. They are especially important for detecting changes in oxygen in the blood, although they also respond to a lesser extent to changes in carbon dioxide and hydrogen ion concentrations. The chemoreceptors transmit nervous signals to the respiratory center in the brain to help regulate respiratory activity.
Most of the chemoreceptors are in the *carotid bodies*. However, a few are also in the *aortic bodies*, shown in the lower part of Figure 41-4, and a very few are located elsewhere in association with other arteries of the thoracic and abdominal regions.

Slide 8

Chemoreceptor Control of Breathing





Chemical Control of Respiration

Oxygen, in contrast, with CO2 does not have a significant *direct* effect on the respiratory center of the brain in controlling respiration. Instead, it acts almost entirely on peripheral *chemoreceptors* located in the *carotid*and *aortic bodies*, and these in turn transmit appropriate nervous signals to the respiratory center for control of respiration.

Slide 9

Effect of blood CO2 level on central chemoreceptors

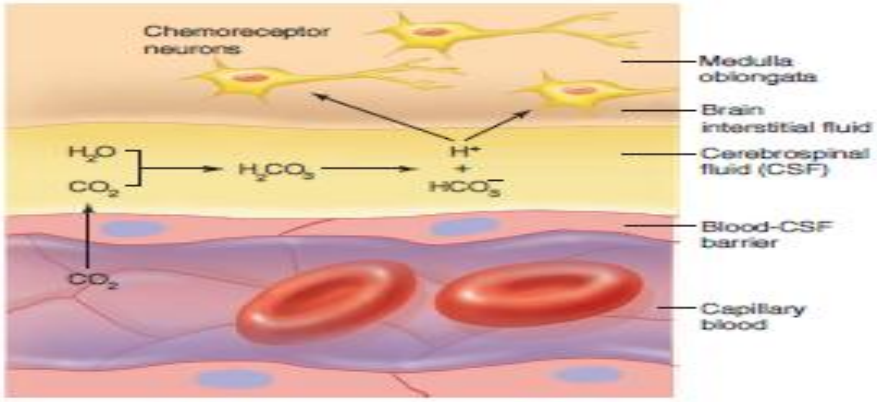
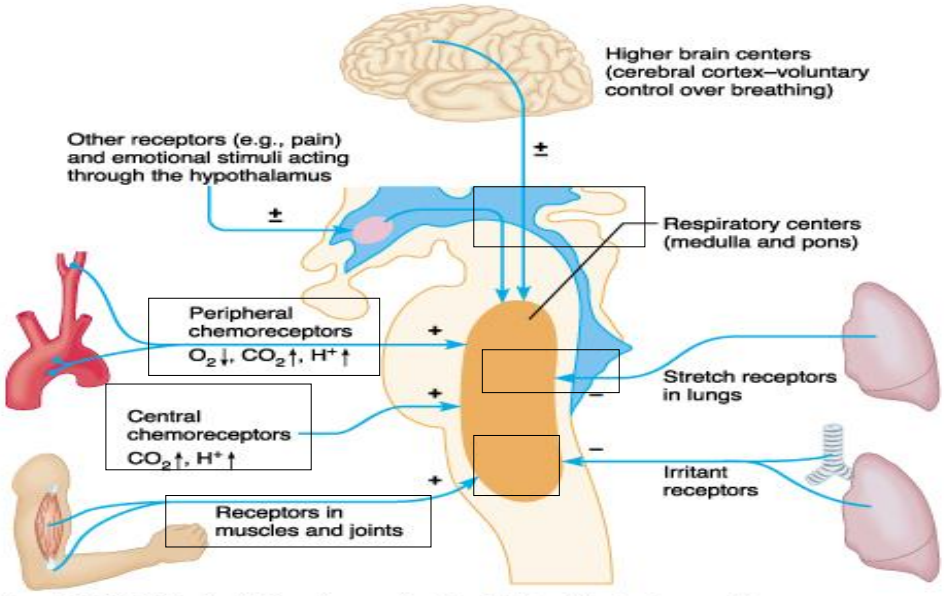


Figure 16.29 How blood CO_2 affects chemoreceptors in the medulla oblongata. An increase in blood CO_2 stimulates breathing indirectly by lowering the pH of blood and cerebrospinal fluid (CSF). This figure illustrates how a rise in blood CO_2 increases the H^+ concentration (lowers the pH) of CSF and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

Slide 10

Factors Influencing Respiration



Slide 11

Hering-Breuer inflation reflex

- When the lung becomes overstretched (tidal volume is 1 L or more), stretch receptors located in the wall 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 increase the rate of respiration as does the pneumotaxic center.

