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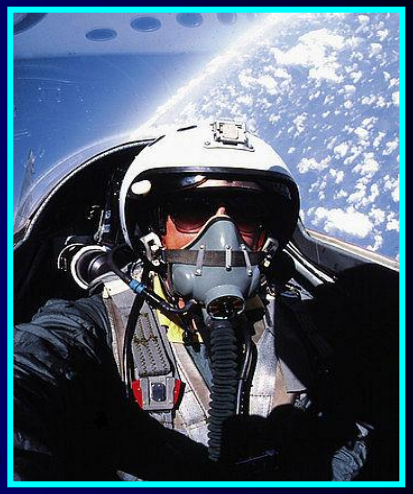

Lecture № 13

# Control of respiration. Aviation, High-Altitude, and Space Physiology. Physiology of Deep-Sea Diving and Other Hyperbaric Conditions

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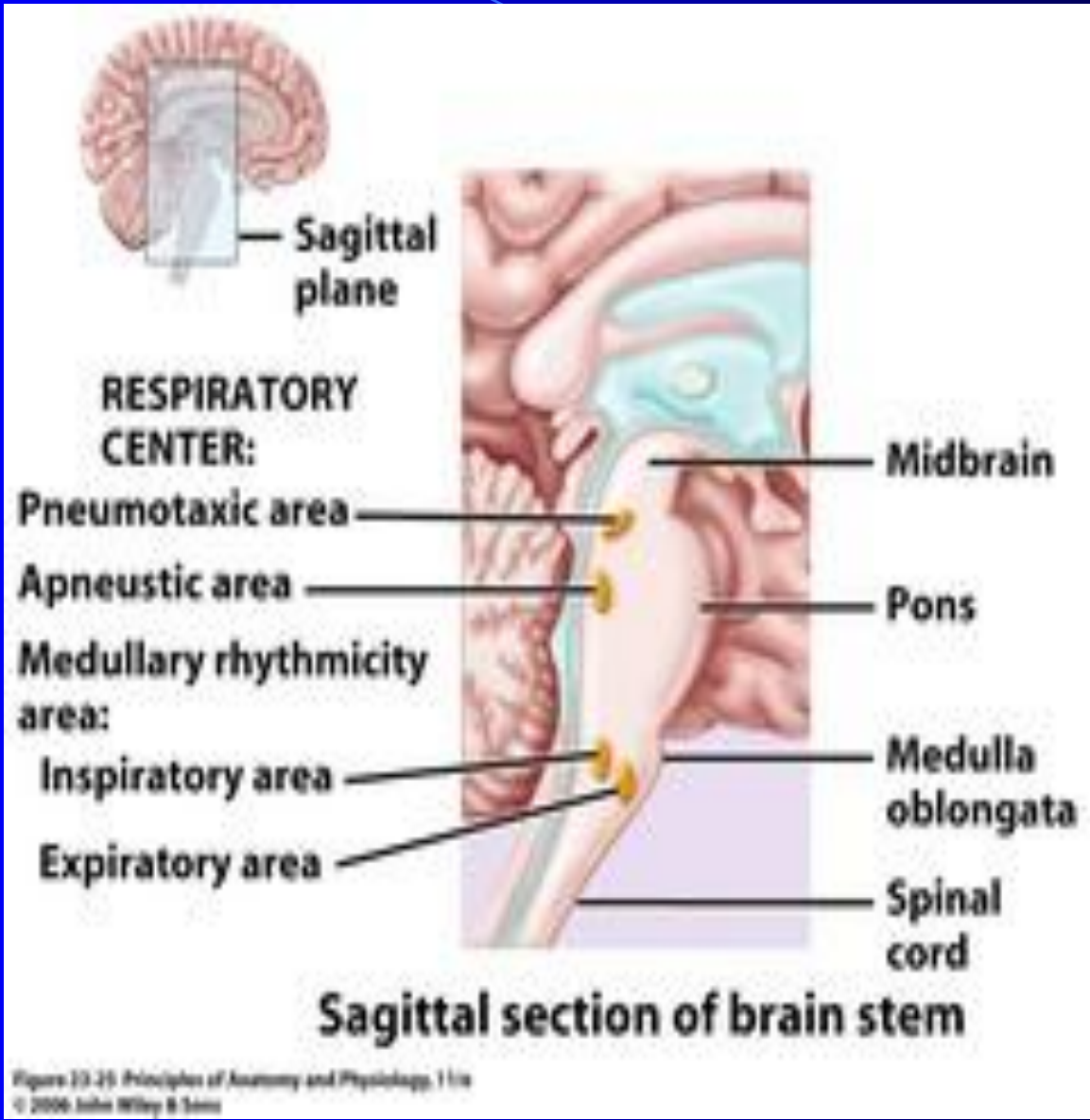
# Control of respiration

- The system of control works using negative feed back mechanism of regulation.
- There are 2 types of regulation: voluntary and automatic.
- The regulated parameters are $pCO_2$ and $pO_2$ of arterial blood.
- This system performs its effect changing alveolar ventilation.

# Respiratory Center

- 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; and
- (3) the *pneumotaxic center,* located dorsally in the superior portion of the pons, which mainly controls rate and depth of breathing.
- The dorsal respiratory group of neurons plays the most fundamental role in the control of respiration.

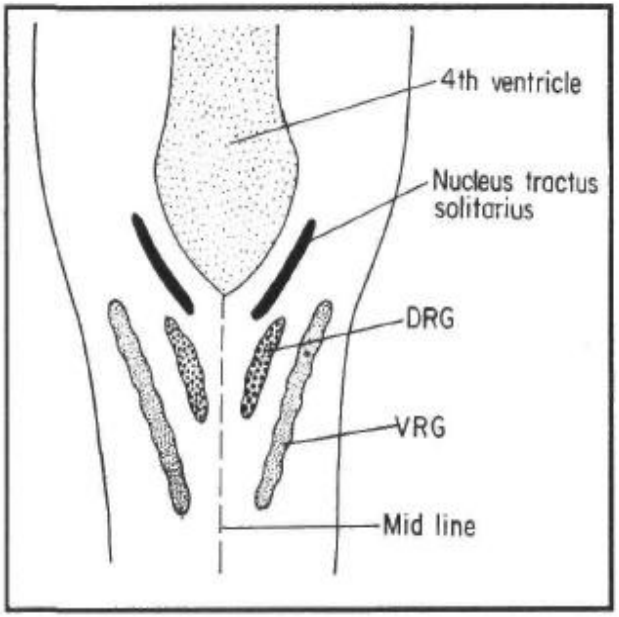
# Respiratory centers



# Dorsal Respiratory Group of Neurons

- The dorsal respiratory group of neurons extends most of the length of the medulla. Most of its neurons are located within the *nucleus of the tractus solitarius*, although additional neurons in the adjacent reticular substance of the medulla also play important roles in respiratory control.
- The nucleus of the tractus solitarius is the sensory termination of both the vagal and the glossopharyngeal nerves, which transmit sensory signals into the respiratory center from (1) peripheral chemoreceptors, (2) baroreceptors, and (3) several types of receptors in the lungs.

