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Medical physiology one

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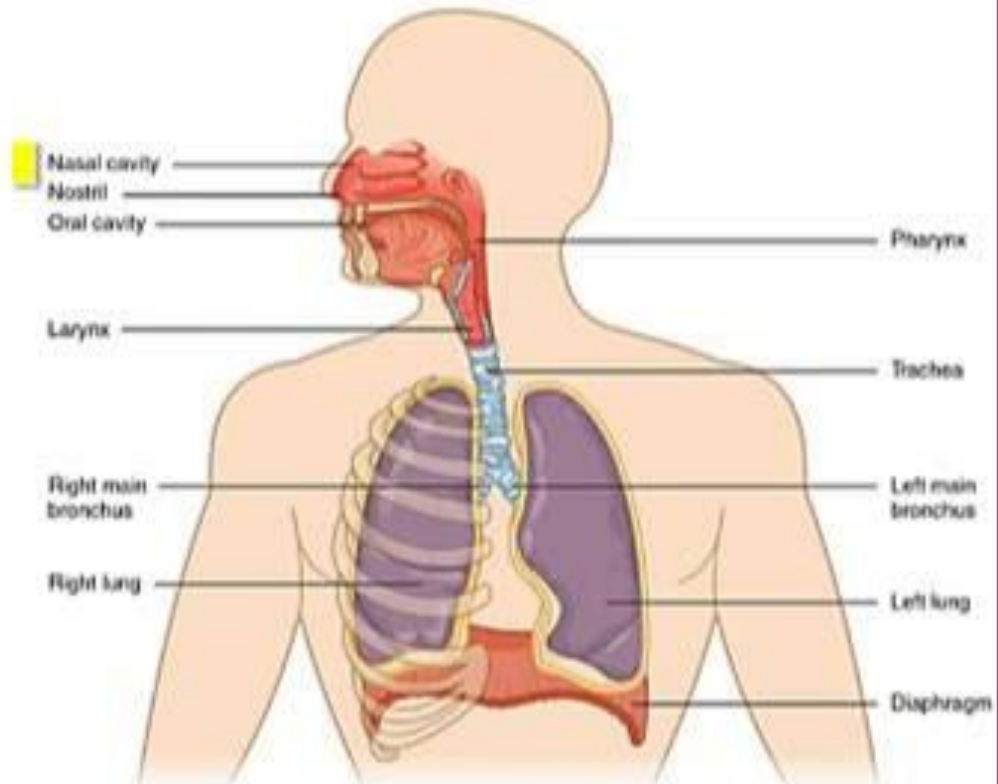
The Respiratory System 1

Function of the respiratory system

Functions of the Respiratory System:

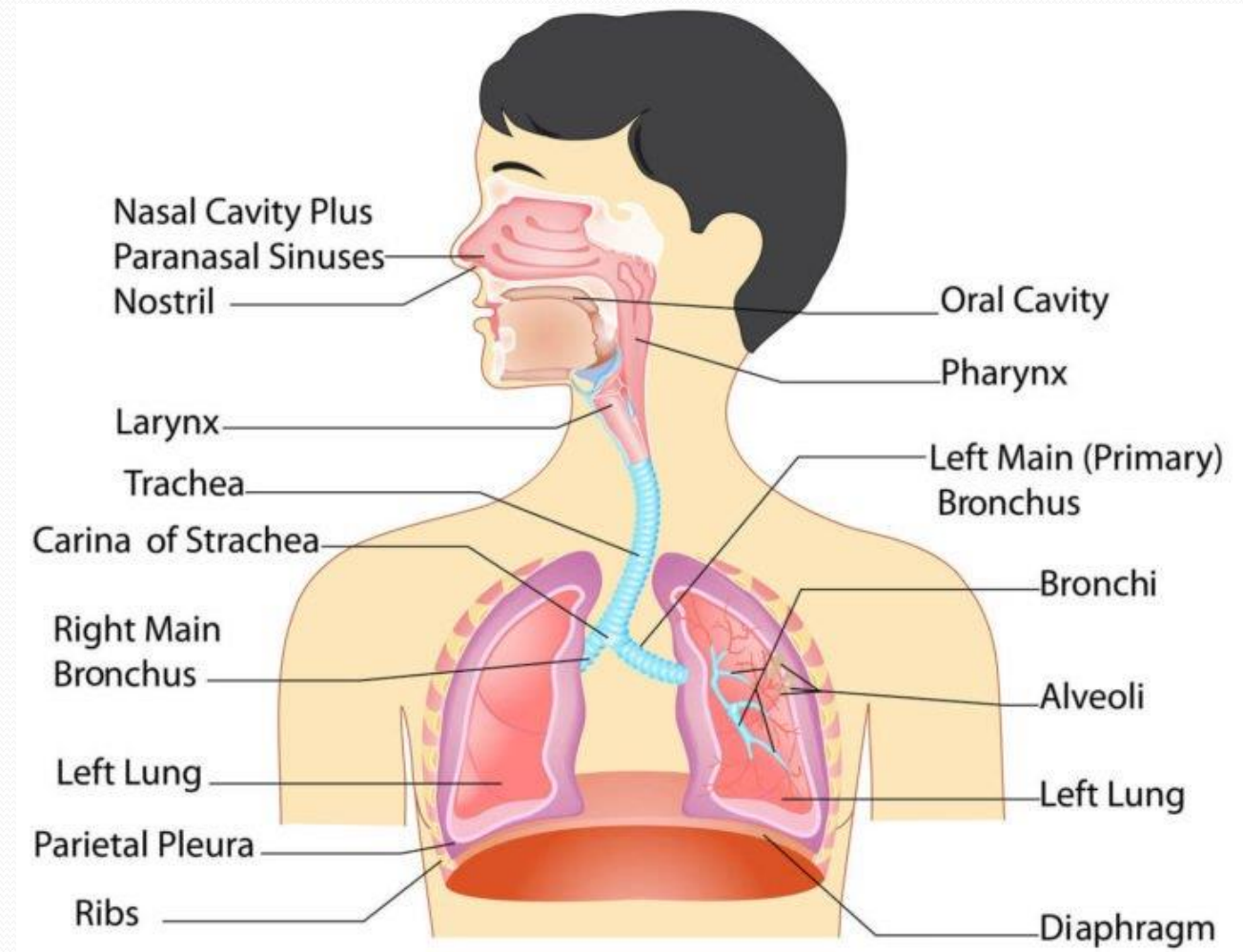
- Gaseous exchange (Intake of O_2 and removal of CO_2).
- Regulation of blood pH.
- Olfactory sensation.
- Phonation (vocalization).
- Excretion (water and heat).

Defensive role against microbes



Anatomy of the respiratory system

- Upper airways: The nose, mouth, pharynx, and larynx
- Lower airways: The trachea, two bronchi, bronchioles, alveolar ducts and sacs



Anatomy of the respiratory system

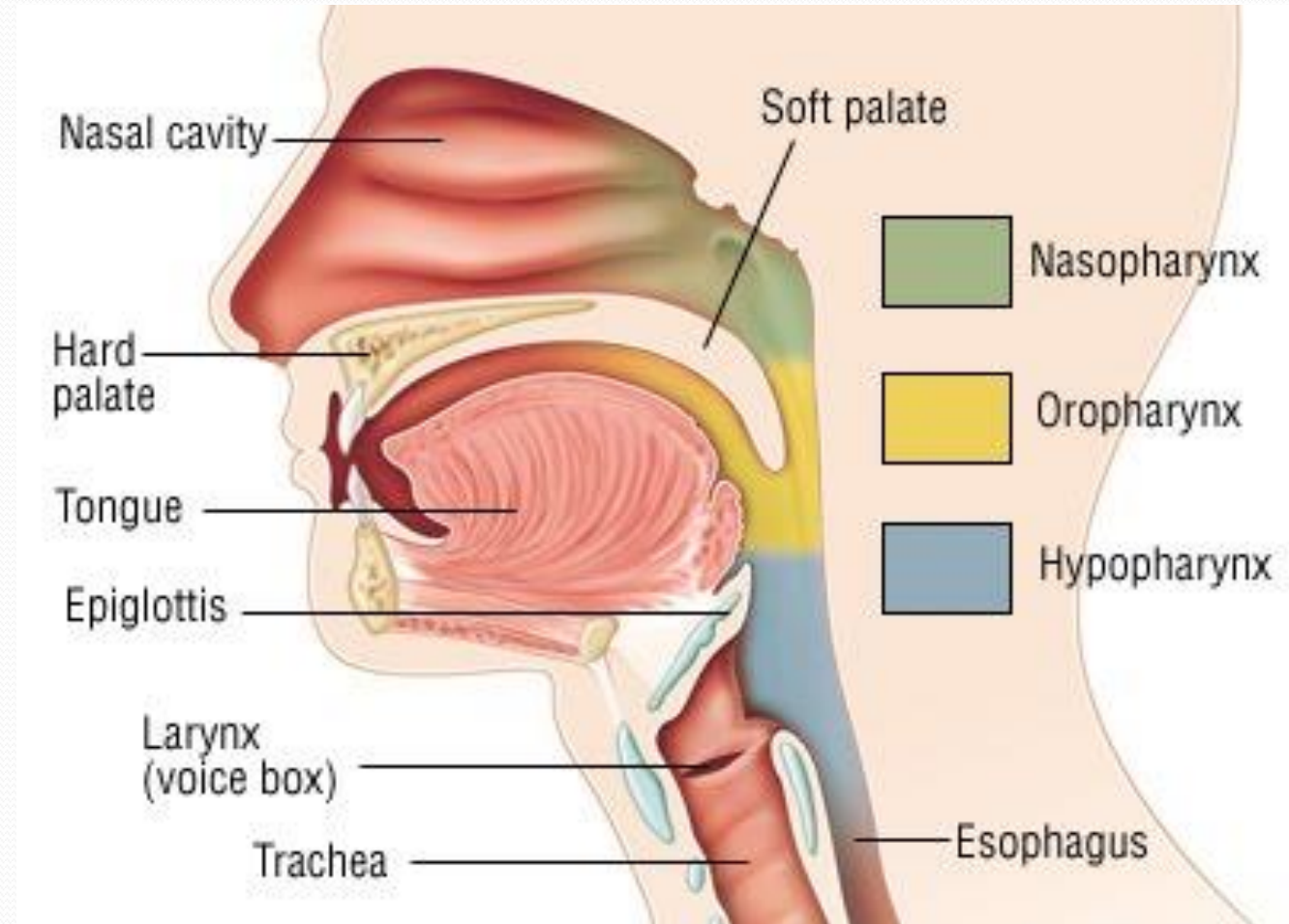
Nasal Cavity

- The nose and nasal cavity constitute the main external opening of the respiratory system.
- Nasal cavity has 2 symmetrical chambers separated by the nasal septum.
- The cavity is lined with mucus membranes and little hairs that can filter the air before it goes into the respiratory tract.
- Nasal Function
 1. Filtering all that air and retaining particles (turbulent precipitation, particles larger than 6 micrometer in diameter)
 1. Humidifying the air that you breathe, adding moisture to the air to prevent dryness of the lining of the lungs and bronchial tubes.
 1. Warming cold air through the extensive surfaces of the turbinate and the septum

Anatomy of the respiratory system

Pharyngeal Cavity

- Musculomembranous tube running from the base of the skull to the 6th cervical vertebra
- 12 cm in length
- Continues down into the esophagus
- It divided into 3 areas:
 - Nasopharynx
 - Oropharynx
 - Laryngopharynx



Anatomy of the respiratory system

Airway branching

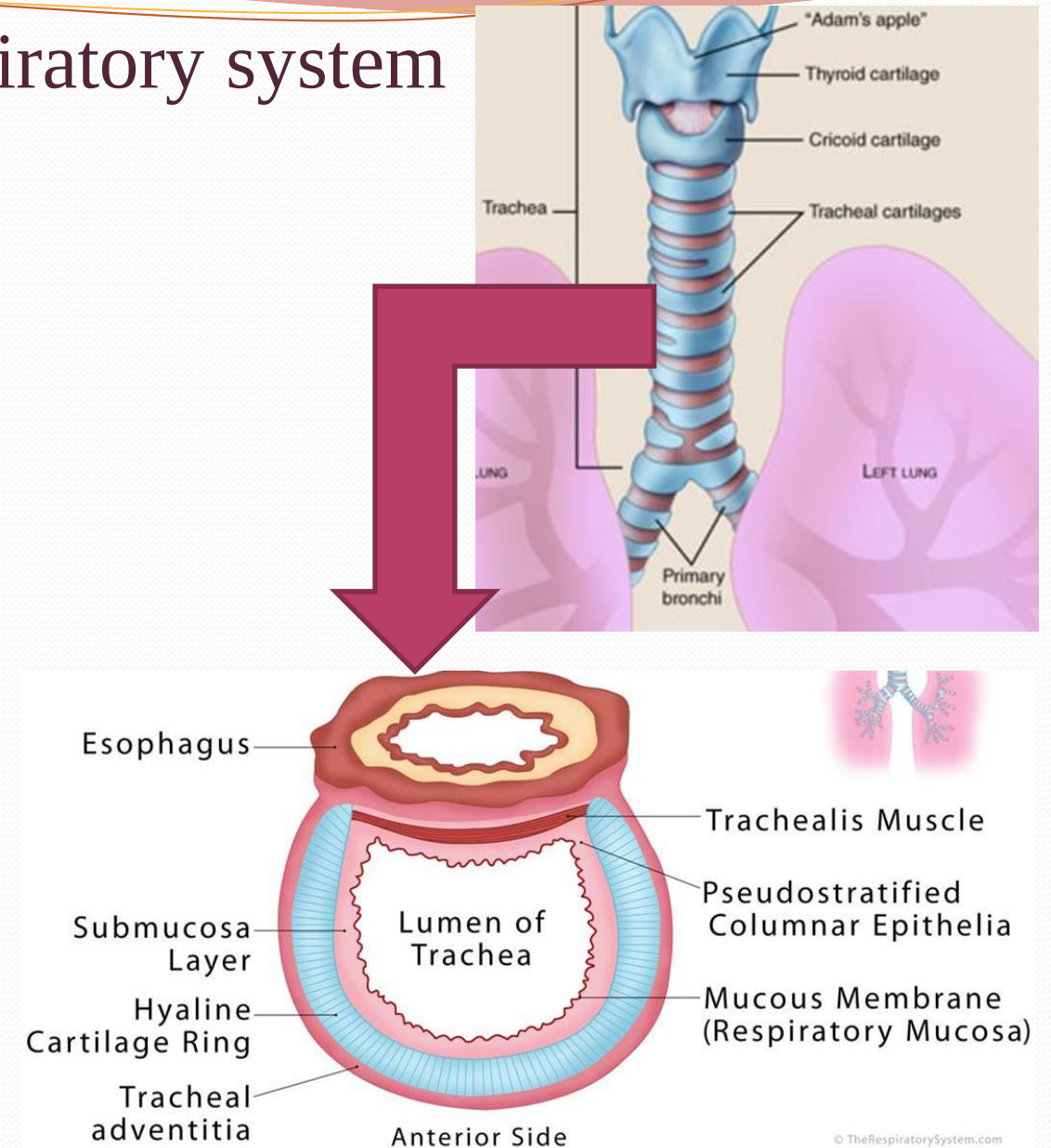
The larynx opens into a long tube, the trachea, which in turn branches into two bronchi (singular, bronchus), one of which enters each lung. Within the lungs, there are more than 20 generations of branchings, each resulting in narrower, shorter, and more numerous tubes

	Name of branches	Number of tubes in branch
Conducting zone	Trachea	1
	Bronchi	2
		4
		8
		16
	Bronchioles	32
Respiratory zone	Terminal bronchioles	6×10^4
	Respiratory bronchioles	5×10^5
	Alveolar ducts	
	Alveolar sacs	8×10^6

Anatomy of the respiratory system

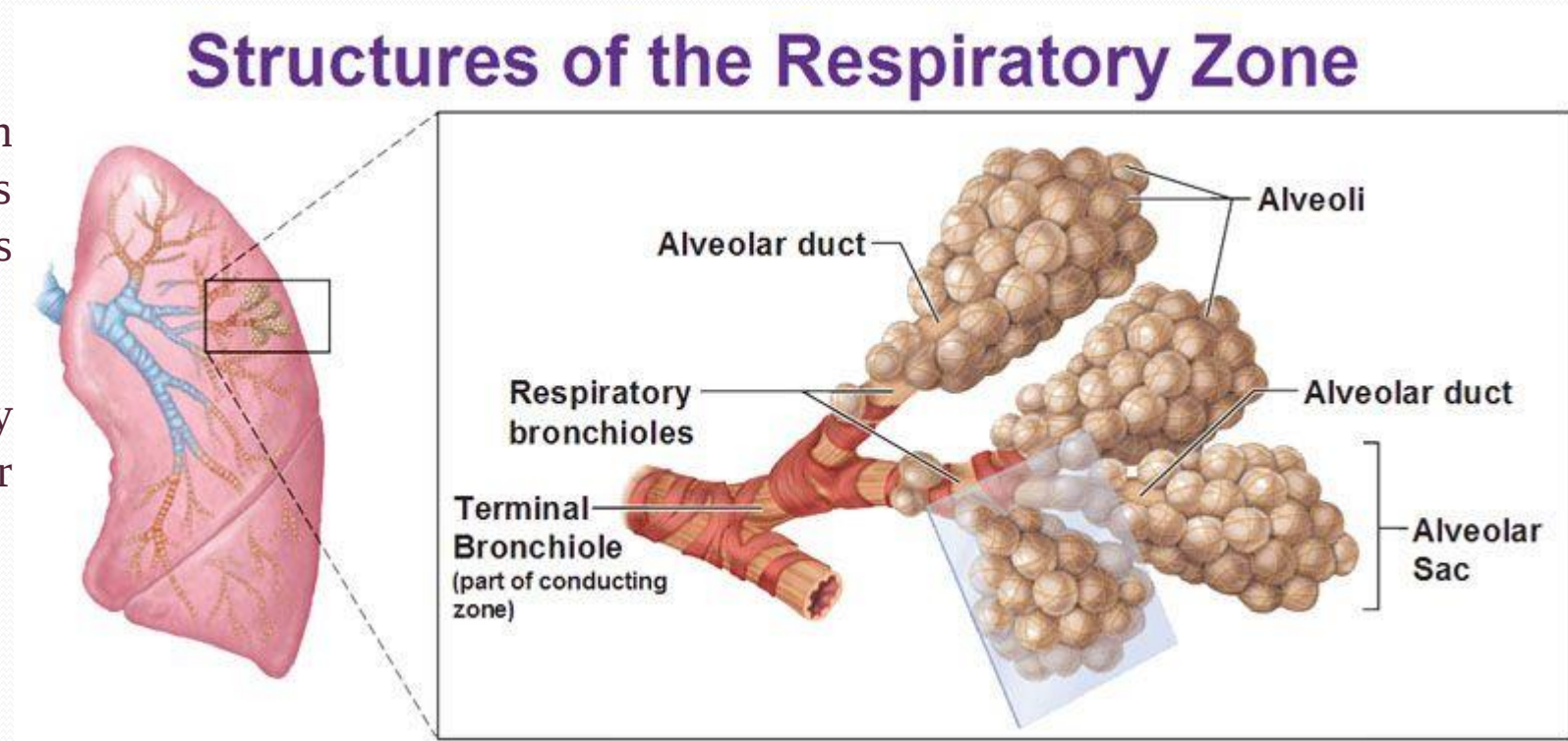
Trachea

- Provides transition of air in and out of thoracic cavity
- Composed of 16-20 C-shaped cartilaginous rings
- The rings hold the trachea open
- Posterior wall has trachealis muscle to fill the gap between the C-rings
- Trachea lined inside with ciliated epithelial mucous membrane
- Mucous glands secrete mucous to moisten incoming air and move particles out of the trachea with its sweeping cilia



Anatomy of the respiratory system

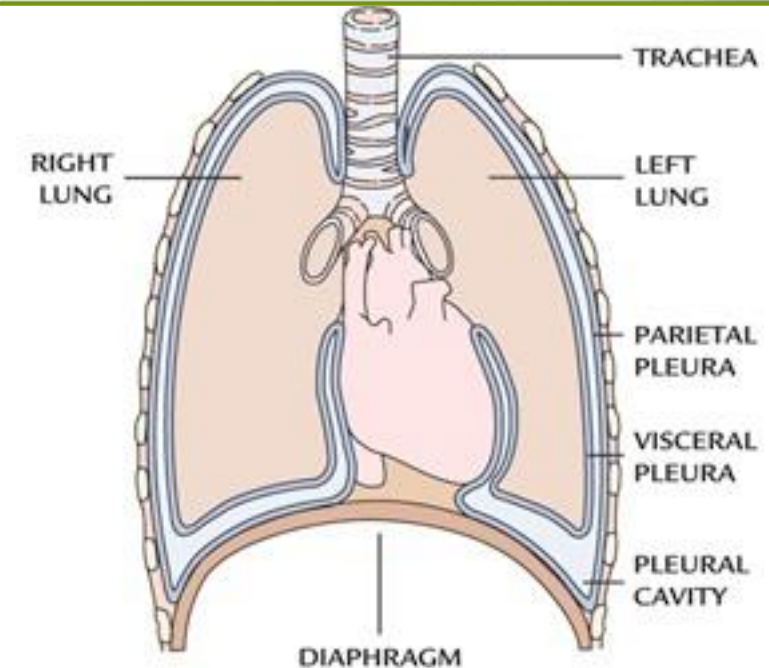
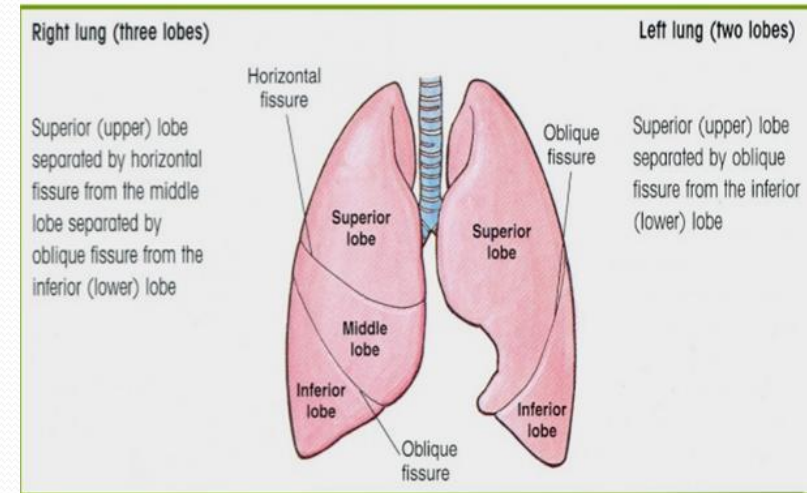
- Like the trachea, bronchi contain rings of cartilage, which give them their cylindrical shape and support them.
 - Bronchioles are the first airway branches that have no cartilage.
 - Alveoli first begin to appear on the walls of the respiratory bronchioles.
-
- The number of alveoli increases in the alveolar ducts, and the airways then end in grapelike clusters consisting entirely of alveoli.
 - The airways, are surrounded by smooth muscle, which contracts or relaxes to alter airway radius



Anatomy of the respiratory system

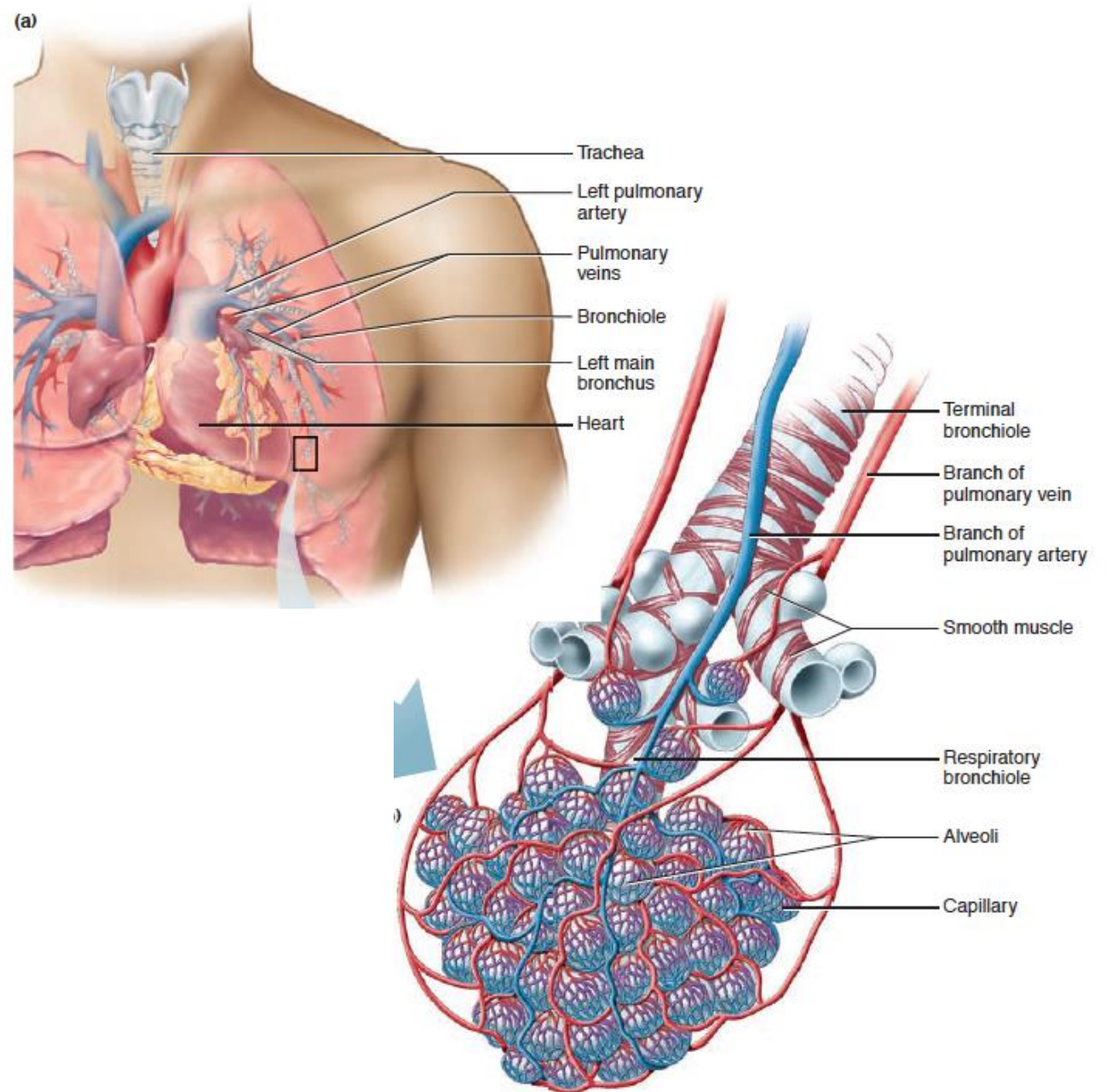
Lungs

- Lungs composed of tissue having a light, and spongy texture. They are highly elastic
- Pleurae: coverings for lungs and pleural fluid lubricates lung movement
- Lungs are passive, complete dependence on surrounding musculature and air pressure to “pump” the air in and out.
- The lung is suspended at its hilum from the mediastinum, with no attachment between the lung and the chest wall
- Base of lungs are concave and ride on the diaphragm



Anatomy of the respiratory system

- The pulmonary blood vessels accompany the airways
- The pulmonary capillaries form networks that richly supply the alveoli.
- The resistance as well as the pressure of the pulmonary circulation is low compared to the systemic circulation.



Respiration

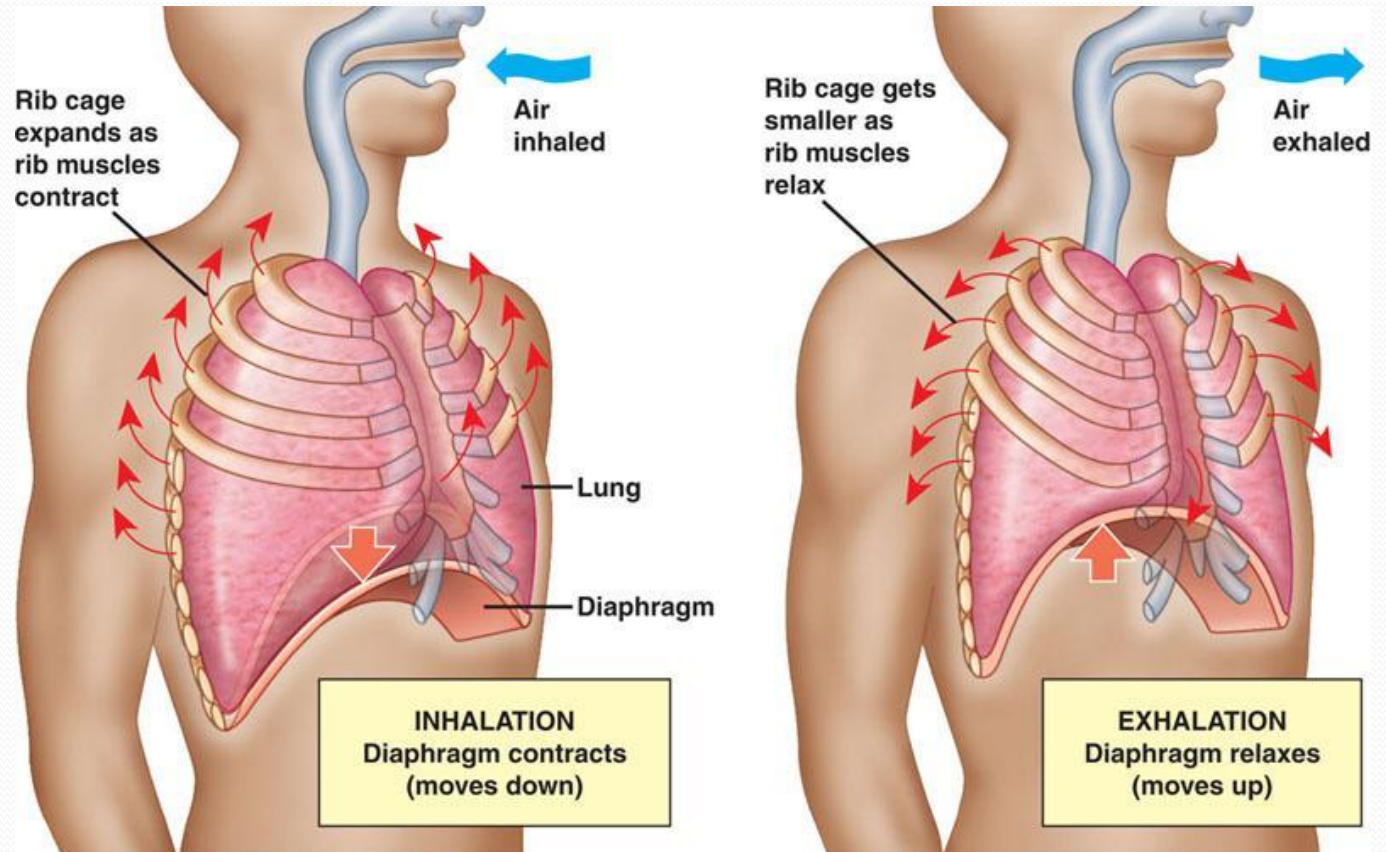
- The main function of the respiratory system is to supply the body tissues with oxygen and dispose of carbon dioxide generated by cellular metabolism.
- Respiration is collectively made up of 4 processes:
 1. Pulmonary ventilation (breathing)
 2. External respiration (movement of O_2 from lungs into blood; CO_2 from blood to lungs)
 3. Transport of respiratory gases in the blood
 4. Internal respiration (movement of O_2 from blood into tissue cells; CO_2 from cells into blood)

Mechanics of Pulmonary Ventilation

Lungs can be expanded or contracted by two ways:

1- Lengthening and shortening of the chest cavity by the downward and upward movement of the diaphragm.

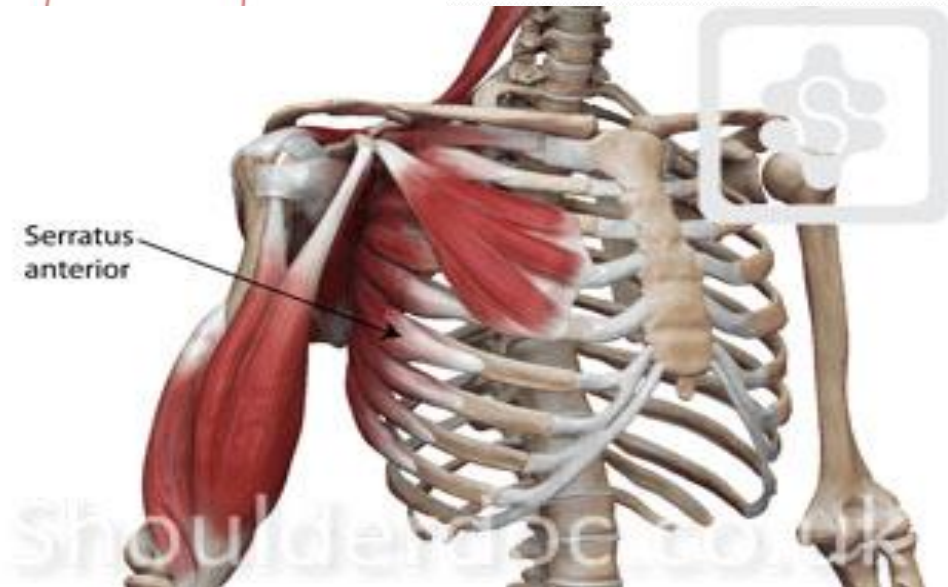
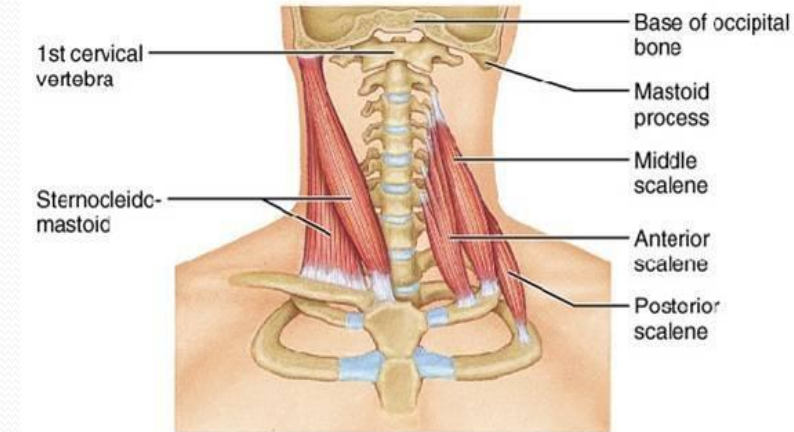
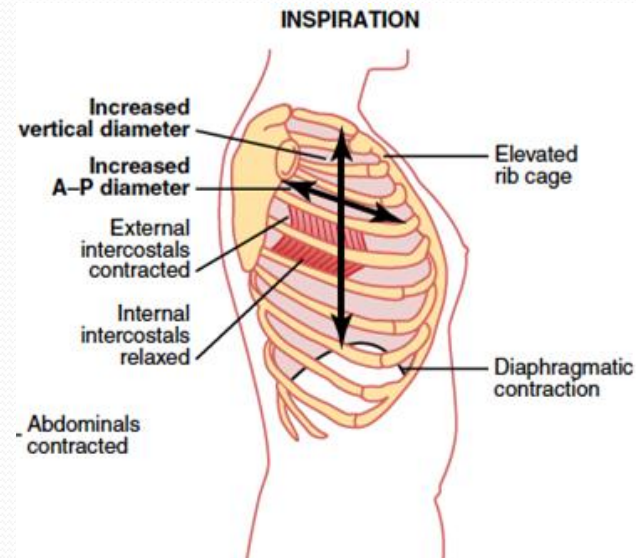
2- Increasing and decreasing anteroposterior diameter of the chest cavity by elevation and depression of the ribs.



