Lecture 09- Respiration part I Chapters 38, 39, 40:

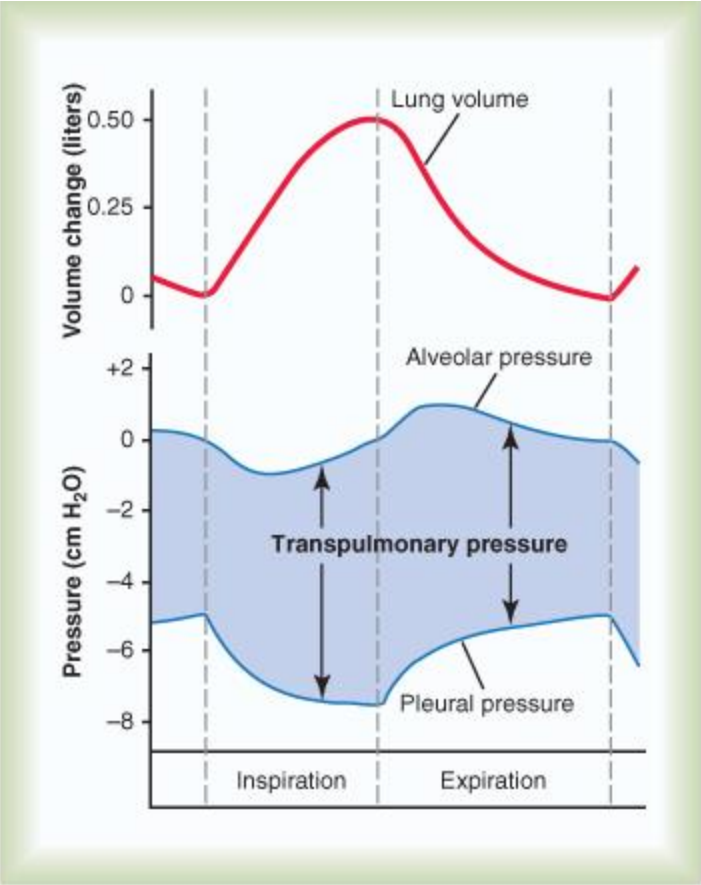
Pulmonary ventilation:

The goals of respiration are to provide oxygen to the tissues and to remove carbon dioxide. This can be divided into 4 major functions: 1) pulmonary ventilation= the inflow and outflow of air between the atmosphere and the lung alveoli; 2) diffusion of oxygen and carbon dioxide between the alveoli and the blood; 3) transport of oxygen and carbon dioxide in the blood and body fluids to and from the body's tissue cells; and 4) regulation of ventilation and other facets of respiration.

Alveolar Pressure:

- Alveolar pressure is the pressure of the air inside the lung alveoli. When the glottis is open and no air is flowing into or out of the lungs, the pressures in all parts of the respiratory tree, all the way to the alveoli, is equal to atmospheric pressure, which is considered to be zero reference pressure in the airways- that is, 0 centimeters water pressure.
- To cause inward flow of air into the alveoli during inspiration, the pressure in the alveoli must fall to a value slightly below atmospheric pressure (below 0). The second curve (labeled alveolar pressure) of **Figure 37-2** demonstrates that during normal inspiration, alveolar pressure decreases to about -1 centimeter of water.

Changes in lung volume, alveolar pressure, pleural pressure, and transpulmonary pressure during normal breathing.



This slight negative pressure is enough to pull 0.5 liter of air into the lungs in the 2 seconds required for normal quiet inspiration.

During expiration, opposite pressure occur: the alveolar pressure rises to about +1 centimeter of water, and this forces the 0.5 liter of inspired air out of the lungs during the 2-3 seconds of expiration.

Compliance of the Lungs.

- The extent to which the lungs will expand for each unit increase in transpulmonary pressure if enough time is allowed to reach equilibrium, is called the lung compliance.