Lung Inflation Signals Limit Inspiration—The Hering-BreuerInflation Reflex

In addition to the central nervous system respiratory control mechanisms operating entirely within the brain stem, sensory nerve signals from the lungs also help control respiration. Most important, located in the muscular portions of the walls of the bronchi and bronchioles throughout the lungs are *stretch receptors* that transmit signals through the *vagi* into the dorsal respiratory group of neurons when the lungs become overstretched. These signals affect inspiration in much the same way as signals from the pneumotaxic center; that is, when the lungs become overly inflated, the stretch receptors activate an appropriate feedback response that ‘‘switches off’’ the inspiratory ramp and thus stops further inspiration. This is called the *Hering-Breuer inflation reflex*. This reflex also increases the rate of respiration, as is true for signals from the pneumotaxic center.

In humans, the Hering-Breuer reflex probably is not activated until the tidal volume increases to more than three times normal (>≈ 1.5 liters per breath). Therefore, this reflex appears to be mainly a protective mechanism for preventing excess lung inflation rather than an important ingredient in normal control of ventilation.

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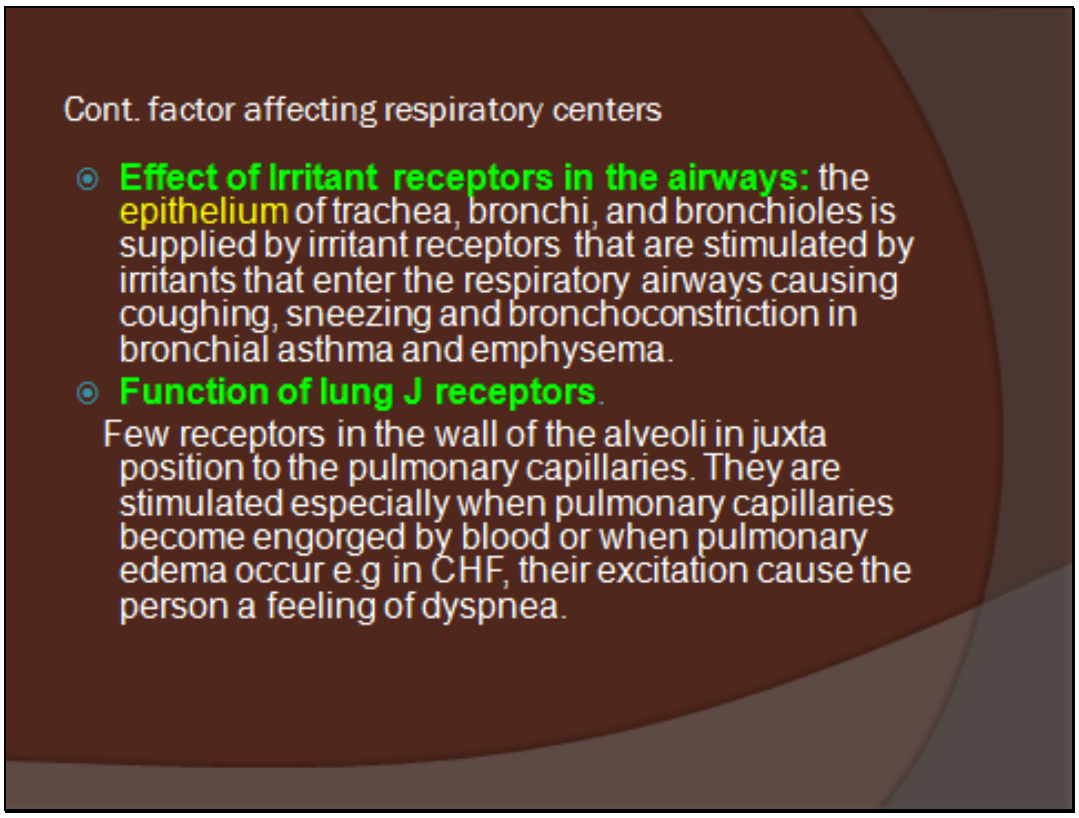
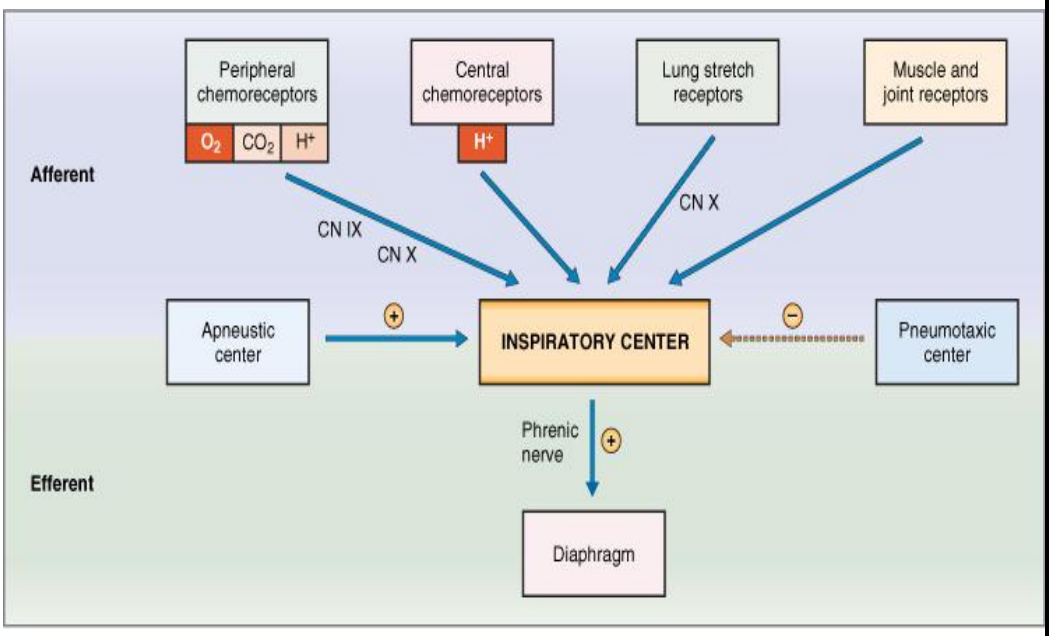