Mechanics of Pulmonary Ventilation

Muscles that elevate the chest cage; inspiratory muscles;

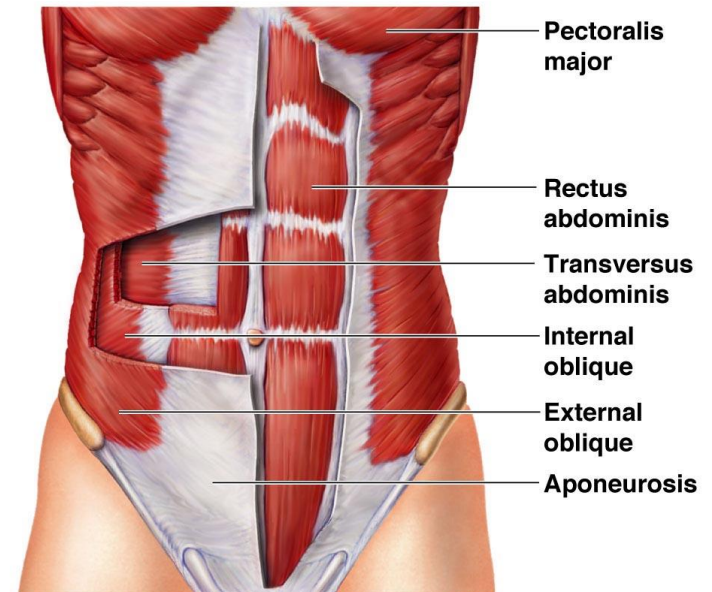
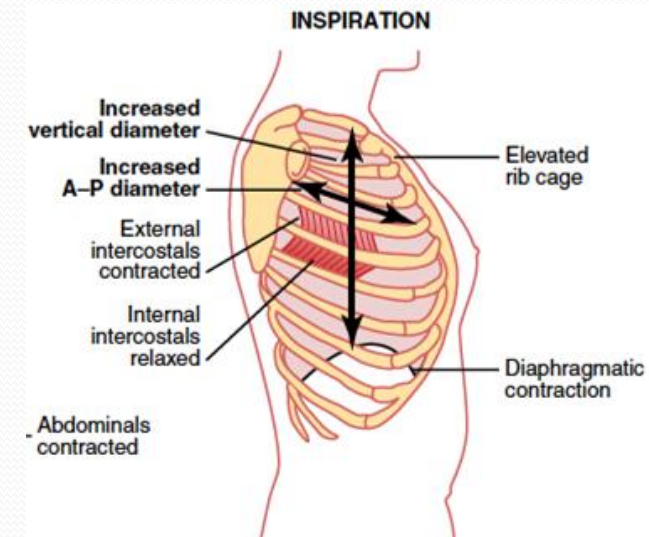
external intercostal muscles (the most important), other helper muscles; sternocleidomastoid muscles, which lift upward on the sternum; anterior serrati, which lift many of the ribs; and scaleni, which lift the first two ribs.



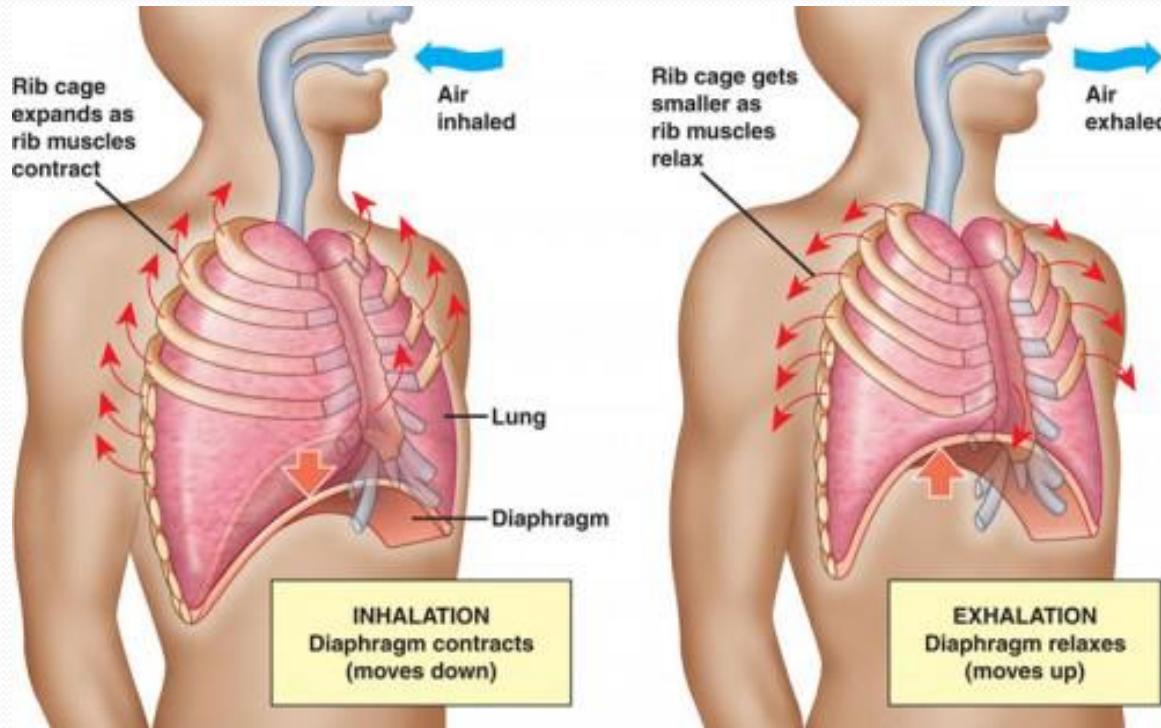
Mechanics of Pulmonary Ventilation

**Muscles that depress the chest cage;
muscles of expiration**

Abdominal recti and internal intercostal muscles

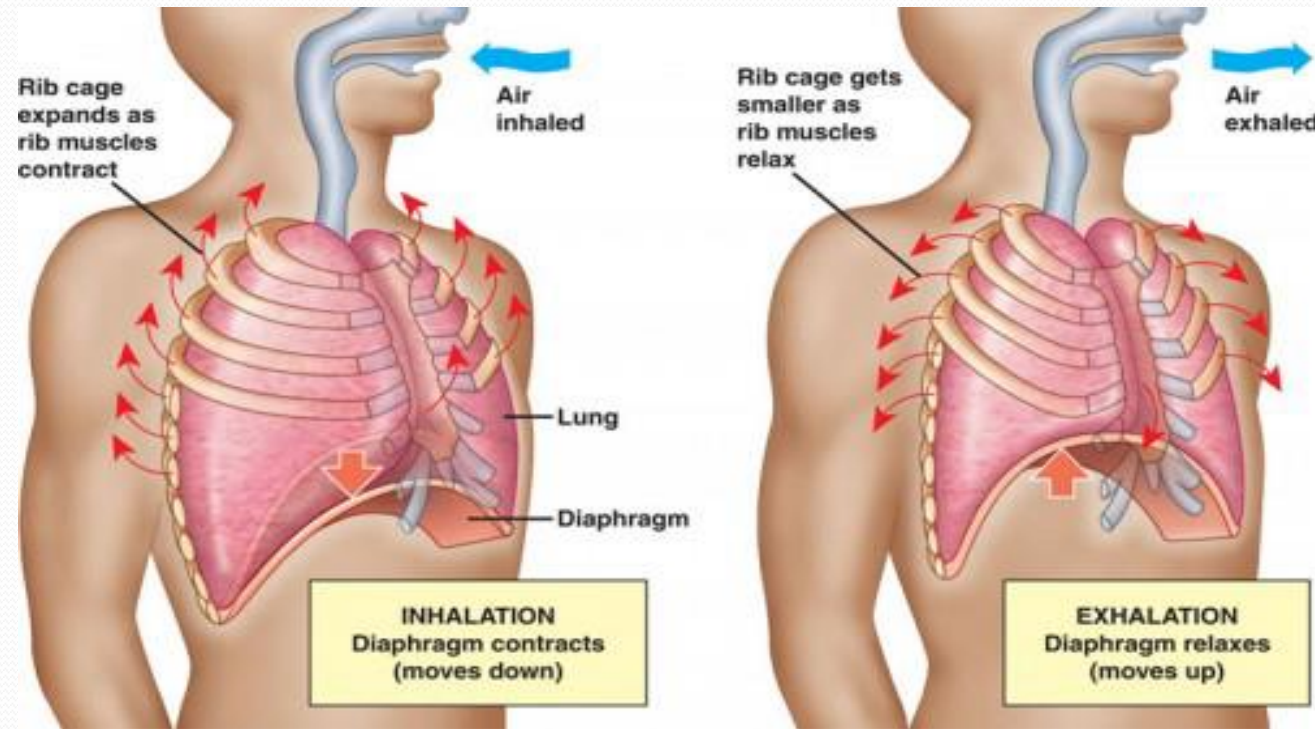


Mechanics of Pulmonary Ventilation



Inhalation: the diaphragm contracts and is drawn inferiorly into the abdominal cavity until it is flat. At the same time, the external intercostal muscles between the ribs elevate the anterior rib cage and spread the ribs. The thoracic cavity becomes deeper and larger, drawing in air from the atmosphere until pressure within lungs is same as atmospheric pressure

Mechanics of Pulmonary Ventilation



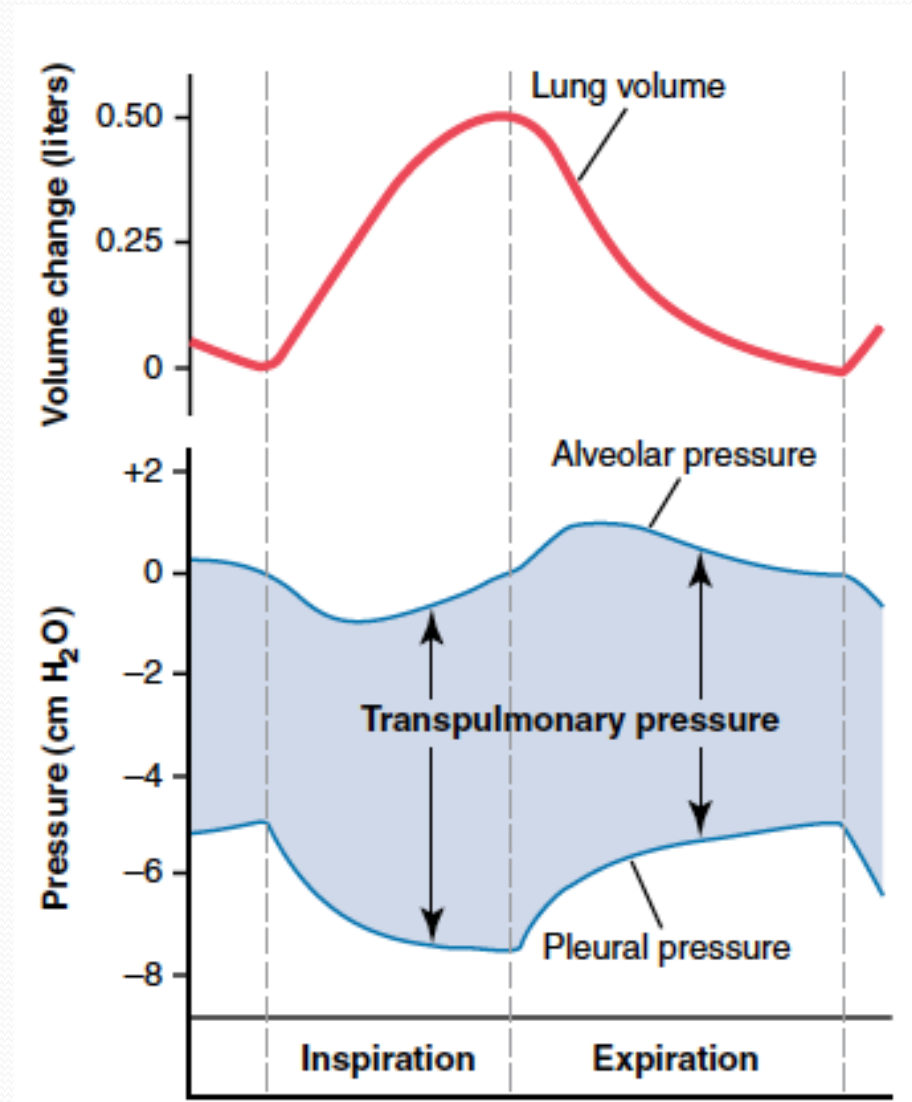
Exhalation: the diaphragm relaxes and elevates to its dome-shaped position in the thorax, the internal intercostal muscles pull the ribs inferiorly and closer together. The rib cage then drops to its resting position. The compression of the ribs decreases the volume of the thoracic cavity, resulting in the forced exhalation of air from the lungs.

Pressures that cause the movement of air in and out of the lungs

Pleural pressure:

it is a negative (sub-atmospheric) due to continuous suction of excessive fluid into lymphatic channels. This pressure (amount of suction, -5) is important to prevent lung collapse.

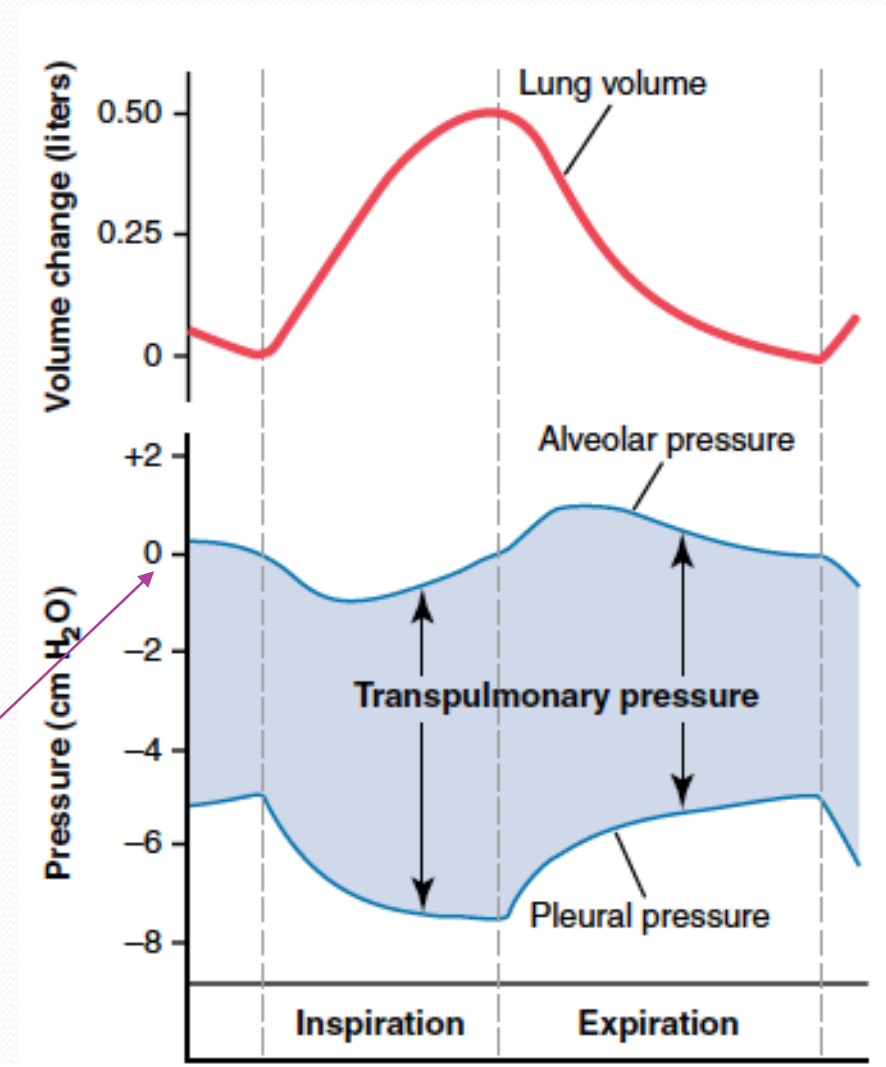
During normal inspiration, more negative pressure will developed (- 7.5)



Pressures that cause the movement of air in and out of the lungs

Alveolar pressure:

It is the pressure of the air inside the lung alveoli. When the glottis is open and no in or out movement of air, the pressures in all parts of the respiratory tree, are equal to atmospheric pressure, which is considered to be zero reference pressure in the airways (0 cm water pressure).



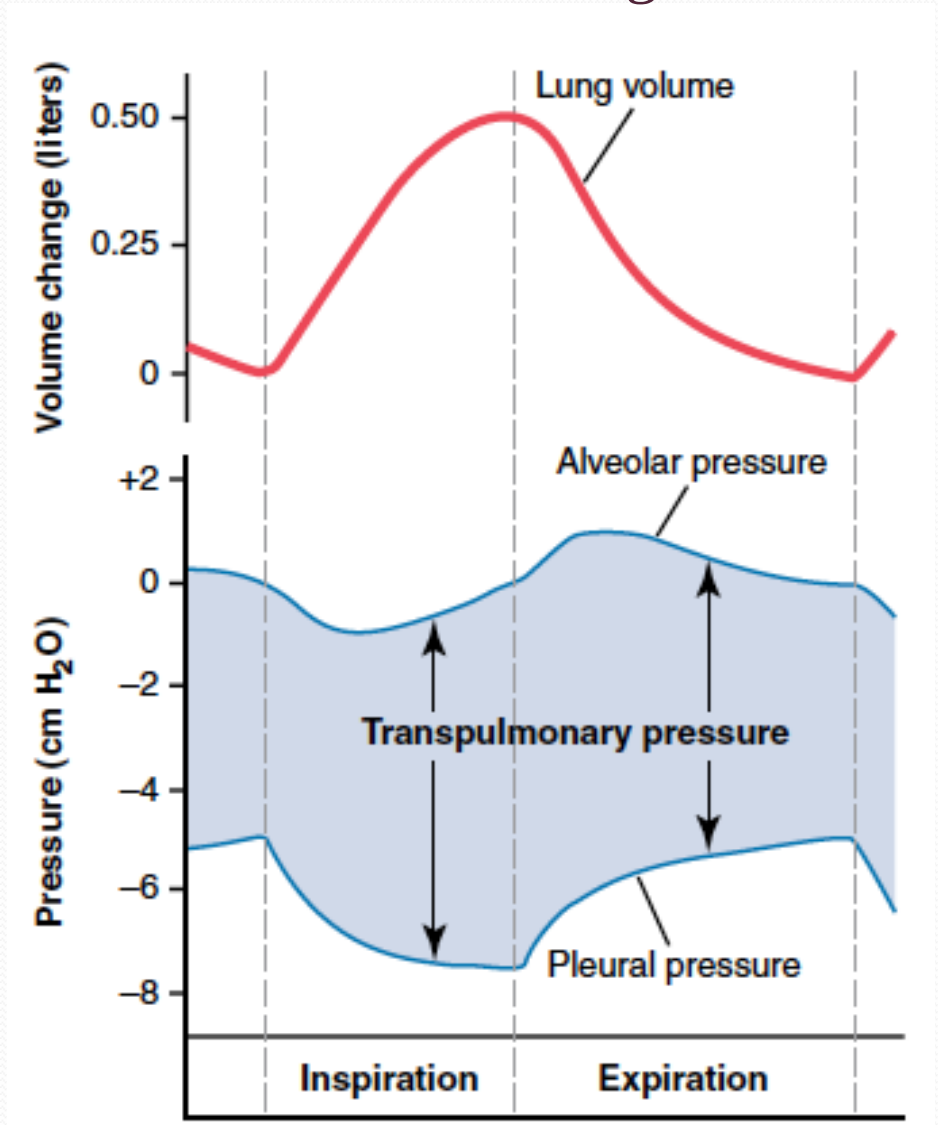
Pressures that cause the movement of air in and out of the lungs

Transpulmonary pressure:

It is the pressure difference between the alveolar and the pleural pressure

It is a **measure of the elastic forces** in the lungs that tend to collapse the lungs at each instant of respiration, called the **recoil pressure**.

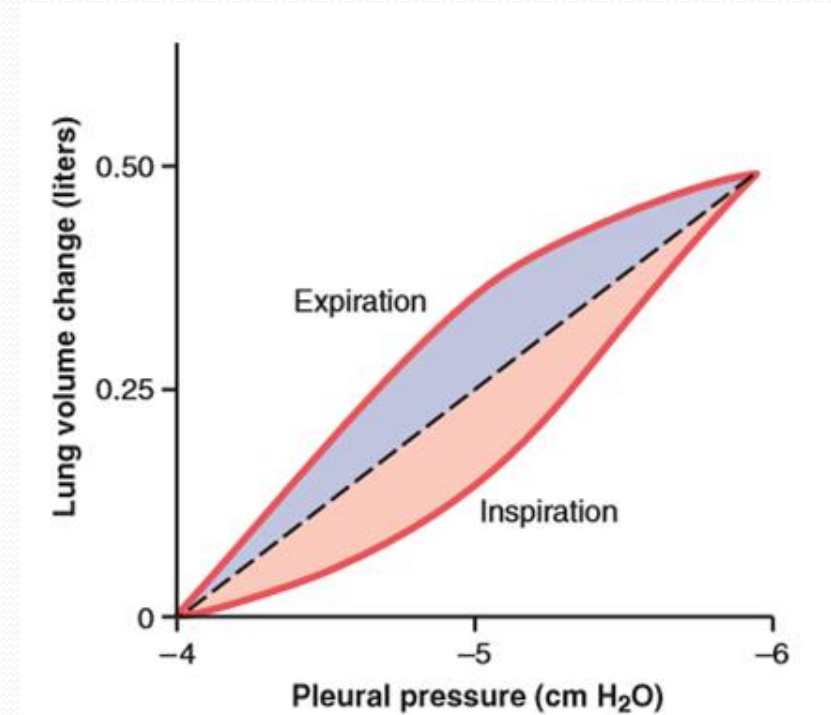
The transpulmonary pressure is equal and opposite to the elastic recoil pressure of the lung



Mechanics of Pulmonary Ventilation

Compliance diagram of the Lungs

- Lung compliance: the extent to which the lungs will expand for each unit increase in transpulmonary pressure
- In normal adult human, the total compliance of both lungs is about 200 milliliters of air per centimeter of water transpulmonary pressure.
- Two elastic forces of the lungs can affect the compliance diagram:
 1. The elastic forces of the lung tissue
 1. The surface tension at the air-water interfaces within the alveoli



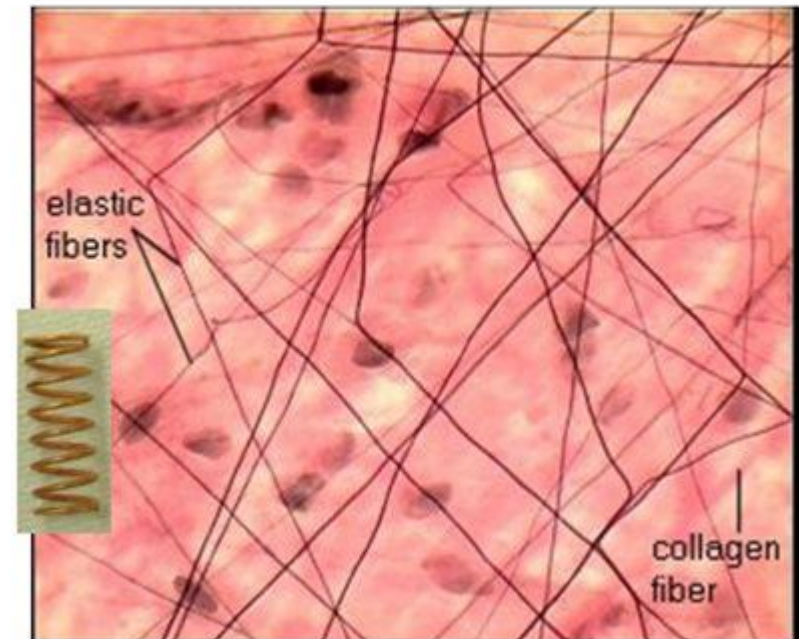
Mechanics of Pulmonary Ventilation

Compliance diagram of the Lungs

The elastic forces of the lung tissue:

- The elastin and collagen fibers of the lung determine the forces of the lung tissue. During lung deflation, these fibers are contracted and kinked, and lung expansion stretches and unkinks the fibers
- The tissue elastic force represent only about one third of the total lung elasticity that tends to collapse the air-filled lung

Elastin + Collagen fibres

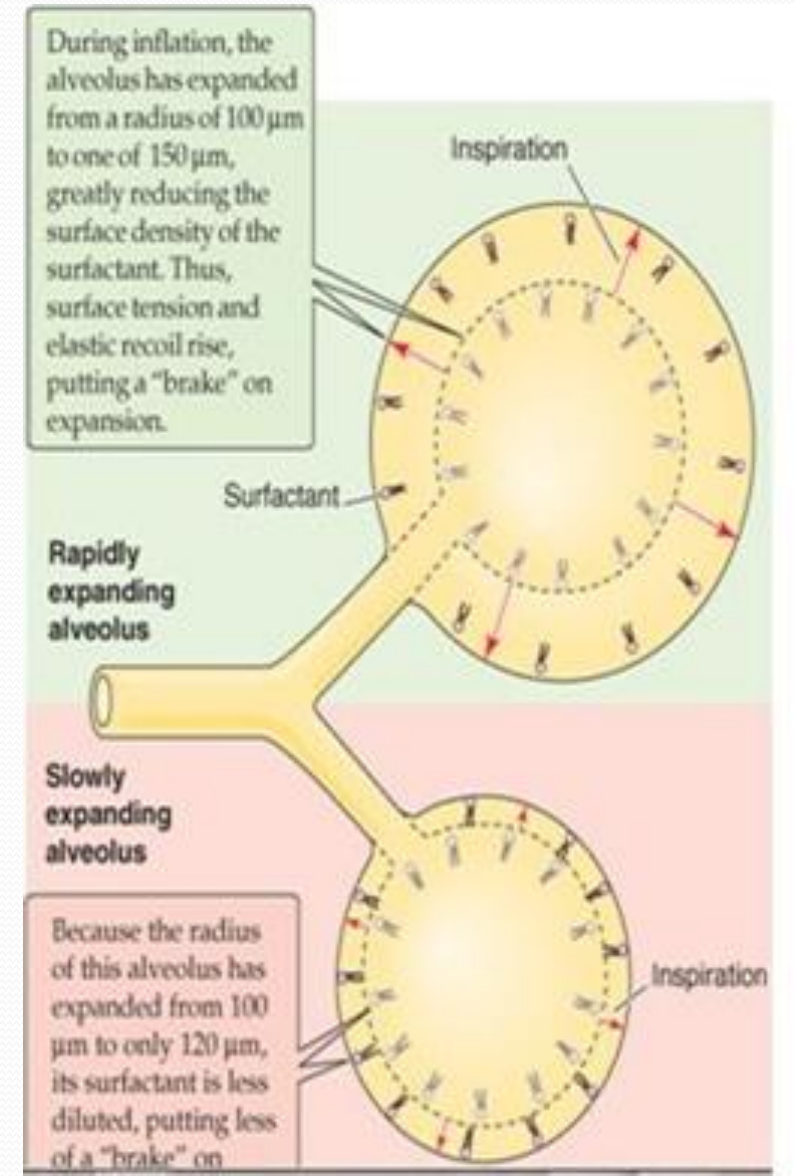


Mechanics of Pulmonary Ventilation

Compliance diagram of the Lungs

Surface tension elastic coil

- The fluid-air surface tension forces in the alveoli represent two thirds of the total lung elasticity that tends to collapse the air-filled lung.
- The important of surfactant: surfactant is a surface active agent secreted by special epithelial cells; type II alveolar cells, these cells account for 10 % of surface area of alveoli.
- Surfactant is composed of mixture of several phospholipids, proteins, and ions. The phospholipids are responsible for reducing the surface tension. The surface tension in the fluid of the alveoli without surfactant is 50 dynes/cm, with surfactant, it is between 5 and 30 dynes/cm.
- Immature baby?