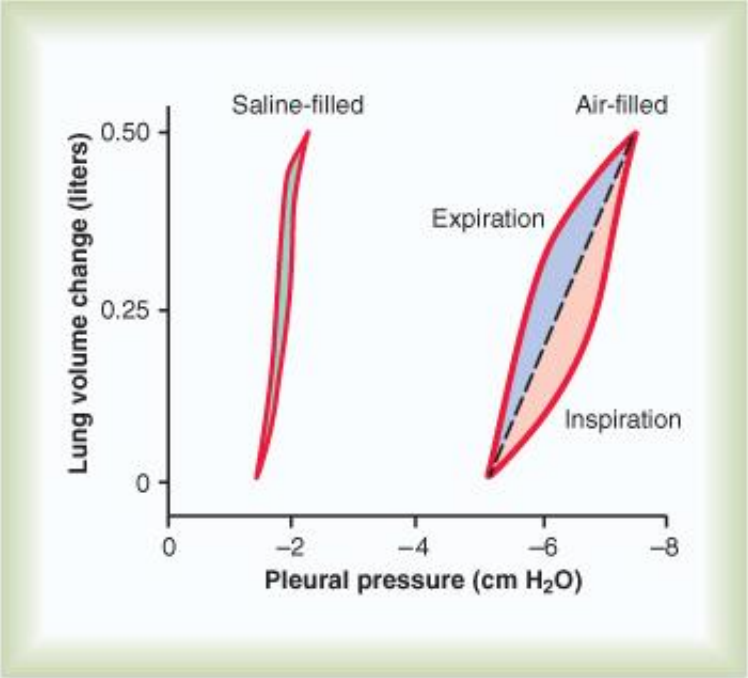
Compliance-2

- The characteristics of the compliance diagram are determined by the elastic forces of the lungs. These can be divided into two parts: 1) elastic forces of the lung tissue itself and 2) elastic forces caused by surface tension of the fluid that lines the inside walls of the alveoli and other lung air spaces.
- The elastic forces of the lung tissue are determined mainly by **elastin** and **collagen** fibers interwoven among the lung parenchyma. In deflated lungs, these fibers are in an elastically contracted and kinked state; then, when the lungs expand, the fibers become stretched and unlinked, thereby elongating and exerting even more elastic force.

Compliance-3

- The elastic forces caused by surface tension are much more complex. The significance of surface tension is shown in Figure **37-4** which compares the compliance diagram of the lungs when filled with saline solution and when filled with air. When the lungs are filled with air, there is an interface between the alveolar fluid and the air in the alveoli. In the case of the saline solution-filled lungs, there is no air-fluid interface; therefore, the surface tension effect is not present- only tissue elastic forces are operative in the saline solution-filled lungs.

Compliance-4



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Compliance-5

- Note that transpleural pressures required to expand air-filled lungs are about three times as great as those required to expand saline solution-filled lungs. Thus one can conclude that the tissue elastic forces tending to cause collapse of the air-filled lung represent only about one third of the total lung elasticity, whereas the fluid-air surface tension forces in the alveoli represent about two thirds.
- The fluid-air surface tension elastic forces of the lungs also increase tremendously when the substance called surfactant is not present in the alveolar fluid.

Surfactant, surface tension, and collapse of the alveoli.

- Principle of surface tension. When water forms a surface with air, the water molecules on the surface of the water have an especially strong attraction for one another—thus the water surface is always attempting to contract- this is what holds raindrops together.
- The same principle can be applied to the inner surface of the alveoli—here the water surface is also attempting to contract.
- This results in an attempt to force the air out of the alveoli through the bronchi and in doing so, causes the alveoli to try to collapse.
- The net effect is to cause an elastic contractile force of the entire lungs, which is called the surface tension elastic force.

Surfactant and its effect on surface tension

- Surfactant is a surface active agent in water, which means that it greatly reduces the surface tension of water.
- It is secreted by special surfactant-secreting epithelial cells called type II alveolar epithelial cells, which constitute about 10% of the surface area of the alveoli- these cells are granular, containing lipid inclusions that are secreted in the surfactant into the alveoli.

Surfactant-2

- Surfactant= complex mixture of several phospholipids, protein, and ions. The most important components are the phospholipid dipalmitoylphosphatidylcholine (dipalmitoyl-PC), surfactant apoproteins, and calcium ions.
- The dipalmitoyl-PC is responsible for reducing the surface tension= part of the molecule dissolves, while the remainder spreads over the surface of the water in the alveoli- (why does this happen?). this surface has from 1/12 to ½ the surface tension of a pure water surface

Pressure in occluded alveoli caused by surface tension

- If the air passages leading from the alveoli of the lungs are blocked, the surface tension in the alveoli tends to collapse the alveoli.
- This creates positive pressure in the alveoli, attempting to push the air out.

Represented by the following formula:

- Pressure= (2 x surface tension)/radius of alveolus

- --From this formula one can see how important surfactant is in reducing the alveolar surface tension and therefore also reducing the effort required by the respiratory muscles to expand the lungs