Juxta: placed close together

Slide 13

Cont..factors affecting respiration



Slide 14

Respiratory Acidosis

- Hypoventilation.
- Accumulation of CO_2 in the tissues.
  - P_{CO2} increases
  - pH decreases.

Respiratory Alkalosis

- Hyperventilation.
- Excessive loss of CO_2.
  - P_{CO2} decreases (↓35 mmHg).
  - pH increases.

Slide 15

Effects of low and high gas pressure on the body

Objectives

- **By the end of this lecture you should be able to:**
- 1-Describe the effects of exposure to low and high barometric pressures on the body.
- 2- Describe the body acclimatization to low barometric pressure.
- 3-Define decompression sickness and explain how it can be avoided.
- 4-Understand the effects of high nitrogen pressure, and nitrogen narcosis.

Effect of increased barometric pressure
(Deep sea diving).

- When human descend below the sea, the pressure around them increased.
- To prevent the lungs from collapse , air must be supplied also under high pressure.
- This exposes the blood in the lungs to extremely high alveolar gas pressure (hyperbarism).
- Under certain limits these high pressures cause tremendous alterations in the physiology of the body.

Cont..

- The surrounding pressure increases by 1 atmosphere for every 10 meter (33 feet) of depth in sea water.
- Therefore at a depth of 31 meter (100 feet) in the ocean the diver is exposed to a pressure of 4 atmospheres.
- These problems confront SCUBA (self contained under water breathing apparatus.

Slide 19

Deep-Sea Diving (High pressure)

- Relationship of Pressure to Sea Depth: a person 33 feet beneath the ocean surface is exposed to 2 atmospheres pressure
- At 66 feet the pressure is 3 atmospheres, and so forth..

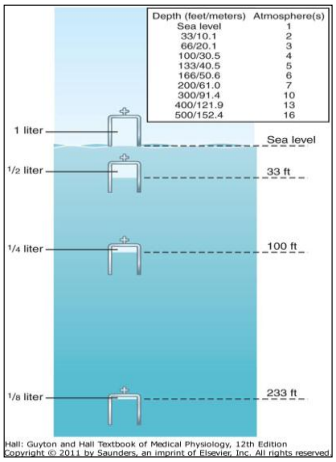


Figure 44-1 Effect of sea depth on pressure (top table) and on gas volume (bottom).