Mechanics of Pulmonary Ventilation

Surface tension elastic coil

- If the air passage from the alveoli is blocked, the pressure generated by the surface tension that attempts to collapse the alveoli can be calculated:

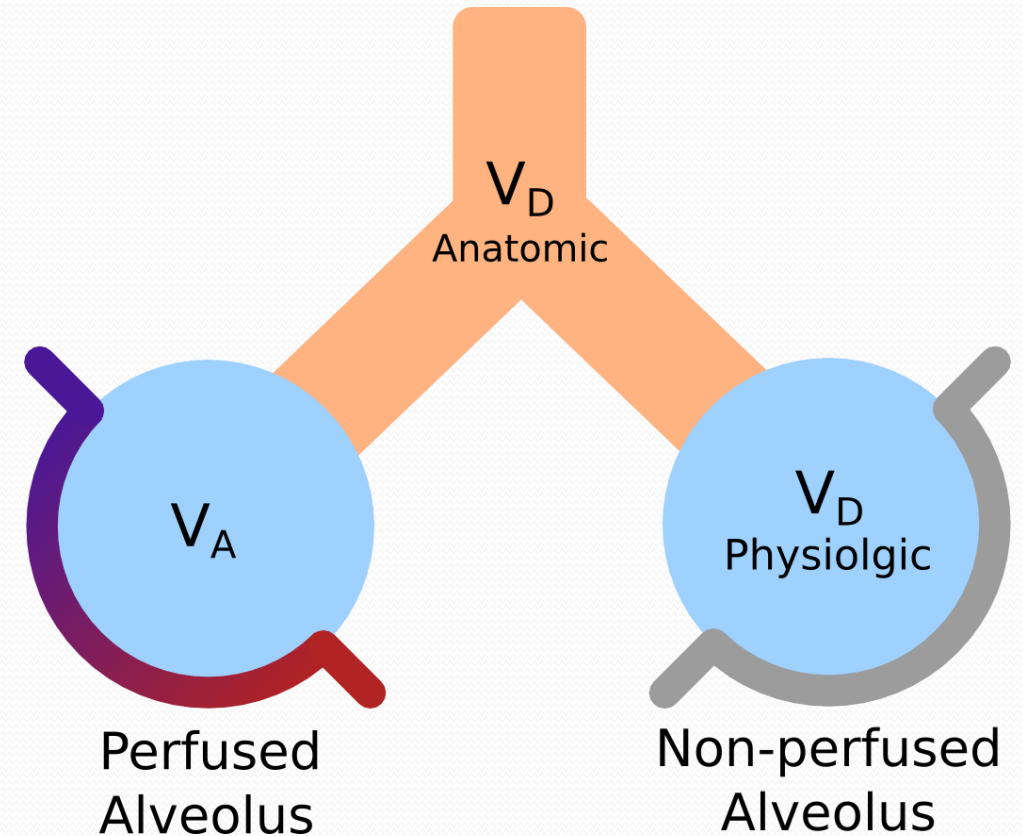
$$\text{Pressure} = \frac{2 \times \text{Surface tension}}{\text{Radius of alveolus}}$$

Important of the surfactant on surface tension and the radius of the alveoli

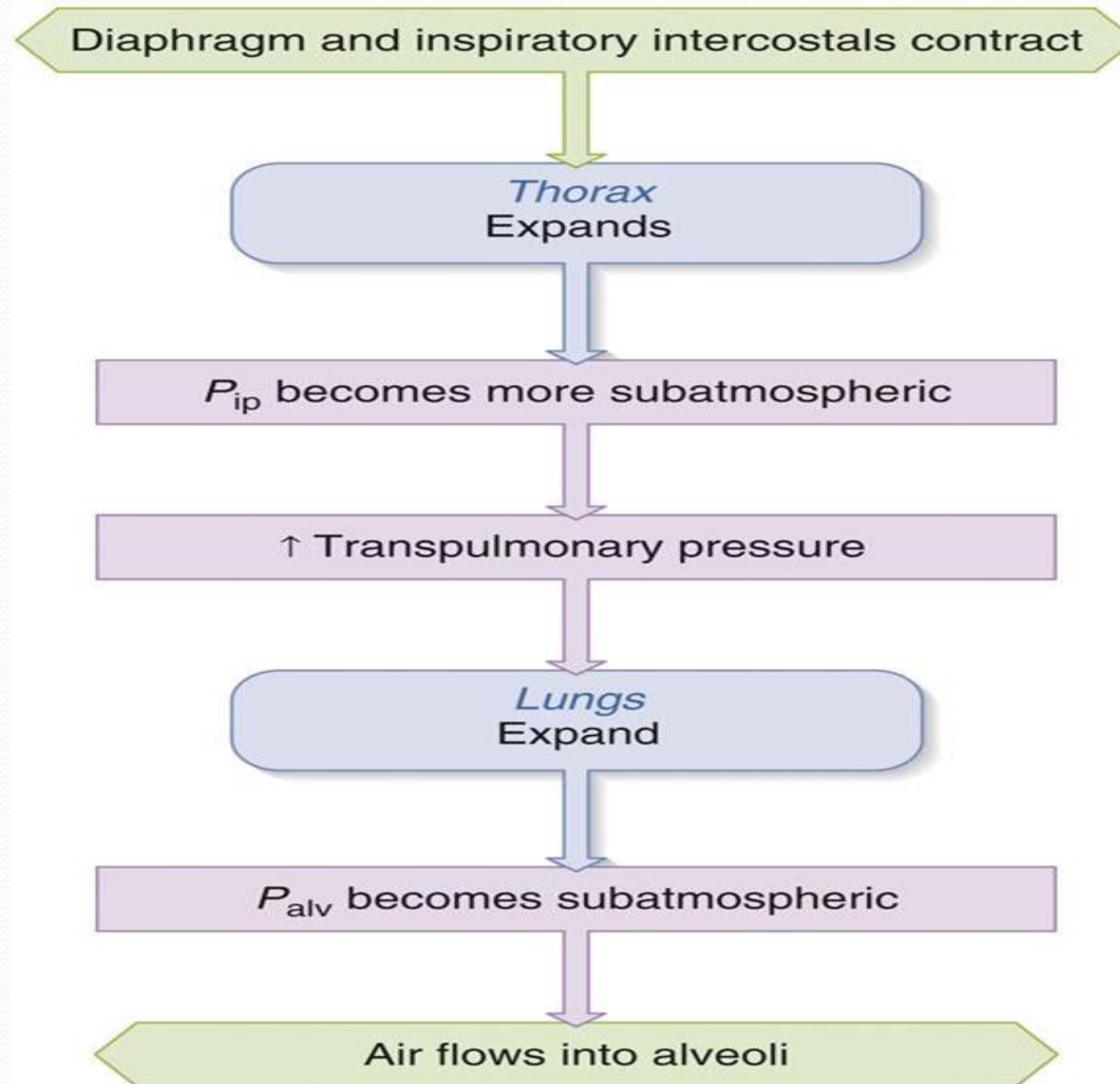
- The compliance of the thoracic cage and lung together (entire pulmonary system): The compliance of entire pulmonary system (110 milliliters of volume per centimeter of water pressure) is about half that of the lung alone (200 milliliters of volume per centimeter of water pressure)

Dead space

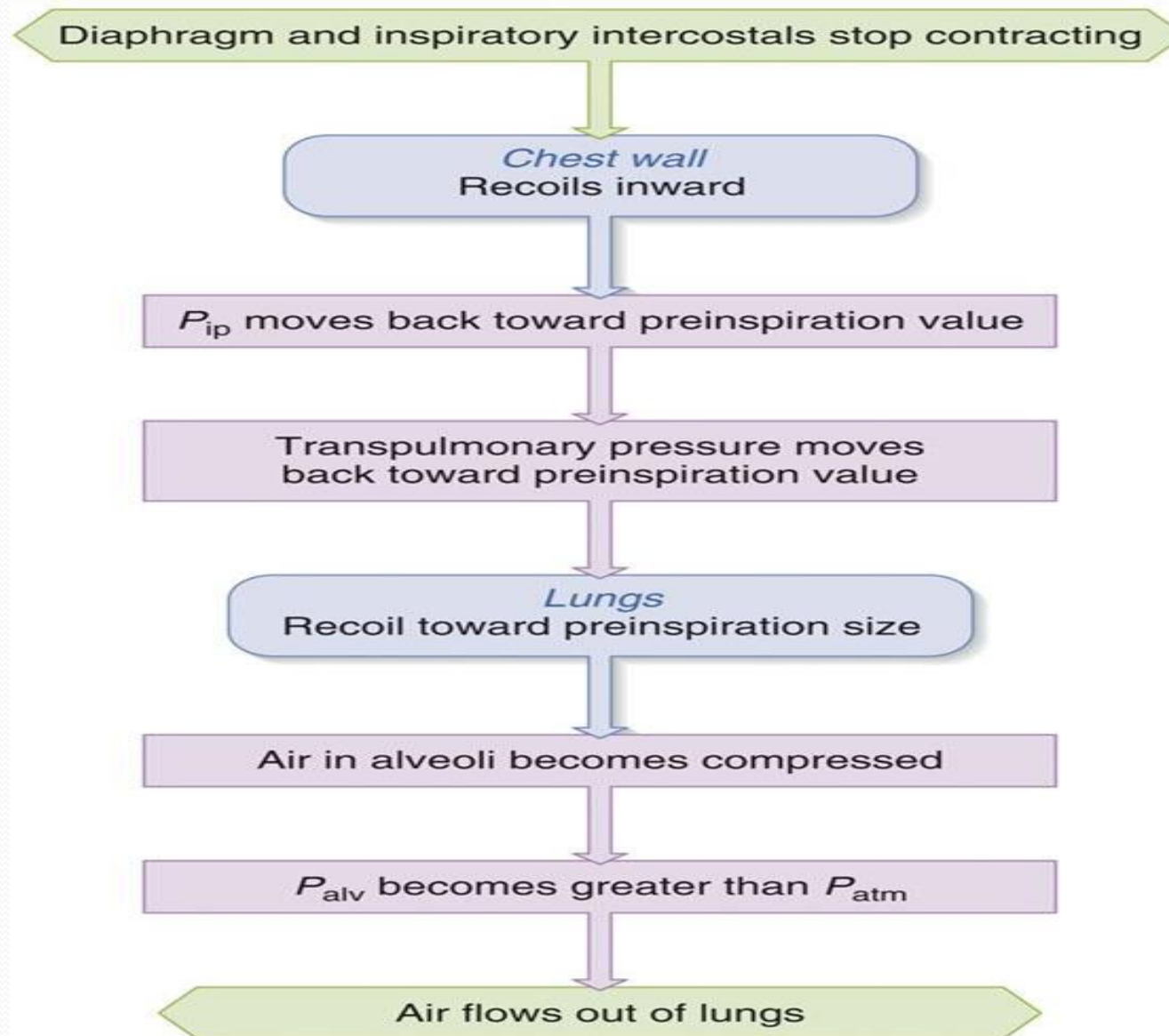
- Some of the air a person breathes never reaches the gas exchange areas but simply fills respiratory passages where gas exchange does not occur, such as the nose, pharynx, and trachea. This air is called dead space air because it is not useful for gas exchange
- Anatomic V_D vs physiological dead space



Inspiration



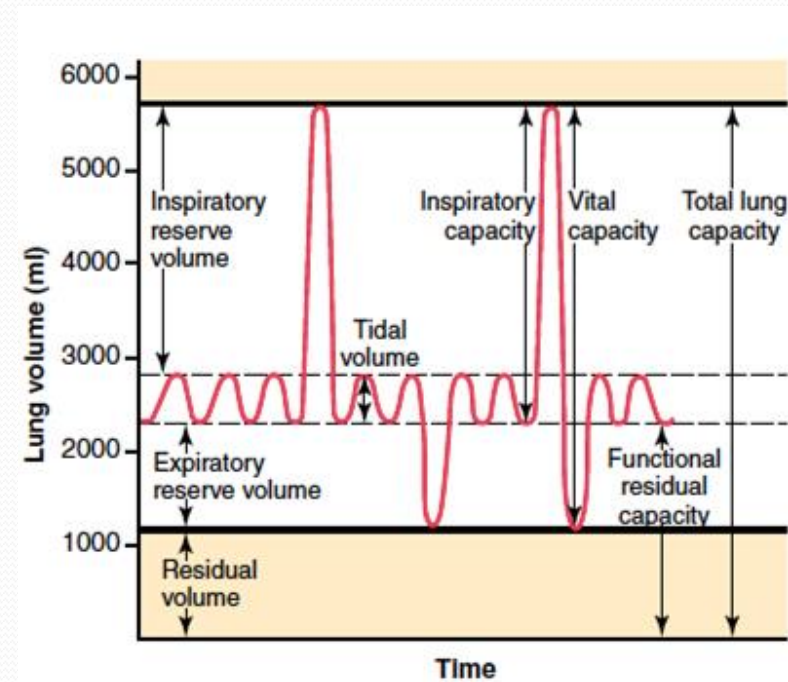
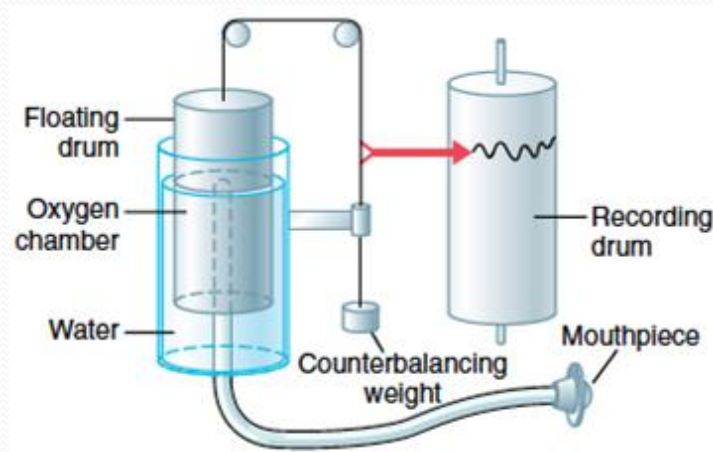
Expiration



Mechanics of Pulmonary Ventilation

Pulmonary volumes and capacities

Spirometry : a method to record the volume of air moves into and out of the lungs



Mechanics of Pulmonary Ventilation

Pulmonary volumes and capacities

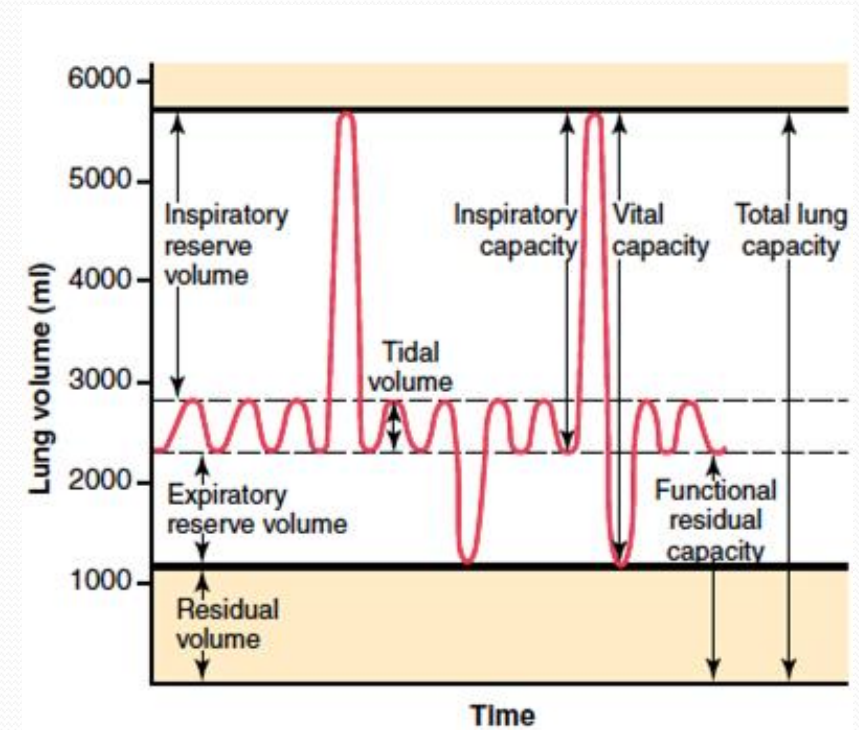
There are four pulmonary volume:

1. The tidal volume is the volume of air inspired or expired with each normal breath; it amounts to about 500 milliliters in the adult male.

2. The inspiratory reserve volume is the extra volume of air that can be inspired over and above the normal tidal volume when the person inspires with full force; it is usually equal to about 3000 milliliters.

3. The expiratory reserve volume is the maximum extra volume of air that can be expired by forceful expiration after the end of a normal tidal expiration; this normally amounts to about 1100 milliliters.

4. The residual volume is the volume of air remaining in the lungs after the most forceful expiration; this volume averages about 1200 milliliters.



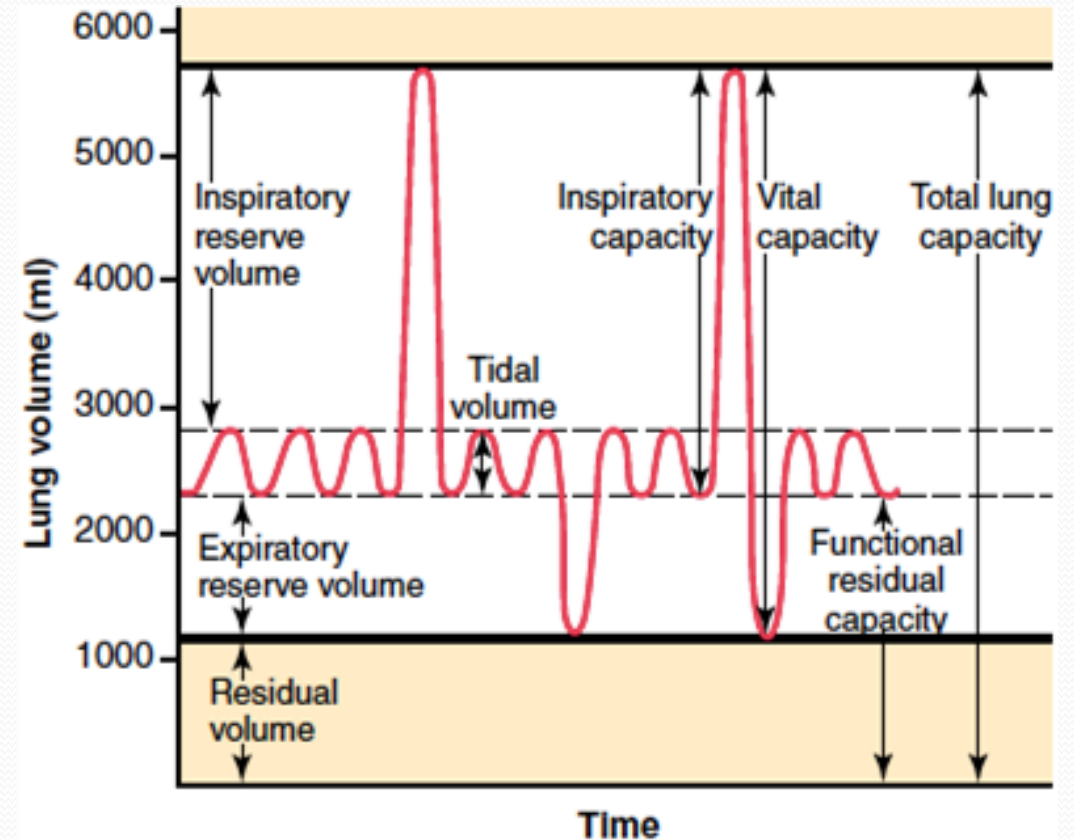
Mechanics of Pulmonary Ventilation

Pulmonary volumes and capacities

Pulmonary capacities

1. The inspiratory capacity equals the tidal volume plus the inspiratory reserve volume. This is the amount of air (about 3500 milliliters) a person can breathe in, beginning at the normal expiratory level and distending the lungs to the maximum amount.

2. The functional residual capacity equals the expiratory reserve volume plus the residual volume. This is the amount of air that remains in the lungs at the end of normal expiration (about 2300 milliliters).



Mechanics of Pulmonary Ventilation

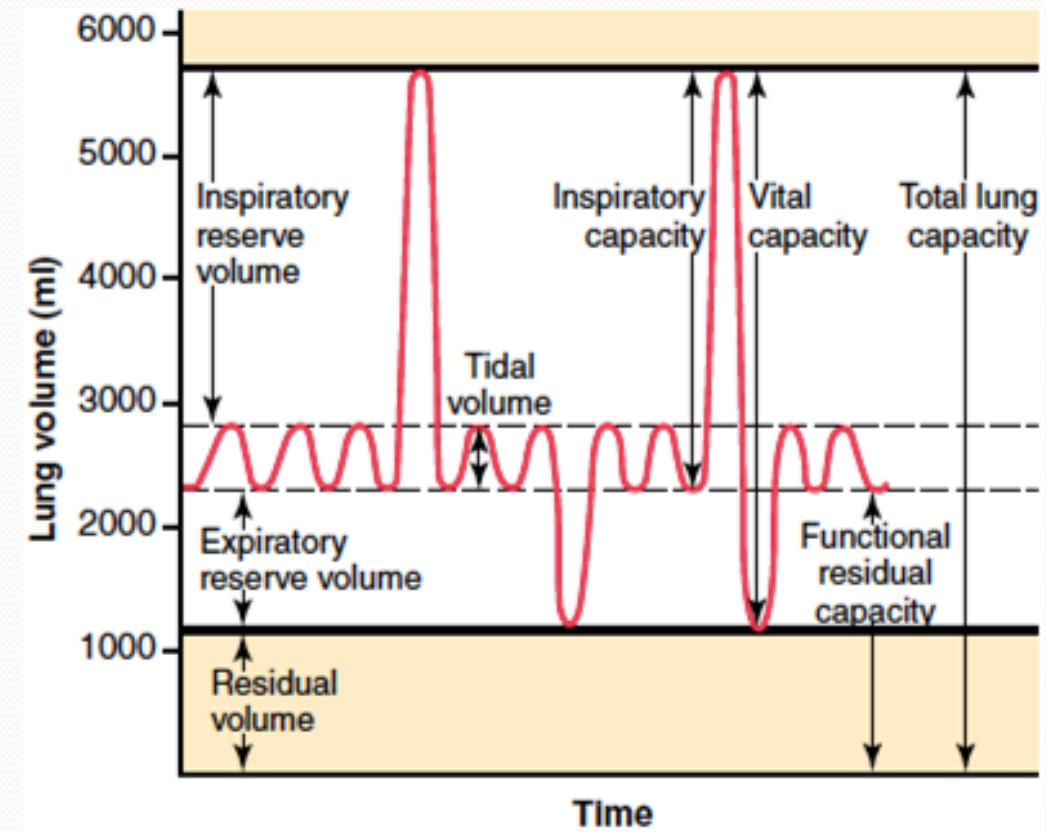
Pulmonary volumes and capacities

Pulmonary capacities

3. The vital capacity equals the inspiratory reserve volume plus the tidal volume plus the expiratory reserve volume. This is the maximum amount of air a person can expel from the lungs after first filling the lungs to their maximum extent and then expiring to the maximum extent (about 4600 milliliters).

4. The total lung capacity is the maximum volume to which the lungs can be expanded with the greatest possible effort (about 5800 milliliters); it is equal to the vital capacity plus the residual volume.

The pulmonary volumes and capacities in female are about 20 to 25 % less than in male, and these volume and capacities are also greater in large and athletic people than in small and asthenic people.



Mechanics of Pulmonary Ventilation

Spirometry Interpretation: Obstructive vs. Restrictive Defect

Obstructive Disorders

FVC normal
or slightly
decreased

FEV1 ↓

FEV1/FVC
↓

TLC normal
or ↑

RV ↑

Restrictive Disorders

FVC ↓

FEV1 ↓

FEV1/FVC
normal, or
increased

TLC ↓

RV ↓

Mechanics of Pulmonary Ventilation

Spirometry Interpretation: Obstructive vs. Restrictive Defect

- In a normal person, FEV_1 / FVC is approximately 0.8, meaning that 80% of the vital capacity can be expired in the first second of forced expiration
- In a patient with an obstructive lung disease such as asthma, both FVC and FEV_1 are decreased, but FEV is decreased more than FVC is.
- In a patient with a restrictive lung disease such as fibrosis, both FVC and FEV are decreased, but FEV_1 is decreased less than FVC is. Thus, in fibrosis, FEV_1 / FVC is actually increased or normal

Mechanics of Pulmonary Ventilation

Abbreviations and symbols Used in pulmonary function studies

$$VC = IRV + VT + ERV$$

$$VC = IC + ERV$$

$$TLC = VC + RV$$

$$TLC = IC + FRC$$

$$FRC = ERV + RV$$

V_T	tidal volume	P_B	atmospheric pressure
FRC	functional residual capacity	P_{alv}	alveolar pressure
ERV	expiratory reserve volume	P_{pl}	pleural pressure
RV	residual volume	P_{O_2}	partial pressure of oxygen
IC	inspiratory capacity	P_{CO_2}	partial pressure of carbon dioxide
IRV	inspiratory reserve volume	P_{N_2}	partial pressure of nitrogen
TLC	total lung capacity	P_{aO_2}	partial pressure of oxygen in arterial blood
VC	vital capacity	P_{aCO_2}	partial pressure of carbon dioxide in arterial blood
R_{aw}	resistance of the airways to flow of air into the lung	P_{aO_2}	partial pressure of oxygen in alveolar gas
C	compliance	P_{ACO_2}	partial pressure of carbon dioxide in alveolar gas
V_D	volume of dead space gas	P_{AH_2O}	partial pressure of water in alveolar gas
V_A	volume of alveolar gas	R	respiratory exchange ratio
$\dot{V}_I$	inspired volume of ventilation per minute	$\dot{Q}$	cardiac output
$\dot{V}_E$	expired volume of ventilation per minute		
$\dot{V}_s$	shunt flow		
$\dot{V}_A$	alveolar ventilation per minute	Ca_{O_2}	concentration of oxygen in arterial blood
$\dot{V}_{O_2}$	rate of oxygen uptake per minute	Cv_{O_2}	concentration of oxygen in mixed venous blood
$\dot{V}_{CO_2}$	amount of carbon dioxide eliminated per minute	So_2	percentage saturation of hemoglobin with oxygen
$\dot{V}_{CO}$	rate of carbon monoxide uptake per minute	Sa_{O_2}	percentage saturation of hemoglobin with oxygen in arterial blood
DLO_2	diffusing capacity of the lungs for oxygen		
DL_{CO}	diffusing capacity of the lungs for carbon monoxide		

Mechanics of Pulmonary Ventilation

- The minute respiratory volume: is the total amount of new air moved into the respiratory passages each minute
- The minute respiratory volume = tidal volume (V_T) times the respiratory rate per minute
- The minute respiratory volume averages about 6 L/min (normal V_T is 500 milliliters, normal respiratory rate is about 12 breaths/minute)
- We can live for a short period with a minute respiratory volume as low as 1.5 L/min and a respiratory rate of only 2 to 4 breaths per minute.
- The respiratory rate occasionally could rise to 40 to 50 per minute, and the tidal volume can increase to be equal vital capacity, about 4600 milliliters in a young adult man, but most of us cannot sustain more than one half to two thirds of these values for longer than 1 minute.

Respiration

The respiratory cycle: inspiration and expiration

- The physiologic pattern of breathing expresses the rate, duration, and depth of breathing
- Rate: at rest it is 12-15 times/min, while it increases to thirty times during strenuous exercise
- Duration: the duration of inspiration is 1.5-2 seconds, the same is for expiration and there is a pause of no breathing that continues for 2 seconds too.
- Depth: it is about 500 ml (tidal volume)
- During phonic respiration (breathing during speech), the inhalation time is reduced (sometimes to as little as half a second), whereas the exhalation time is increased to about 5 - 10 seconds

Mechanics of Pulmonary Ventilation

How the respiratory passages are kept open?

1. Multiple cartilage rings
1. The transpulmonary pressure expands the alveoli as well as the bronchioles where no cartilage ring is found
- All areas of the trachea and bronchi that are not supported by cartilage plates, and the walls of the bronchioles, are composed mainly of **smooth muscle**, with the exception of the most terminal bronchiole
- The **respiratory bronchiole** is mainly composed of **pulmonary epithelium** and underlying **fibrous tissue plus a few smooth muscle fibers**.
- Under normal condition the greatest resistance to airflow occurs in some of the larger bronchioles and bronchi more than in small one, why?

Mechanics of Pulmonary Ventilation

Control of the diameter of the airways:

1. Bronchiole is under the control of sympathetic (dilation) and parasympathetic (mild to moderate constriction)

Irritation of the epithelial membrane of the respiratory passageways, (for example by noxious gases, dust, cigarette smoke, or bronchial infection), and pulmonary embolism can activate the parasympathetic system.

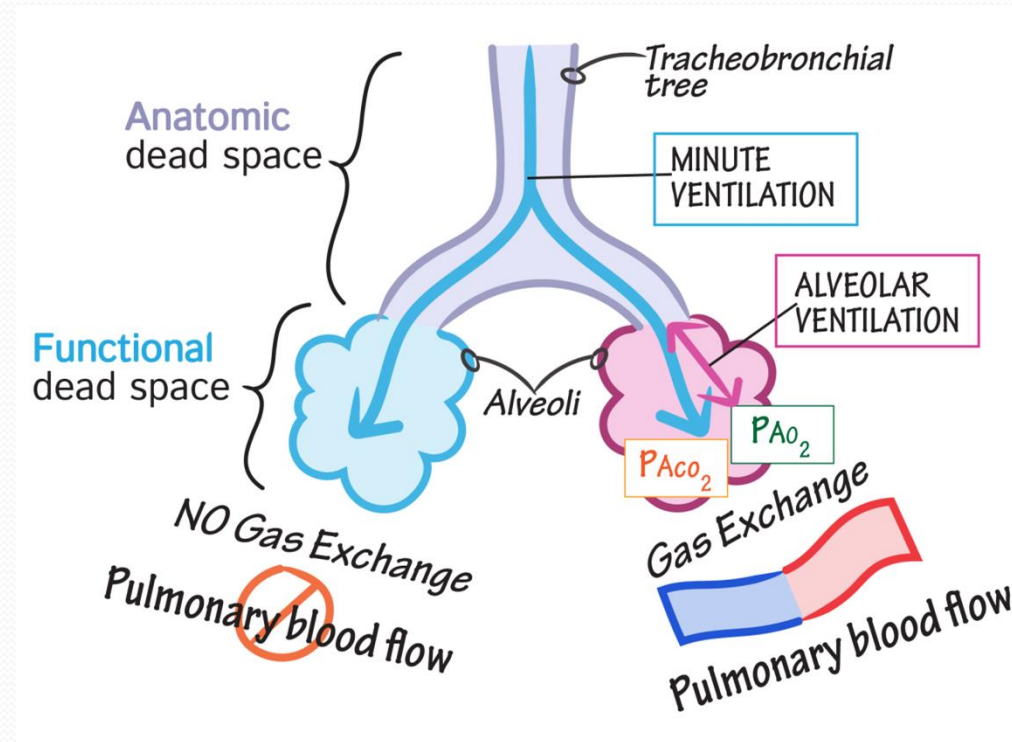
2. Irritants can also act directly on the lung and cause local, non-nervous reaction resulting in bronchiolar constriction.
3. Local secretory factors, such as histamine and slow reactive substance of anaphylaxis, cause constriction of the bronchiole

Alveolar ventilation

- The ultimate importance of pulmonary ventilation is to continually renew the air in the gas exchange areas of the lungs, where air is in proximity to the pulmonary blood.
- Gas exchange areas of the lungs: the alveoli, alveolar sacs, alveolar ducts, and respiratory bronchioles.
- Alveolar ventilation: is the rate at which new air reaches these areas

Alveolar ventilation

- Remember what is dead space???
- The ratio of physiologic dead space to tidal volume provides an estimate of how much ventilation is “wasted” (either in the conducting airways or in nonperfused alveoli)



Alveolar ventilation

Rate of alveolar ventilation

- Alveolar ventilation per minute is the total volume of new air entering the alveoli and adjacent gas exchange areas each minute.

$$\dot{V}_A = \text{Freq} \times (V_T - V_D)$$

- V_A is the volume of alveolar ventilation per minute
- Freq is the frequency of respiration per minute
- V_T is the tidal volume
- V_D is the physiologic dead space volume.

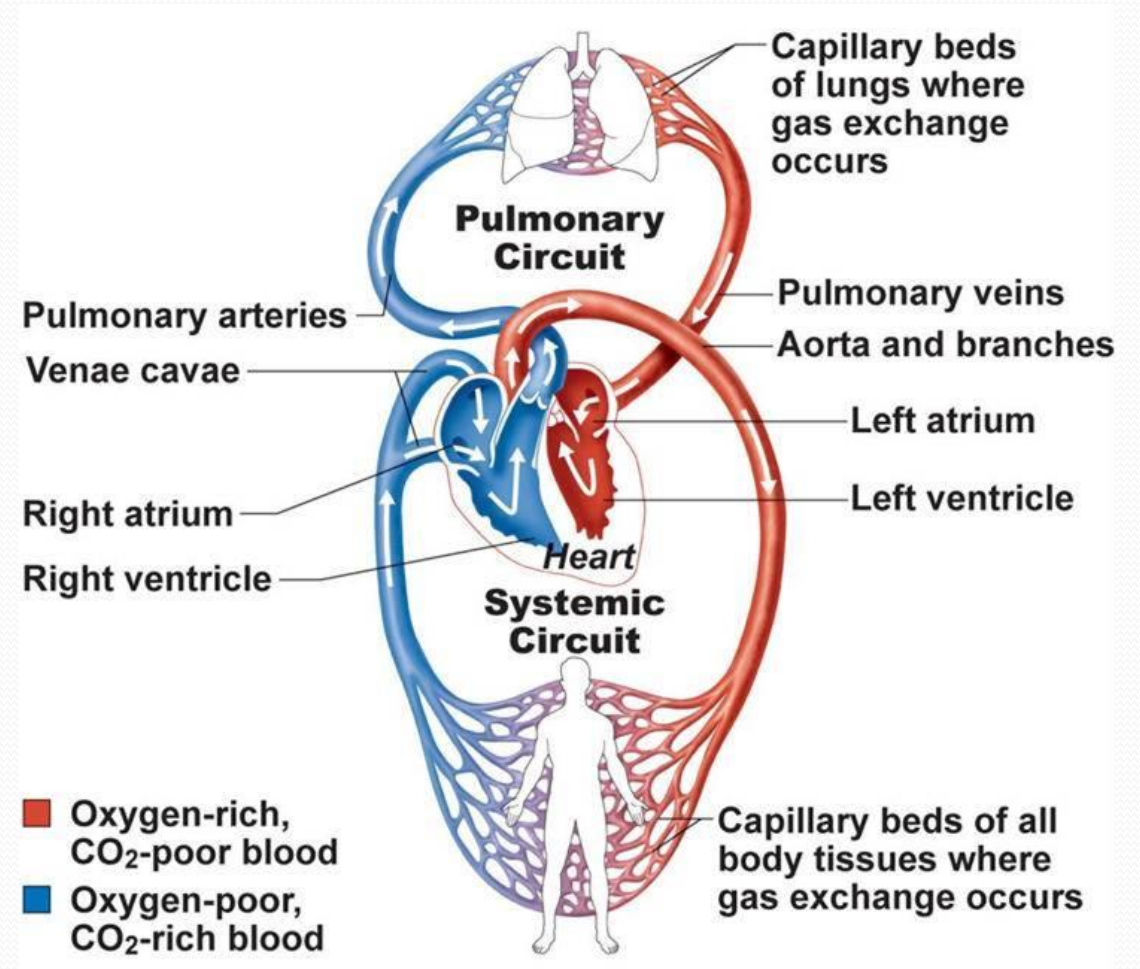
With a normal tidal volume of 500 milliliters, a normal dead space of 150 milliliters, and a respiratory rate of 12 breaths per minute, alveolar ventilation equals 4200 ml/min.

Alveolar ventilation is one of the major factors determining the concentrations of oxygen and carbon dioxide in the alveoli

Pulmonary circulation

1. Systemic Circulation:

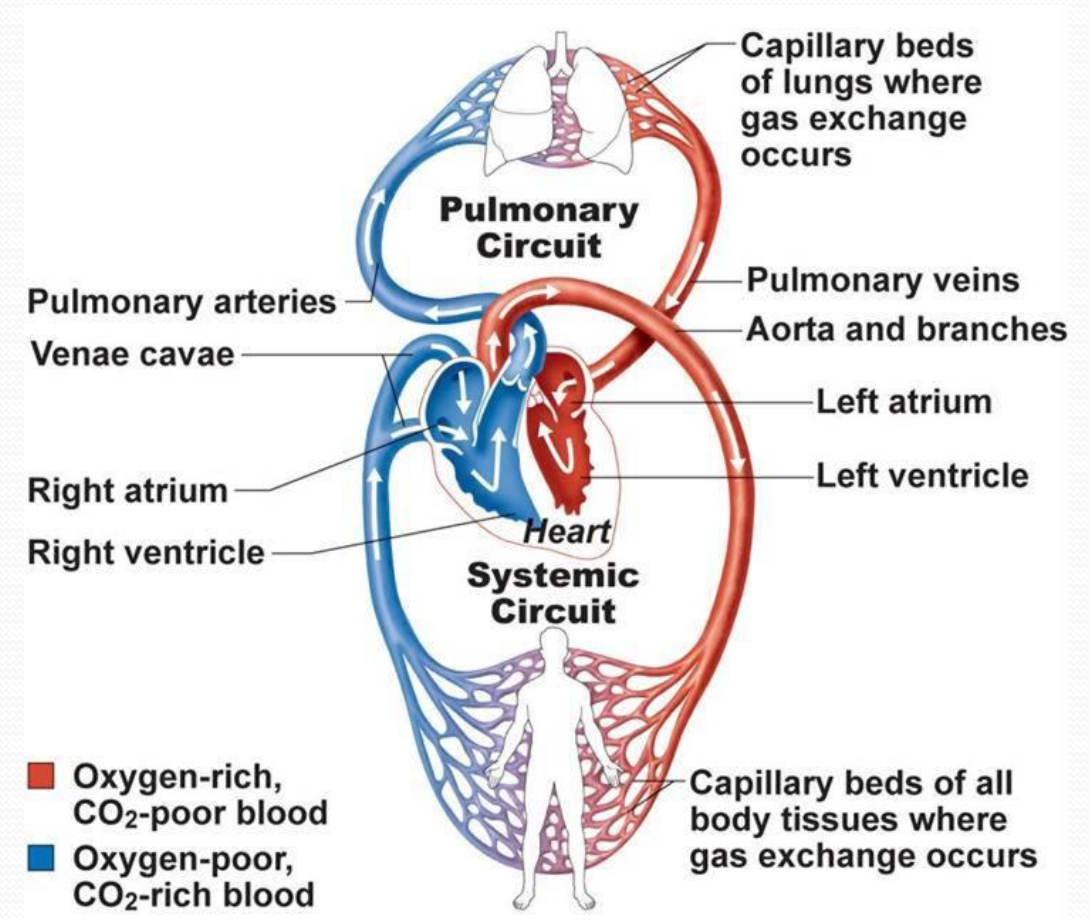
- bronchial arteries: supply of oxygenated blood to the trachea, the bronchial tree including the terminal bronchioles, the supporting tissues of the lung including the connective tissue, and the outer coats (adventia) of the pulmonary arteries and veins.
- Systemic supply to the lung equals 1-2 % of the total cardiac output.
- Systemic supply do not participate in gas exchange
- The venous return of the lung go directly to pulmonary veins and enters the left atrium (Physiological shunt).