Effect of alveolar radius on the pressure caused by surface tension

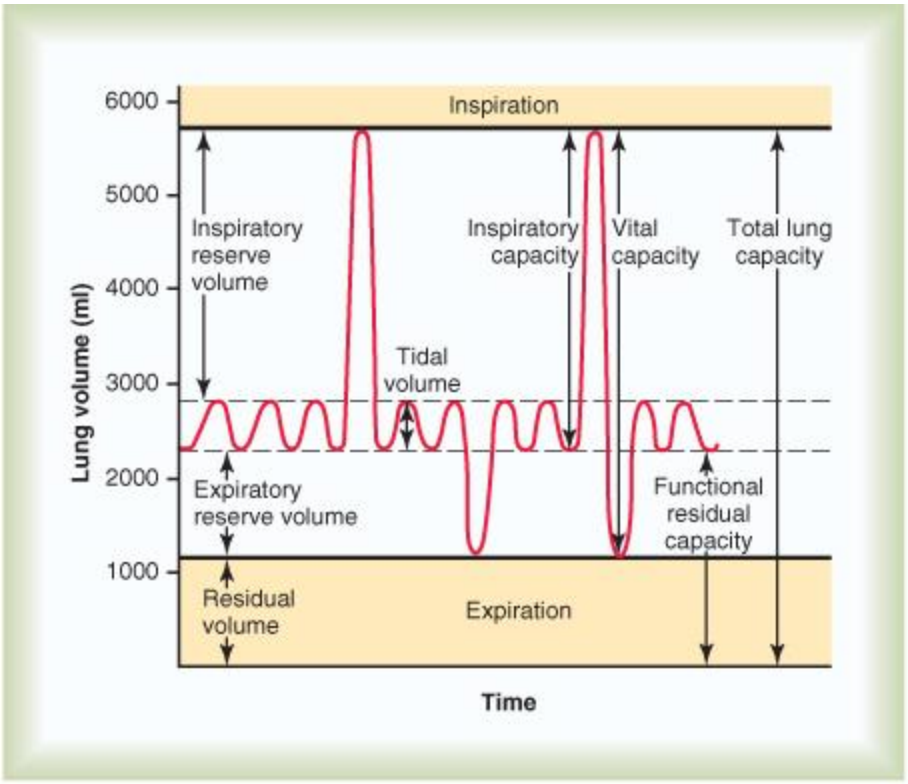
- Note from the preceding formula that the pressure generated as a result of surface tension in the alveoli is inversely affected by the radius of the alveolus.
- Thus the smaller the alveolus the greater the alveolar pressure caused by the surface tension.
- Thus when the alveoli have half the normal radius (50 instead of 100 micrometers), the pressure would be doubled.
- This is especially significant in small premature babies, many of whom have alveoli with radii less than one quarter that of an adult person. Furthermore, surfactant does not normally begin to be secreted into the alveoli until between the sixth and seventh months of gestation. Therefore, many premature babies have the condition called respiratory distress syndrome of the newborn.
- It is fatal if not treated with strong measures, especially properly applied continuous positive pressure breathing.

The work of breathing

- During normal quiet breathing, all respiratory muscle contraction occurs during inspiration; expiration is almost entirely a passive process caused by elastic recoil of the lungs and chest cage.
- Thus under resting conditions the respiratory muscles normally perform work to cause inspiration but not to cause expiration.

- <u>Energy required for respiration</u>
- During normal quiet respiration, only 3 to 5 percent of the total energy expended by the body is required for pulmonary ventilation.
- But during heavy exercise this amount can increase as much as 50-fold. Therefore, one of the major limitations on the intensity of exercise that can be performed is the person's ability to provide enough muscle energy for the respiratory process alone.

Pulmonary volumes



- Figure 37-6 lists four pulmonary lung volumes that, when added together, equal the maximum volume to which the lungs can be expanded. The significance of each is as follows:
- Tidal volume= the volume of air inspired or expired with each normal breath= 500ml in adult male.
- *Inspiratory reserve volume= extra volume of air that can be inspired* over and above the tidal when the person inspires with full force= 3000 ml.
- Expiratory reserve volume=maximum extra volume of air expired by forceful expiration after the end of a normal tidal expiration; normally= 1100 ml.
- Residual volume= volume of air remaining in the lungs after the most forceful expiration; averages about 1200 ml.

Pulmonary capacities

- In describing events in the pulmonary cycle, it is sometimes desirable to consider two or more of the volumes together. Such combinations are called pulmonary capacities.

- All pulmonary volumes and capacities are about 20 to 25% less in women than in men, and they are greater in large and athletic people than in small and asthenic people.

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.
- These areas include the alveoli, alveolar sacs, alveolar ducts, and respiratory bronchioles. The rate at which new air reaches these areas is called alveolar ventilation.
- Concept of dead space (see textbook)

Functions of the respiratory passageways:

- *Nervous and local control of the bronchiolar musculature- sympathetic dilation of the bronchioles*.
- Direct control of the bronchioles by sympathetic nerve fibers is relatively weak because few of these fibers penetrate to the central portions of the lung.
- However, the bronchial tree is very much exposed to norepinephrine and epinephrine released into the blood by sympathetic stimulation of the adrenal glands.
- Both of these hormones, especially epinephrine, because of its greater stimulation of beta-adrenergic receptors, cause dilation of the bronchial tree.