- **Effect of depth on the volume of the gases**:

  is compression of gases to smaller and smaller volumes. 1L (sea level)→1/2 L at 33 feet and so on

- **Effect of depth on density of gases**

  increase in density of gas and hence increased work of breathing.

- **Nitrogen effect at high nitrogen pressure**

  has 2 principle effects:

  * Nitrogen narcosis (anesthetic effect)
  * Decompression thickness.

Slide 21

Nitrogen Narcosis at High Nitrogen Pressures

- About four fifths of the air is nitrogen. At sea-level pressure, the nitrogen has no significant effect on bodily function but at high pressures it can cause varying degrees of narcosis
- Nitrogen narcosis has characteristics similar to those of alcohol intoxication

Nitrogen narcosis Cont..

- Nitrogen like most other anesthetic gases, dissolve freely in the fats of the body including the membranes and other lipid structures of the neurons.
- This leads to alteration of the electrical conductance of the membranes, reduces their excitability and subsequent narcosis develops.
- At 120 feet: the diver lose many of his cares.
- At 150 feet: there is a feeling of euphoria (happiness)and drowsiness and impaired performance.
- At higher pressure: loss of coordination and finally coma might develop.

decompression sickness and how it can be avoided.

- Breathes air under high pressure for a long time--nitrogen dissolved in the body fluids increases
- And because nitrogen is not metabolized by the body, it remains dissolved in all the body tissues until the nitrogen pressure in the lungs is decreased back to some lower level, however, this removal often takes hours to occur and is the source of multiple problems collectively called **decompression sickness**

decompression sickness and how it can be avoided. Cont…

- if diver suddenly comes back to the surface of the sea, nitrogen bubbles can develop in the body fluids either intracellularly or extracellularly decompression sickness.
- Due to decompression gases can escape from the dissolved state and form actual bubbles, in both tissues and blood where they plug many small blood vessels. The bubbles may not appear for many minutes to hours because sometimes the gases can remain dissolved in the "supersaturated" state for hours before bubbling.

Decompression sickness (Cassion's disease)

- It is a syndrome caused by a decrease in the ambient pressure which occur in animal and men when the tissues of the body contain an excess of physically inert gas.
- During descent , the high partial pressure of nitrogen (encountered when breathing compressed air at depth) forces this poorly soluble gas into solution in body tissue particularly in fat (it has a high N2 solubility).
- On ascending, this inert gas comes out of physical solution forming a gaseous phase (bubbles), leading to symptoms and signs.

Cont.. Decompression sickness

- **During slow ascent** N2 is slowly removed from the tissues since the partial pressure there is higher than that in the arterial blood and alveolar gas.
- **If decompression is rapid** bubbles of gaseous nitrogen are released, in tissues and blood, causing the symptoms of decompression sickness (the bends or caisson disease)

Symptoms & signs of decompression sickness(DS)

- The mildest form of DS is fatigue or drowsiness after decompression.
- Locally there is skin itch
- Other sever symptoms may occur e.g.:

bubbles in the tissues cause sever pains particularly around the joints.

Neurological symptoms include paresthesia, itching, paralysis, and inner ear disturbances.

Cont.. DS

- Thoracic pains: dyspnea, substernal pain, cyanosis, and cough.
- Bubbles in the coronary arteries may cause myocardial damage.
- Decompression sickness shock, capillaries become permeable to plasma and hypovolemia rapidly develop.
- Edema may be prominent and shock is also usually complicated by pulmonary edema

Treatment of decompression symptoms

- Rapid recompression in a pressure chamber followed by slower decompression. This reduces the volume of the bubbles and forces them back into solution.
- In a very deep dives, the risk of decompression sickness can be reduced if a helium-O2 mixture is breathed during the dive..

Cont.. Treatment of DS

- Helium is more desirable than nitrogen in deep dives because it has:
- ¼-1/5 the narcotic effect of nitrogen on CNS.
- 1/7 the molecular weight of nitrogen.
- low density leading to decreased air way resistance of diver.
- High diffusion through tissues.
- Helium is about 1/2 as soluble as nitrogen in body fluids. This reduces the quantity of bubbles that can form in tissues when the diver is decompressed after diving

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Treatment of Decompression Sickness

- Put the diver into a pressurized tank to lower the pressure gradually back to normal atmospheric pressure, by using this time schedule.