# Medullary respiratory centres: dorsal respiratory group (DRG)




- The DRG is autorhythmic and can maintain somewhat rhythmic respiration in absence of all other inputs.
- For normal rhythmic respiration it is helped by feedback information from peripheral chemoreceptors, vagal inputs, central chemoreceptors and inputs from other centres.

# Rhythmical Inspiratory Discharges from the Dorsal Respiratory Group

- **The basic rhythm** of respiration is generated mainly in the dorsal respiratory group of neurons.
- Even when all the peripheral nerves entering the medulla have been sectioned and the brain stem transected both above and below the medulla, this group of neurons still emits repetitive bursts of *inspiratory neuronal action potentials.*
- The nervous signal that is transmitted to the inspiratory muscles (the diaphragm and external intercostal muscles) is not an instantaneous burst of action potentials.
- Instead, in normal respiration, it begins weakly and increases steadily in a ramp manner for about 2 seconds.
- Then it ceases abruptly for approximately the next 3 seconds, which turns off the excitation of the diaphragm and allows elastic recoil of the lungs and the chest wall to cause expiration.

- ***There are two qualities of the inspiratory ramp that are controlled, as follows:***
- 1. Control of the *rate of increase of the ramp signal,* so that during heavy respiration, the ramp increases rapidly and therefore fills the lungs rapidly.
- 2. Control of the *limiting point at which the ramp suddenly ceases. This is the usual method for* controlling the rate of respiration; that is, the earlier the ramp ceases, the shorter the duration of inspiration. This also shortens the duration of expiration. Thus, the frequency of respiration is increased.

- ***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.
- The function of the pneumotaxic center is primarily to limit inspiration.

# Ventral Respiratory Group of Neurons - Functions in Both Inspiration and Expiration

- Located in each side of the medulla, about 5mm anterior and lateral to the dorsal respiratory group of neurons, is the *ventral respiratory group of neurons*, found in the *nucleus ambiguus rostrally and the nucleus retroambiguus caudally*.
- *The function of this* neuronal group differs from that of the dorsal respiratory group in several important ways:
- 1. The neurons of the ventral respiratory group remain almost totally *inactive during normal quiet* respiration. Therefore, normal quiet breathing is caused only by repetitive inspiratory signals from the dorsal respiratory group transmitted mainly to the diaphragm, and expiration results from elastic recoil of the lungs and thoracic cage.

- 2. There is no evidence that the ventral respiratory neurons participate in the basic rhythmical oscillation that controls respiration.
- 3. When the respiratory drive for increased pulmonary ventilation becomes greater than normal, respiratory signals spill over into the ventral respiratory neurons from the basic oscillating mechanism of the dorsal respiratory area. As a consequence, the ventral respiratory area contributes extra respiratory drive as well.

- 4. Electrical stimulation of a few of the neurons in the ventral group causes inspiration, whereas stimulation of others causes expiration. Therefore, these neurons contribute to both inspiration and expiration. They are especially important in providing the powerful expiratory signals to the abdominal muscles during very heavy expiration.
- Thus, this area operates more or less as an overdrive mechanism when high levels of pulmonary ventilation are required, especially during heavy exercise.

# Lung Inflation Signals Limit Inspiration - The Hering-Breuer Inflation Reflex

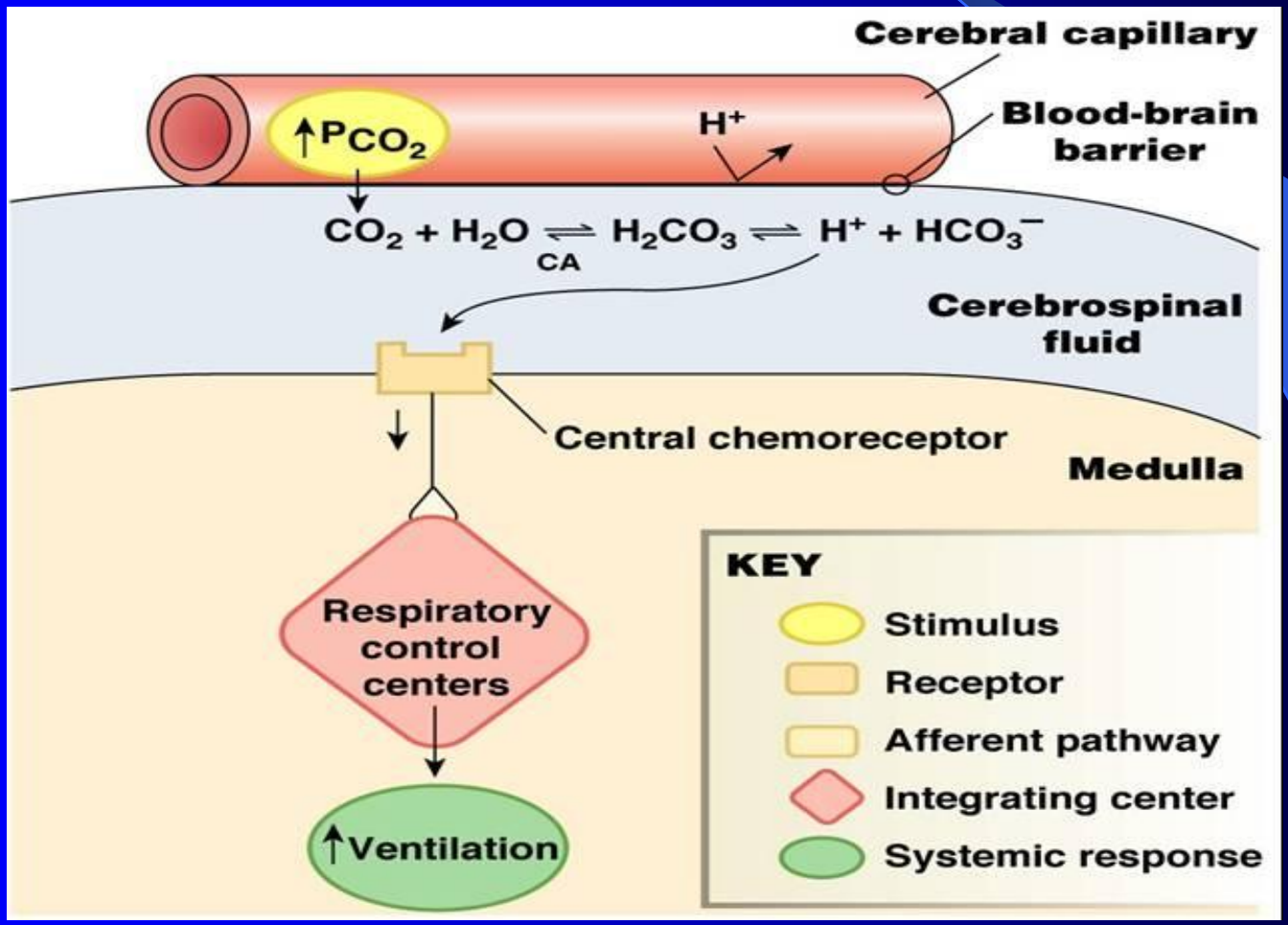
- In addition to the central nervous system respiratory control mechanisms operating entirely within the brain stem, sensory nerve signals from the lungs also help control respiration.
- Most important, located in the muscular portions of the walls of the bronchi and bronchioles throughout the lungs 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 human beings, the Hering-Breuer reflex probably is not activated until the tidal volume increases to more than three times normal (greater than about 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.