Parasympathetic constriction of the bronchioles

- A few parasympathetic nerve fibers derived from the vagus nerves penetrate the lung parenchyma.
- These nerves secrete acetylcholine and when activated, cause mild to moderate constriction of the bronchioles.
- When a disease such as asthma has already caused some bronchiolar constriction, superimposed parasympathetic nervous stimulation often worsens the condition.
- When this occurs, administration of drugs that block the effects of acetylcholine, such as atropine, can sometimes relax the respiratory passages enough to relieve obstruction

Local secretory factors often cause bronchiolar constriction

- Several substances formed in the lungs themselves are often quite active in causing bronchiolar constriction= histamine and slow reactive substance of anaphylaxis—
- both of these are released in the lung tissues by mast cells during allergic reactions, especially those caused by pollen in the air.
- They therefore play key roles in causing the airway obstruction that occurs in allergic asthma

Mucous lining the respiratory passageways and action of cilia to clear the passageways

- All the respiratory passages, from the nose to the terminal bronchioles are kept moist by a layer of mucous that coats the entire surface.
- This mucous is secreted by mucous goblet cells in the epithelium lining of the passages and by small submucosal glands. Mucous keeps the cell surface moist and also traps small particles out of the inspired air and keeps these from reaching the alveoli

- The respiratory passages are lined with ciliated epithelium, with about 200 cilia on each epithelial cell; each cilia beat continually at a rate of 10 to 20 times per second.
- Direction of their “power stroke” is ***always toward the pharynx***.
- Thus cilia in the lungs beat upward whereas those in nose beat downward.
- The collected mucous and its entrapped particles are either swallowed or coughed to the exterior

Cough reflex

- Very slight amounts of foreign matter or other causes of irritation to the bronchi or trachea initiate the cough reflex.
- First, up to 2.5 liters of air is rapidly inspired. 2nd, the epiglottis closes and the vocal cords shut tightly to entrap the air within the lungs.
- 3rd the abdominal muscles contract forcefully, pushing against the diaphragm, consequently rapidly raising the pressure in the lungs to as much as 100 mm Hg or more.
- 4th, the vocal cords and epiglottis suddenly open widely, so that air under this high pressure in the lungs explodes outward.

Cough reflex-2

- This air can reach velocities from 75-100 mph.
- importantly, the strong compression of the lungs collapses the bronchi and trachea by causing their noncartilaginous parts to invaginate inward, so that the exploding air actually passes through bronchial and tracheal slits.
- The rapidly moving air usually carries with it any foreign matter that is present in the bronchi or trachea
- Sneeze reflex
- Very much like the cough reflex. In this case the uvula is depressed, so that large amounts of air pass rapidly through the nose, thus helping to clear the nasal passages of foreign matter

Normal respiratory functions of the nose

- 1. The air is warmed;
- 2. Air is humidified;
- 3. Air is filtered.
-
- These essential functions are illustrated by the effects of breathing air through a tube directly into the trachea (as through a tracheostomy), the cooling and especially the drying effect in the lower lung can lead to serious lung crusting and infection.

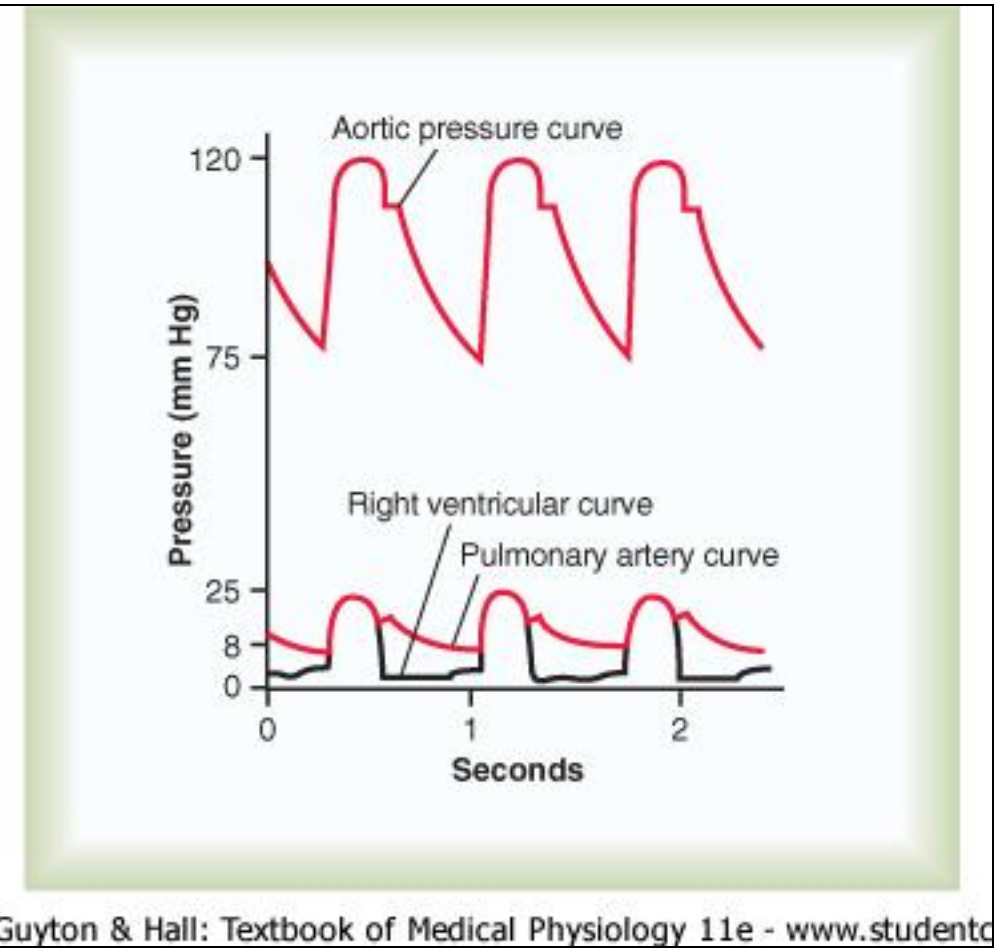
Size of particles trapped in respiratory passages