10 minutes at 50 feet depth
17 minutes at 40 feet depth
19 minutes at 30 feet depth
50 minutes at 20 feet depth
84 minutes at 10 feet depth

Effects of low oxygen pressure on the body
(Aviation-ascend to high altitude)

- At the sea level the barometric pressure is 760 mmHg.
- At 10,000 feet is 523 mmHg
- At 50,000 feet 87 mmHg.
- This decrease in barometric pressure is the basic cause of all the hypoxia problems in high altitude in physiology.

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High altitude (Low pressure) Cont ..

Table 43-1. Effects of Acute Exposure to Low Atmospheric Pressures on Alveolar Gas Concentrations and Arterial Oxygen Saturation*

			Breathing Air			Breathing Pure Oxygen		
Altitude (ft/meters)	Barometric Pressure (mm Hg)	P_{O_2} in Air (mm Hg)	P_{CO_2} in Alveoli (mm Hg)	P_{O_2} in Alveoli (mm Hg)	Arterial Oxygen Saturation (%)	P_{CO_2} in Alveoli (mm Hg)	P_{O_2} in Alveoli (mm Hg)	Arterial Oxygen Saturation (%)
0	760	159	40 (40)	104 (104)	97 (97)	40	673	100
10,000/3048	523	110	36 (23)	67 (77)	90 (92)	40	436	100
20,000/6096	349	73	24 (10)	40 (53)	73 (85)	40	262	100
30,000/9144	226	47	24 (7)	18 (30)	24 (38)	40	139	99
40,000/12,192	141	29				36	58	84
50,000/15,240	87	18				24	16	15

*Numbers in parentheses are acclimatized values.

Guyton & Hall: Textbook of Medical Physiology 12E

Alveolar PO2 at different altitudes

- As the barometric pressure decreases, the oxygen partial pressure decreases proportionally, remaining less than 21 % of the total barometric pressure.
- At sea level PO2= 159 mmHg.
- At 20,000 feet PO2= 40 mmHg.
- At 50,000 feet PO2= only 18 mmHg.

Cont…

- Even at high altitude CO2 is continuously excreted from the pulmonary blood into the alveoli. Also, water vaporizes into the inspired air from the respiratory surfaces.
- Therefore, these two gases dilute the oxygen in the alveoli, thus reducing the oxygen concentration and therefore hypoxia develops.

Effects of acute hypoxia

- Some of the important acute effects of hypoxia beginning at an altitude of approximately 12,000 feet, are:
- Drowsiness, lassitude, mental and muscle fatigue, sometimes headache, occasionally nausea and sometimes euphoria.
- All these progress to a stage of twitching or convulsions above 18,000.
- Above 23,000 feet the un acclimatized person can enter into coma.

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Acclimatization to low PO2

- A person remaining at high altitudes for days , weeks or years becomes more and more acclimatized to low PO2.
- So that it causes fewer deleterious effects on the body and it becomes possible for the person to work harder without hypoxic effects or to ascend to still higher altitude.

A person remaining at high altitudes for days, weeks, or years becomes more and more **acclimatized** to the low Po2

The principal of acclimatization summarized in

1-a great increase in pulmonary ventilation : low Po2 stimulates the arterial chemoreceptors, and this increases alveolar ventilation to a maximum of about 1.65 times normal

then lead to reducing the Pco2 and increasing the pH of the body fluids -- inhibit the brain stem respiratory center -- oppose the effect of low Po2 -- after 2 to 5 days inhibition fades away

2- Increase in Red Blood Cells and Hemoglobin Concentration

exposed to low oxygen for weeks at a time, the hematocrit rises slowly from a normal value of 40 to 45 to an average of about 60, with an average increase in whole blood hemoglobin concentration from normal of 15 g/dl to about 20 g/dl

the blood volume also increases, often by 20 to 30 percent

3-increased diffusing capacity of the lungs

normal diffusing capacity of oxygen through the pulmonary membrane is about 21 ml/mm Hg/min

at high altitude increased similar to exercise performance--increased pulmonary capillary blood volume --expands the capillaries and increases the surface area of oxygen can diffuse into the blood.