# Chemical Control of Respiration – the role of central and periferal chemoreceptors

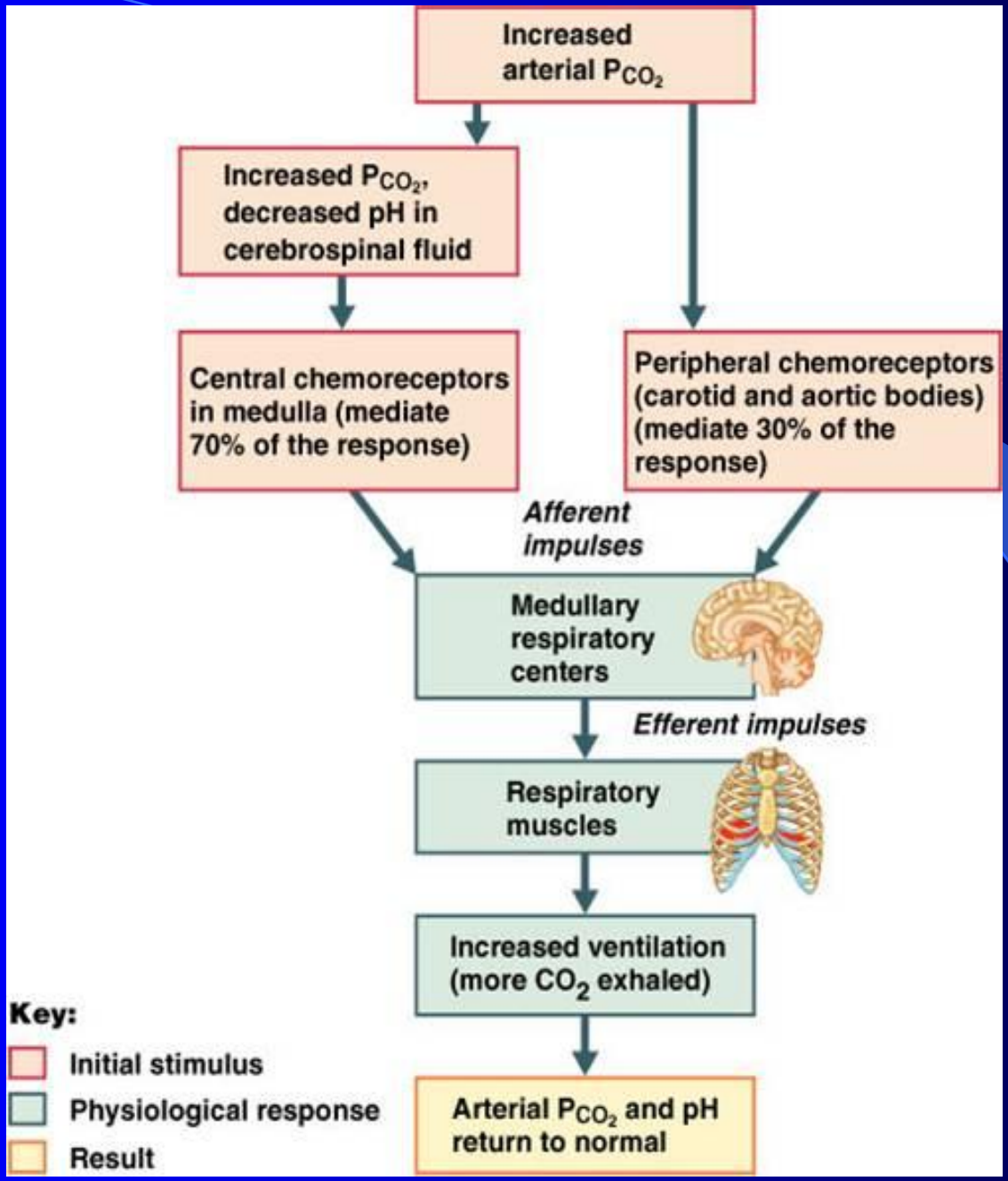
- **Role of central chemoreceptors**
- Direct Chemical Control of Respiratory Center Activity by Carbon Dioxide and Hydrogen Ions
- Unimportance of Oxygen for Control of the Respiratory Center

*Changing $pCO_2$ levels are monitored by chemoreceptors of the brain stem
*Carbon dioxide in the blood diffuses into the cerebrospinal fluid where it is hydrated.
*Resulting carbonic acid dissociates, releasing hydrogen ions.
*$pCO_2$ levels rise (**hypercapnia**) resulting in increased depth and rate of breathing.



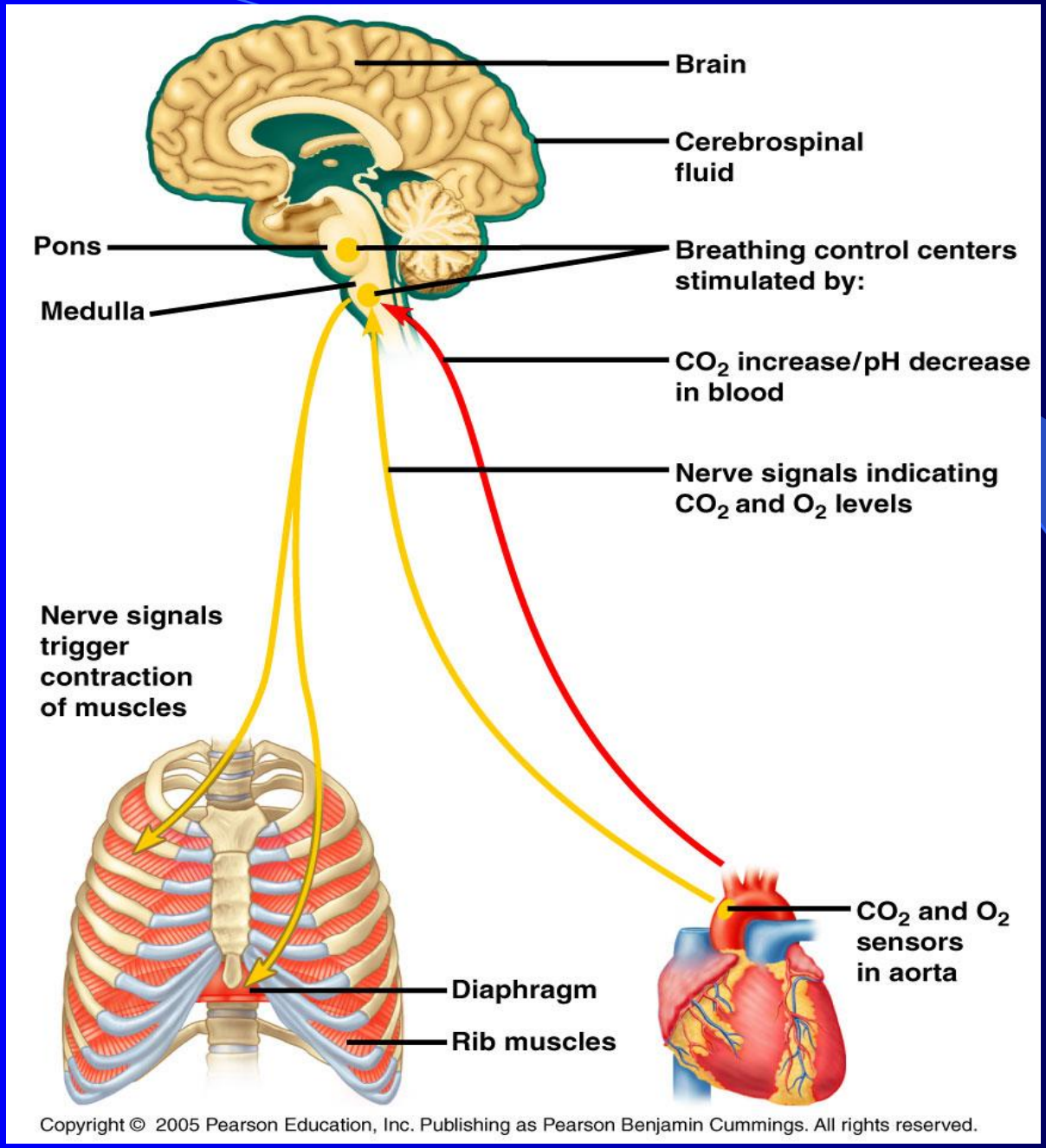
# Effect of Carbon Dioxide and Hydrogen Ion Concentration on Chemoreceptor Activity