- The nasal ***turbulence mechanism*** for removing particles from air is so effective that almost no particles larger than 6 micrometers in diameter enter the lungs through the nose.
- Many particles smaller than 0.5 micrometer in diameter remain suspended in the alveolar air and are expelled by expiration.
- For instance, the particles of cigarette smoke are about 0.3 micrometer. Almost none of these particles are precipitated in the respiratory passageways before they reach the alveoli.
- And unfortunately, up to one third of them do precipitate in the alveoli by the diffusion process, with the balance remaining suspended and expelled in the expired air.

Chap. 38
Pulmonary vessels

- The pulmonary artery extends only 5 centimeters beyond the apex of the right ventricles and then divides into right and left main branches that supply blood to the two respective lungs.
- The pulmonary artery is thin, with a wall thickness one third that of the aorta; all the pulmonary arteries have larger diameters than their counterpart systemic arteries.
- This combined with the fact that the vessels are thin and distensible, gives the pulmonary arterial tree a large compliance.
- The pulmonary veins, like the pulmonary arteries, are also short. The immediately empty their effluent blood into the left atrium, to be pumped by the left heart through the systemic circulation.

Pressure in the pulmonary system



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During systole, the pressure in the pulmonary artery is essentially equal to the pressure in the right ventricle (fig. 38-1).

However, after the pulmonary valve closes at the end of systole, the ventricular pressure fall precipitously, whereas the pulmonary arterial pressure falls more slowly as blood flows through the capillaries of the lungs.

Blood flow through the lungs and its distribution

- Blood flow through the lungs is essentially equal to the cardiac output.
- Under most conditions, the pulmonary vessels act as passive, distensible tubes that enlarge with increasing pressure and narrow with decreasing pressure

Effect of diminished alveolar oxygen on local alveolar blood flow- automatic control of pulmonary blood flow distribution

- When the concentration of oxygen in the air of the alveoli decreases below normal (below 70% or normal), the adjacent blood vessels constrict, with the vascular resistance increasing more than fivefold at extremely low oxygen levels.
- This is the opposite to the effect observed in systemic vessels. It is believed that the low oxygen concentration causes some yet undiscovered vasoconstrictor substance to be released from the lung tissue.
- The effect of low oxygen on pulmonary vascular resistance has an important function: to distribute blood flow where it is most effective.
- So if some alveoli are poorly ventilated so that their oxygen concentration becomes low, the local vessels constrict.
- This causes the blood to flow through other areas of the lungs that are better aerated, thus providing and automatic control system for distributing blood flow to the pulmonary areas in proportion to their alveolar oxygen pressures

Length of time blood stays in the pulmonary capillaries

- It has been calculated that when the cardiac output is normal, blood passes through the pulmonary capillaries in about 0.8 sec.
- when the cardiac output increases, this can shorten to as little as 0.3 sec.
- thus in only a fraction of a second, blood passing through the alveolar capillaries becomes oxygenated and loses its excess carbon dioxide.