Another part results from an increase in lung air volume, which expands the surface area of the alveolar-capillary .

A final part results from an increase in pulmonary arterial blood pressure; this forces blood into greater numbers of alveolar capillaries

4- increased vascularity of the peripheral tissues

cardiac output increases as much as 30 percent

growth of increased numbers of systemic circulatory capillaries (or angiogenesis)

5- increased ability of the tissue cells to use oxygen despite low Po2.

In animals native to altitudes of 13,000 to 17,000 feet, cell mitochondria and cellular oxidative enzyme systems are slightly more plentiful than in sea-level inhabitants.

Principle means of acclimatization

- 1- Increase in pulmonary ventilation.
- 2- Increased red blood cells.
- 3-Increased diffusing capacity of the lungs.
- 4- Increased vascularity of the tissues.
- 5-Increased ability of the cells to utilize oxygen despite the low PO2.

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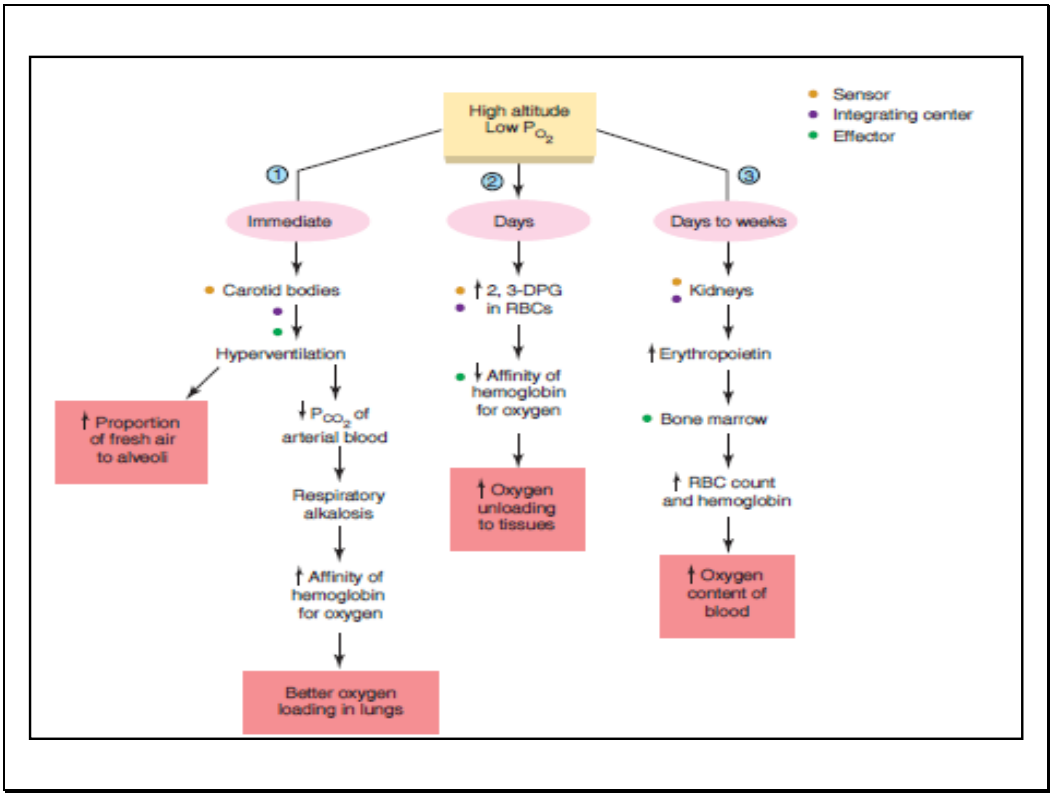
Sensor
Integrating center
Effector
High altitude
Low P_{O_2}
1
2
3
Immediate
Days
Days to weeks
Carotid bodies
Hyperventilation
↑ Proportion of fresh air to alveoli
↓ P_{CO_2} of arterial blood
Respiratory alkalosis
↑ Affinity of hemoglobin for oxygen
Better oxygen loading in lungs
↑ 2, 3-DPG in RBCs
↓ Affinity of hemoglobin for oxygen
↑ Oxygen unloading to tissues
Kidneys
↑ Erythropoietin
Bone marrow
↑ RBC count and hemoglobin
↑ Oxygen content of blood