- An increase in either carbon dioxide concentration or hydrogen ion concentration excites the chemoreceptors and, in this way, indirectly increases respiratory activity.
- However, the direct effects of both these factors in the respiratory center itself are so much more powerful than their effects mediated through the periferal chemoreceptors.

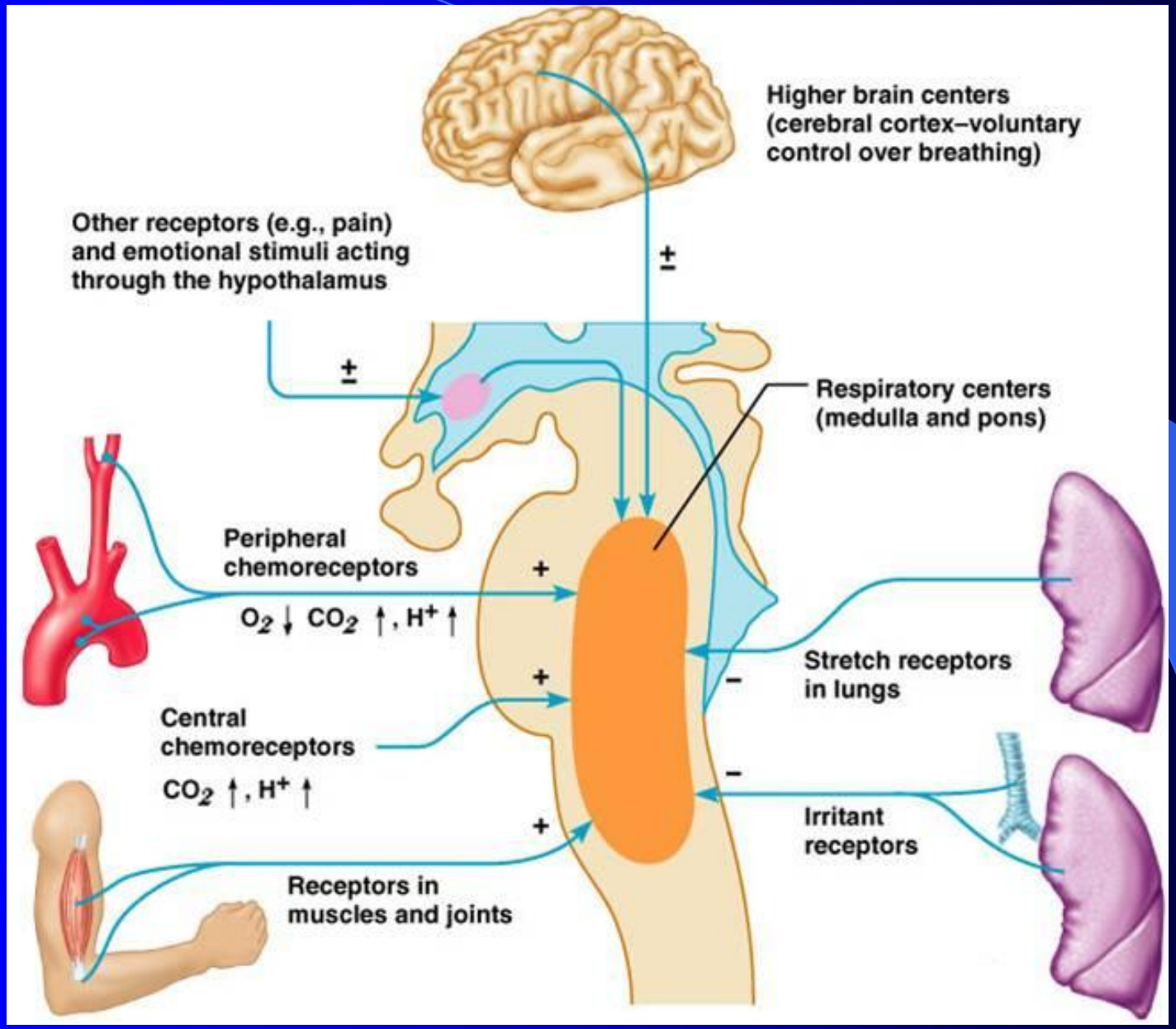

Increased arterial $P_{CO_2}$
Increased $P_{CO_2}$, decreased pH in cerebrospinal fluid
Central chemoreceptors in medulla (mediate 70% of the response)
Peripheral chemoreceptors (carotid and aortic bodies) (mediate 30% of the response)
Afferent impulses
Medullary respiratory centers
Efferent impulses
Respiratory muscles
Increased ventilation (more $CO_2$ exhaled)
Arterial $P_{CO_2}$ and pH return to normal
Key:
Initial stimulus
Physiological response
Result