Pulmonary edema

- Pulmonary edema occurs in the same way that edema occurs elsewhere in the body.
- Any factor that causes the pulmonary interstitial fluid pressure to rise from the negative range into the positive range will cause rapid filling of the pulmonary interstitial spaces and alveoli with large amounts of free fluid.
- The most common causes of pulmonary edema are:
- 1. Left-sided heart failure or mitral valve disease, with consequent great increases in pulmonary venous pressure and pulmonary capillary pressure and flooding of the interstitial spaces and alveoli.
- 2. Damage to the pulmonary blood capillary membranes caused by infection such as pneumonia or breathing noxious gases.
- Each of these causes rapid leakage of both plasma proteins and fluid out of the capillaries and into both the lung interstitial spaces and the alveoli

Pulmonary edema safety factor:
Safety factor in chronic conditions

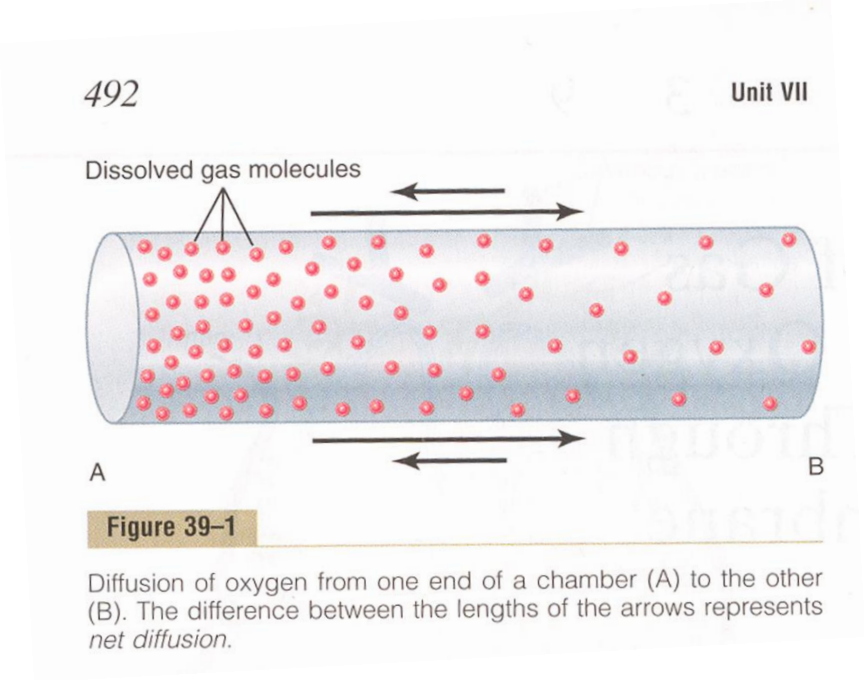
- When the pulmonary capillary pressure remains elevated chronically (for at least two weeks), the lungs become even more resistant to pulmonary edema because the lymph vessels expand greatly, increasing their capability of carrying away fluid from the interstitial spaces perhaps as much as 10-fold.
- In patients with chronic mitral stenosis, pulmonary capillary pressure of 40-45 mm Hg have been measured without the development of lethal pulmonary edema.

- Rapidity of death in acute pulmonary edema.
- When the pulmonary capillary pressure rises even slightly above the safety factor level, lethal pulmonary edema can occur within hours, or even within 20-30 minutes.
- Thus, in acute left-sided heart failure, in which the pulmonary capillary pressure occasionally does rise to 50 mm Hg, death frequently ensues in less than 30 minutes from acute pulmonary edema.

Chapter 39.

- After the alveoli are ventilated with fresh air, the next step in the respiratory process is **diffusion** of oxygen from the alveoli into the pulmonary blood and diffusion of carbon dioxide in the opposite direction, out of the blood.
- One is concerned not only with the basic mechanism by which diffusion occurs but also with the rate at which it occurs.

Molecular basis of gas diffusion



All the gases of concern in respiratory physiology are simple molecules that are free to move among one another, which is the process called diffusion. For diffusion to occur, there must be a source of energy.

This is provided by the kinetic motion of the molecules themselves.
Net diffusion of a gas in one direction- effect of a concentration gradient.
From high to low- show fig. 39-1.

Gas pressures in a mixture of gases- partial pressures of individual gases

- Pressure is caused by multiple impacts of moving molecules against a surface. This means that the pressure is directly proportional to the concentration of the gas molecules.
- In respiratory physiology one deals with mixtures of mainly oxygen, nitrogen, and carbon dioxide. The rate of diffusion of each of these gases is directly proportional to the pressure caused by that gas alone, called the partial pressure of that gas.

Factors that determine the partial pressure of a gas dissolved in a fluid

- The partial pressure of a gas in solution is determined not only by its concentration, but also by the solubility coefficient of the gas.
- Some types of molecules, especially carbon dioxide are physically or chemically attracted to water molecules, whereas others are repelled. These relations are expressed by the following formula, which is Henry's law:
- Partial pressure= Conc. Of dissolved gas/ solubility coefficient.

- The solubility coefficients for example for oxygen is 0.024 and carbon dioxide= 0.57

- From these values one can see that ***carbon dioxide is more than 20 times as soluble as oxygen***. Therefore, the *partial pressure* of carbon dioxide (for a given concentration) is less than one twentieth that exerted by oxygen.

Diffusion of gases between the gas phase in the alveoli and the dissolved phase in the pulmonary blood.