Pulmonary circulation

2. Pulmonary circulation:

- Pulmonary artery has right and left main branches
- The pulmonary artery is thin, with a wall thickness one third that of the aorta.
- All the pulmonary arteries, have larger diameters, are thinner and more distensible compared to their counterpart systemic arteries.

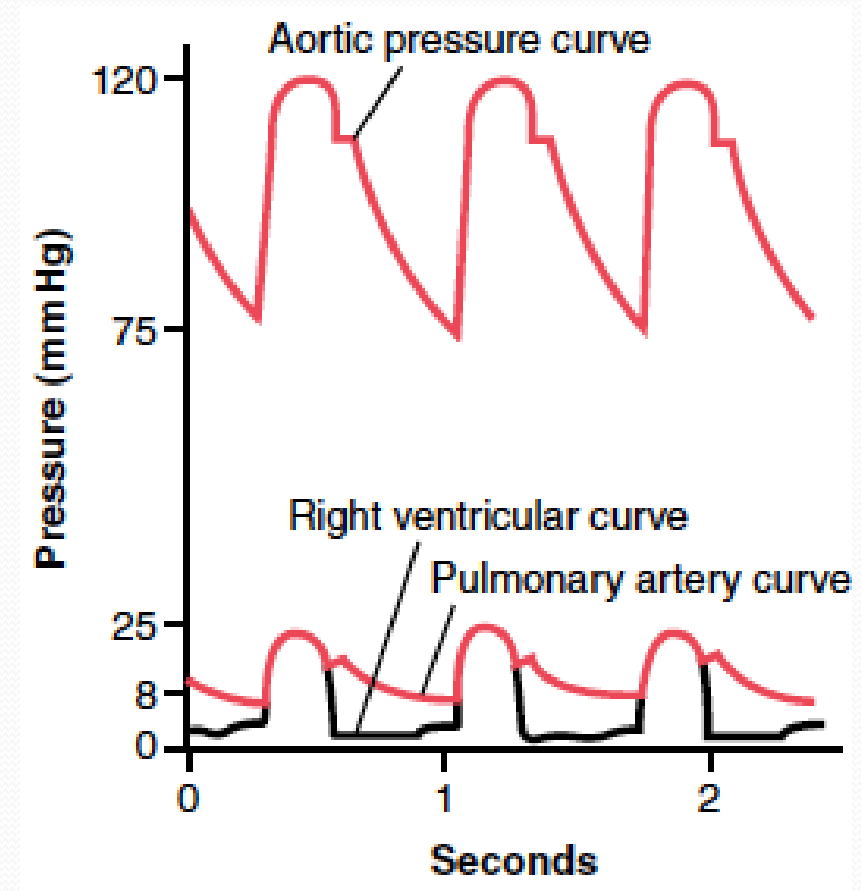


Pulmonary circulation

Lymph vessels are present in all the supportive tissues of the lung, and then mainly into the right thoracic lymph duct. Lymph system removes particulate matter entering the alveoli, and plasma protein leaking from the lung capillaries to prevent pulmonary edema.

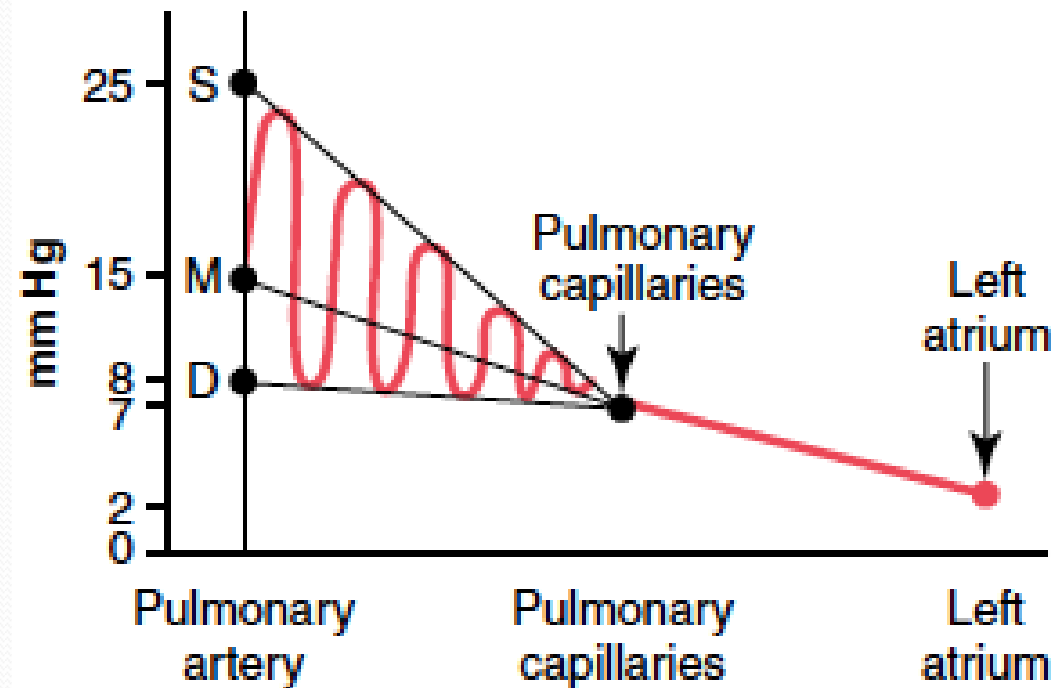
Pressure in the Pulmonary circulation

- During systole, the pressure in the pulmonary artery is essentially equal to the pressure in the right ventricle. However, after the pulmonary valve closes at the end of systole, the ventricular pressure falls precipitously whereas the pulmonary arterial pressure falls more slowly as blood flows through the capillaries of the lungs



Pressure in the Pulmonary circulation

- The average systolic pulmonary arterial pressure is about 25 mm Hg, the diastolic pulmonary arterial pressure is about 8 mm Hg, and the mean pulmonary arterial pressure is 15 mm Hg
- The mean pulmonary capillary pressure is about 7 mm Hg. The mean pressure in the left atrium and the major pulmonary veins averages about 2 mm Hg in the recumbent human being, varying from as low as 1 mm Hg to as high as 5 mm Hg.



Blood volume of the lung

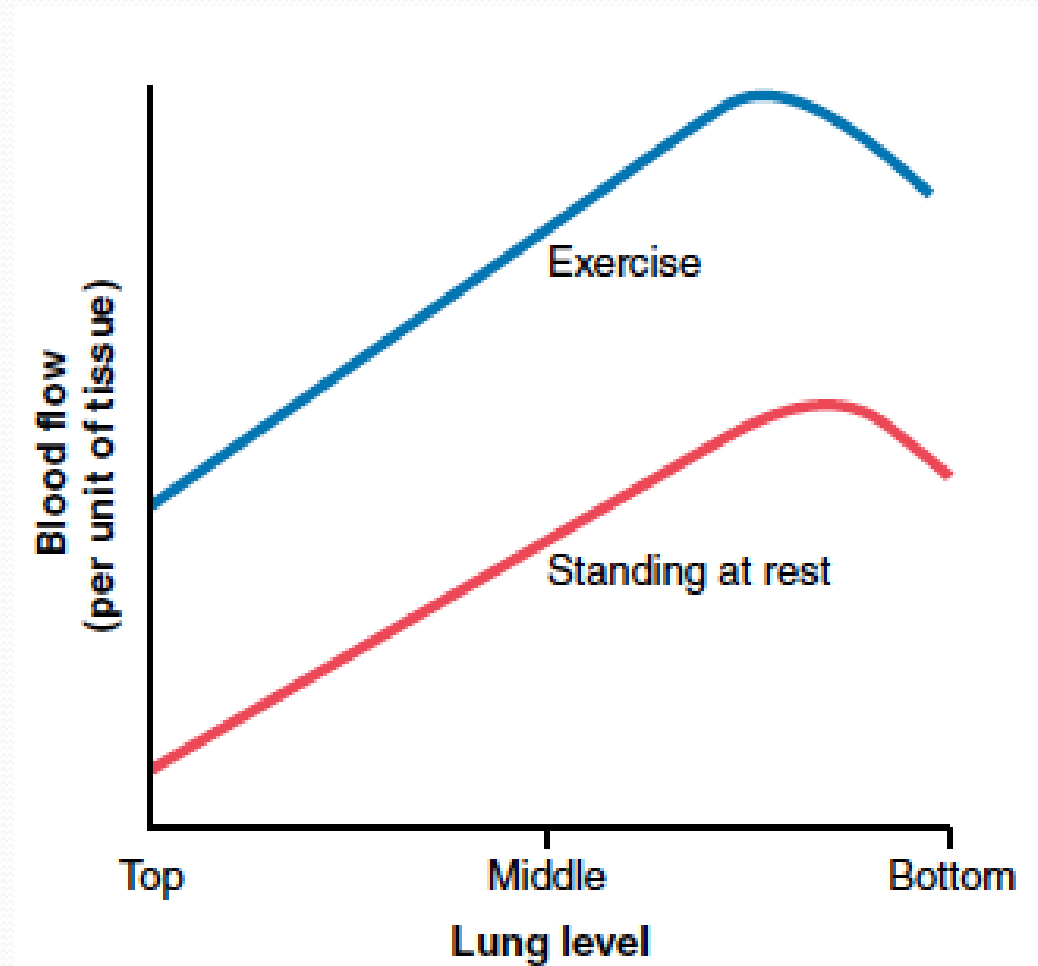
- The blood volume of the lungs (450 milliliters) is about 9 % of the total blood volume of the entire circulatory system.
- The pulmonary capillaries have approximately 70 milliliters of this pulmonary blood volume, the rest is divided about equally between the pulmonary arteries and the veins.
- The blood volume of the lung is variable??

Factors that affect pulmonary blood flow

1. Factors that affect cardiac output
 1. Alveolar oxygen level: if the alveolar oxygen level decreases below normal, especially if less than 70% of normal, this cause vasoconstriction of the adjacent blood vessels.. What is the important of this effect in the lung?
 1. Effect of hydrostatic pressure (pressure caused by the weight of the blood itself in the blood vessels, gravitational effects) on regional pulmonary blood flow.

Factors that affect pulmonary blood flow

Effect of hydrostatic pressure (pressure caused by the weight of the blood itself in the blood vessels) on regional pulmonary blood flow.



Factors that affect pulmonary blood flow

Zones 1, 2, and 3 of pulmonary blood flow

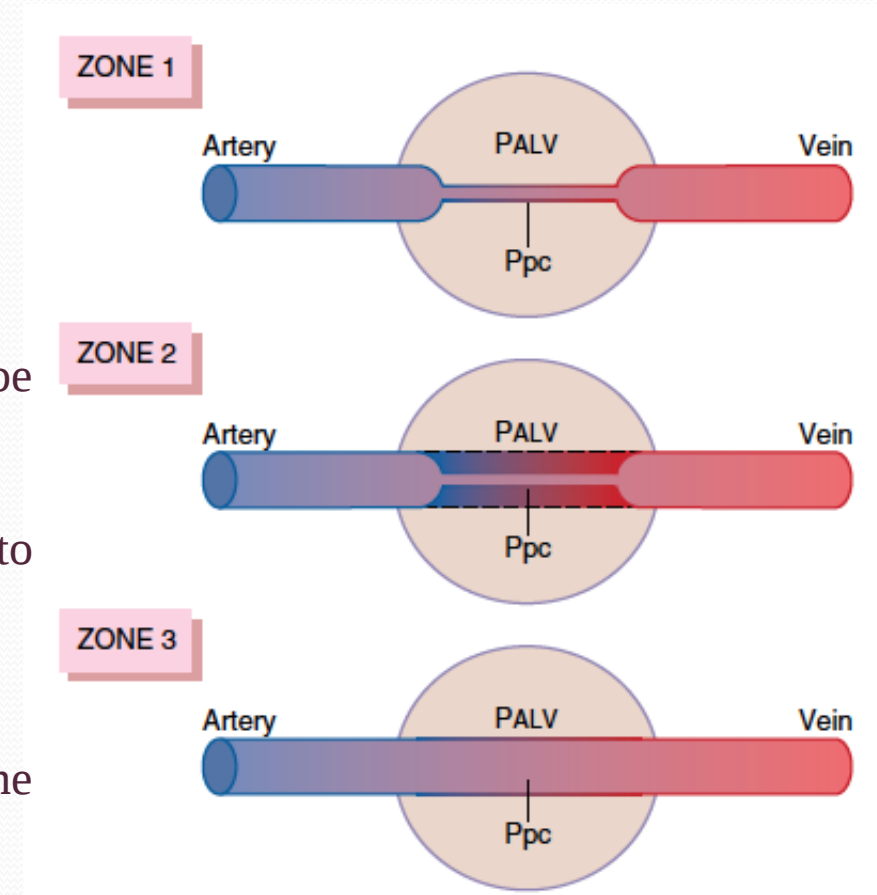
The capillaries in the alveolar walls are under the influence of two force:

1. The blood pressure inside that distend them
2. The alveolar air pressure that compressed them

Zone 1 No blood flow during all portions of the cardiac cycle (zone 1 can be considered as a part of physiological dead space)

Zone 2 (about 10 cm above the midlevel of the heart and extends from there to the top of the lungs): intermittent blood flow

Zone 3 (about 10 cm above the level of the heart all the way to the bottom of the lungs) Continuous blood flow



Factors that affect pulmonary blood flow

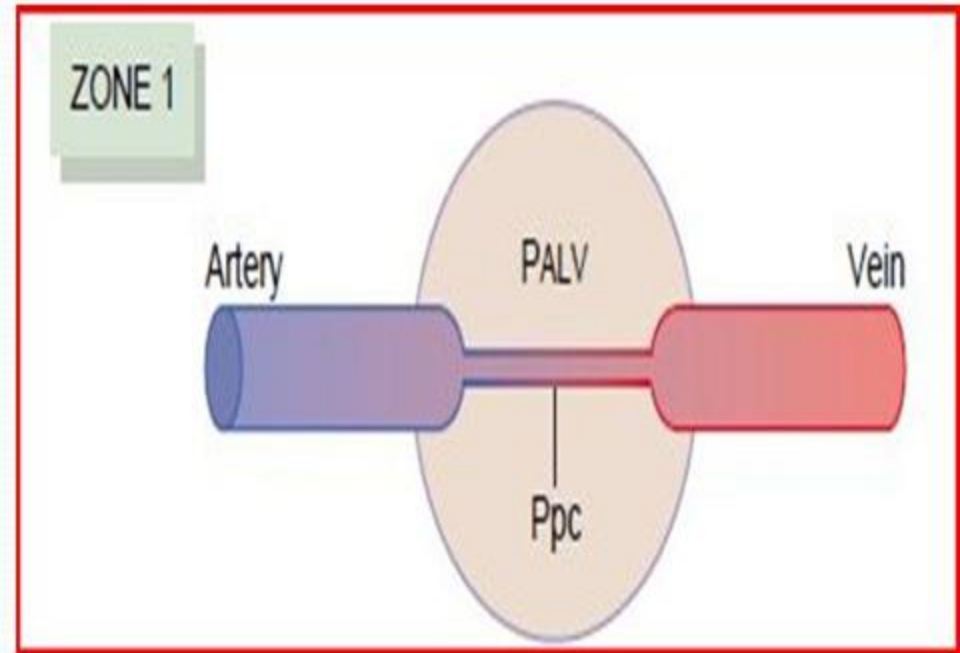
Zones 1, 2, and 3 of pulmonary blood flow

Zone 1 occurs only under abnormal condition:

Raised alveolar pressure above

Decreased pulmonary systolic arterial pressure
as after severe blood loss

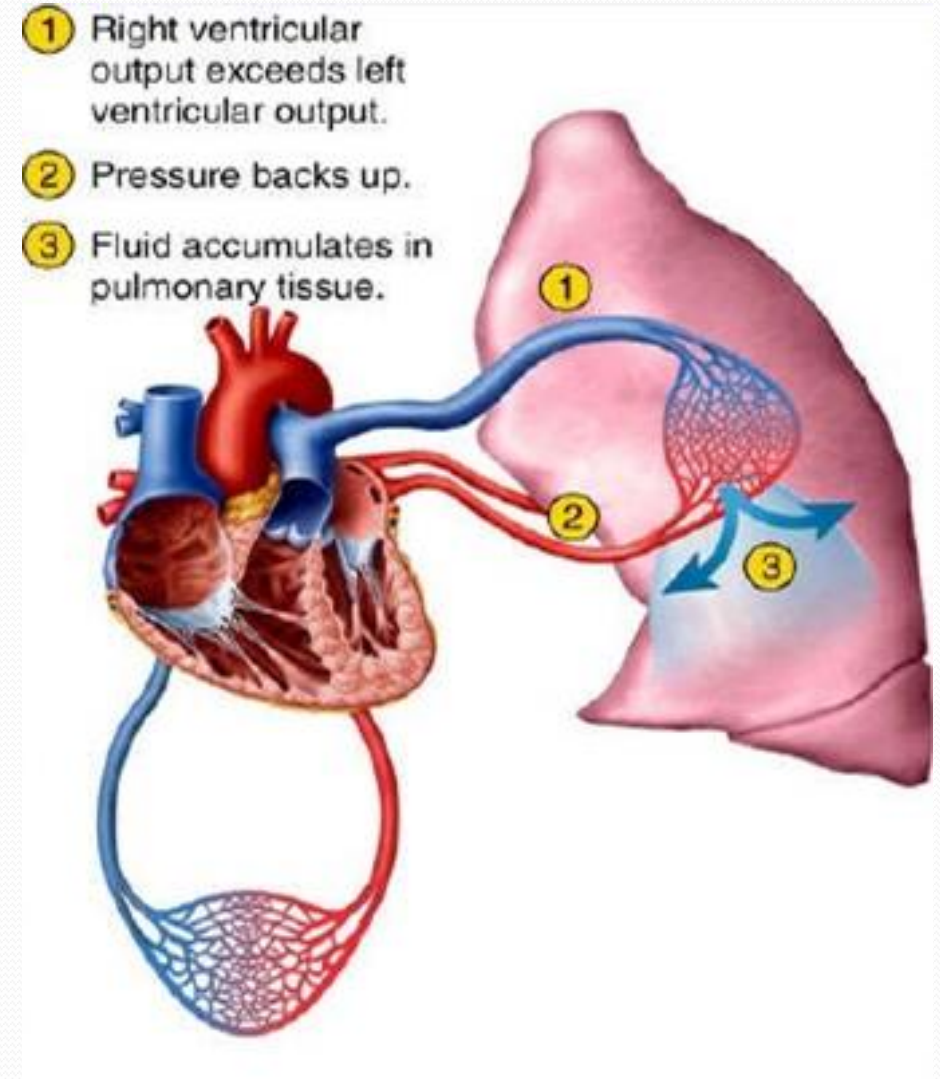
During exercise: the slight increased in the
pulmonary vascular pressures change zone 2
into a zone 3.



Factors that affect pulmonary blood flow

Effects of left sided heart failure on the pulmonary circulation:

- raising the left atrial pressure above 7 mm Hg will cause almost equal increases in pulmonary arterial pressure, and this will increase the load on the right heart, and pulmonary edema due to increased capillary pressure



Pulmonary capillary dynamics

- The capillary blood flows in the alveolar walls are described as a sheet of flow, rather than flow in individual capillaries
- The pulmonary capillary pressure is 7 mm Hg
- In normal cardiac output, blood needs 0.8 seconds to pass through the pulmonary capillaries.
- If the cardiac output increased, the above time decreases to 0.3 seconds, **why?**
- The dynamics of fluid exchange across the lung capillary membranes are qualitatively the same but quantitatively different from that for peripheral tissues.

Pulmonary capillary dynamics

The difference between the pulmonary and peripheral capillary dynamics:

1. The pulmonary capillary pressure (7 mm Hg) is lower than the peripheral capillary pressure (17 mm Hg).
1. Lung interstitial fluid pressure is slightly more negative than interstitial pressure in the peripheral subcutaneous tissue.
3. Pulmonary capillaries are relatively leaky to protein molecules, thus the colloid osmotic pressure of the pulmonary interstitial fluid is about 14 mm Hg (8 mmHg in the interstitial of the systemic circulation)
4. The alveolar walls are extremely thin, and the alveolar epithelium covering the alveolar surfaces is so weak that it can be ruptured by any positive pressure in the interstitial spaces greater than alveolar air pressure (>0 mm Hg), which allows dumping of fluid from the interstitial spaces into the alveoli.

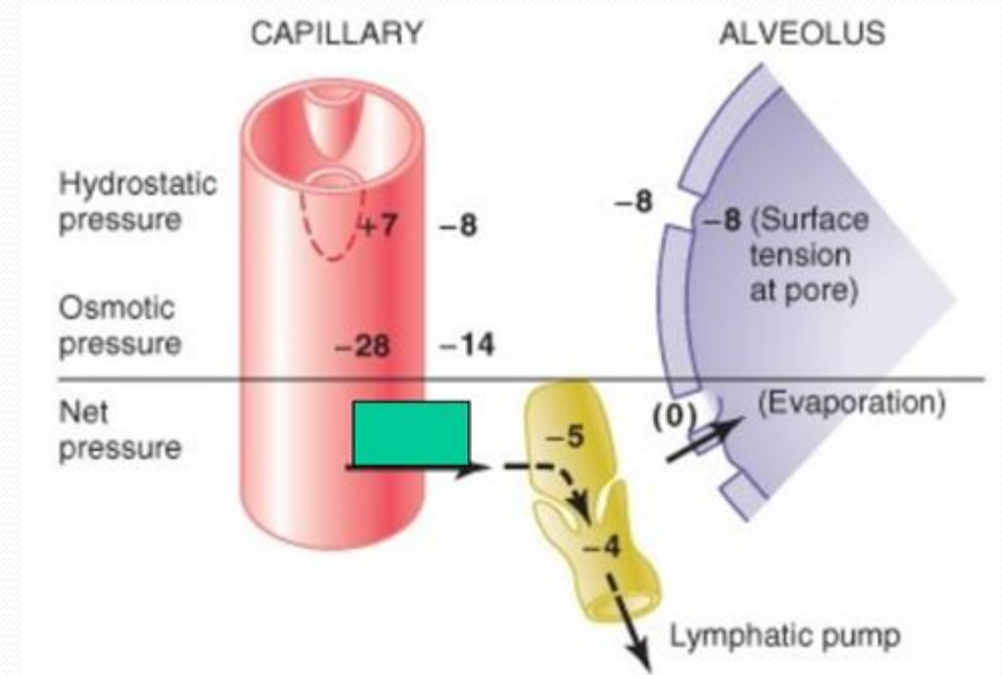
Pulmonary capillary dynamics

	mm Hg
<i>Forces tending to cause movement of fluid outward from the capillaries and into the pulmonary interstitium:</i>	
Capillary pressure	7
Interstitial fluid colloid osmotic pressure	14
Negative interstitial fluid pressure	<u>8</u>
TOTAL OUTWARD FORCE	29
<i>Forces tending to cause absorption of fluid into the capillaries:</i>	
Plasma colloid osmotic pressure	<u>28</u>
TOTAL INWARD FORCE	28

Forces that determine the net movement across the pulmonary capillaries

Pulmonary capillary dynamics

- There is a filtration pressure that causes a slight continual flow of fluid from the pulmonary capillaries into the interstitial spaces
- What prevents the leaking out of the interstitial spaces into the alveoli, since large protein molecules, water, and electrolytes can pass through the opening between the alveolar epithelium?
- The alveoli are kept “dry,” except for a small amount of fluid that seeps from the epithelium onto the lining surfaces of the alveoli to keep them moist
- Negative pulmonary interstitial pressure and lymphatic system



Pulmonary capillary dynamics

Pulmonary edema:

- Accumulation of fluid in the lung interstitial spaces and alveoli
- Can be caused by any factor that increases fluid filtration out of the pulmonary capillaries or that block the pulmonary lymphatic function and causes the pulmonary interstitial fluid pressure to rise from the negative range into the positive range
- **Examples??**
- Safety factor for the development of pulmonary edema: the pulmonary capillary pressure normally must rise to a value at least equal to the colloid osmotic pressure of the plasma inside the capillaries before significant pulmonary edema will occur. (28)
- **Safety factor in acute and chronic conditions????**

Fluid in the pleural cavity

- The pleural space is a potential space between the parietal and visceral pleurae,
- Pleural fluid is a thin layer of mucoid fluid that fills the pleural space to facilitate the sliding back and forth of the lungs during inspiration and expiration.
- Due to porous nature of the pleural membrane, continuous transudation of small amounts of interstitial fluid into the pleural space occurs, carrying with the fluid tissue proteins, and that gives the pleural fluid a mucoid characteristic
- Lymphatic system is responsible for pumping away any excess fluid in the pleural cavity, and for the negative pressure inside the pleural cavity (about -7 mm Hg) which is important to prevent lung collapse.

Fluid in the pleural cavity

Pleural effusion:

- Accumulation of large amounts of free fluid in the pleural space.
- Possible causes
 1. blockage of lymphatic drainage from the pleural cavity
 2. excessive transudation of fluid into the pleural cavity due to cardiac failure, which causes excessively high peripheral and pulmonary capillary pressures
 3. greatly reduced plasma colloid osmotic pressure, thus allowing excessive transudation of fluid
 4. infection or any other cause of inflammation of the surfaces of the pleural cavity, which breaks down the capillary membranes and allows rapid dumping of both plasma proteins and fluid into the cavity.

Gas exchange

- Diffusion: random motion of molecules in all directions through the respiratory membrane and adjacent fluids.
- Concentration gradient
- Partial pressure of a gas in a mixture of gases: it depends on both its concentration and its solubility coefficient. The more the gas is dissolved in water, the less its partial pressure

$$\text{Partial pressure} = \frac{\text{Concentration of dissolved gas}}{\text{Solubility coefficient}}$$

When partial pressure is expressed in atmospheres (1 atmosphere pressure equals 760mm Hg) and concentration is expressed in volume of gas dissolved in each volume of water, the solubility coefficients for important respiratory gases at body temperature are the following:

Oxygen	0.024
Carbon dioxide	0.57
Carbon monoxide	0.018
Nitrogen	0.012
Helium	0.008

Gas exchange

- Diffusion of gases between the gas phase in the alveoli and the dissolved phase in the pulmonary blood
- The net diffusion is determined by the difference between the two partial pressure
- Vapor pressure of water = 47 mm Hg, it is the partial pressure that the water molecules exert to escape through the surface (evaporate) to humidify air
- The net rate of diffusion of a gas in fluid is determined by :
 1. The pressure difference
 2. The solubility of the gas in the fluid
 3. The cross-sectional area of the fluid
 4. The distance through which the gas must diffuse
 5. The molecular weight of the gas
 6. The temperature of the fluid (this remains reasonably constant and usually need not be considered)

Gas exchange

$$D \propto \frac{\Delta P \times A \times S}{d \times \sqrt{MW}}$$

D: diffusion rate

ΔP : the partial pressure difference between the two ends of the diffusion pathway

A: the cross-sectional area of the pathway

S: the solubility of the gas

d: the distance of diffusion

MW: The molecular weight of the gas

Gas exchange

- -The diffusion coefficient of the gas is proportional to S/MW , the relative rates at which different gases at the same partial pressure levels will diffuse are proportional to their diffusion coefficients.

Oxygen	1.0
Carbon dioxide	20.3
Carbon monoxide	0.81
Nitrogen	0.53
Helium	0.95

- Diffusion of gases through tissues: the important gases are highly lipid soluble, so they are highly soluble in cell membranes, so movement through the tissue water is the major factor determining the rate of diffusion through the tissue

Gas exchange

Table 40-1 Partial Pressures of Respiratory Gases (in mm Hg) as They Enter and Leave the Lungs (at Sea Level)

	Atmospheric Air	Humidified Air	Alveolar Air	Expired Air
N ₂	597 (78.62)	563.4 (74.09)	569 (74.9)	566 (74.5)
O ₂	159 (20.84)	149.3 (19.67)	104 (13.6)	120 (15.7)
CO ₂	0.3 (0.04)	0.3 (0.04)	40 (5.3)	27 (3.6)
H ₂ O	3.7 (0.50)	47 (6.20)	47 (6.2)	47 (6.2)
Total	760 (100)	760 (100)	760 (100)	760 (100)

Compositions of alveolar air and atmospheric air are different

Gas exchange

Rate at which alveolar air is renewed by atmospheric air

Multiple breaths are required to exchange most of the alveolar air. This slow replacement of alveolar air is important to prevent sudden changes in blood gas concentration, so respiratory control will be stable, and prevent the occurrence of excessive increase or decrease in O_2 , CO_2 concentration and PH if respiration is temporarily interrupted

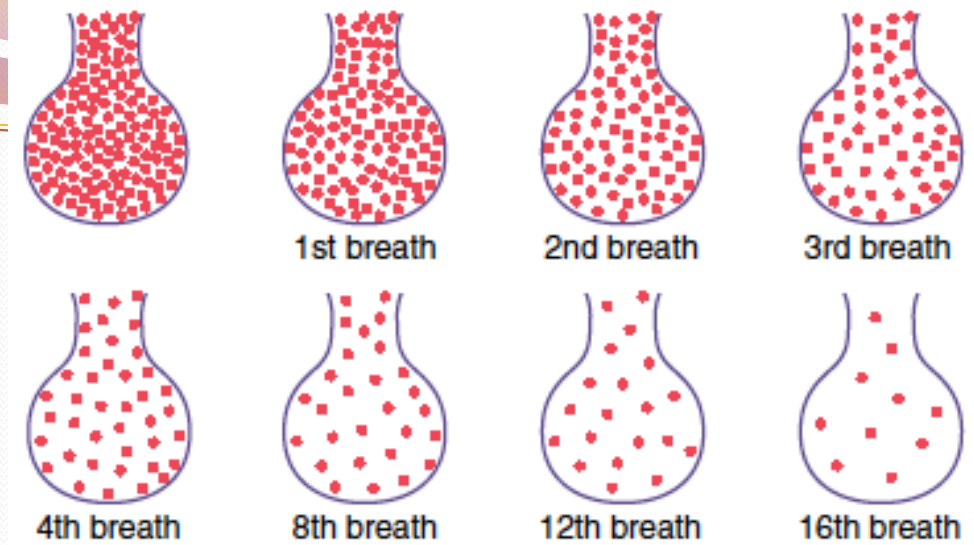


Figure 39-2 Expiration of a gas from an alveolus with successive breaths.

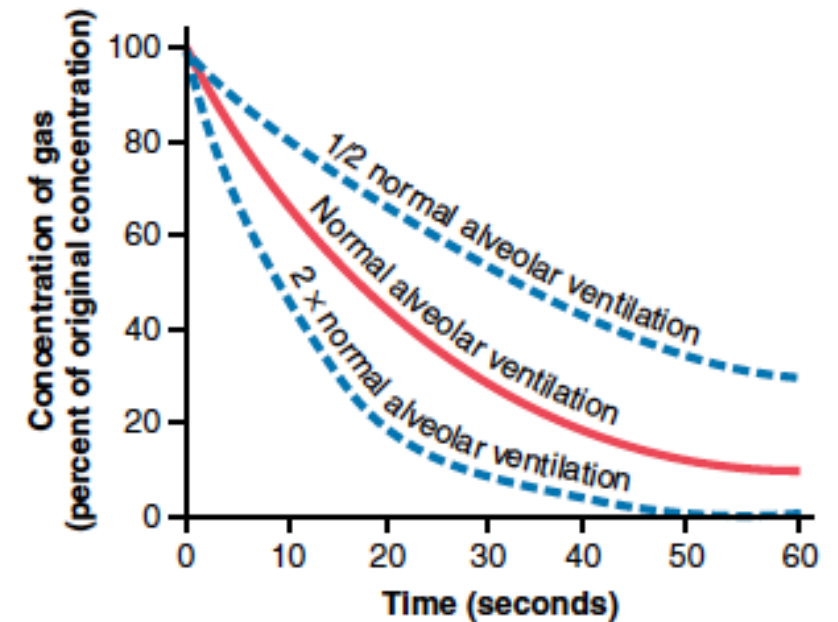


Figure 39-3 Rate of removal of excess gas from alveoli.

Gas exchange

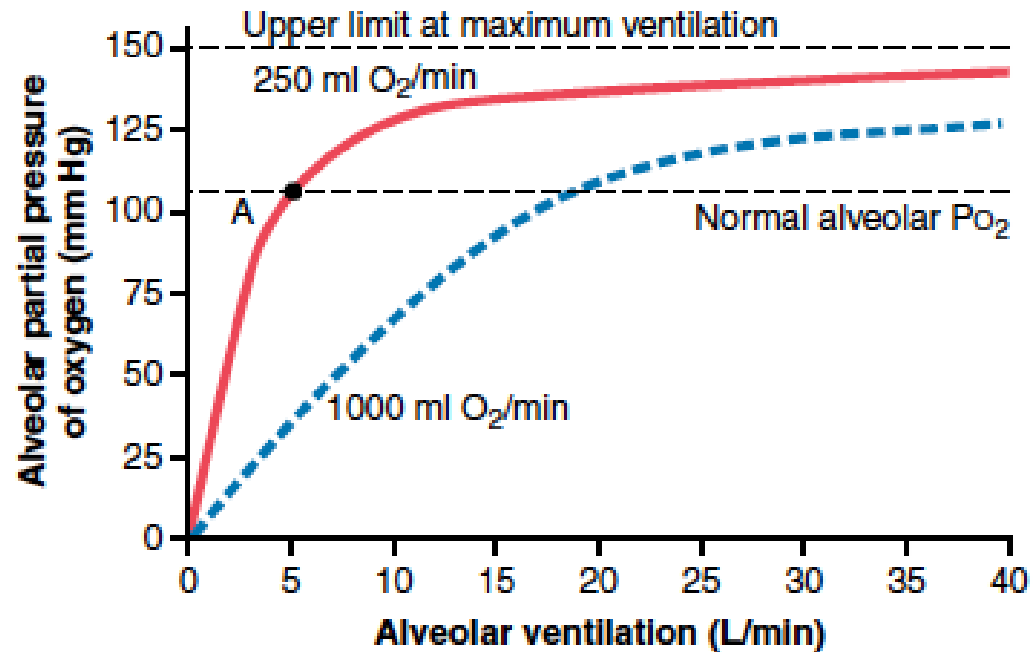


Figure 39-4 Effect of alveolar ventilation on the alveolar P_{O_2} at two rates of oxygen absorption from the alveoli—250 ml/min and 1000 ml/min. *Point A* is the normal operating point.