# Stimulation of the Peripheral Chemoreceptors by *Decreased Arterial* Oxygen.

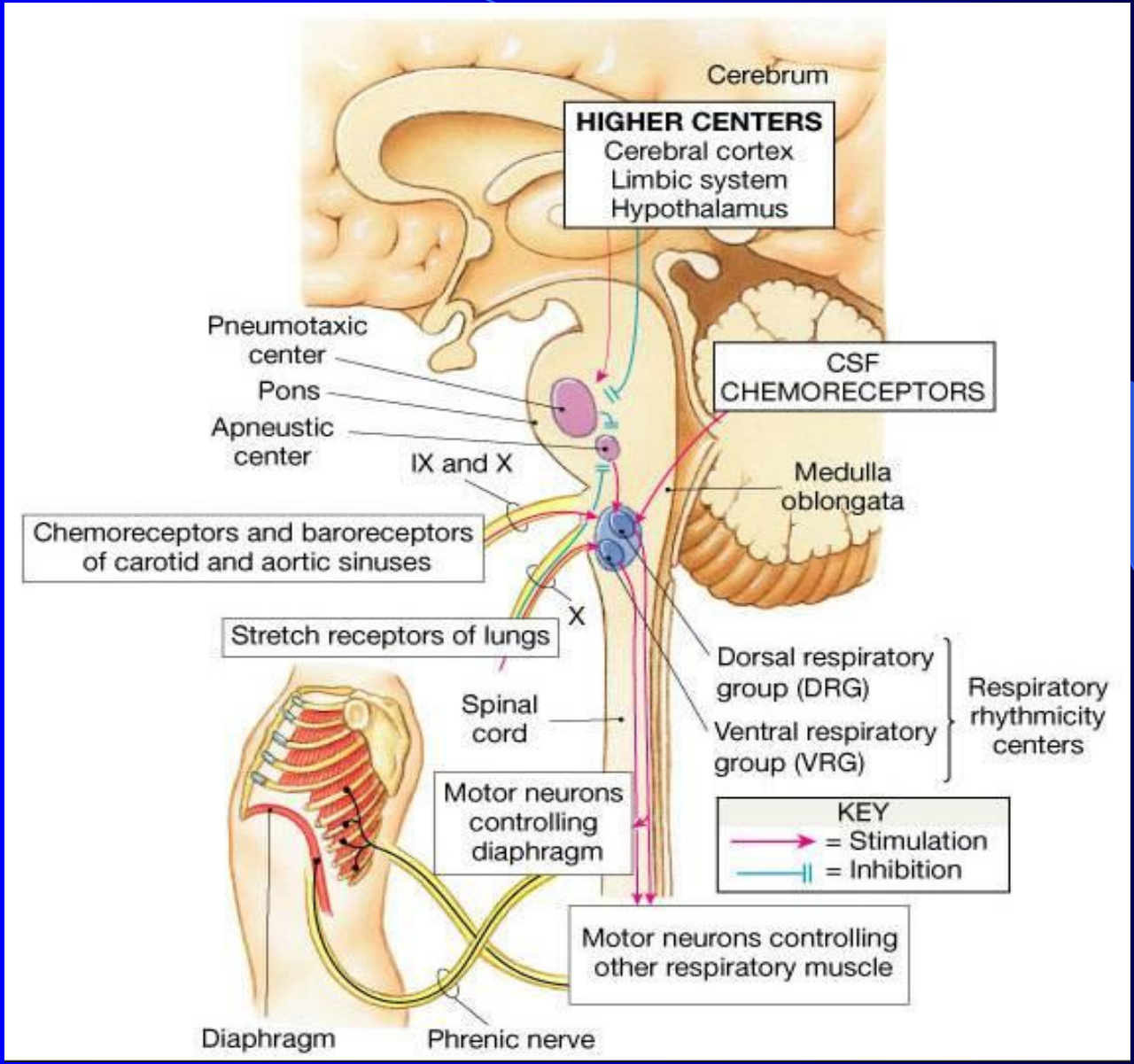
- **When the oxygen concentration in the arterial** blood falls below normal, the chemoreceptors become strongly stimulated.
- Note that the impulse rate from a carotid body is particularly sensitive to changes in arterial $pO_2$ in the range of 60 down to 30 mm Hg, a range in which hemoglobin saturation with oxygen decreases rapidly.



# Reflex control of respiration



# Control of respiration

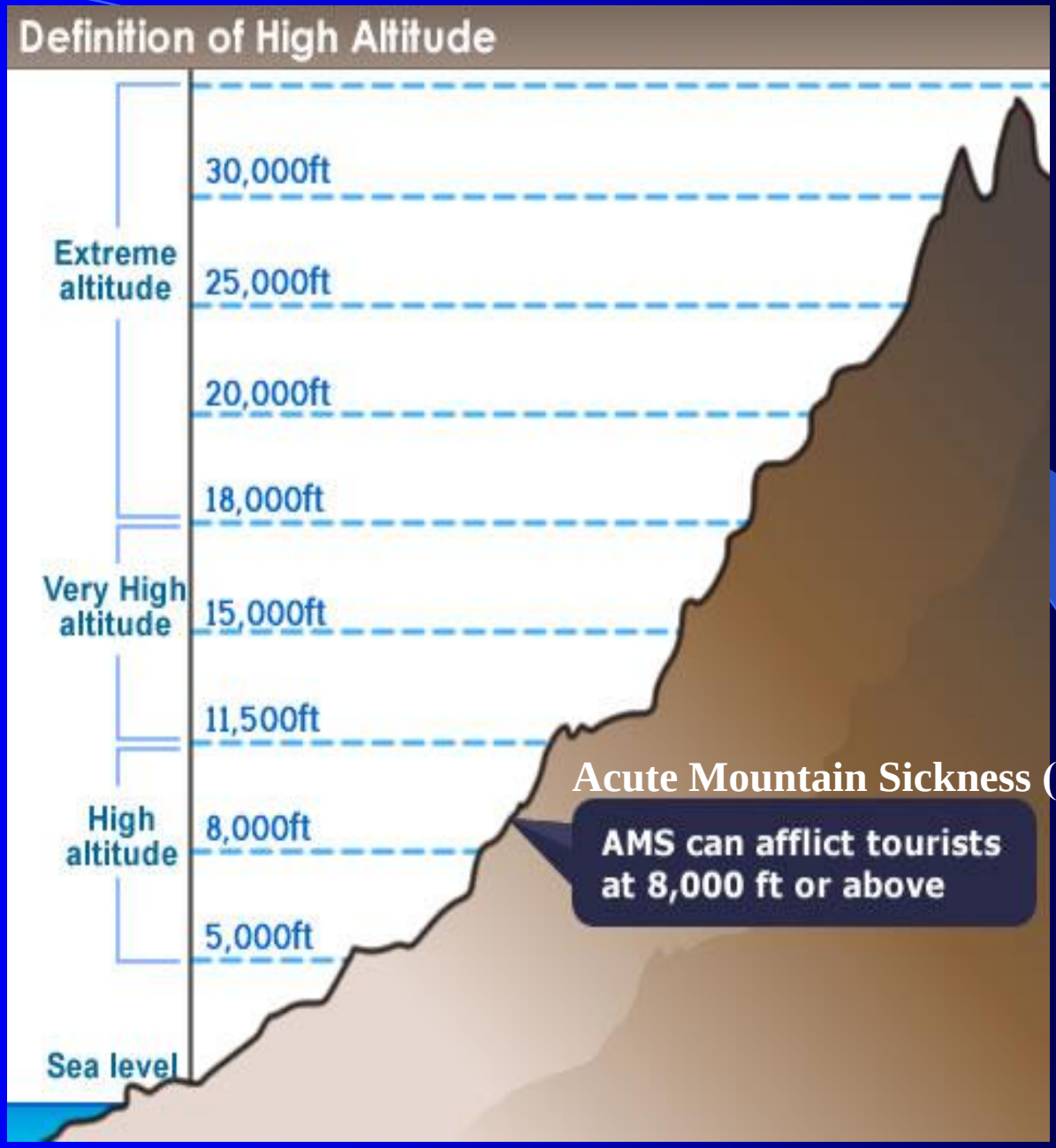


# Aviation, High-Altitude, and Space Physiology

- As we have ascended to higher and higher altitudes in aviation, mountain climbing, and space vehicles, it has become progressively more important to understand the effects of altitude and low gas pressures (as well as several other factors-acceleratory forces, weightlessness, and so forth) on the human body.