- The partial pressure of each gas in the alveolar respiratory gas mixture tends to force molecules of that gas into solution in the blood of the alveolar capillaries.
- Conversely, the molecules of the same gas that have already dissolved in the blood are bouncing randomly in the fluid of the blood, and some of these bouncing molecules escape back into the aveoli.
- The rate at which they escape is directly proportional to their partial pressure in the blood.

Diffusion-2

- But in which direction will net diffusion of the gas occur?
- This is determined by the difference between the two partial pressures.
- If the partial pressure is greater in the gas phase in the alveoli, as is normally true for oxygen, then more molecules will diffuse into the blood than in the other direction.
- Alternatively, if the partial pressure of the gas is greater in the dissolved state in the blood, which is normally true for carbon dioxide, then net diffusion will occur toward the gas phase in the alveoli

Quantifying the net rate of diffusion in fluids

- In addition to the pressure difference, other factors affecting the rate of gas diffusion in a fluid are
- 1) solubility of the gas in the fluid;
- 2) cross-sectional area of the fluid;
- 3) distance through which the gas must diffuse;
- 4) molecular weight of the gas; and
- 5) the temperature of the fluid. In the body, temperature remains reasonably constant and usually need not be considered.
- Therefore:

- >solubility of gas= >#of molecules available to diffuse for any given partial pressure difference.
- >cross sec. area of diffusion pathway=># of molecules that diffuse
- >distance the molecule must diffuse=>time it will take the molecule to diffuse the entire distance
- >velocity of kinetic movement of molecules (inv. Prop. To molec. Weight)=>rate of diffusion of the gas.

Quantifying the net rate of diffusion in fluids-2

- All of these factors can be expressed in a single formula as follows:
- $D \propto \frac{\Delta P \times A \times S}{d \times \sqrt{MW}}$

- in which D is the diffusion rate, ΔP is the partial pressure difference between the two ends of the diffusion pathway, A is the cross-sectional area of the pathway, S= solubility of the gas, d=distance of diffusion, and MW= molecular weight of the gas.

- The characteristics of the gas itself determine two factors of the formula: ***solubility and molecular weight***. Together, these two factors determine the diffusion coefficient of the gas which is proportional to S/√MW.

Diffusion of gases through tissues

- The gases that are of respiratory importance are all highly soluble in lipids and consequently are highly soluble in cell membranes

- Composition of alveolar air- its relation to atmospheric air.
- Alveolar air does not have the same concentrations of gases as atmospheric air by any means. There are several reasons for this:
- 1) alveolar air is only partially replaced by atmospheric air with each breath;
- 2) oxygen is constantly being absorbed into the pulmonary blood from the alveolar air;
- 3) carbon dioxide is constantly diffusing from the pulmonary blood into the alveoli;
- 4) dry atmospheric air that enters the respiratory passages is humidified even before it reaches the alveoli.

Humidification of the air in the respiratory passages

- Table 39-1 in the text shows that atmospheric air is composed almost entirely of nitrogen and oxygen; it normally contains almost ***no CO_2 and little water vapor***.
- However, as soon as the atmospheric air enters the respiratory passages, it is exposed to the fluids that cover the respiratory surfaces.
- Even before the air enters the alveoli, it becomes humidified.
- The partial pressure of water vapor at a normal body temperature of 37deg C is **47 mm Hg, which is therefore the partial pressure of water vapor in the alveolar air**.
- Because the total pressure in the alveoli cannot rise to more than the atmospheric pressure (760 mm Hg at sea level), ***this water vapor dilutes the oxygen partial pressure at sea level*** from an average of 159 mm Hg in atmospheric air to 149 mm Hg in the humidified air.

Rate at which alveolar air is renewed by atmospheric air

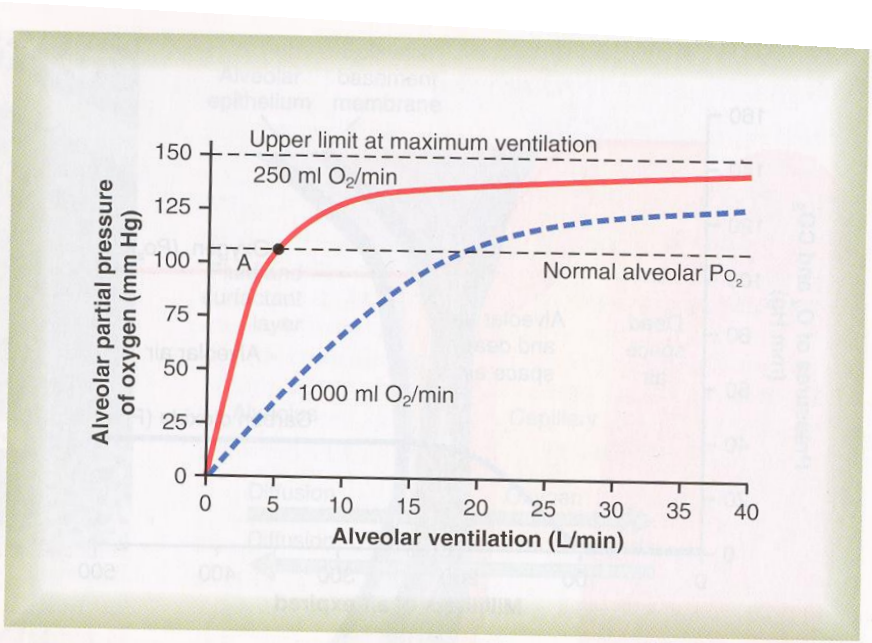
- As previously discussed, the average male functional residual capacity of the lung measure about2300 ml., yet only 350 ml of new air is brought into the alveoli with each normal inspiration, and this same amount of old alveolar air is expired.
- Therefore, the volume of alveolar air that is replaced by new atmospheric air with each breath is only one seventh of the total, so that multiple breaths are required to exchange most of the alveolar air.