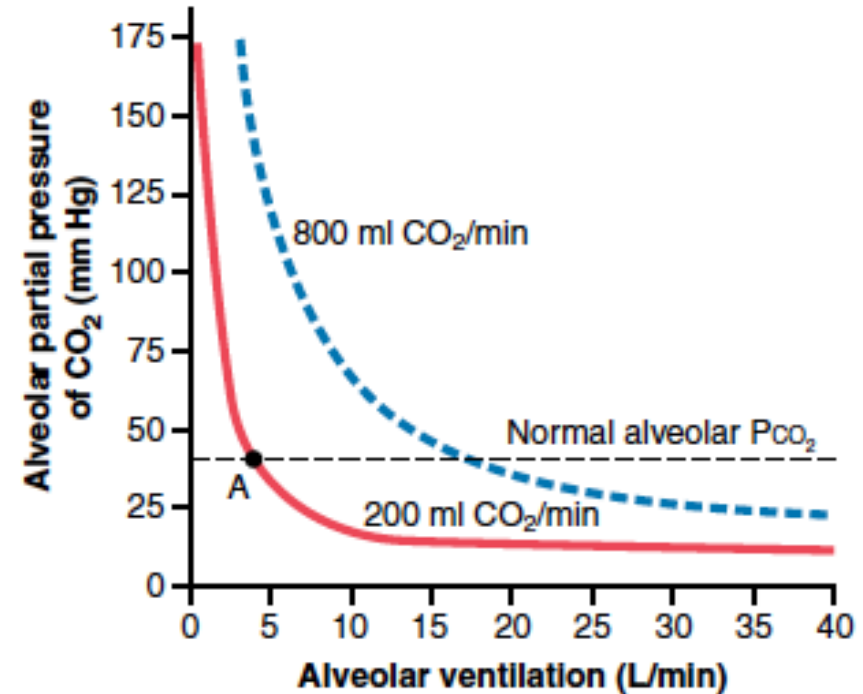
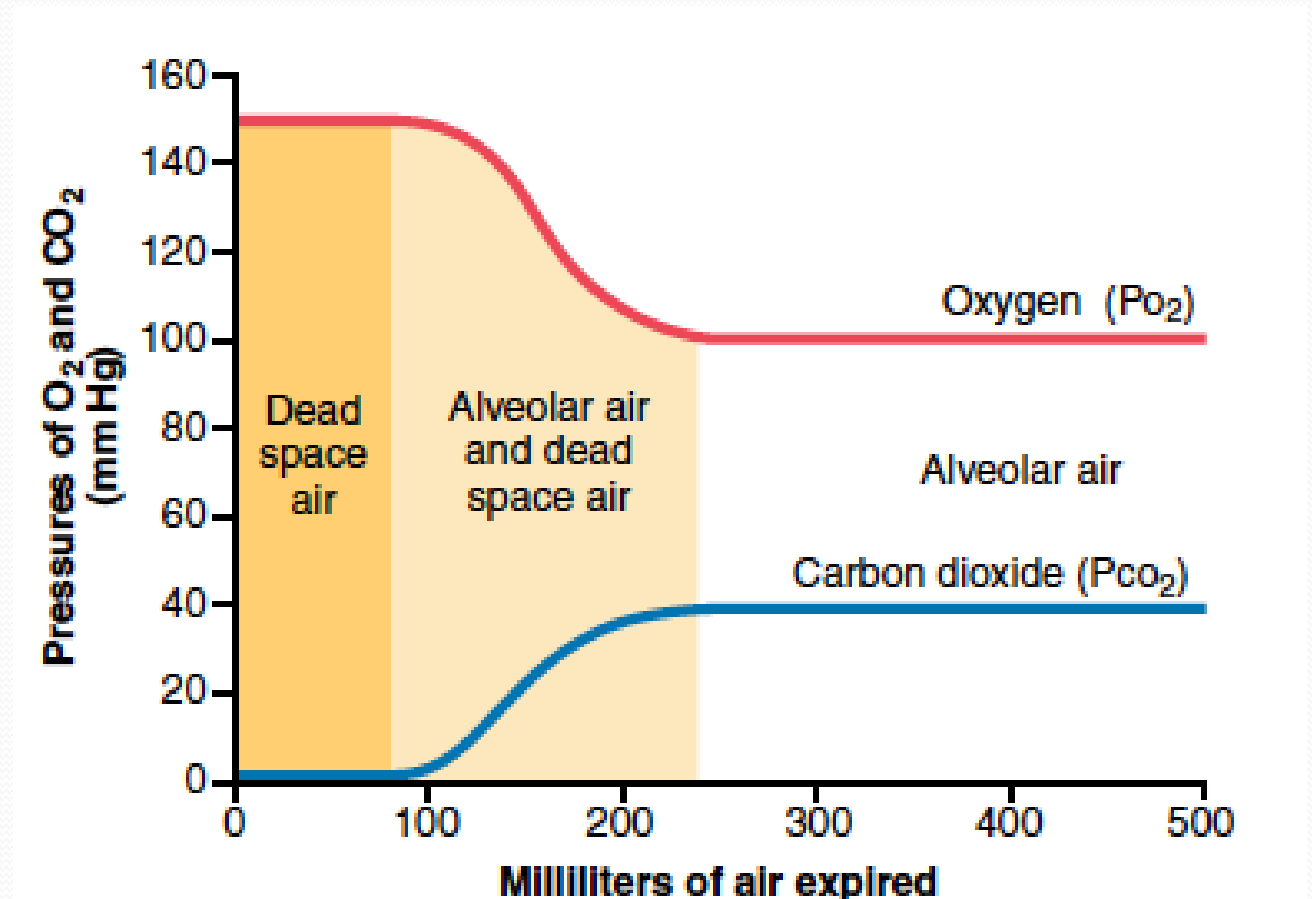


Figure 39-5 Effect of alveolar ventilation on the alveolar P_{CO_2} at two rates of carbon dioxide excretion from the blood—800 ml/min and 200 ml/min. *Point A* is the normal operating point.

If the rate of absorption or excretion of the O_2 and CO_2 gases is changed, the alveolar ventilation must be changed in order to maintain their normal values of the alveolar pressure

Gas exchange

- The first portion of the expired air, the dead space air from the respiratory passageways, is typical humidified air.
- Then, progressively more and more alveolar air becomes mixed with the dead space air until all the dead space air has finally been washed out and nothing but alveolar air is expired at the end of expiration.

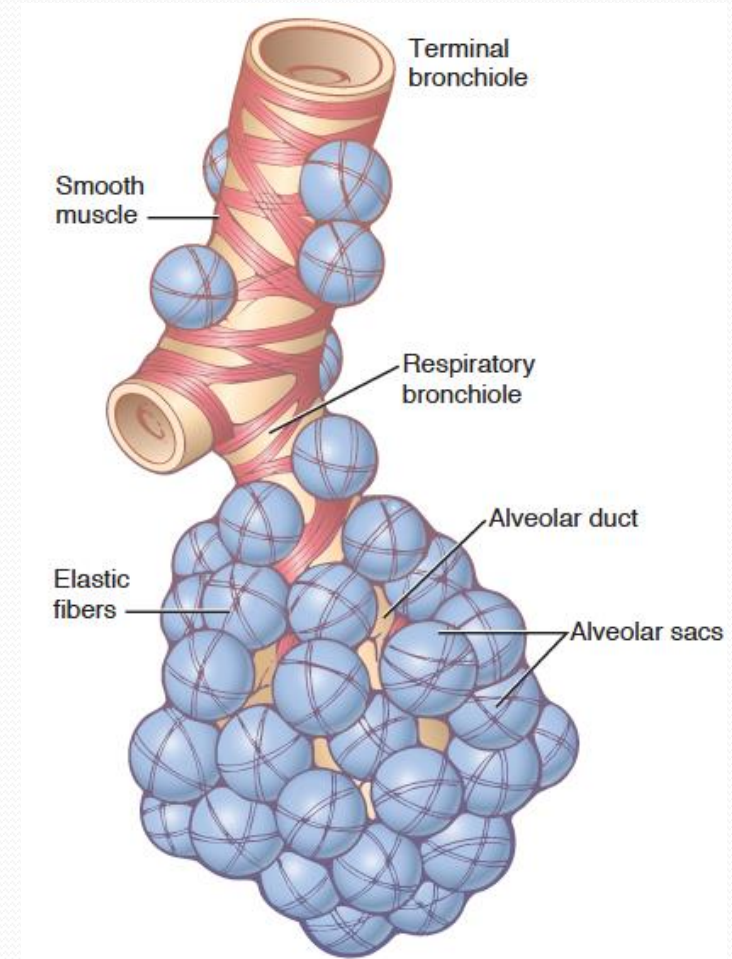


The progressive changes in O_2 and CO_2 partial pressures in the expired air during the course of expiration.

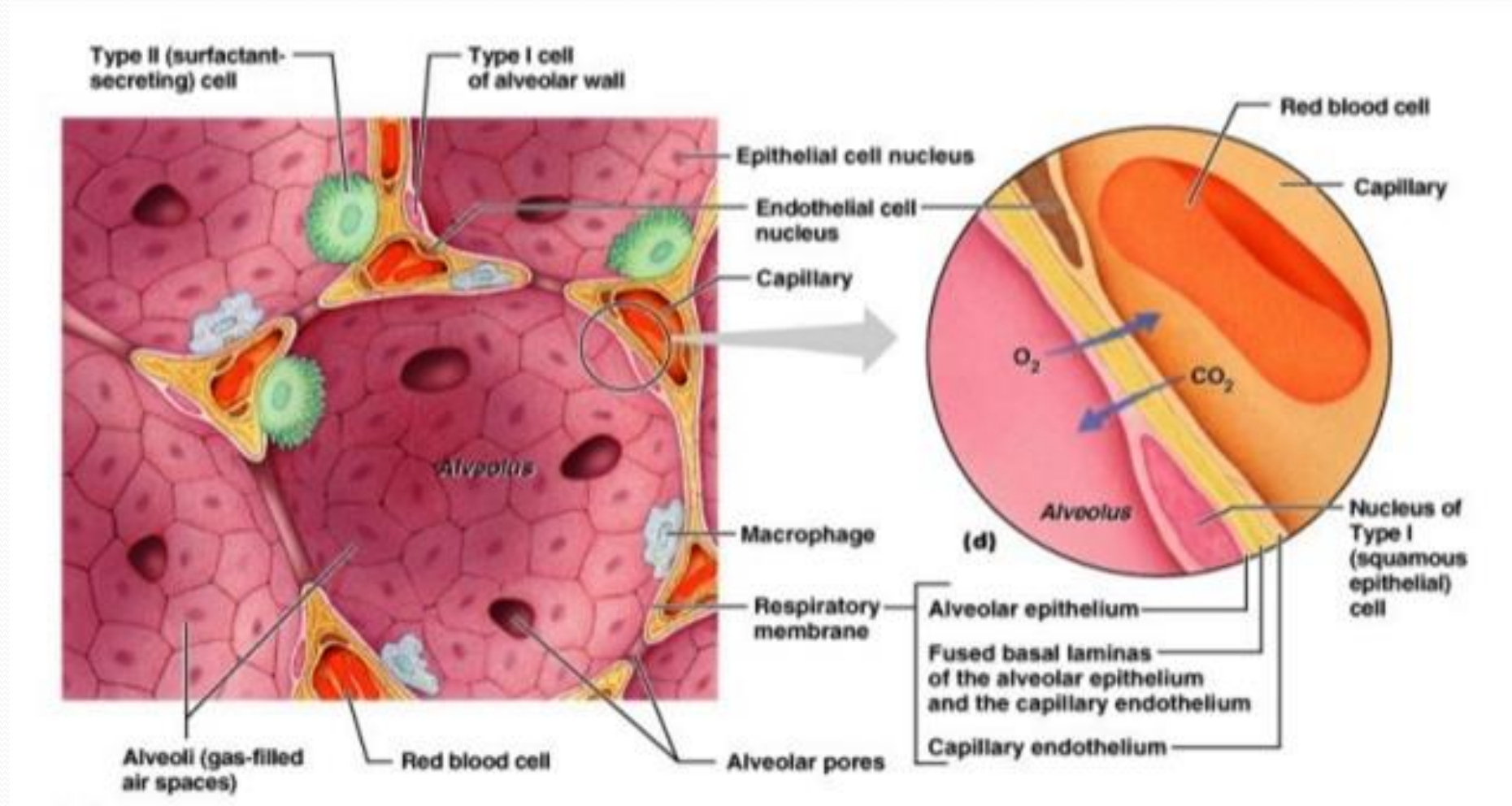
Gas exchange

Diffusion of gases through the respiratory membrane

- Respiratory unit or the respiratory lobule is composed of a respiratory bronchiole, alveolar ducts, atria, and alveoli.
- There are about 300 million alveoli in the two lungs, with average diameter of about 0.2 for each alveolus.
- The alveolar walls are extremely thin, and between the alveoli is an almost solid network of interconnecting capillaries.
- The flow of blood in the alveolar wall has a “sheet” flow characteristics
- Respiratory or pulmonary membrane of the bronchial tree: The membrane of all the terminal portions of the lungs where gas exchanges occur (not only the alveoli)



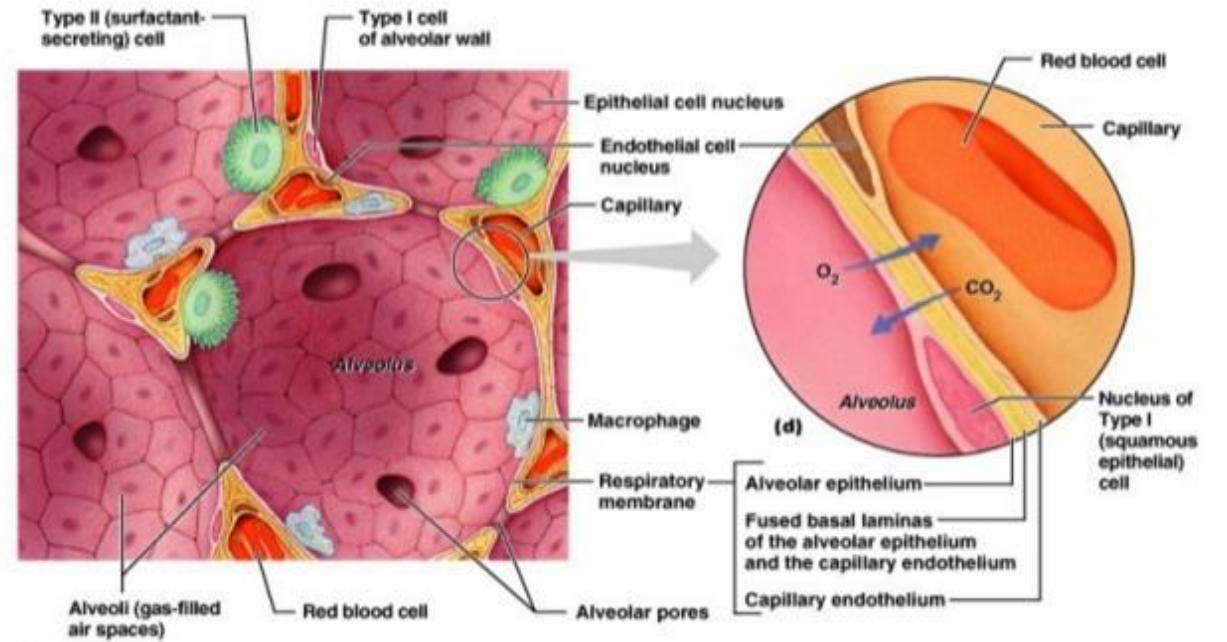
The Respiratory Membrane



The capillary and alveolar walls and their fused basement membranes form the **respiratory membrane**, a 0.6- μm thick blood air barrier that has blood flowing past on one side and gas on the other

The Respiratory Membrane

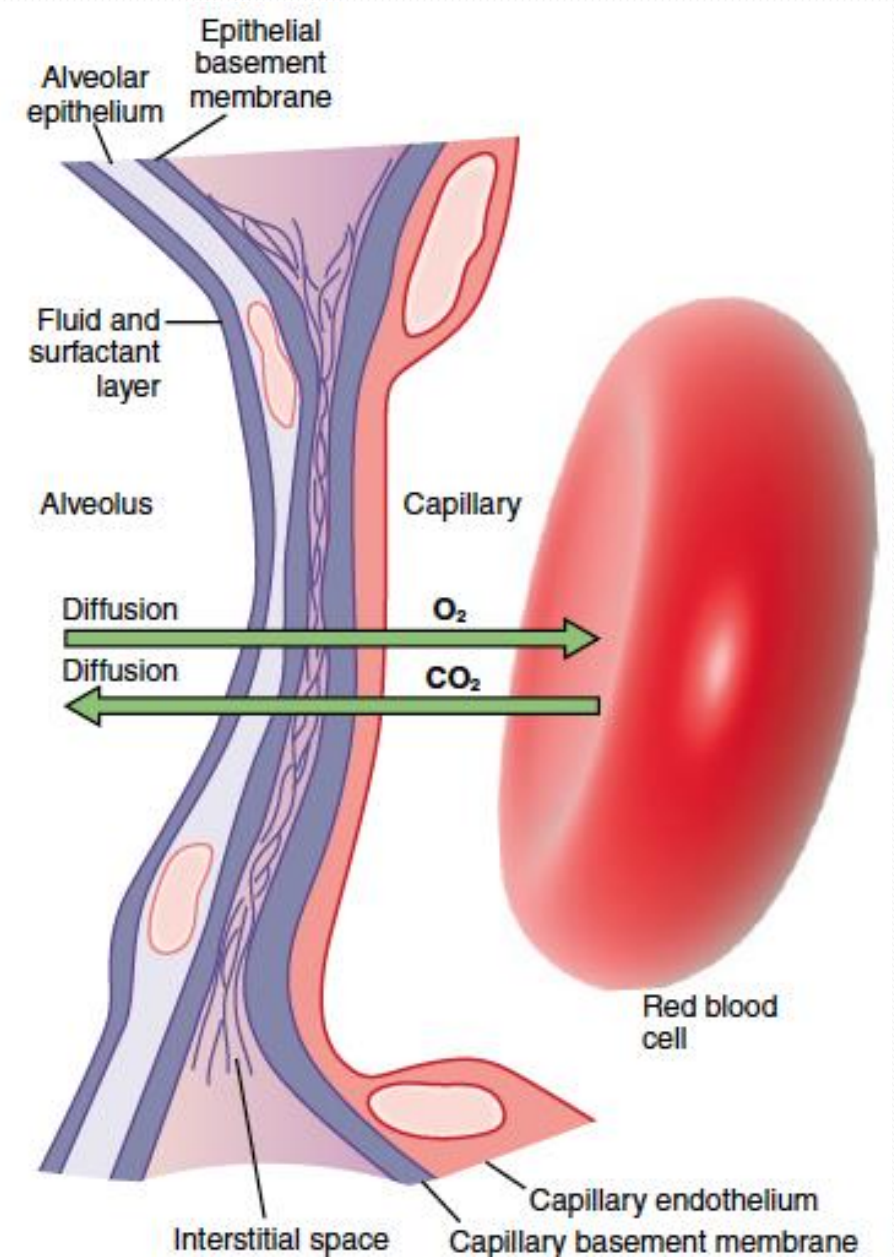
- The walls of the alveoli are composed primarily of a single layer of squamous epithelial cells; *type I alveolar cells*
- Scattered amid the squamous type I alveolar cells are cuboidal type II alveolar cells.
- Type II alveolar cells secrete surfactant and a number of antimicrobial proteins
- Surfactant is a detergent-like substance that coats the gas-exposed alveolar surfaces, preventing alveolar collapse by decreasing the surface tension
- Alveolar macrophages



Gas exchange

The average thickness of the respiratory membrane is about 0.6 micrometer and is composed of the following layers :

1. A layer of fluid lining the alveolus and containing the surfactant
2. The alveolar epithelium composed of thin epithelial cells
3. An epithelial basement membrane
4. A thin interstitial space
5. A capillary basement membrane that in many places fuses with the alveolar epithelial basement membrane
6. The capillary endothelial membrane



Gas exchange

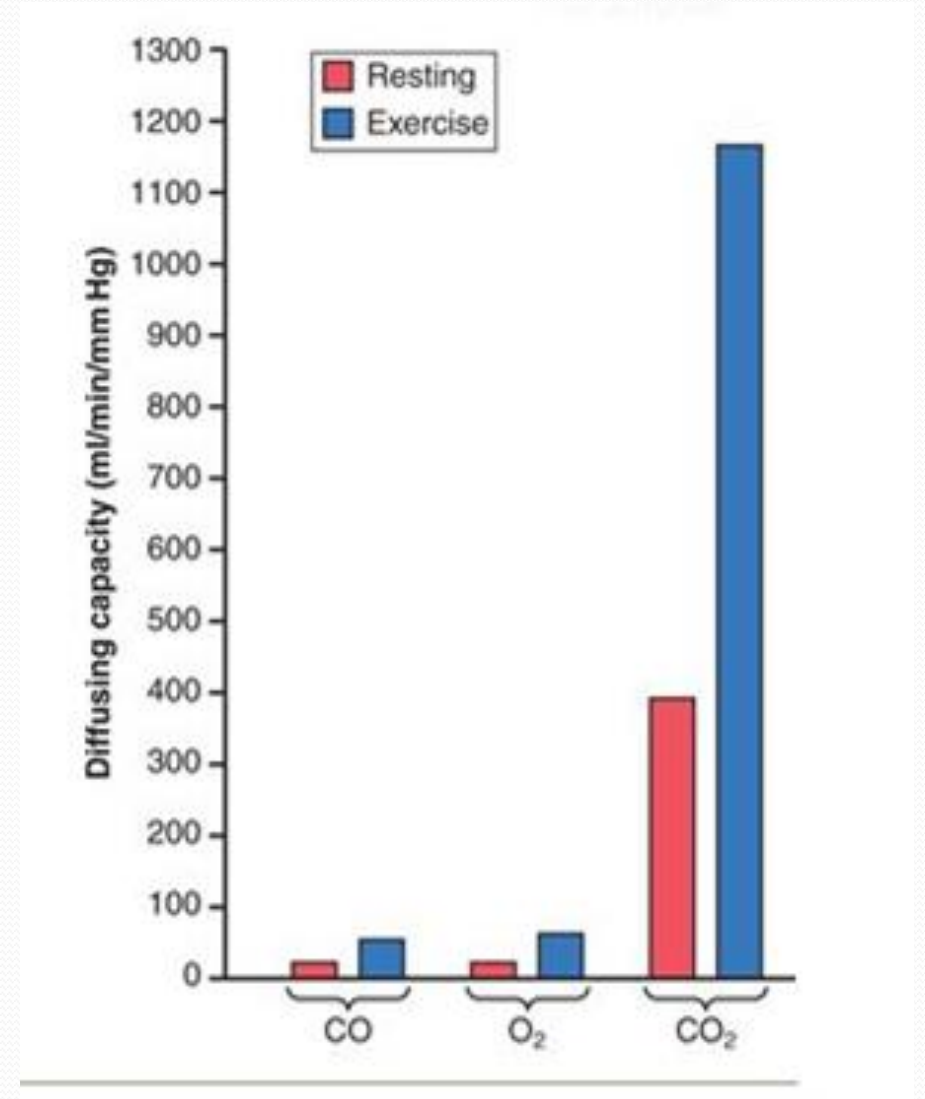
- The exchange of the gas through the respiratory membrane is rapid due to
 - A. Large surface area of the pulmonary capillaries (70 square meters) with small blood volumes
 - B. The diameter of pulmonary capillaries is small, so gases diffuse into RBCs without passing through the plasma.
- Factors that affect the rate of gas diffusion through the respiratory membrane:
 1. the thickness of the membrane. Effects of pulmonary edema and fibrosis?
 2. the surface area of the membrane. Removal of the lung and emphysema?
 3. the diffusion coefficient of the gas in the substance of the membrane
 4. the partial pressure difference of the gas between the two sides of the membrane.

Gas exchange

- The respiratory membrane's diffusing capacity: is the volume of a gas that will diffuse through the membrane each minute for a partial pressure difference of 1 mm Hg. The above mentioned factors affect the diffusion capacity
- Diffusion capacity of O₂ : 21 ml/min/mm Hg, is equal to the rate at which the resting body uses oxygen.
- Increasing the alveolar ventilation or pulmonary blood flow, increases the diffusion capacity of O₂ to 65 ml/min/mm Hg due to opening of pulmonary capillaries or dilation of the already opened one, and better match between ventilation of the alveoli and the perfusion of the alveolar capillaries with blood (ventilation-perfusion ratio)

Gas exchange

- The diffusing capacity for carbon dioxide: The diffusing capacity for carbon dioxide has never been measured.
- It is expected that the diffusing capacity for carbon dioxide under resting conditions is about 400 to 450 ml/min/mm Hg and during exercise of about 1200 to 1300 ml/min/mm Hg.



Gas exchange

Ventilation-perfusion ratio = $\dot{V}_A/\dot{Q}$ alveolar ventilation/blood flow

- If the ventilation and perfusion for the same alveolus is normal: $\dot{V}_A/\dot{Q}$ is normal.
- If the ventilation is zero but normal perfusion, the $\dot{V}_A/\dot{Q}$ is zero.
- If the ventilation is normal but no perfusion, $\dot{V}_A/\dot{Q}$ is infinity.
- In both gases ($\dot{V}_A/\dot{Q}$ is zero or infinity) no gas exchange occurs

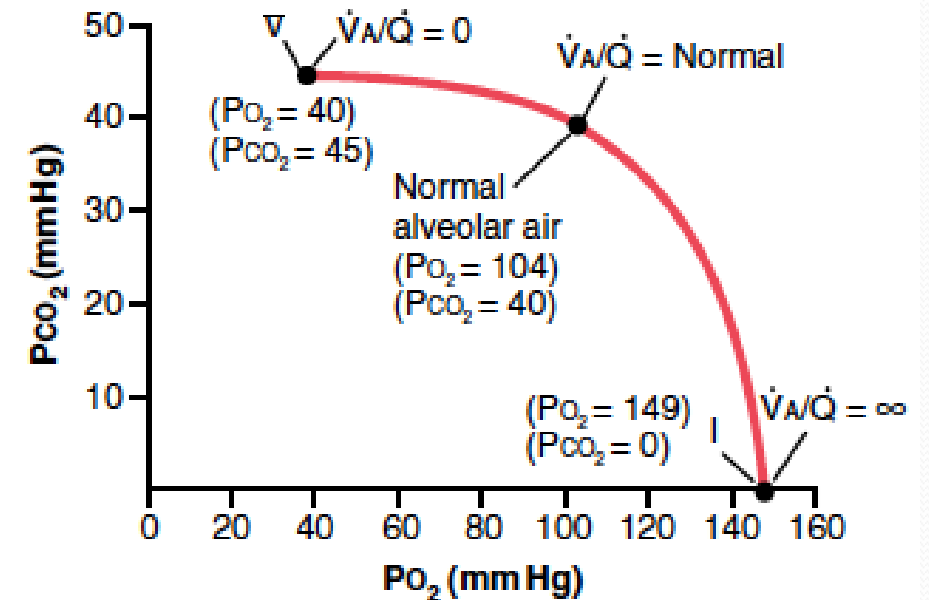


Figure 39-11 Normal P_{O_2} - P_{CO_2} , $\dot{V}_A/\dot{Q}$ diagram.

Gas exchange

Physiologic shunt: VA/Q is below normal

- There is inadequate ventilation to provide the oxygen needed to fully oxygenate the blood flowing through the alveolar capillaries. This means that a certain fraction of the venous blood passing through the pulmonary capillaries does not become oxygenated. This fraction is called shunted blood.
- Blood from the bronchial veins goes directly to pulmonary veins rather than through alveolar capillaries, this accounts for about 2 percent of the cardiac output; this is unoxygenated, shunted blood.
- The physiologic shunt is the total quantitative amount of shunted blood per minute.

Physiologic dead space: VA/Q is above normal, good ventilation but low blood flow. So we said that the ventilation of these alveoli is wasted.

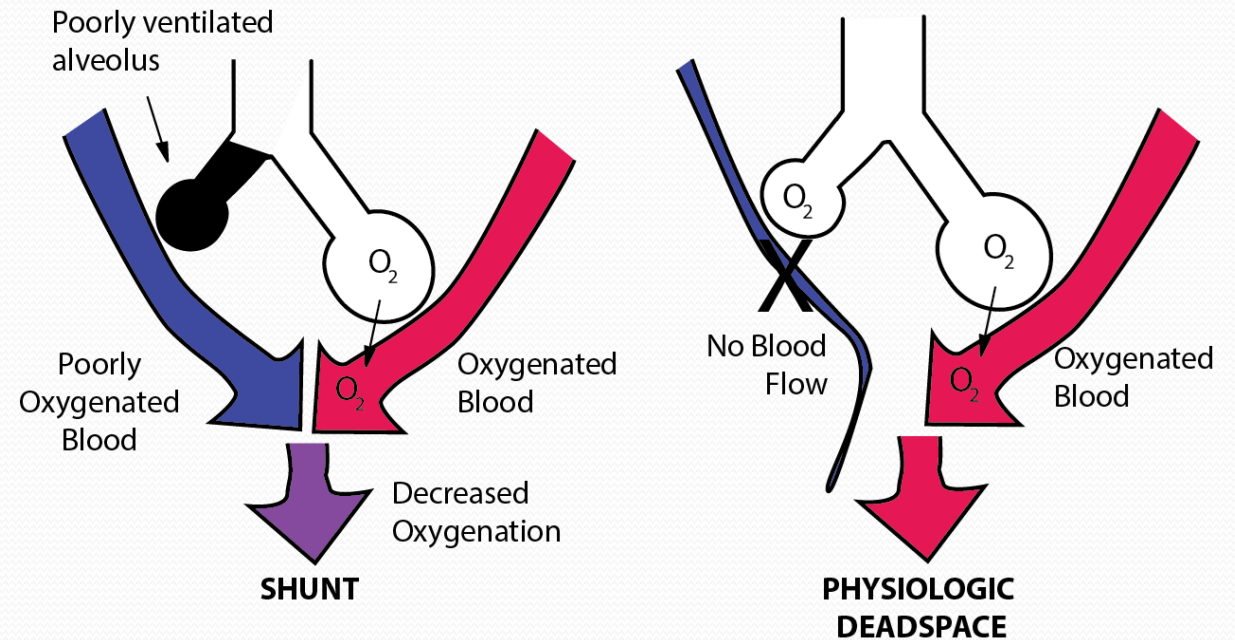
The top of the lung has a moderate degree of physiologic dead space, in lower lung there is a slight shunt

Gas exchange

Emphysema is a complex obstructive and destructive disease of the lungs caused by many years of smoking

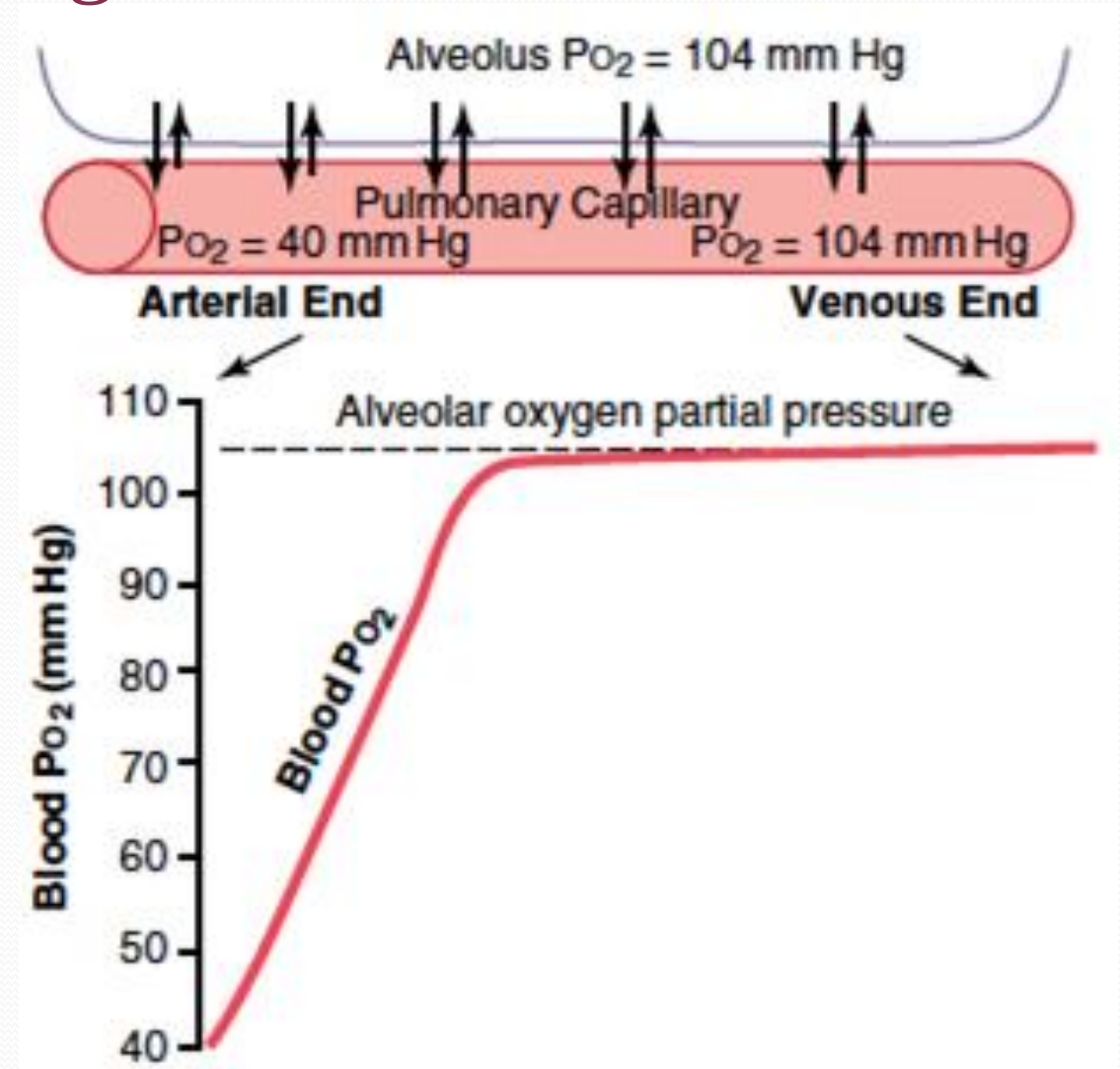
Emphysema cause abnormal VA/Q:

- Obstruction of the small bronchiole causes physiological shunt, since the alveoli beyond the obstructions are unventilated, but has normal perfusion (VA/Q approaches zero).
- The area of the lung where the alveoli are ventilated but the alveolar walls have been mainly destroyed, most of the ventilation is wasted because of inadequate blood flow to transport the blood gases (physiologic dead space).