12

1ft =0,304m


Definition of High Altitude
30,000ft
Extreme altitude
25,000ft
20,000ft
18,000ft
Very High altitude
15,000ft
11,500ft
Acute Mountain Sickness (AMS)
AMS can afflict tourists at 8,000 ft or above
High altitude
8,000ft
5,000ft
Sea level

# Barometric Pressures at Different Altitudes

- At sea level, the barometric pressure is 760 mm Hg; at 10,000 feet only - 523 mm Hg; and at 50,000 feet - 87 mm Hg.
- This decrease in barometric pressure is the basic cause of all the hypoxia problems in high-altitude physiology because, as the barometric pressure decreases, the atmospheric oxygen partial pressure decreases proportionately, remaining at all times slightly less than 21 % of the total barometric pressure - $pO_2$ at sea level about 159 mm Hg, but at 50,000 feet only 18 mm Hg.

# Alveolar $pO_2$ at Different Elevations

- Carbon Dioxide and Water Vapor Decrease the Alveolar $O_2$
- In the case of carbon dioxide, during exposure to very high altitudes, the alveolar $pCO_2$ falls from the sea-level value of 40 mm Hg to lower values.
- In the *acclimatized person, who increases his or her ventilation about five fold, the* $pCO_2$ falls to about 7 mm Hg because of increased respiration.
- Now let us see how the pressures of these two gases affect the alveolar oxygen. For instance, assume that the barometric pressure falls from the normal sea-level value of 760 mm Hg to 253 mm Hg, which is the usual measured value at the top of Mount Everest.
- 47 mm Hg of this must be water vapor, leaving only 206 mm Hg for all the other gases.

- In the *acclimatized person, 7 mm of the 206 mm Hg must be carbon dioxide, leaving* only 199 mm Hg. If there were no use of oxygen by the body, one fifth of this 199 mm Hg would be oxygen and four fifths would be nitrogen; that is, the $pO_2$ in the alveoli would be 40 mm Hg.
- However, some of this remaining alveolar oxygen is continually being absorbed into the blood, leaving about 35 mm Hg oxygen pressure in the alveoli.
- At the summit of Mount Everest, only the best of acclimatized people can barely survive when breathing air.

# Alveolar $pO_2$ at Different Altitudes

- *At sea* level, the alveolar $pO_2$ is 104 mm Hg; at 20,000 feet altitude, it falls to about 40 mm Hg in the unacclimatized person but only to 53 mm Hg in the acclimatized.
- The difference between these two is that alveolar ventilation increases much more in the acclimatized person than in the unacclimatized person, as we discuss later.

# Saturation of Hemoglobin with Oxygen at Different Altitudes

- ***Arterial blood oxygen saturation at different altitudes while a person is breathing air and while breathing oxygen:***
- Up to an altitude of about 10,000 feet, even when air is breathed, the arterial oxygen saturation remains at least as high as 90 %.
- Above 10,000 feet, the arterial oxygen saturation falls rapidly, until it is slightly less than 70 % at 20,000 feet and much less at still higher altitudes.

# Acute Effects of Hypoxia

- Some of the important acute effects of hypoxia in the unacclimatized person breathing air, beginning at an altitude of about 12,000 feet, are drowsiness, lassitude, mental and muscle fatigue, sometimes headache, occasionally nausea, and sometimes euphoria.
- These effects progress to a stage of twitchings or seizures above 18,000 feet and end, above 23,000 feet in the unacclimatized person, in coma, followed shortly thereafter by death.
- One of the most important effects of hypoxia is decreased mental proficiency, which decreases judgment, memory, and performance of discrete motor movements.
- For instance, if an unacclimatized aviator stays at 15,000 feet for 1 hour, mental proficiency ordinarily falls to about 50 % of normal, and after 18 hours at this level it falls to about 20 % of normal.

# Acclimatization to Low $pO_2$

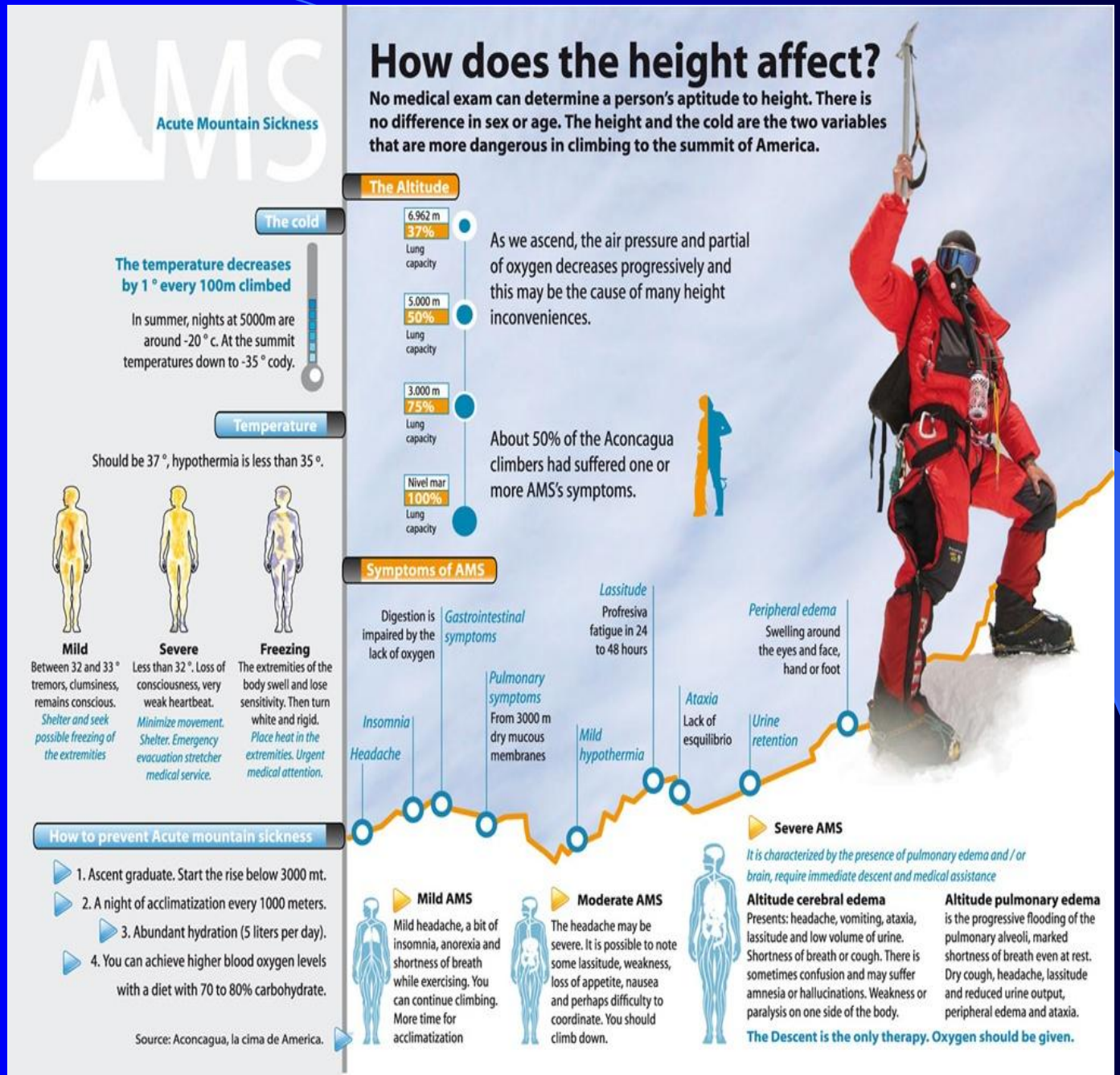
- A person remaining at high altitudes for days, weeks, or years becomes more and more *acclimatized to the* low $pO_2$, so that it causes fewer deleterious effects on the body. And it becomes possible for the person to work harder without hypoxic effects or to ascend to still higher altitudes.
- The principal means by which acclimatization comes about are:
- (1) a great increase in pulmonary ventilation,
- (2) increased numbers of red blood cells,
- (3) increased diffusing capacity of the lungs,
- 4) increased vascularity of the peripheral tissues, and
- (5) increased ability of the tissue cells to use oxygen despite low $pO_2$.