- The slow replacement of alveolar air is of particular importance in preventing sudden changes in gas concentration in the blood.
- This makes the respiratory control mechanism much more stable than it would otherwise be, and it helps ***prevent excessive increases and decreases in tissue oxygenation, tissue carbon dioxide concentration, and tissue pH*** when respiration is temporarily interrupted ---(holding one's breath under water?)

Oxygen concentration and partial pressure in the alveoli

- Oxygen concentration in the alveoli and its partial pressure as well, is controlled by
- 1) the rate of absorption of oxygen into the blood and
- 2) the rate of entry of new oxygen into the lungs by the ventilator process.

Alveolar ventilation vs. PO_2



1. Fig. 39-4 shows the effect of both alveolar ventilation and rate of oxygen absorption into the blood on the alveolar partial pressure of oxygen (**PO_2**). When 1000 ml of oxygen is being absorbed each minute, as occurs during moderate exercise, the rate of alveolar ventilation must increase fourfold to maintain the alveolar PO_2 at the normal value of 104 mm Hg.

2. Another effect shown in fig. 39-4 is that an extremely marked increase in alveolar ventilation can never increase the alveolar PO_2 above 149 mm Hg as long as the person is breathing normal atmospheric air at sea level pressure, because this is the maximum PO_2 in humidified air at this pressure. If the person breathes gases that contain partial pressure of oxygen higher than 149 mm Hg, the alveolar PO_2 can approach these higher pressures at high rates of ventilation (football player and oxygen on the sidelines?)

CO_2 concentration and partial pressure in the alveoli

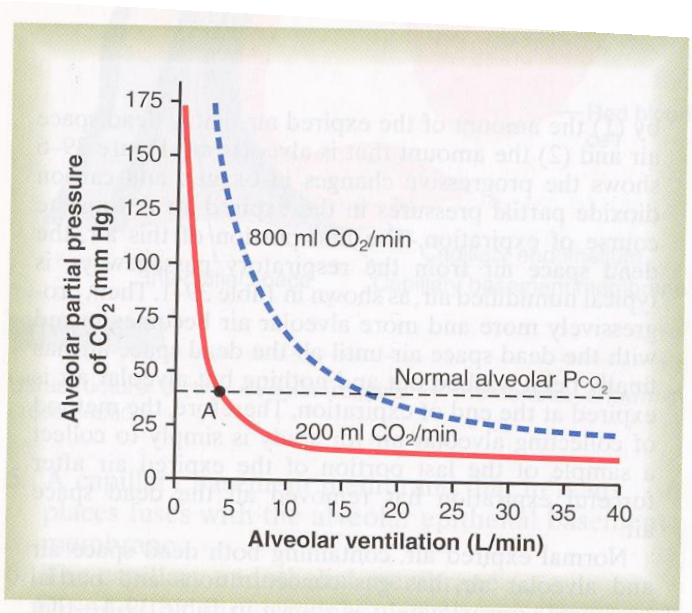


Figure 39–5

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.

CO_2 is continually being formed in the body and then carried in the blood to the alveoli; it is continually being removed from the alveoli by ventilation.

Fig. 39-5 shows the effects on the alveolar partial pressure of carbon dioxide (**PCO_2**) of both alveolar ventilation and two rates of CO_2 excretion.

Two facts are evident from this figure:

1) the alveolar PCO_2 increases directly in proportion to the rate of CO_2 excretion, as represented by the 4-fold elevation of the curve when 800 ml of CO_2 are excreted per/min compared to the normal 200 ml/min.
2) 2nd) the alveolar PCO_2 decreases in ***proportion*** to alveolar ventilation.

Therefore, the concentrations and partial pressures of both oxygen and carbon dioxide in the alveoli are determined by the rates of absorption or excretion of the two gases and by the amount of alveolar ventilation.

End!