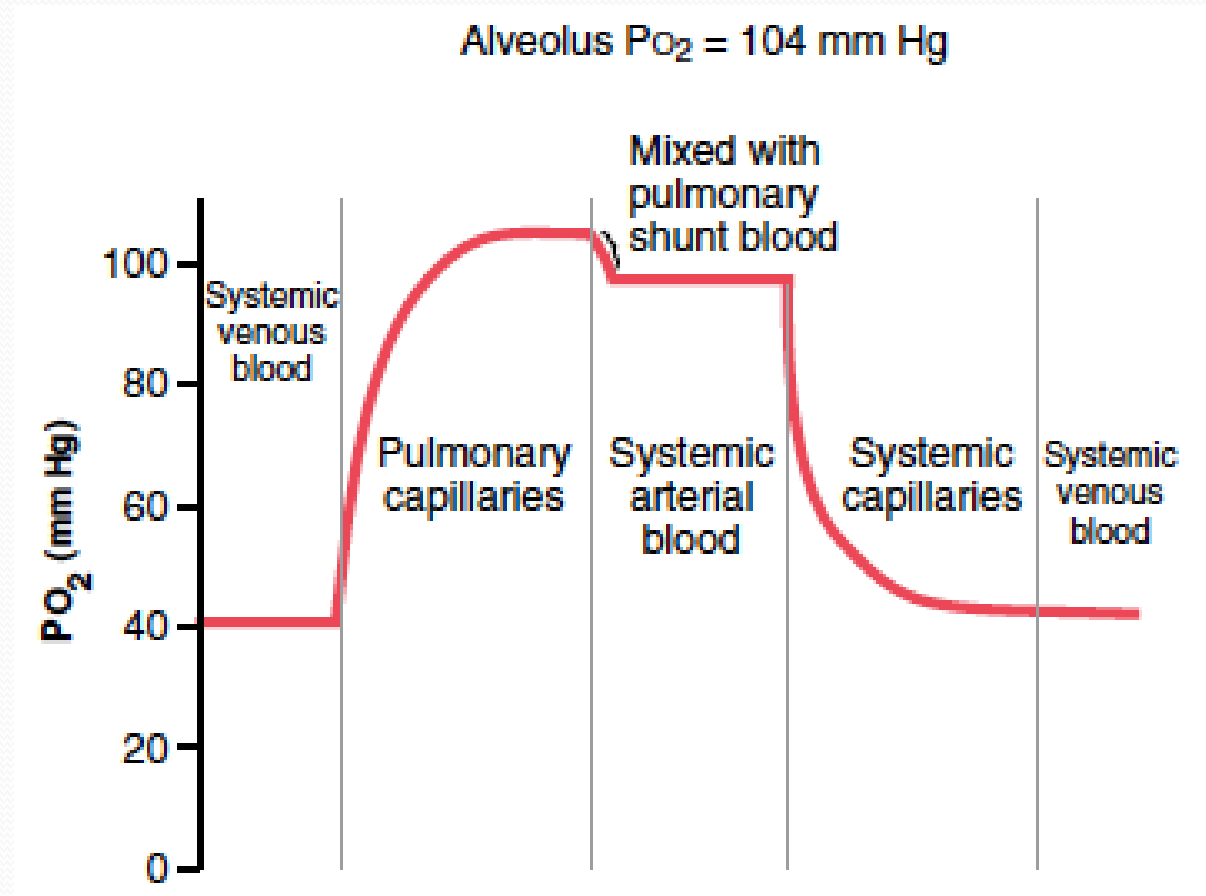
Gas exchange

- The diffusing capacity for O₂ increases almost threefold during exercise; this results mainly from increased surface area of capillaries participating in the diffusion and also from a more nearly ideal ventilation-perfusion ratio in the upper part of the lungs.
- Under non-exercising conditions, the blood becomes almost saturated with O₂ by the time it has passed through one third of the pulmonary capillary, and little additional O₂ normally enters the blood during the latter two thirds of its transit. That is, the blood normally stays in the lung capillaries about three times as long as needed to cause full oxygenation.
- During exercise, the body needs almost 20 times more oxygen



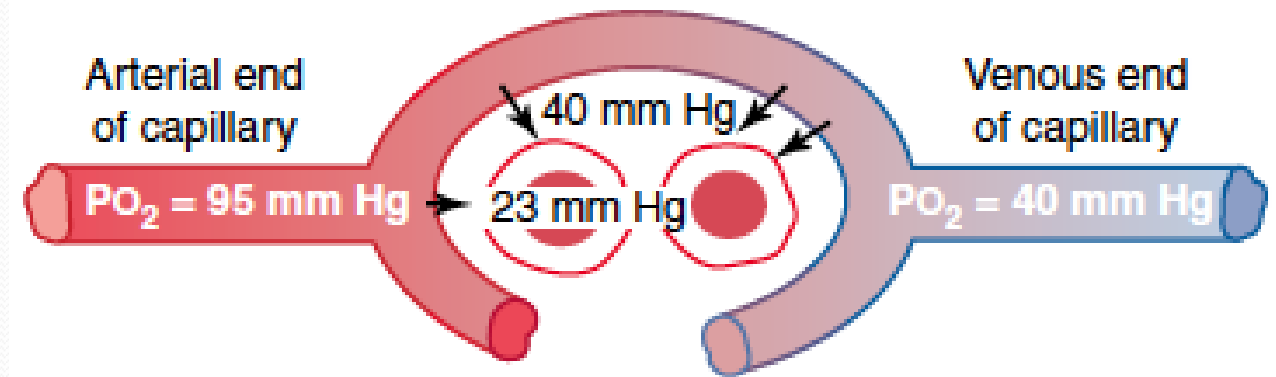
Gas exchange

- About 98 percent of the blood that enters the left atrium from the lungs has just passed through the alveolar capillaries and has become oxygenated up to a PO_2 of about 104 mm Hg.
- Another 2 percent of the blood has passed from the aorta through the bronchial circulation, which supplies mainly the deep tissues of the lungs and is not exposed to lung air.
- Upon leaving the lungs, the PO_2 of the shunt blood is approximately that of normal systemic venous blood—about 40 mm Hg.
- When this blood combines in the pulmonary veins with the oxygenated blood from the alveolar capillaries, this so-called *venous admixture of blood* causes the PO_2 of the blood entering the left heart and pumped into the aorta to fall to about 95 mm Hg.



Gas exchange

- When the arterial blood reaches the peripheral tissues, its PO_2 in the capillaries is still 95 mm Hg. Yet, the PO_2 in the interstitial fluid that surrounds the tissue cells averages only 40 mm Hg.
- There is a large initial pressure difference that causes O_2 to diffuse rapidly from the capillary blood into the tissues—so rapidly that the capillary PO_2 falls almost to equal the 40 mm Hg pressure in the interstitium. Therefore, the PO_2 of the blood leaving the tissue capillaries and entering the systemic veins is also about 40 mm Hg.

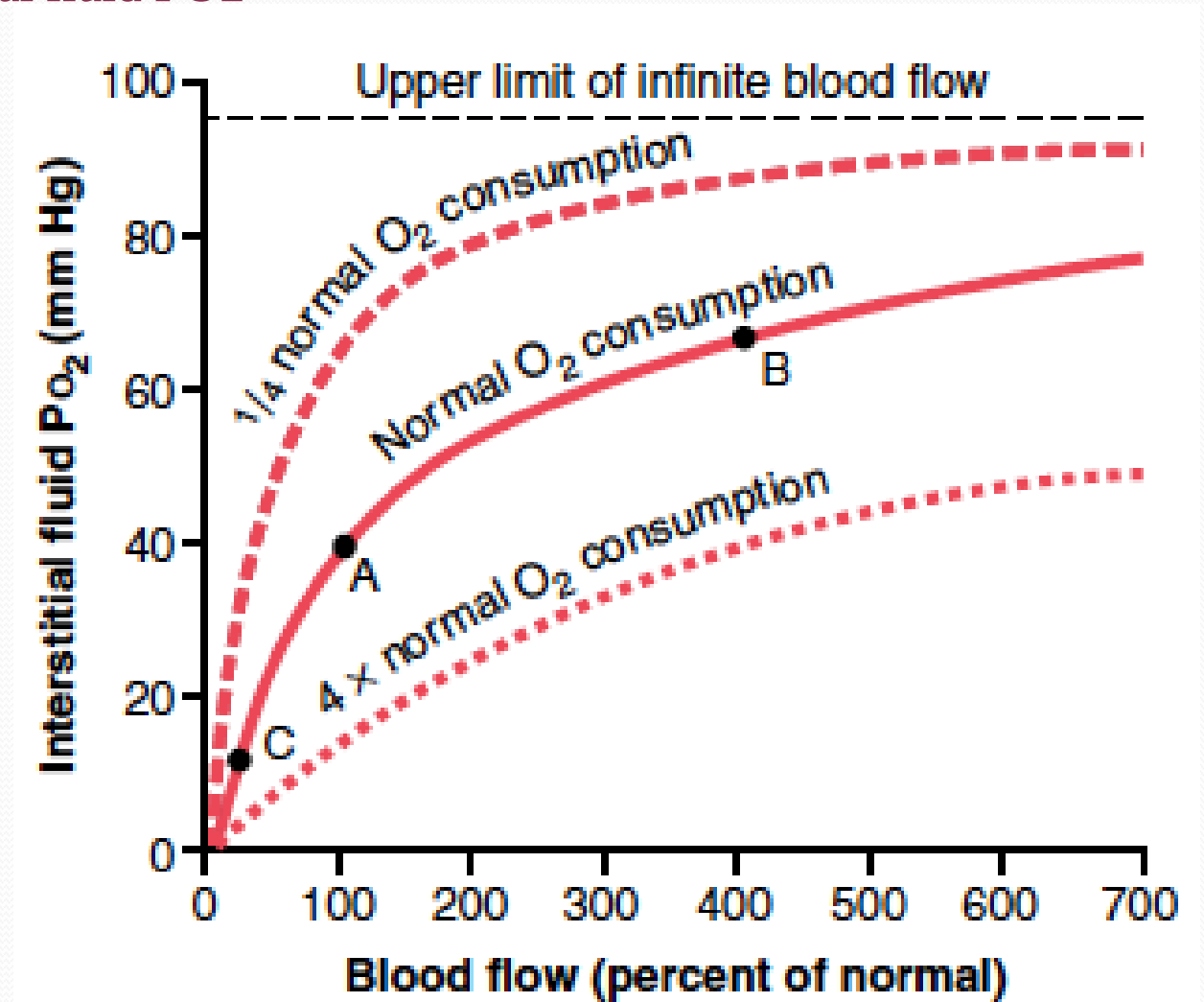


Gas exchange

Effect of rate of blood flow and rate of tissue metabolism on interstitial fluid PO₂

Tissue PO₂ is determined by a balance between:

- (1) the rate of oxygen transport to the tissues in the blood
- (1) the rate at which the oxygen is used by the tissues.



Transport of O₂ in the blood

O₂ is transported in the blood in two forms:

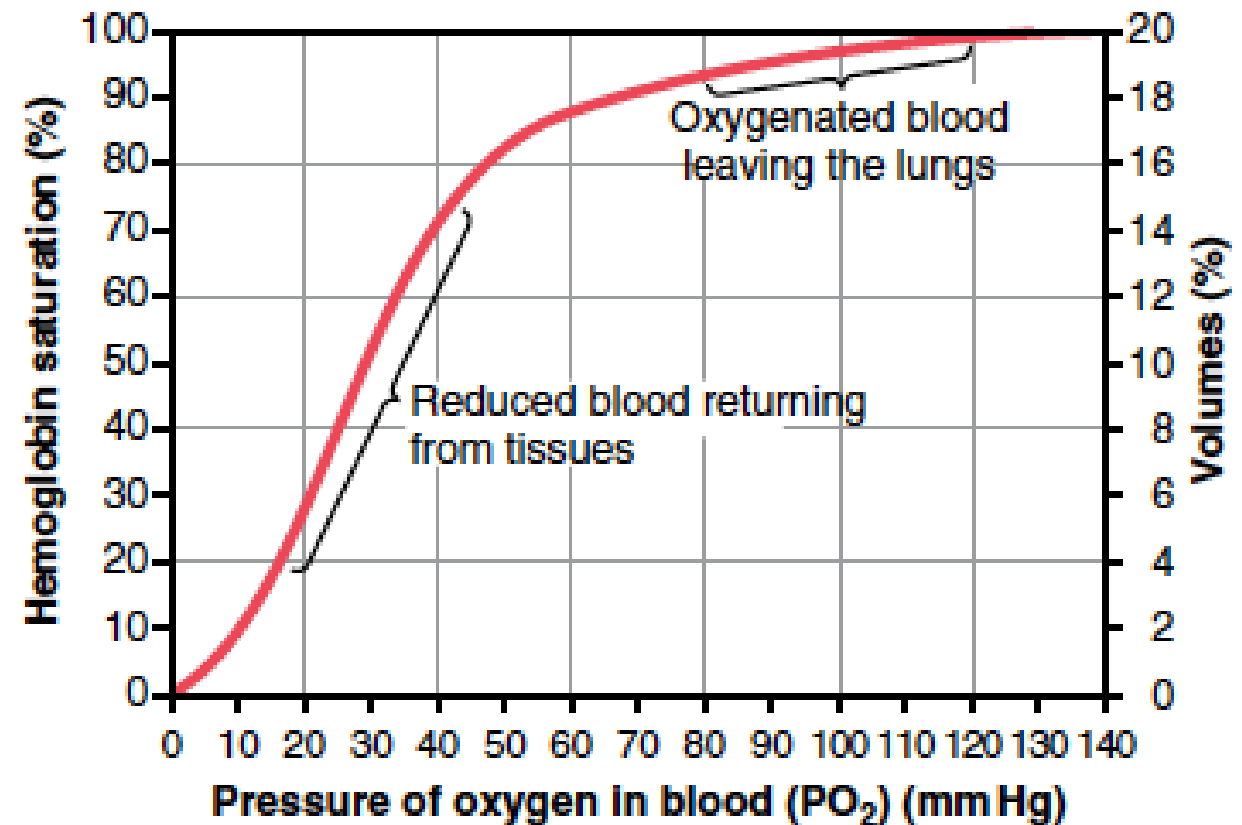
1. In chemical combination with hemoglobin: 97% of oxygen in the blood is carried in this form. The oxygen molecule combines loosely and reversibly with the heme portion of hemoglobin
1. Dissolved in the water of the plasma and blood cells: only 3% is transported in this form

Hemoglobin works as O₂ transporter, and as a tissue oxygen buffer system that stabilizes O₂ pressure in the tissues

Transport of O₂ in the blood

The percent saturation of hemoglobin

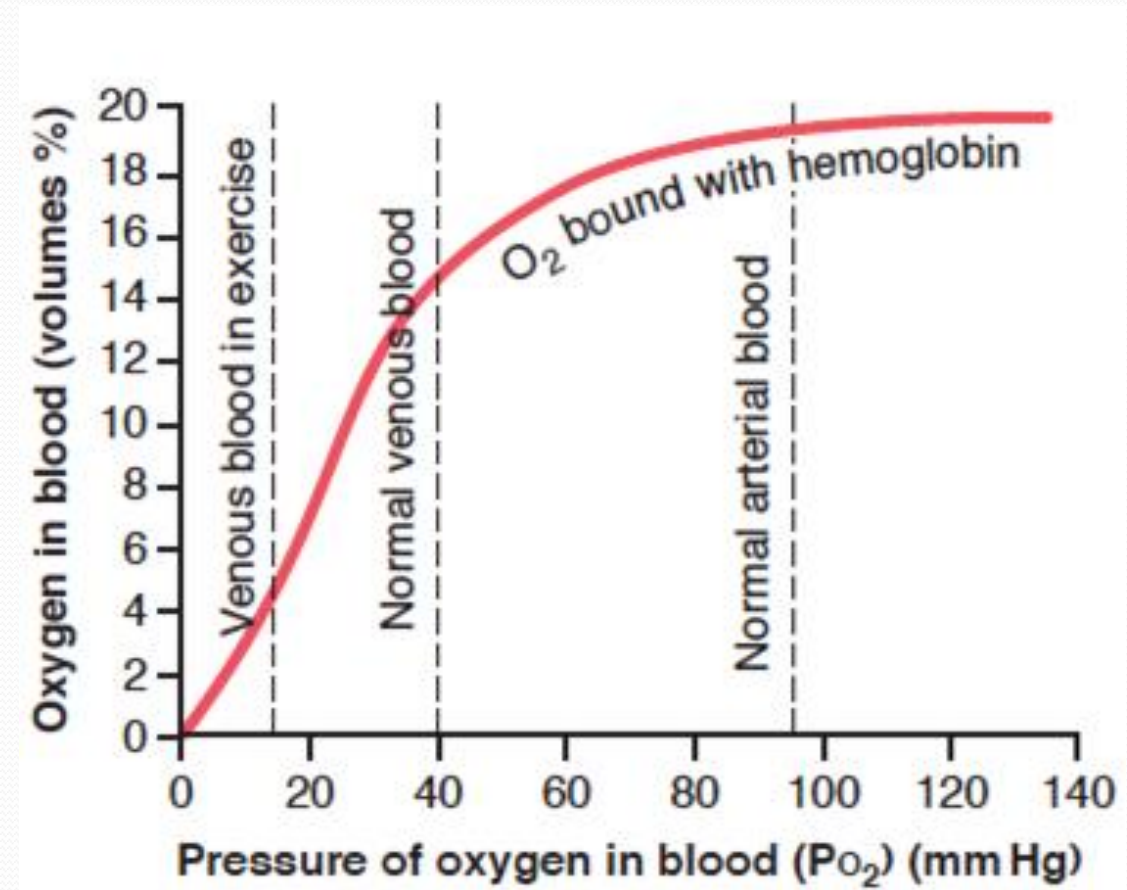
- Systemic arterial blood has PO₂ of 95 mm Hg, and O₂ saturation of hemoglobin averages 97 %
- Venous blood has PO₂ of 40 mm Hg, and O₂ saturation of hemoglobin averages 75 %
- Normally, blood contains 15 grams of hemoglobin in each 100 milliliters of blood, and each gram of hemoglobin can bind with a maximum of 1.34 milliliters of oxygen, so on average, the 15 grams of hemoglobin in 100 milliliter of blood can combine with a total of about 20 milliliters of oxygen if the hemoglobin is 100 percent saturated



Transport of O₂ in the blood

The amount of O₂ delivered to the tissue

- Normally about 5 milliliters of oxygen are transported from the lungs to the tissues by each 100 milliliters of blood flow.
- During exercise the amount of O₂ transferred to the tissue is three times the normal level. And if the cardiac output increases, tissue O₂ delivery will increase many fold
- The utilization coefficient: is the percentage of the blood that gives up its oxygen as it passes through the tissue capillaries. Normally, it is about 25 %, it can reach 75-85 % in exercise.

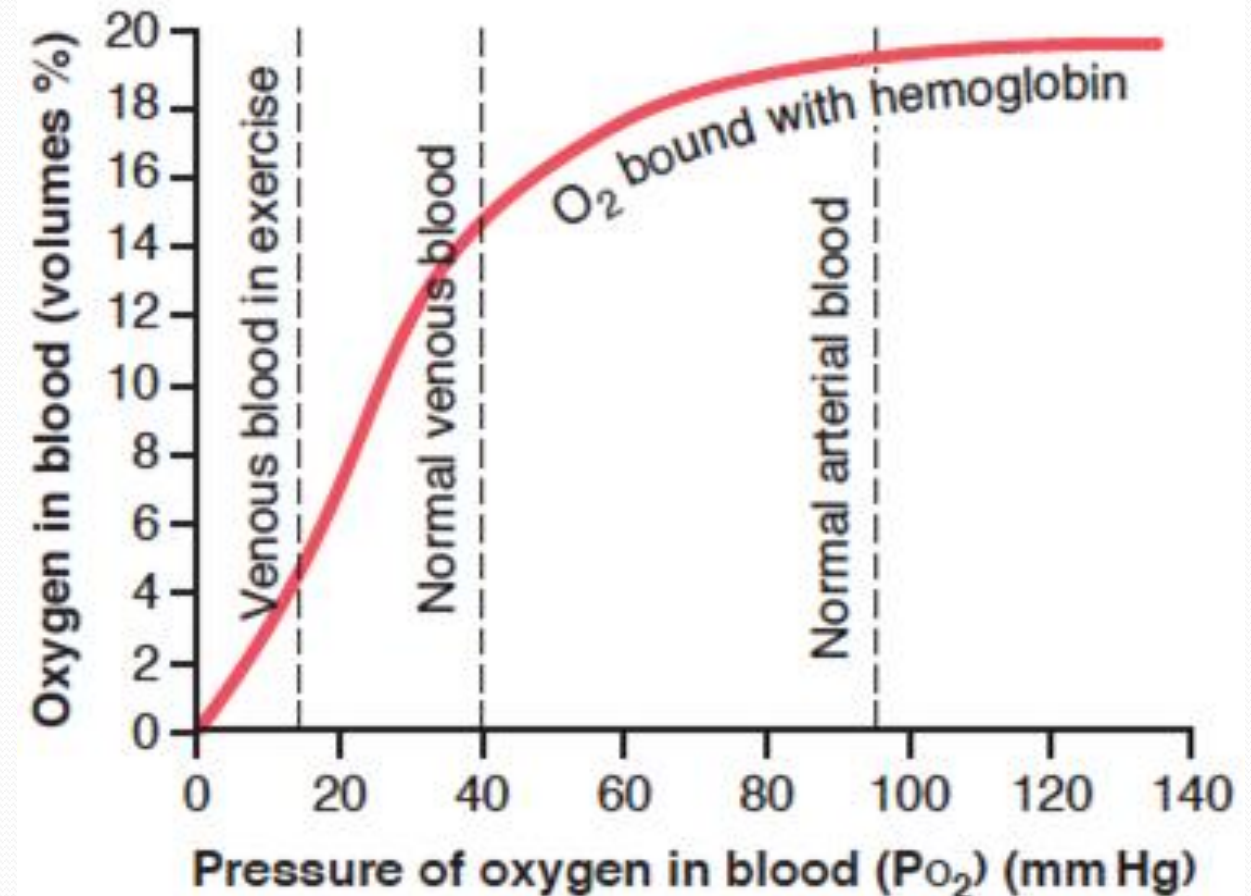


Transport of O₂ in the blood

Hemoglobin as tissue oxygen buffer system

Hemoglobin in the blood automatically delivers oxygen to the tissues at a pressure that is held rather tightly between about 15 and 40 mm Hg in the tissue.

What if the atmospheric oxygen changes??



Transport of O₂ in the blood

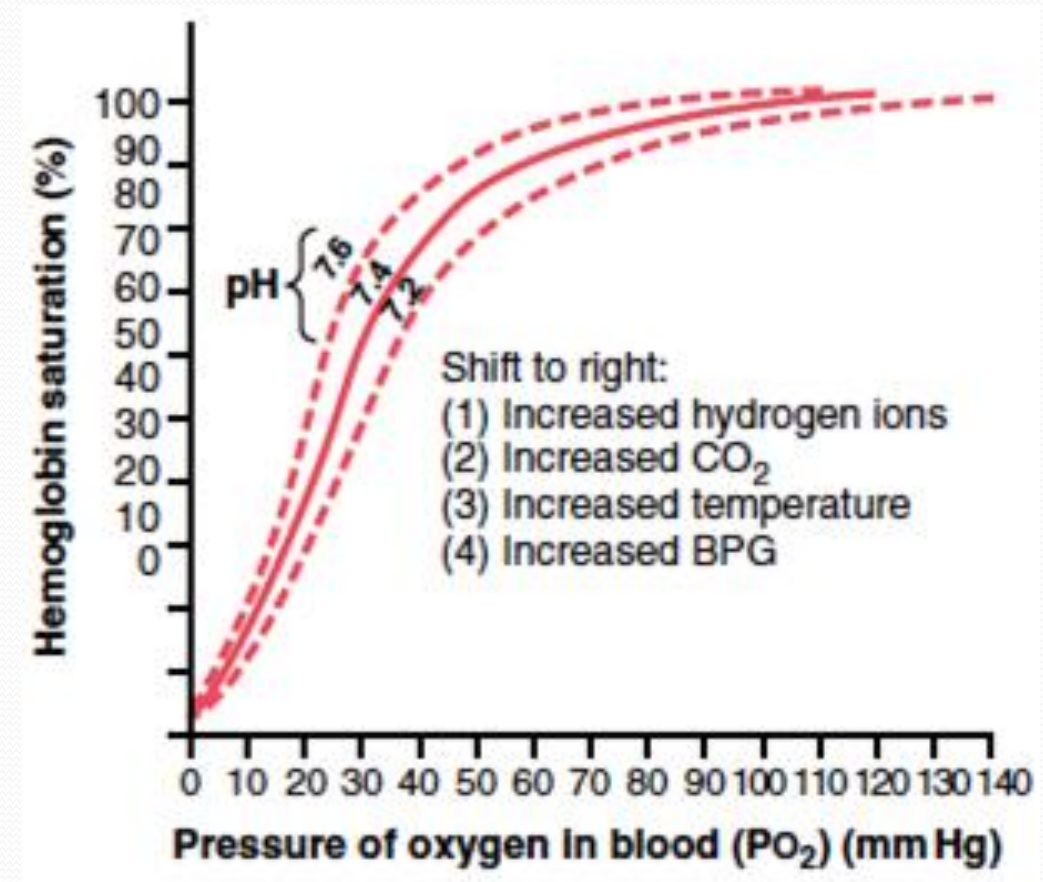
Factors that affect the oxygen-hemoglobin dissociation curve

Factors that cause right sided shift of the oxygen-hemoglobin dissociation curve:

1. Increased CO₂ level: Bohr effect: increased CO₂ and hydrogen ions enhances the releasing of O₂ from the hemoglobin.
1. Increased 2,3-biphosphoglycerate (BPG). BPG is a phosphate compound present in the blood in different concentrations under different metabolic conditions. It is mainly increased under hypoxic condition
1. Increased temperature

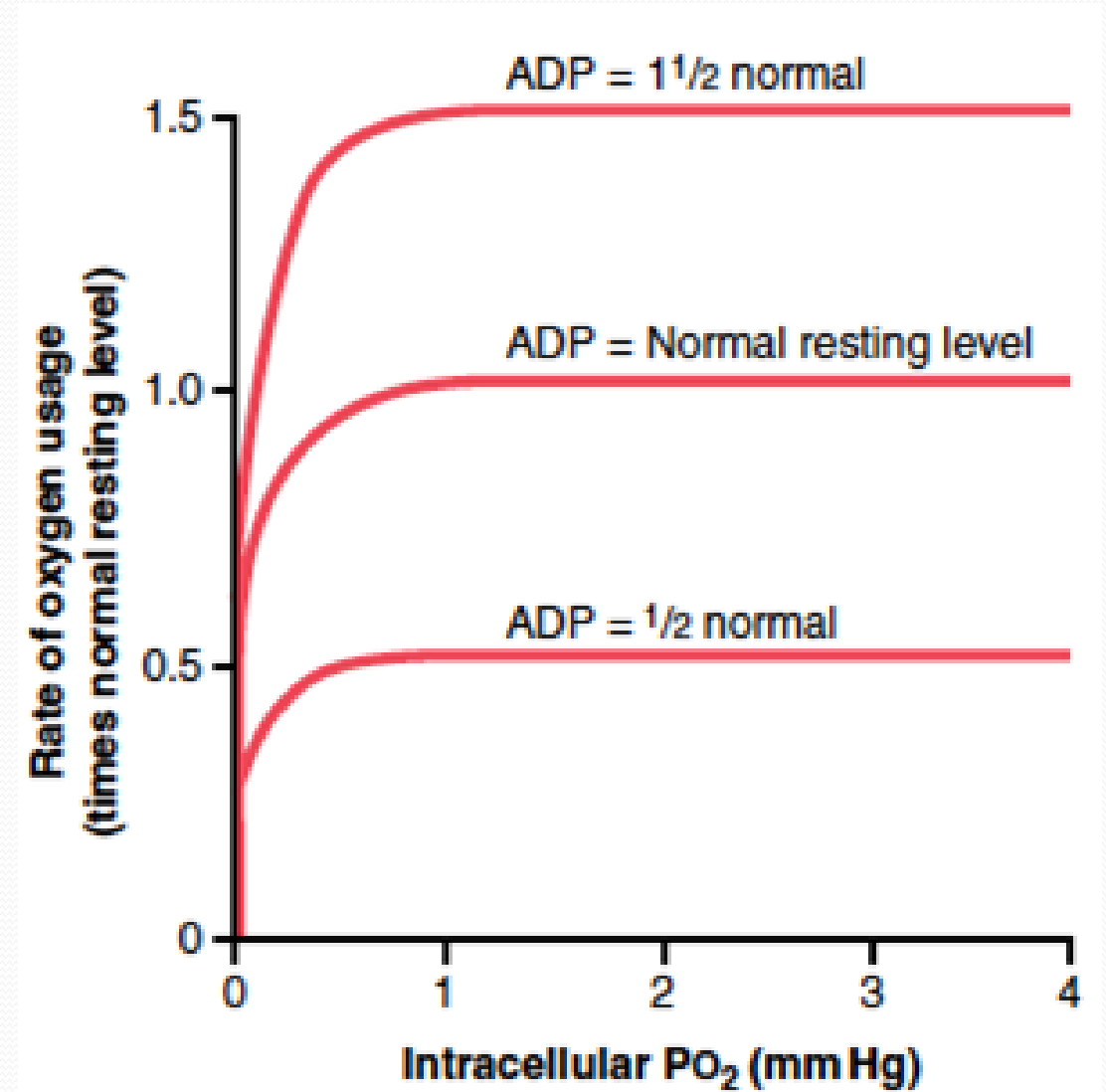
What about left sided shift?

During exercise?



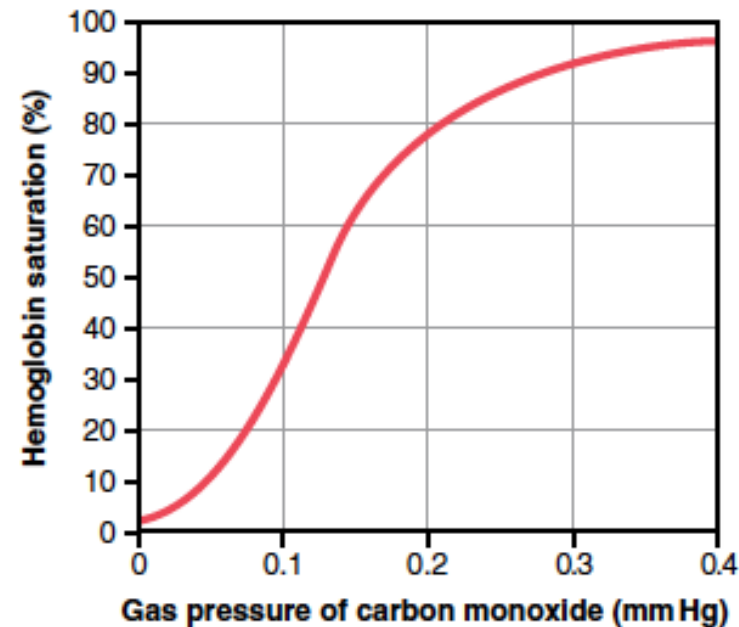
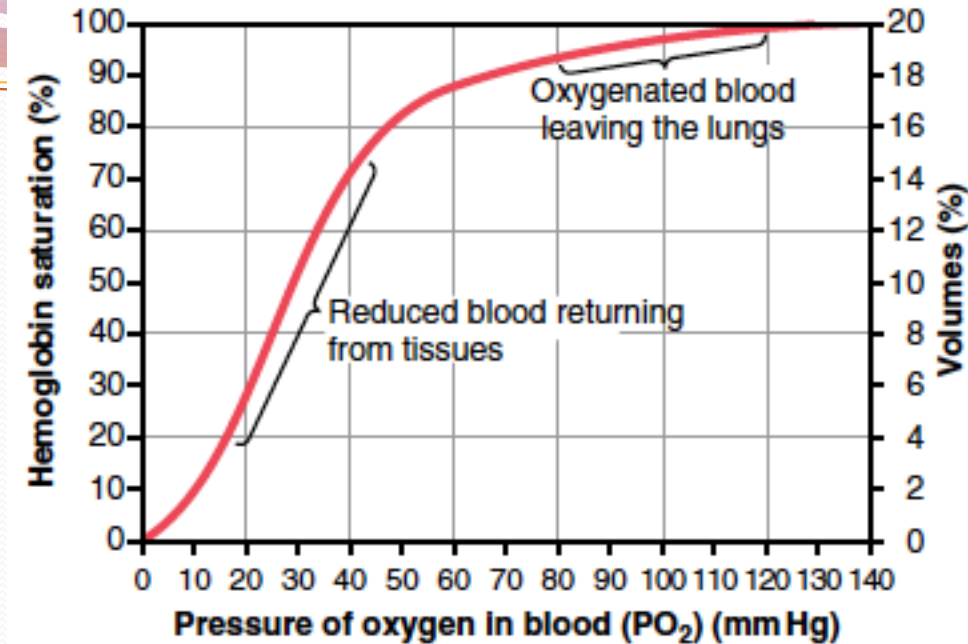
Transport of O₂ in the blood

- If the cellular PO₂ is more than 1 mm Hg, O₂ availability is no longer a limiting factor in the rates of the chemical reactions inside the cells
- O₂ usage is ADP limited: this under normal conditions.
- O₂ usage is diffusion or blood flow limited: this under pathological condition
- O₂ poisoning?