# Acute Mountain Sickness and High-Altitude Pulmonary Edema

- A small percentage of people who ascend rapidly to high altitudes become acutely sick and can die if not given oxygen or removed to a low altitude.
- The sickness begins from a few hours up to about 2 days after ascent. Two events frequently occur:
- **1. *Acute cerebral edema.*** *This is believed to result* from local vasodilatation of the cerebral blood vessels, caused by the hypoxia. Dilation of the arterioles increases blood flow into the capillaries, thus increasing capillary pressure, which in turn causes fluid to leak into the cerebral tissues.
- The cerebral edema can then lead to severe disorientation and other effects related to cerebral dysfunction.

- **2. *Acute pulmonary edema.*** *The cause of this is still* unknown, but a suggested answer is the following:
- The severe hypoxia causes the pulmonary arterioles to constrict potently, but the constriction is much greater in some parts of the lungs than in other parts, so that more and more of the pulmonary blood flow is forced through fewer and fewer still unconstricted pulmonary vessels.
- The postulated result is that the capillary pressure in these areas of the lungs becomes especially high and local edema occurs.
- Extension of the process to progressively more areas of the lungs leads to spreading pulmonary edema and severe pulmonary dysfunction that can be lethal.
- Allowing the person to breathe oxygen usually reverses the process within hours.

# Acute mountain sickness



# Physiologic Problems of Weightlessness

Astronauts in space

# Physiologic Problems of Weightlessness (Microgravity)

- The physiologic problems of weightlessness have not proved to be of much significance, as long as the period of weightlessness is not too long.
- Most of the problems that do occur are related to three effects of the weightlessness:
- (1) motion sickness during the first few days of travel,
- (2) translocation of fluids within the body because of failure of gravity to cause normal hydrostatic pressures, and
- (3) diminished physical activity because no strength of muscle contraction is required to oppose the force of gravity.

- Almost 50 % of astronauts experience motion sickness, with nausea and sometimes vomiting, during the first 2 to 5 days of space travel. This probably results from an unfamiliar pattern of motion signals arriving in the equilibrium centers of the brain, and at the same time lack of gravitational signals.
- The observed effects of prolonged stay in space are the following:
- (1) decrease in blood volume,
- (2) decrease in red blood cell mass,
- (3) decrease in muscle strength and work capacity,
- (4) decrease in maximum cardiac output, and
- (5) loss of calcium and phosphate from the bones, as well as loss of bone mass.
- Most of these same effects also occur in people who lie in bed for an extended period of time. For this reason, exercise programs are carried out by astronauts during prolonged space missions.

# Physiology of Deep-Sea Diving

# Physiology of Deep-Sea Diving

- When human beings descend beneath the sea, the pressure around them increases tremendously.
- To keep the lungs from collapsing, air must be supplied at very high pressure to keep them inflated.
- This exposes the blood in the lungs also to extremely high alveolar gas pressure, a condition called *hyperbarism.*
- Beyond certain limits, these high pressures can cause tremendous alterations in body physiology and can be lethal.
- A person 33 feet beneath the ocean surface is exposed to 2 atmospheres pressure, 1 atmosphere of pressure caused by the weight of the air above the water and the second atmosphere by the weight of the water itself.
- At 66 feet the pressure is 3 atmospheres, and so forth.

# Effect of Sea Depth on the Volume of Gases - Boyle's Law

- Another important effect of depth is compression of gases to smaller and smaller volumes.
- At 33 feet beneath the sea, where the pressure is 2 atmospheres, the volume has been compressed to only one-half liter, and at 8 atmospheres (233 feet) to one-eighth liter.
- Thus, the volume to which a given quantity of gas is compressed is inversely proportional to the pressure. This is a principle of physics called *Boyle's law,* which is extremely important in diving physiology because increased pressure can collapse the air chambers of the diver's body, especially the lungs, and often causes serious damage.

# Effect of High Partial Pressures of Individual Gases on the Body

- The individual gases to which a diver is exposed when breathing air are *nitrogen, oxygen, and carbon dioxide; each of these at times can cause significant* physiologic effects at high pressures.
- **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.
- When the diver remains beneath the sea for an hour or more and is breathing compressed air, the depth at which the first symptoms of mild narcosis appear is about 120 feet. At this level the diver begins to exhibitjoviality and to lose many of his or her cares.

- At 150 to 200 feet, the diver becomes drowsy.
- At 200 to 250 feet, his or her strength wanes considerably, and the diver often becomes too clumsy to perform the work required.
- Beyond 250 feet (8.5 atmospheres pressure), the diver usually becomes almost useless as a result of nitrogen narcosis if he or she remains at these depths too long.
- Nitrogen narcosis has characteristics similar to those of alcohol intoxication, and for this reason it has frequently been called “raptures of the depths.”
- The mechanism of the narcotic effect is believed to be the same as that of most other gas anesthetics. That is, it dissolves in the fatty substances in neuronal membranes and, because of its *physical effect on altering* ionic conductance through the membranes, reduces neuronal excitability.

# Oxygen Toxicity at High Pressures

- When the $pO_2$ in the blood rises above 100 mm Hg, the amount of oxygen dissolved in the water of the blood increases markedly.
- Note that in the normal range of alveolar $pO_2$ (below 120 mm Hg), almost none of the total oxygen in the blood is accounted for by dissolved oxygen, but as the oxygen pressure rises into the thousands of millimeters of mercury, a large portion of the total oxygen is then dissolved in the water of the blood, in addition to that bound with hemoglobin.
- Thus, once the alveolar $pO_2$ rises above a critical level, the hemoglobin-oxygen buffer mechanism is no longer capable of keeping the tissue $pO_2$ in the normal, safe range between 20 and 60 mm Hg.