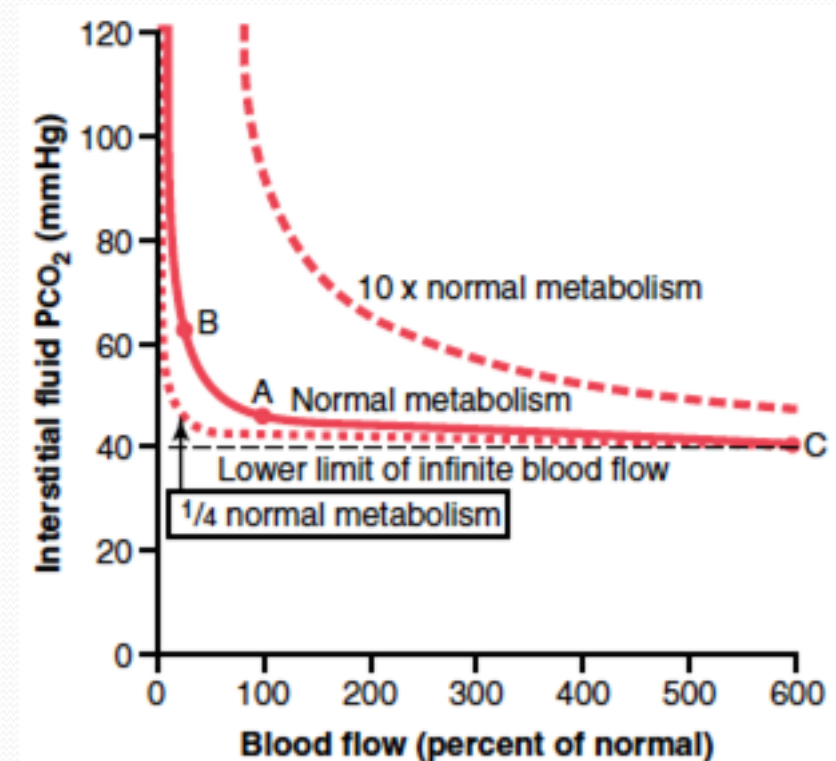
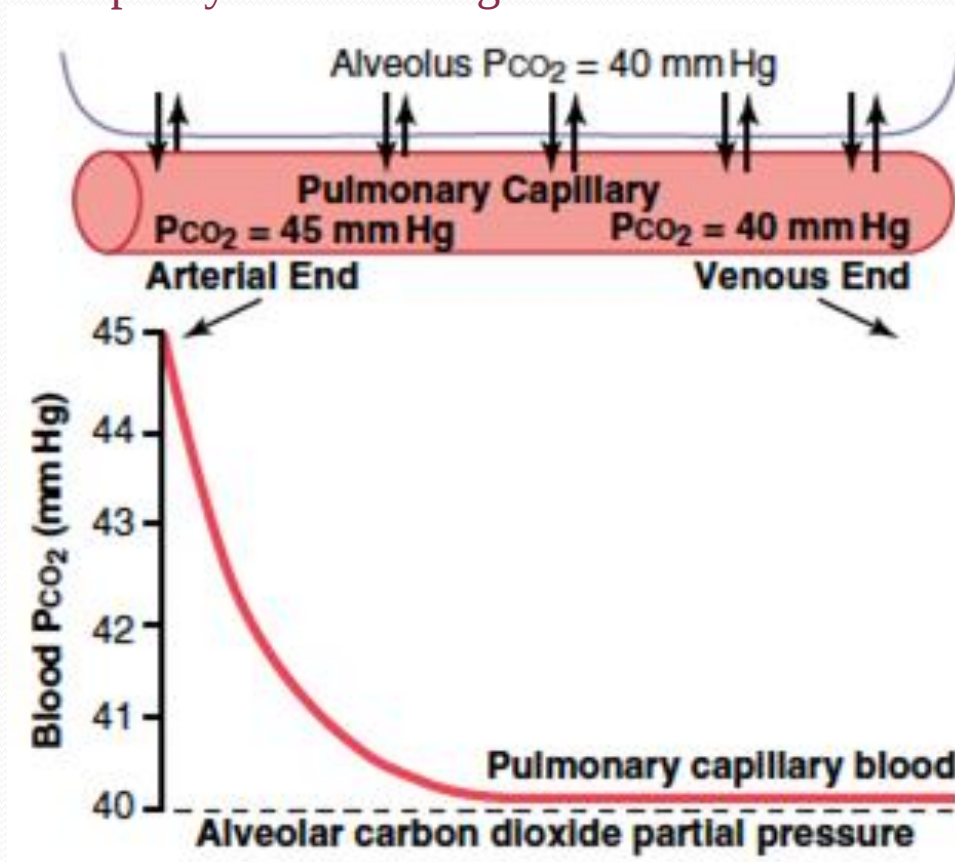
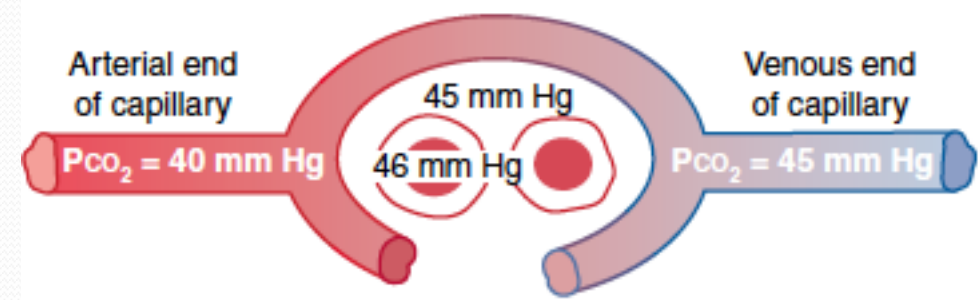
CO poisoning

- CO decreases the oxygen carrying capacity of the blood since it binds with hemoglobin on the same point where O₂ binds, and causes displacement of the oxygen from the hemoglobin
- The binding affinity of CO is higher than that of O₂
- CO poisoning causes hypoxemia without cyanosis, since the carboxyhemoglobin has a characteristic cherry-red colour
- In CO poisoning, the PO₂ is normal, so the reflex mechanisms to increase O₂ are not stimulated, the person becomes disoriented and unconscious before being aware of the danger
- Treatment : O₂ or 5% CO₂



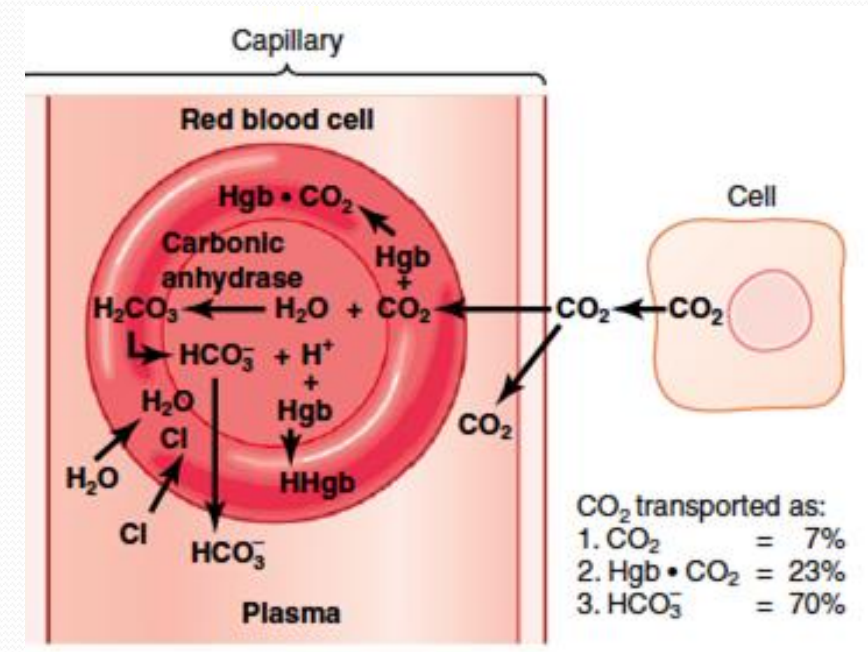
Transport of CO₂

The pressure differences required to cause carbon dioxide diffusion are less than the pressure difference required for O₂ since the diffusion capacity of CO₂ is higher than O₂



Transport of CO₂

- CO₂ concentration has an important role in the acid-base balance of the body fluids
- Under normal resting conditions, an average of 4 milliliters of carbon dioxide is transported from the tissues to the lungs in each 100 milliliters of blood
- CO₂ is transported in the blood in three forms
 1. Dissolved form: only 7 % of CO₂
 2. In form of bicarbonate (HCO₃⁻): 70% of CO₂
 - Carbonic anhydrase
 - Bicarbonate-chloride carrier protein
 - Chloride shift: the chloride content of venous red blood cells is greater than that of arterial red cells
 3. In combination with hemoglobin and plasma protein: carbaminohemoglobin (CO₂Hgb).



Transport of CO₂

- The Bohr effect: Increase of CO₂ in the blood causes oxygen to be displaced from the hemoglobin
- Haldane effect: Binding of oxygen with hemoglobin tends to displace carbon dioxide from the blood.
- Haldane effect is quantitatively far more important in promoting carbon dioxide transport than is the Bohr effect in promoting oxygen transport.

Mechanism of Haldane effect

Combination of oxygen with hemoglobin in the lungs causes the hemoglobin to become a stronger acid. The more acidic hemoglobin:

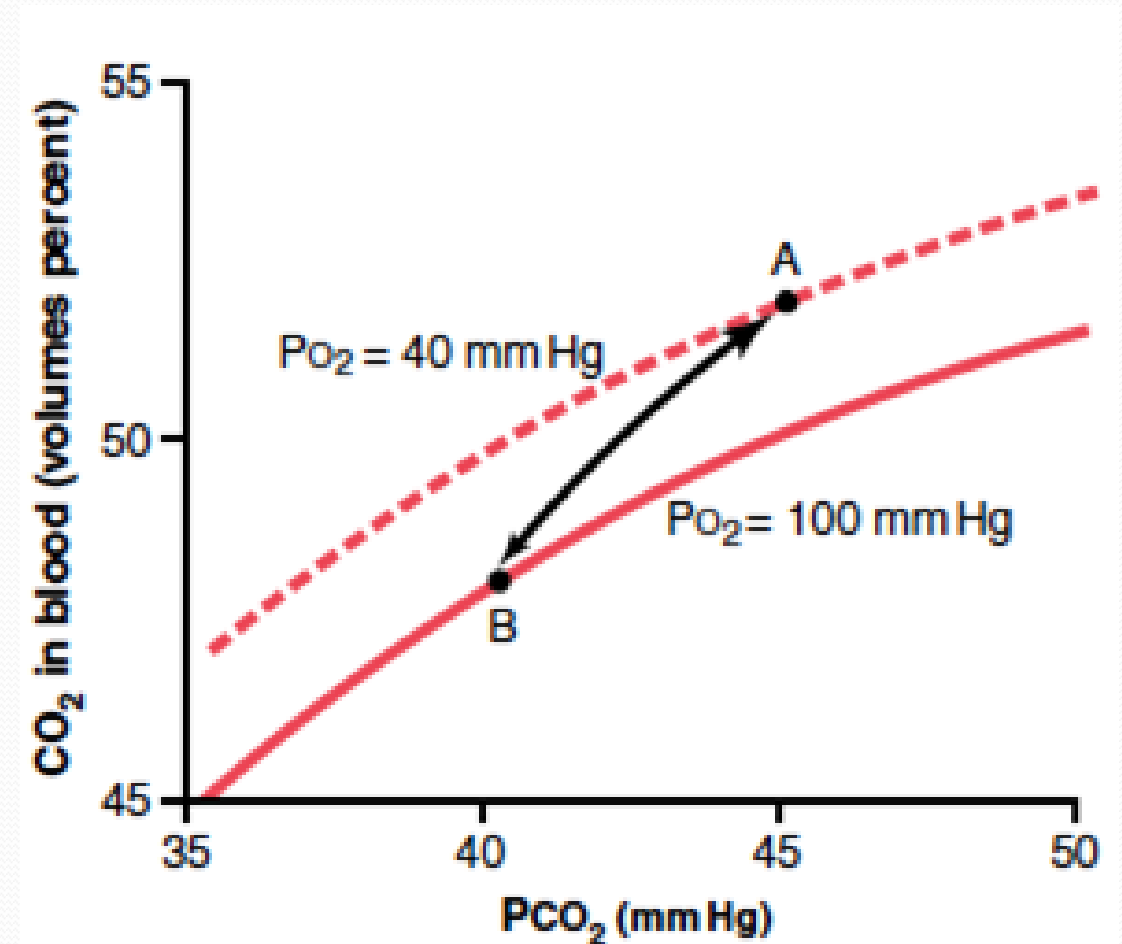
1. Has less affinity to carbon dioxide to form carbaminohemoglobin, thus displacing much of the carbon dioxide that is present in the carbamino form from the blood.
1. Causes hemoglobin to release an excess of hydrogen ions, and these bind with bicarbonate ions to form carbonic acid, which then dissociates into water and carbon dioxide, and the carbon dioxide is released from the blood into the alveoli and, finally, into the air

Transport of CO₂

The importance of Haldane effect

It approximately doubles the amount of carbon dioxide released from the blood in the lungs and approximately doubles the pickup of carbon dioxide in the tissues

Transport of CO₂ in form of carbonic cause slight acidosis of venous blood compared to arterial one. In heavy exercise, high metabolic rate, or decrease blood flow to the tissue, the acidosis is more significant.





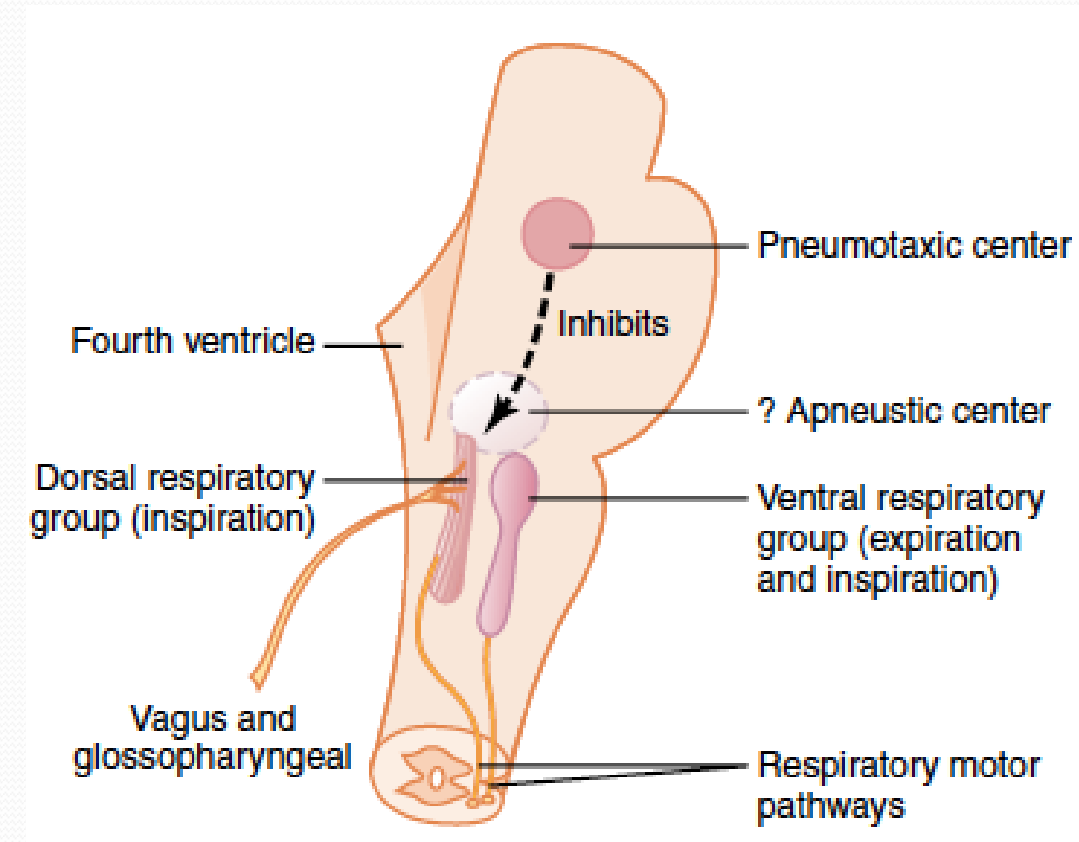
Regulation of respiration

Regulation of respiration

The respiratory center: several groups of neurons located bilaterally in the medulla oblongata and pons of the brain stem.

The center is divided into three major collections of neurons:

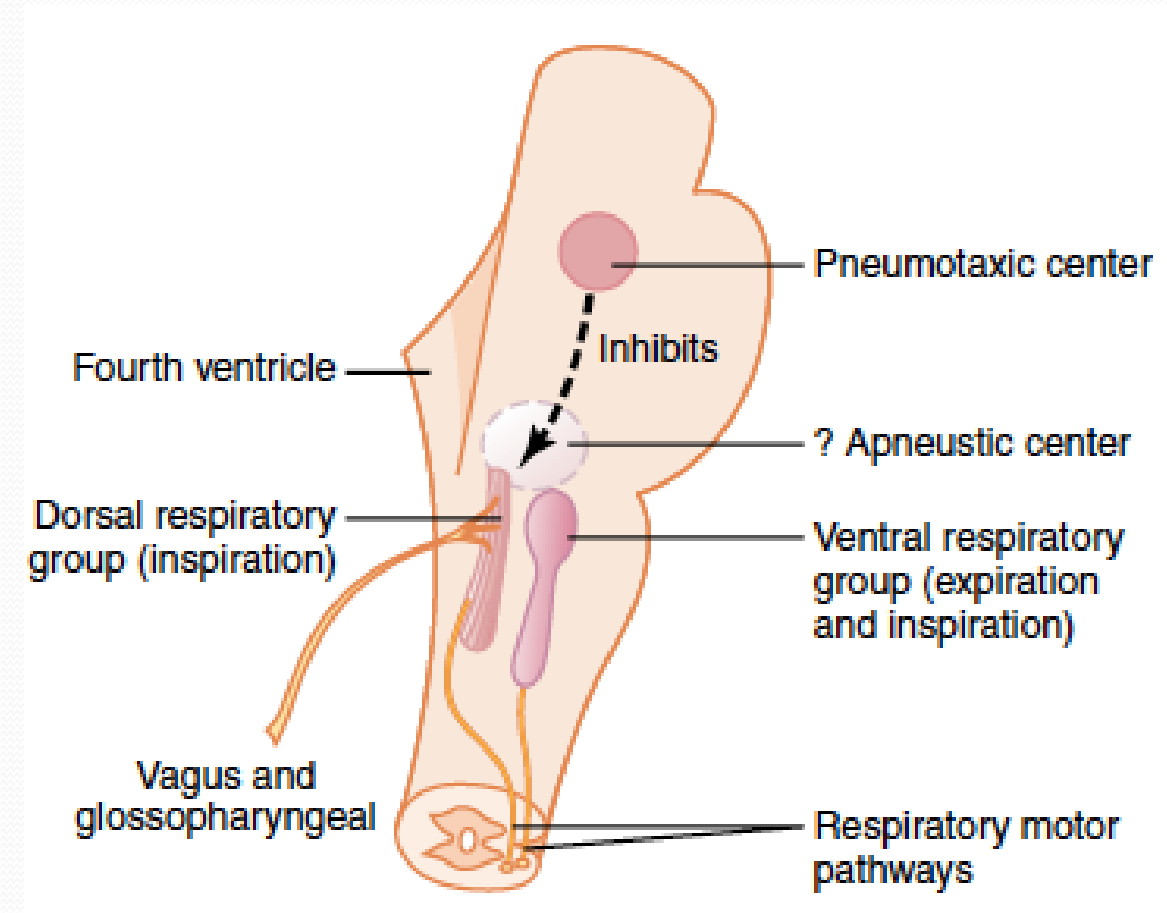
1. A dorsal respiratory group, in the dorsal portion of the medulla (inspiration)
1. A ventral respiratory group, in the ventrolateral part of the medulla (expiration)
1. The pneumotaxic center, located dorsally in the superior portion of the pons, which mainly controls rate and depth of breathing



Regulation of respiration

The dorsal respiratory group:

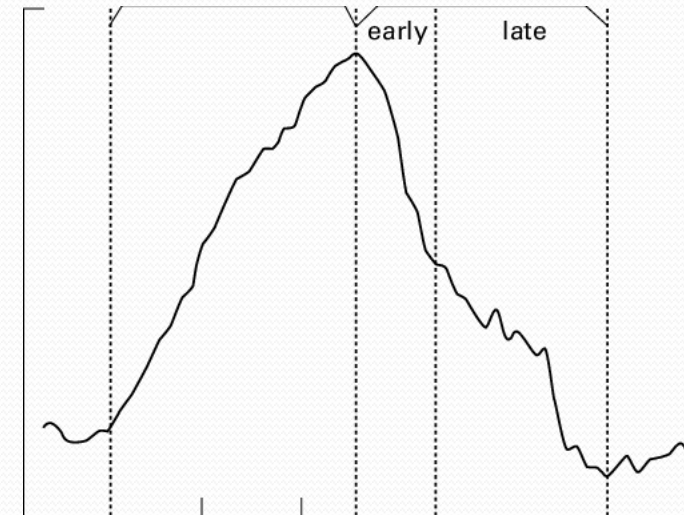
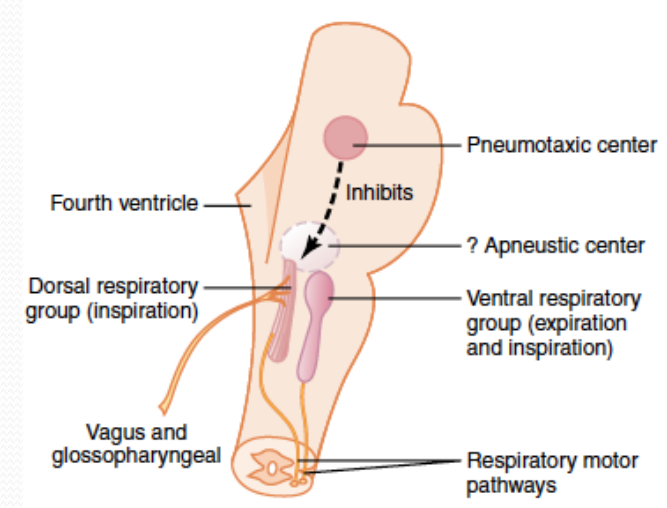
- The most important group in respiratory control
- The dorsal group is responsible for the rhythm of respiration as it emits repetitive bursts of inspiratory neuronal action potentials
- Most of dorsal group neurons are located within the nucleus of the tractus solitarius (NTS)
- Signals from:
 - (1) peripheral chemoreceptors
 - (2) Baroreceptors
 - (3) several types of receptors in the lungs reaches the NTS through the sensory termination of both the vagal and the glossopharyngeal nerves



Regulation of respiration

The dorsal respiratory group:

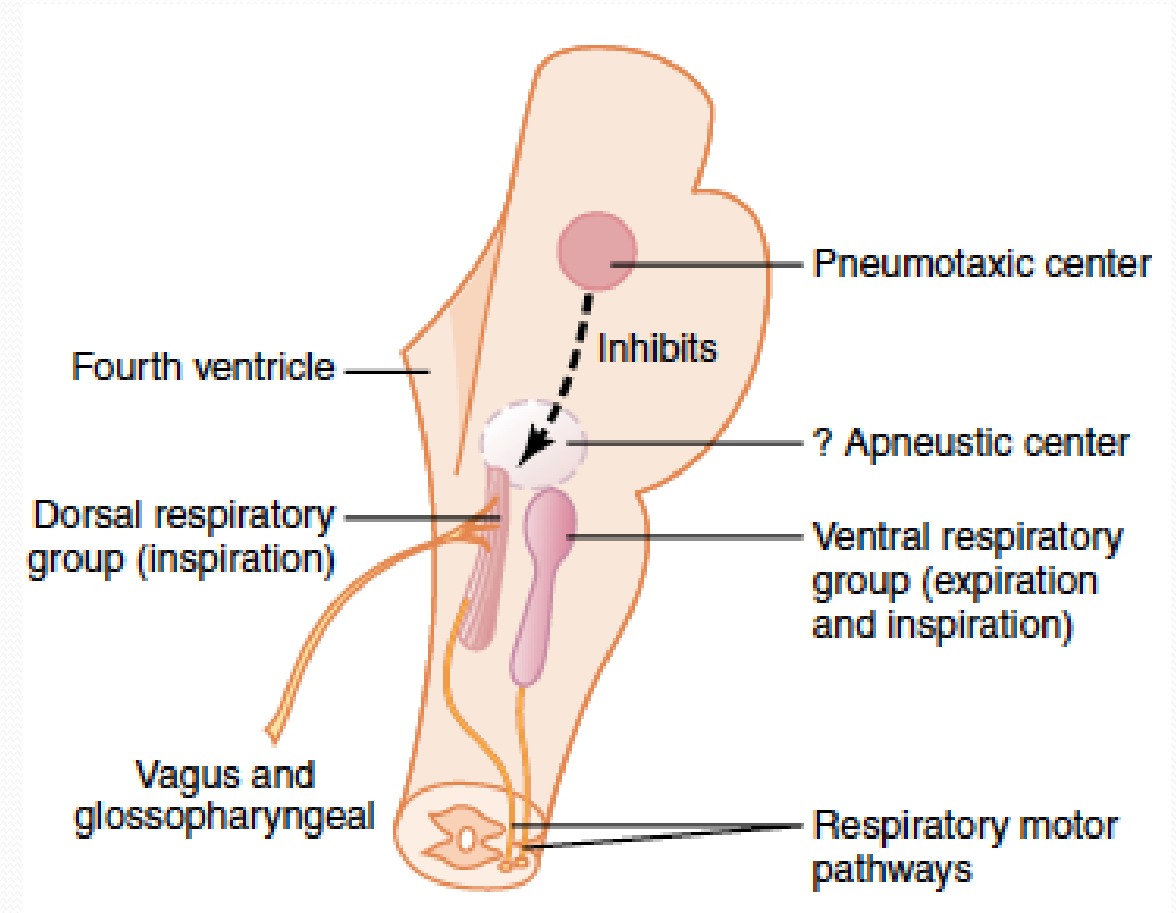
- The inspiratory signal from the dorsal respiratory group begins weakly and increases steadily in a ramp manner for about 2 seconds in normal respiration. Then it ceases abruptly for approximately the next 3 seconds, so no excitation of the diaphragm, allowing expiration
- This cycle repeats again and again, with expiration occurring in between
- There are two qualities of the inspiratory ramp that are controlled:
 1. The rate of increase of the ramp signal
 2. The limiting point at which the ramp suddenly ceases.



Regulation of respiration

Pneumotaxic center:

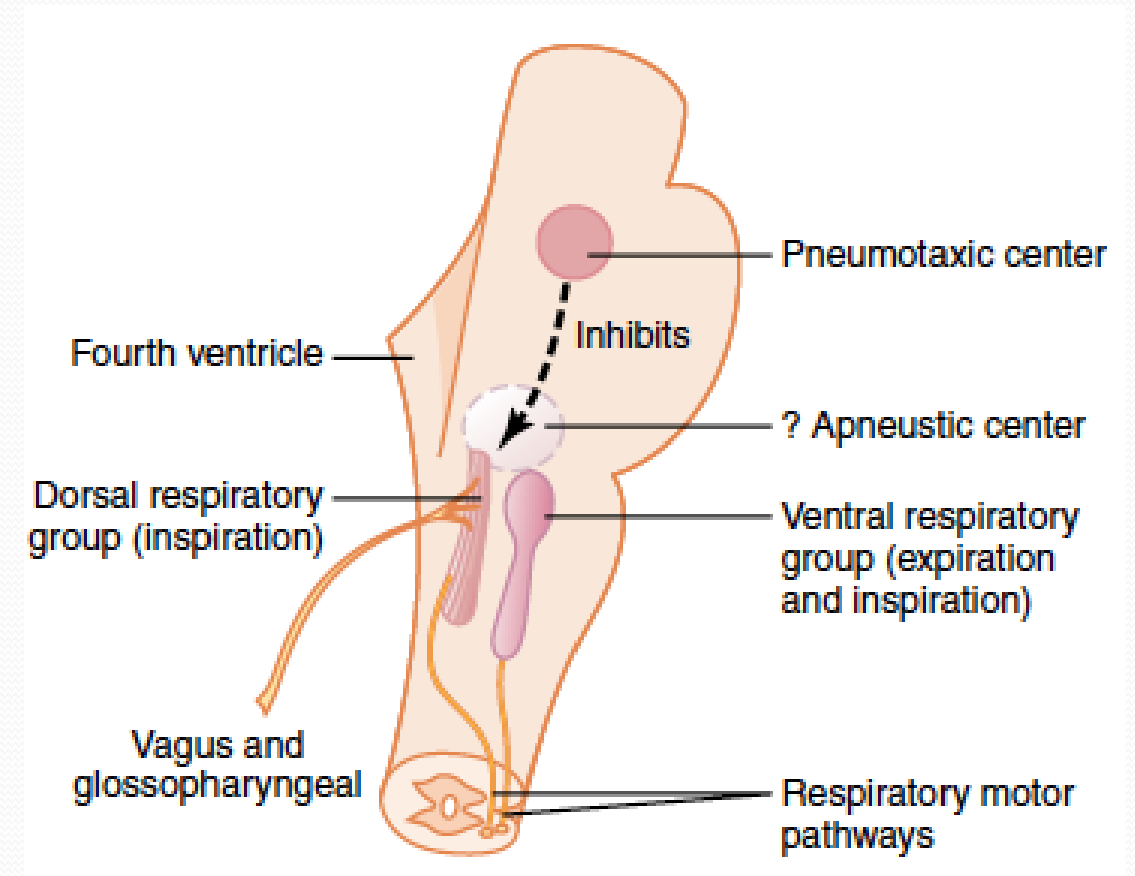
- It is located dorsally in the upper pons.
- It controls the switch-off point of the inspiratory ramp by transmitting inhibitory signals to the inspiratory area.
- It controls the duration of the filling phase of the lung cycle (inspiration), and indirectly control the rate of breathing.



Regulation of respiration

Ventral Respiratory Group

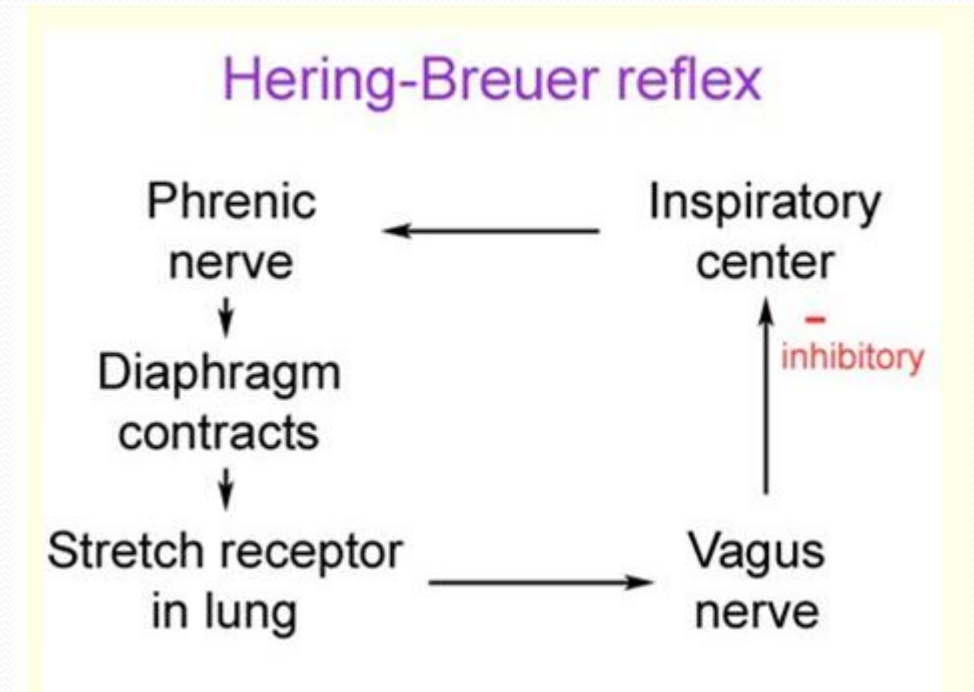
- It is Located in each side of the medulla
- The neurons of this group are inactive during normal quiet breathing
- They do not participate in the basic rhythmical oscillation that controls respiration.
- These neurons are stimulated by the dorsal respiratory groups when there is a need to increase the pulmonary ventilation (exercise)
- Some neurons of this group cause inspiration and others cause expiration
- These neurons send signals to the accessory muscles of respiration



Regulation of respiration

The Hering-Breuer inflation reflex:

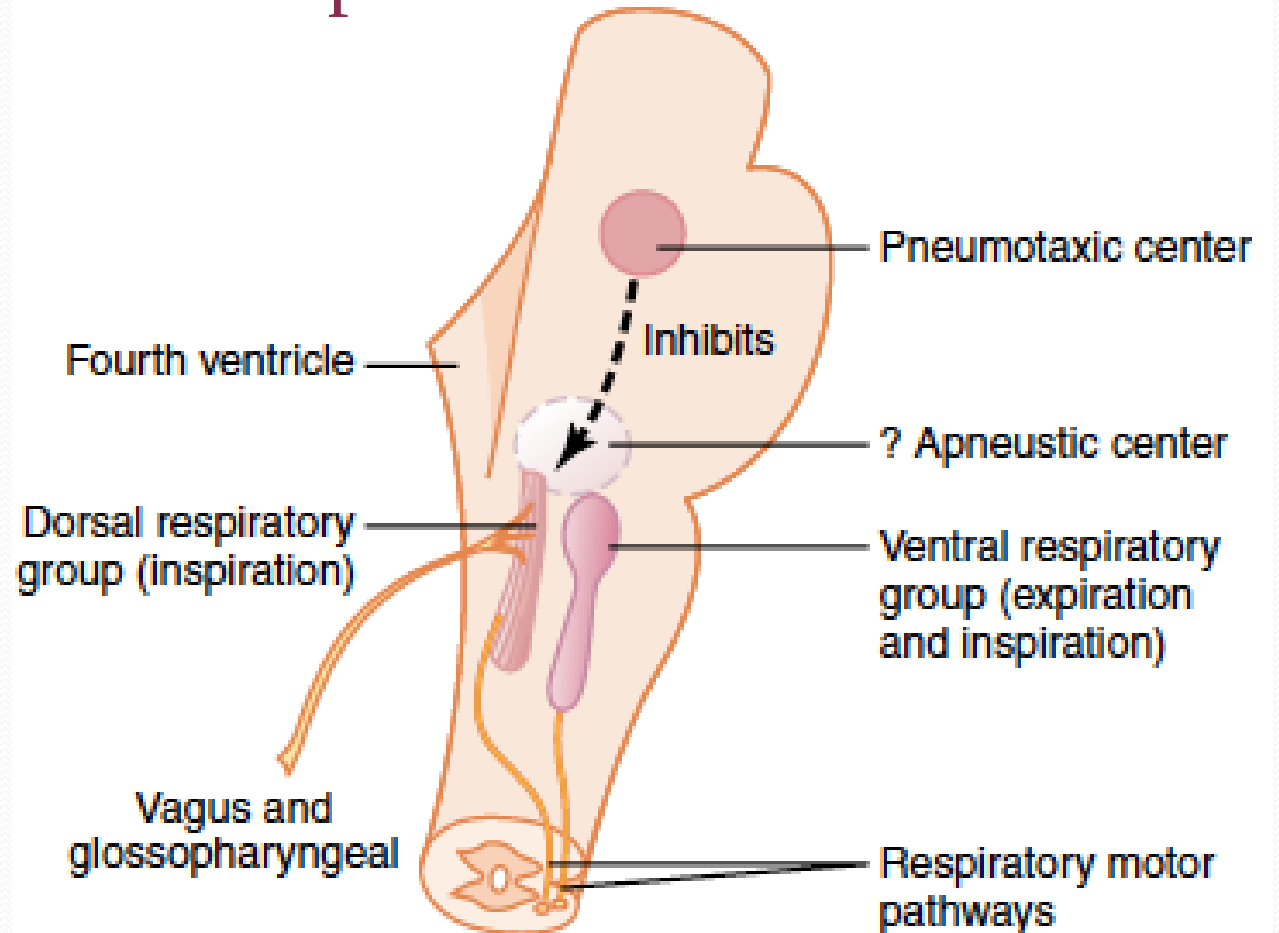
- It is a protective mechanism that prevent over-inflation of the lungs
- Mechanism: over-inflation of the lungs (TV increases to more than three times normal ($>\approx 1.5$ liters per breath)), stimulates the stretch receptors located in the muscular portions of the walls of the bronchi and bronchioles throughout the lungs, which then transmit signals through the vagi into the dorsal respiratory group of neurons to activate an appropriate feedback response that “switches off” the inspiratory ramp and thus stops further inspiration



Regulation of respiration

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 the pneumotaxic center of pons.
- controls the intensity of breathing.
- The apneustic center is inhibited by pulmonary stretch receptors. However, it gives positive impulses to the inspiratory neurons.