- **Acute Oxygen Poisoning**
- **The extremely high tissue** $pO_2$ that occurs when oxygen is breathed at very high alveolar oxygen pressure can be detrimental to many of the body's tissues.
- For instance, breathing oxygen at 4 atmospheres pressure of oxygen ($pO_2$ = 3040 mm Hg) will cause brain *seizures followed by coma in most* people within 30 to 60 minutes.
- The seizures often occur without warning and, for obvious reasons, are likely to be lethal to divers submerged beneath the sea.
- Other symptoms encountered in acute oxygen poisoning include nausea, muscle twitchings, dizziness, disturbances of vision, irritability, and disorientation.
- Exercise greatly increases the diver's susceptibility to oxygen toxicity, causing symptoms to appear much earlier and with far greater severity than in the resting person.

- ***Chronic Oxygen Poisoning*** *Causes Pulmonary Disability.*
- A person can be exposed to only 1 atmosphere pressure of oxygen almost indefinitely without developing the *acute oxygen toxicity of the nervous system* just described. However, after only about 12 hours of 1 atmosphere oxygen exposure, *lung passageway congestion, pulmonary edema, and atelectasis caused by* damage to the linings of the bronchi and alveoli begin to develop.
- The reason for this effect in the lungs but not in other tissues is that the air spaces of the lungs are directly exposed to the high oxygen pressure, but oxygen is delivered to the other body tissues at almost normal $pO_2$ because of the hemoglobin-oxygen buffer system.

# Carbon Dioxide Toxicity at Great Depths in the Sea

- If the diving gear is properly designed and functions properly, the diver has no problem due to carbon dioxide toxicity because depth alone does not increase the carbon dioxide partial pressure in the alveoli.
- This is true because depth does not increase the rate of carbon dioxide production in the body, and as long as the diver continues to breathe a normal tidal volume and expires the carbon dioxide as it is formed, alveolar carbon dioxide pressure will be maintained at a normal value.
- In certain types of diving gear, however, such as the diving helmet and some types of rebreathing apparatuses, carbon dioxide can build up in the dead space air of the apparatus and be rebreathed by the diver.

- Up to an alveolar carbon dioxide pressure ($pCO_2$) of about 80 mm Hg, twice that in normal alveoli, the diver usually tolerates this buildup by increasing the MRV a maximum of 8- to 11-fold to compensate for the increased carbon dioxide.
- Beyond 80-mm Hg alveolar $pCO_2$, the situation becomes intolerable, and eventually the respiratory center begins to be depressed, rather than excited, because of the negative tissue metabolic effects of high $pCO_2$. The diver's respiration then begins to fail rather than to compensate.
- In addition, the diver develops severe respiratory acidosis, and varying degrees of lethargy, narcosis, and finally even anesthesia.

# Decompression of the Diver After Excess Exposure to High Pressure

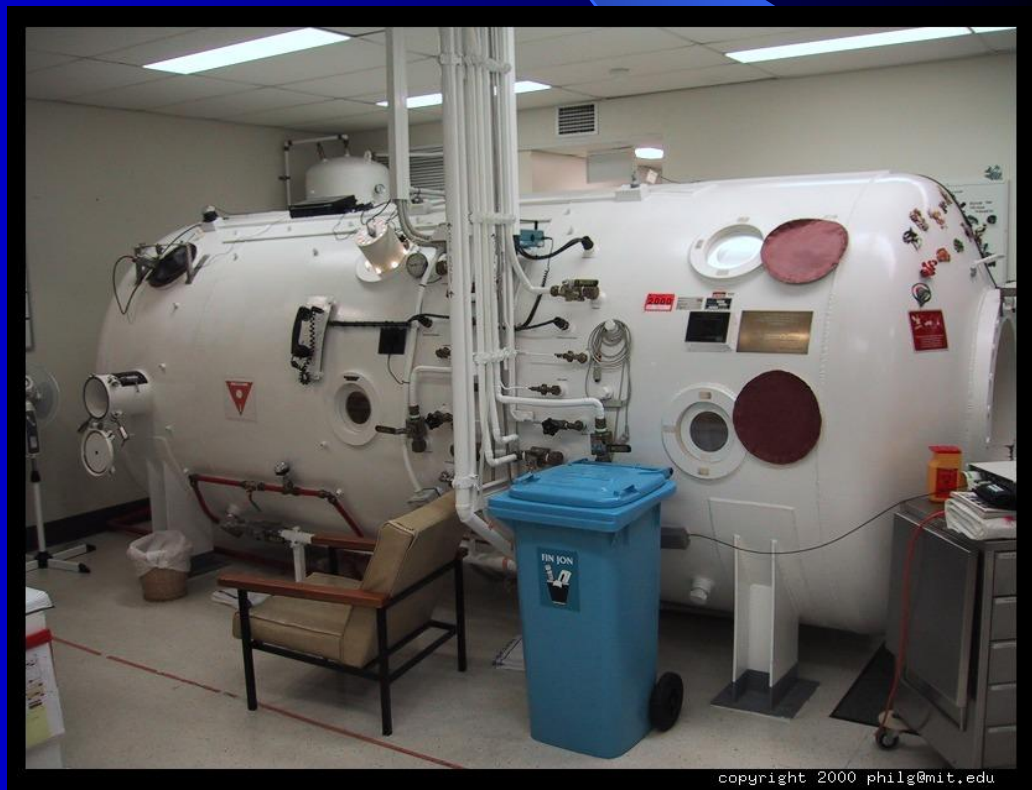
- When a person breathes air under high pressure for a long time, the amount of nitrogen dissolved in the body fluids increases.
- Because nitrogen is not metabolized by the body, it remains dissolved in all the body tissues until the nitrogen pressure in the lungs is decreased back to some lower level, at which time the nitrogen can be removed by the reverse respiratory process; however, this removal often takes hours to occur and is the source of multiple problems collectively called *decompression sickness*.

- If a diver has been beneath the sea long enough that large amounts of nitrogen have dissolved in his or her body and the diver then suddenly comes back to the surface of the sea, significant quantities of nitrogen bubbles can develop in the body fluids either intracellularly or extracellularly and can cause minor or serious damage in almost any area of the body, depending on the number and sizes of bubbles formed; this is called *decompression sickness*.
- The symptoms of decompression sickness are caused by gas bubbles blocking many blood vessels in different tissues. At first, only the smallest vessels are blocked by minute bubbles, but as the bubbles coalesce, progressively larger vessels are affected.

## Decompression chamber

The main chamber can be used as a rescue chamber for diving accidents.

It can additionally be used for treatment of decompression sickness and hyperbaric oxygen treatment.



- Decompression tables have been prepared by the U.S. Navy that detail procedures for safe decompression.
- To give the student an idea of the decompression process, a diver who has been breathing air and has been on the sea bottom for 60 minutes at a depth of 190 feet is decompressed according to the following 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
- Thus, for a work period on the bottom of only 1 hour, the total time for decompression is about 3 hours.

# Thanks for your attention!