Regulation of respiration

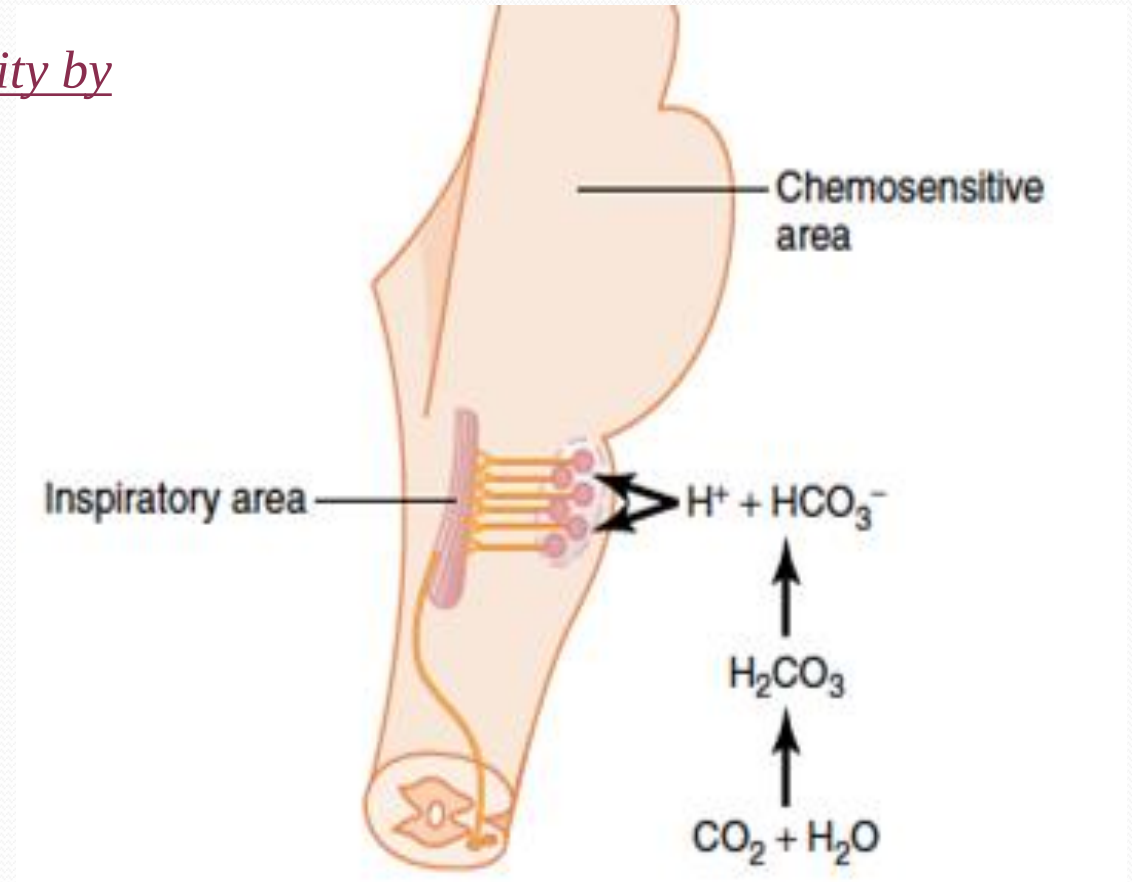
Control of ventilation in accord with the respiratory needs of the body is done through two main mechanisms:

1. The effect of CO₂ on the central chemosensitive area (direct effect)
1. The effect of O₂ through the peripheral chemoreceptors (indirect effect)

Regulation of respiration

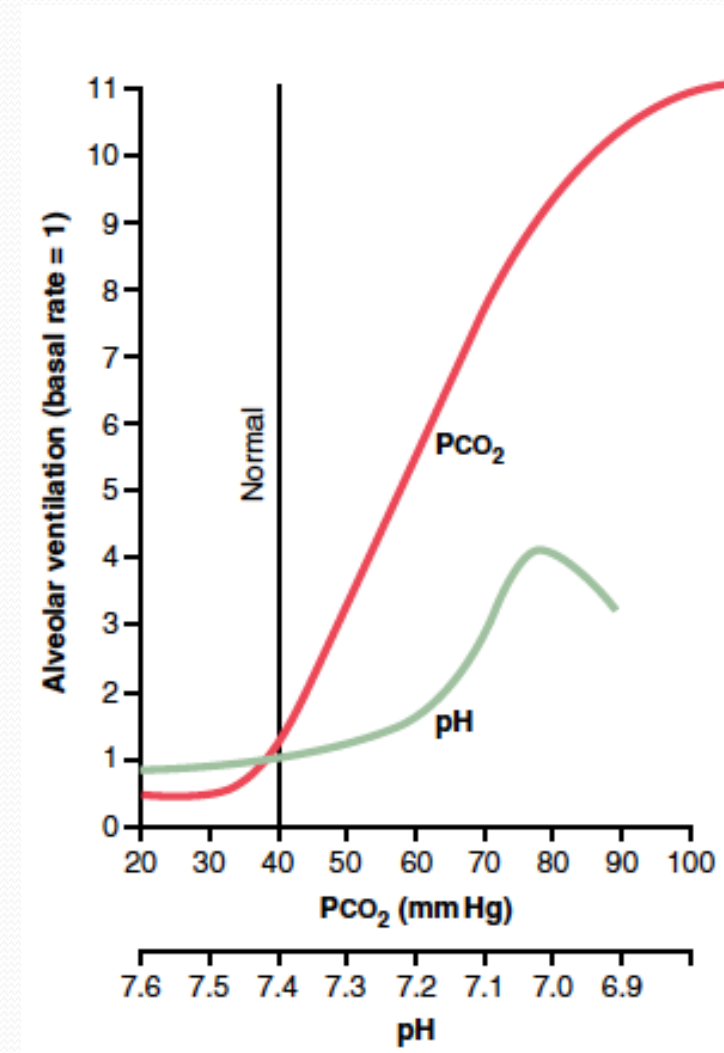
Direct chemical control of respiratory center activity by carbon dioxide and hydrogen ions

- The chemosensitive area, located bilaterally beneath the ventral surface of the medulla, is highly sensitive to hydrogen and CO₂ concentration.
- The sensor neurons in the chemosensitive area are especially excited by hydrogen ions, but it is the CO₂ that will stimulate this area, **why?**
- A change in blood carbon dioxide concentration has a potent acute effect on controlling respiratory drive but only a weak chronic effect after a few days (adaptation), **why?**



Regulation of respiration

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.



Regulation of respiration

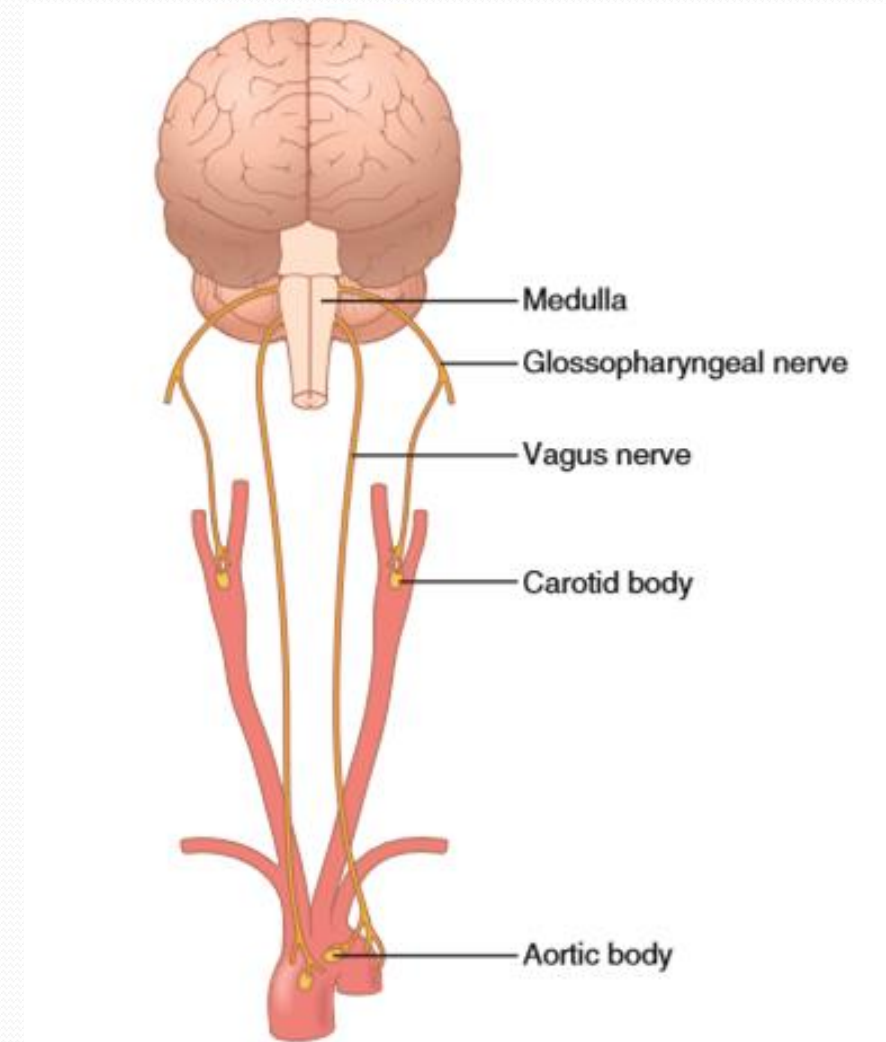
Regulation by O₂

- Changes in oxygen have little direct effect on control of the respiratory center
- Oxygen changes work indirectly on the respiratory center, acting through the peripheral chemoreceptors. However, this mechanism responds when the blood oxygen falls too low, mainly below a PO₂ of 70 mm Hg

Regulation of respiration

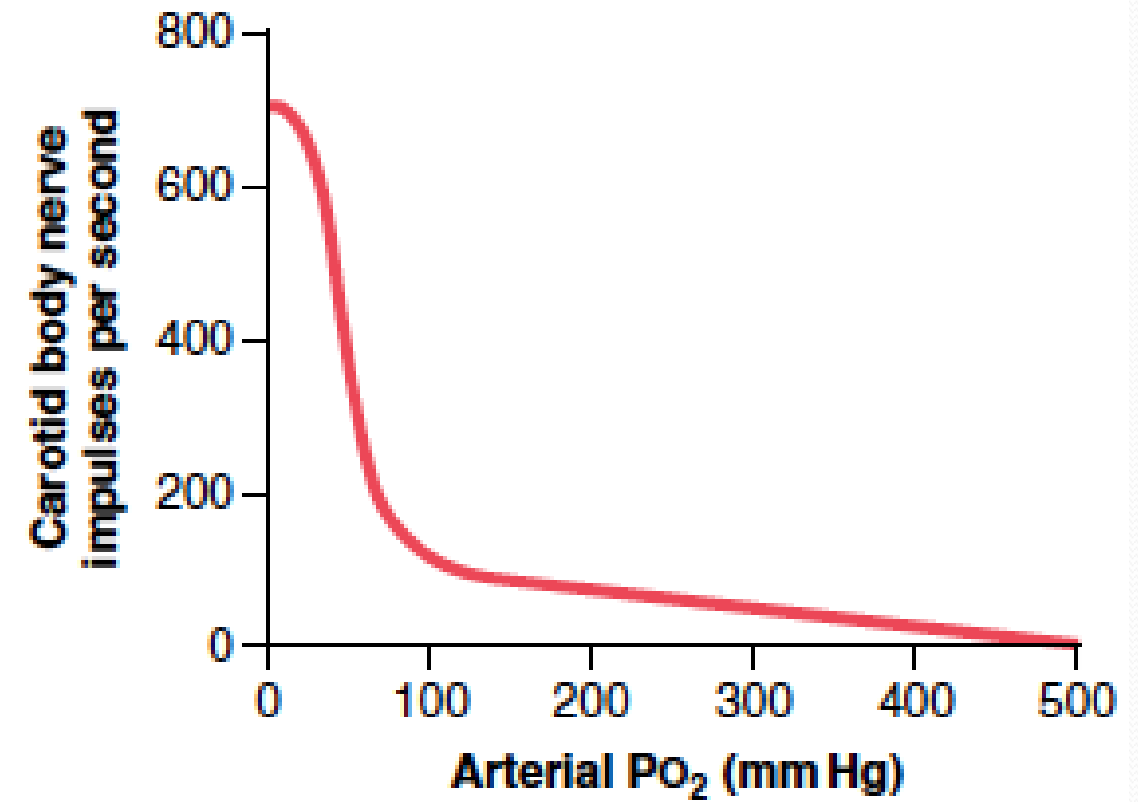
Peripheral chemoreceptor system for control of respiratory activity

- Special nervous chemical receptors, called chemoreceptors, are located in several areas outside the brain.
- chemoreceptors are especially important for detecting changes in O_2 in the blood, although they also respond to a lesser extent to changes in CO_2 and hydrogen ion concentrations. The chemoreceptors transmit nervous signals to the respiratory center in the brain to help regulate respiratory activity.



Regulation of respiration

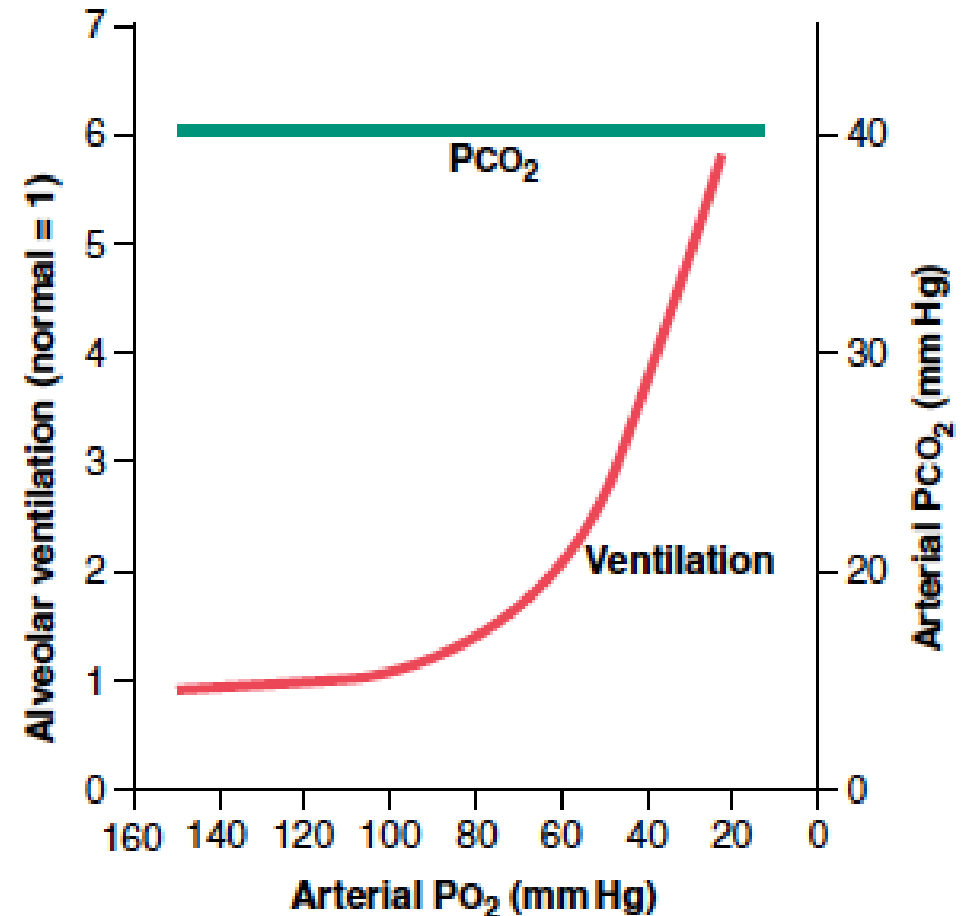
- When the oxygen concentration in the arterial blood falls below normal, the chemoreceptors become strongly stimulated. the impulse rate is particularly sensitive to changes in arterial PO_2 in the range of 60 down to 30 mm Hg, a range in which hemoglobin saturation with oxygen decreases rapidly
- Increase in either the CO_2 or hydrogen stimulates the chemoreceptors, however the direct effect of CO_2 and hydrogen is much more powerful, but the indirect effect is more rapid, this increases the rapidity of response to carbon dioxide at the onset of exercise.



Regulation of respiration

Effect of low arterial PO₂ to stimulate alveolar ventilation when arterial carbon dioxide and hydrogen ion concentrations remain normal

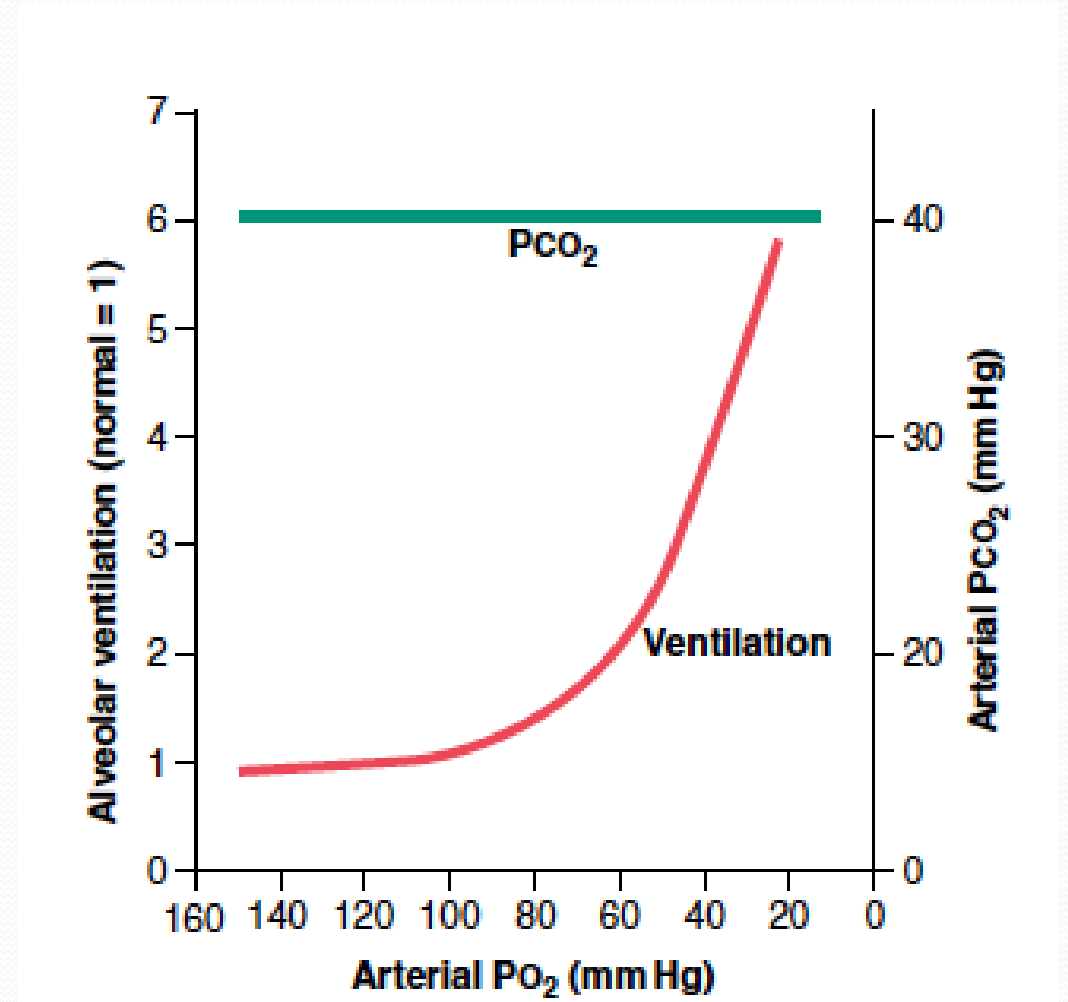
- If the PO₂ is greater than 60 to 80 mm Hg, the effect of hypoxia on ventilation is modest, and at this level of O₂, the PCO₂ and the hydrogen ion have the main control on respiration, (at sea level)
- Chronic breathing of low oxygen has more effect on respiration than acute exposure to low oxygen: Acclimatization



Regulation of respiration

Effect of low arterial PO₂ to stimulate alveolar ventilation when arterial carbon dioxide and hydrogen ion concentrations remain normal

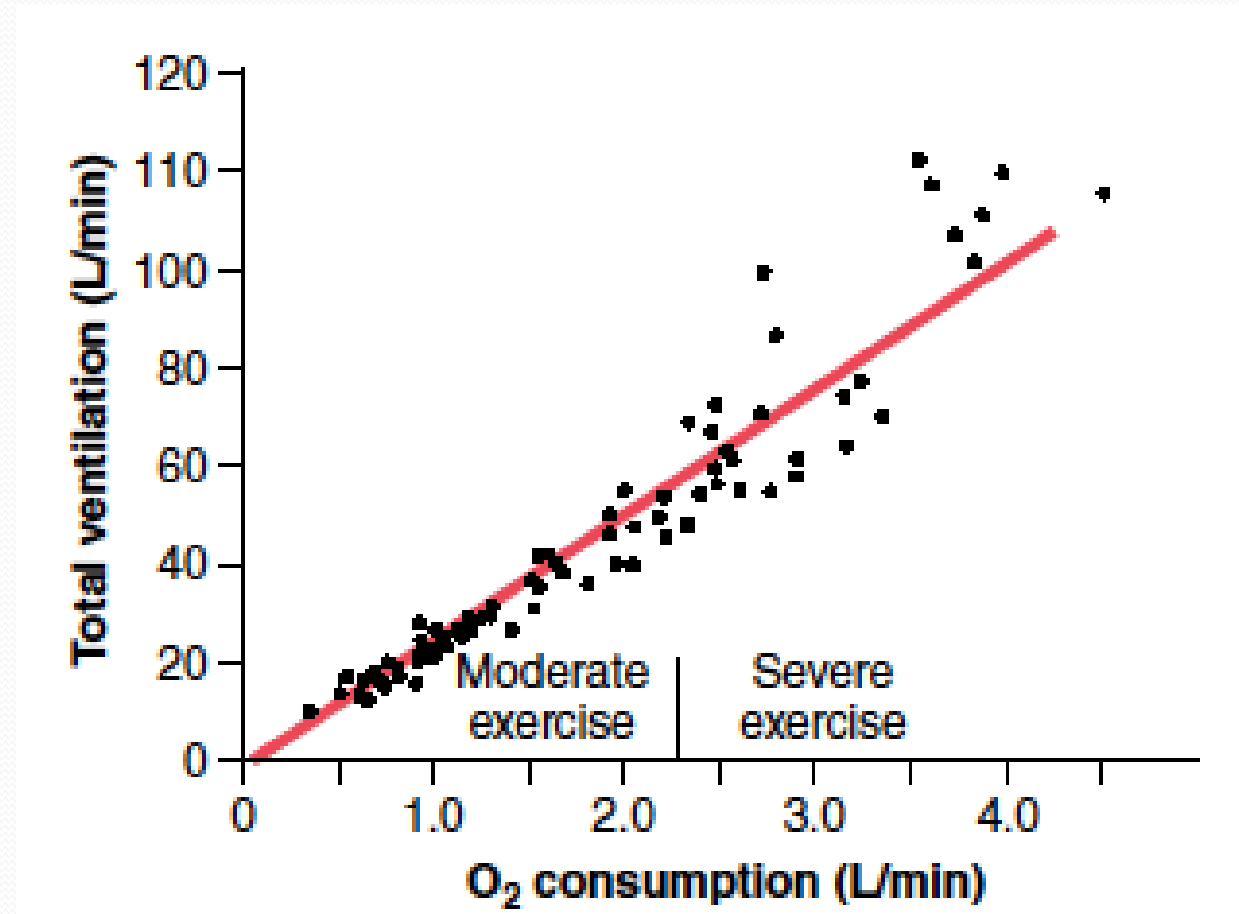
- Mechanism: within 2 to 3 days of living at high altitude, the respiratory center in the brain stem loses most of its sensitivity to changes in PCO₂ and hydrogen ions (adapted), what is the importance of this?
- Acute exposure to low oxygen leads to 70 % increase in ventilation, while chronic low O₂ increases the ventilation 400 to 500 % after 2 to 3 days of low oxygen



Regulation of respiration

Regulation of respiration during exercise

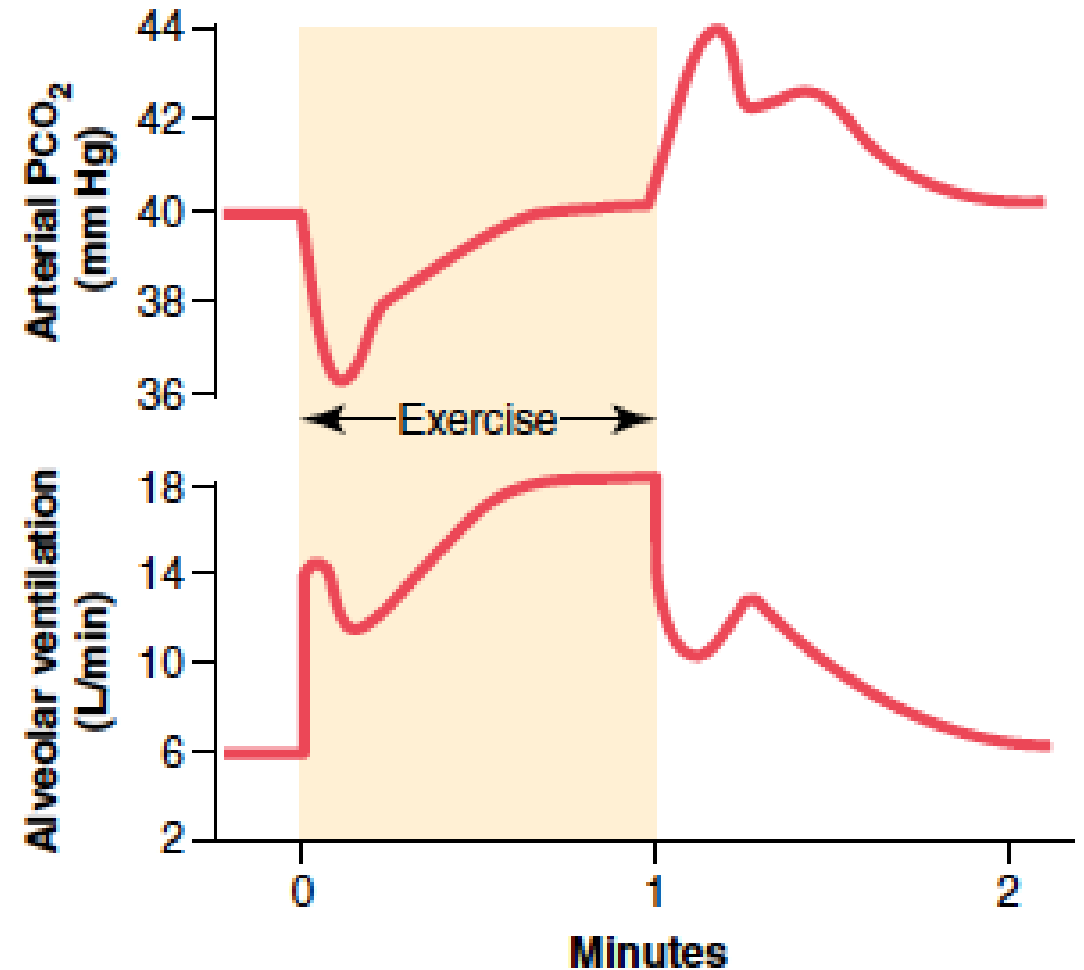
- During exercise, alveolar ventilation ordinarily increases almost exactly in step with the increased level of oxygen metabolism, and the arterial PO_2 , PCO_2 , and pH remain almost exactly normal.
- Since PO_2 and PCO_2 and pH do not change, what stimulates the ventilation?



Regulation of respiration

Regulation of respiration during exercise

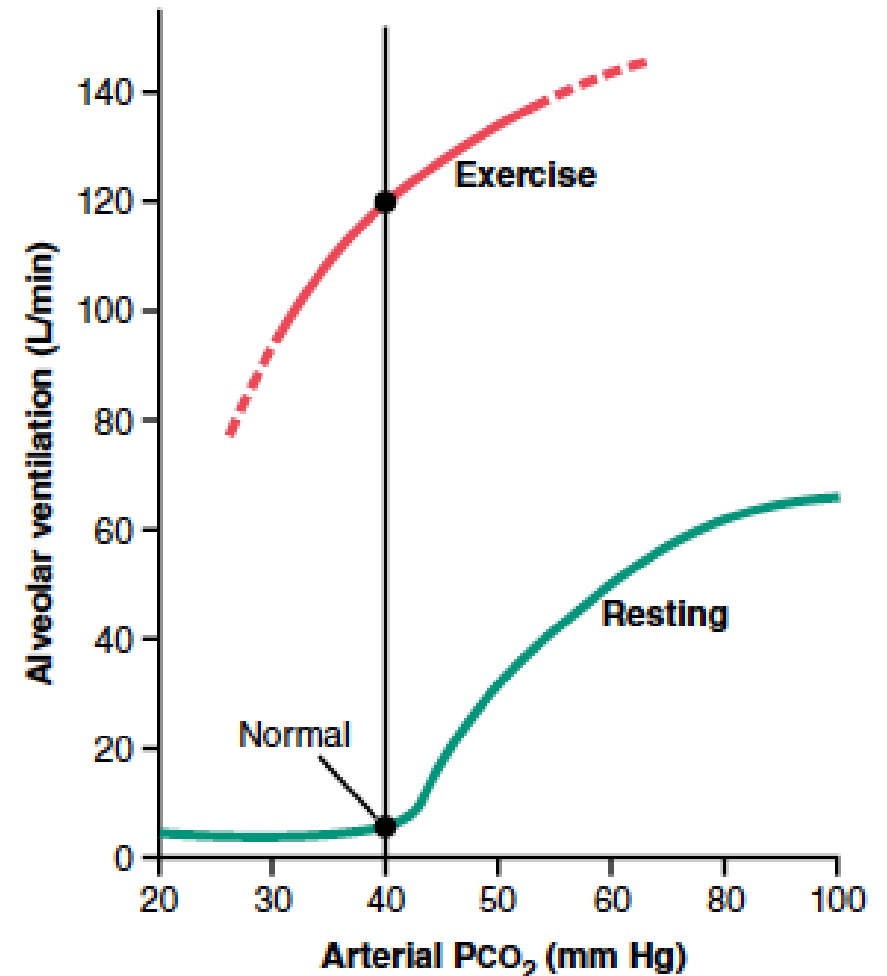
- At the onset of exercise, the alveolar ventilation increases almost instantaneously, without an initial increase in arterial PCO₂
- This increase in ventilation is usually great enough so that at first it actually decreases arterial PCO₂ below normal
- The presumed reason that the ventilation forges ahead of the buildup of blood CO₂ is that the brain provides an “anticipatory” stimulation of respiration at the onset of exercise, causing extra alveolar ventilation even before it is necessary.
- After about 30 to 40 seconds, the amount of CO₂ released into the blood from the active muscles approximately matches the increased rate of ventilation, and the arterial PCO₂ returns essentially to normal even as the exercise continues.



Regulation of respiration

Regulation of respiration during exercise

- In both resting and exercising states the PCO_2 is at the normal level of 40 mm Hg. In other words, the neurogenic factor shifts the curve about 20fold in the upward direction, so ventilation almost matches the rate of CO_2 release, thus keeping arterial PCO_2 near its normal value.
- During exercise, the arterial PCO_2 does change from its normal value of 40 mm Hg, it has an extra stimulatory effect on ventilation at a PCO_2 value greater than 40 mm Hg and a depressant effect at a PCO_2 value less than 40 mm Hg.



Regulation of respiration

Other factors that affect respiration

1. Voluntary control of respiration.
2. Stimulation of pulmonary irritant receptors in the the epithelium of the trachea, bronchi, and bronchioles causes coughing and sneezing, and they may also cause bronchial constriction in asthma and emphysema.
3. Stimulation of the lung J Receptors, which are sensory nerve endings in the alveolar walls in juxtaposition to the pulmonary capillaries, give the person a feeling of dyspnea. These receptors are stimulated when the pulmonary capillaries become engorged with blood or when pulmonary edema occurs as in congestive heart failure
4. Brain edema depresses or inactivates the respiratory center by blocking the cerebral blood flow. **Treatment options?**
5. Anesthesia. overdose with anesthetics or narcotics is the most prevalent cause of respiratory depression and respiratory arrest