WCHP Respiratory Physiology 2009-2010
PULMONARY VENTILATION

Clinical rationale and overall goal:

Acute and chronic respiratory disorders affecting ventilation are among the most common problems seen in a primary care setting. The overall goal of this classroom session is to provide the student with an understanding of the mechanics of ventilation, the physiological basis for pulmonary function testing, and the concepts of dead space and alveolar ventilation - concepts that must be understood in order to appreciate the pathophysiology of arterial hypoxemia in a patient with respiratory disease.

Sources of information:

The sources of information that will be sufficient for the individual student to master the specific objectives listed below include the following:

- The required text: Guyton & Hall, *Textbook of Medical Physiology, 11th edition*, Chap. 37;
- Handouts, reprints, URLs, or other supplementary materials provided by faculty;
- Lecture notes

Nota bene: Students are expected to be prepared for class by having read the relevant sections in the text(s) prior to the classroom sessions on individual topics, to take their own notes during classroom sessions, to participate actively in any large-group or break-out group activities, and to try all online quizzes. Students are encouraged to contact the instructor via email (jnorton@une.edu) with any questions. Students are strongly discouraged from using class notes provided by a note service as the sole or even the primary source of information in this course.

Learning objectives:

Following study of appropriate sections in the assigned texts (or similar sections in other texts available to the student and approved by the instructor) and attendance at the lectures on this topic, the student should be able to:

1. Define or otherwise indicate an understanding of the following words or phrases: ventilation; perfusion; oxygen consumption; carbon dioxide production; diffusion; convection; inspiration; expiration; anatomic dead space; physiologic dead space; work of breathing; partial pressure; water vapor pressure; frequency; tidal volume; minute ventilation; dead space ventilation; alveolar ventilation; pulmonary volumes and capacities; hyperventilation; hypoventilation; alveolar ventilation equation; alveolar air equation; atelectasis; surface tension.

2. Identify the primary and accessory muscles of inspiration and expiration, and indicate whether each is active in quiet breathing and/or in conditions when minute ventilation is increased significantly;

3. Demonstrate an understanding of the relationships among minute ventilation, respiratory frequency, and tidal volume, as described in the following expression:

$$\dot{V}_E = f \cdot V_T$$

4. Demonstrate an understanding of the relationships among minute ventilation, dead space ventilation, and alveolar ventilation, as described in the following expression:

$$\dot{V}_E = \dot{V}_D + \dot{V}_A$$

5. Demonstrate an understanding of the changes in *alveolar pressure* and *intrapleural pressure* that occur during a normal quiet respiratory cycle, and identify typical values for these pressures at the onset and end of inspiration and the end of expiration;

6. Demonstrate an understanding of the changes in *lung volume* during a normal quiet respiratory cycle, and

identify typical values for lung volume in a 70 kg healthy human subject at the end of inspiration and the end of expiration;

7. Identify, in words or on a representation of a spirometric tracing, the four *pulmonary volumes* and four *pulmonary capacities* and recognize typical values for these volumes and capacities in a healthy human subject;

8. Recognize each of the following quantities derived from spirometry and identify the usefulness of each in determining the presence of *restrictive* and/or *obstructive* lung disease: FVC, $FEV_{1.0}$, and the $FEV_{1.0}$/FVC ratio;

9. Identify the physical forces that combine to generate a *negative intrapleural pressure* in a healthy human subject at rest;

10. Demonstrate an understanding of differences between *anatomic* and *physiologic* dead spaces with respect to their magnitude in a healthy human subject; method of measurement; clinical importance;

11. Demonstrate an understanding of *alveolar ventilation*, including appropriate units, and recognize its significance in pulmonary gas exchange;

12. Demonstrate an understanding of the *alveolar ventilation equation* with respect to the effects (increase, decrease, no change) of changes in alveolar ventilation or changes in the rate of CO_2 production on the alveolar partial pressure of carbon dioxide, as described in the following expression:

$$P_A CO_2 = \frac{\dot{V}CO_2}{\dot{V}_A} \cdot K$$

13. Recognize the effects (increase, decrease, no change) of *hypoventilation* and *hyperventilation* on the alveolar and arterial partial pressures of oxygen and carbon dioxide.

14. Recognize the effects (increase, decrease, no change) of changes in either *respiratory frequency* or *tidal volume* on minute ventilation and alveolar ventilation;

15. Demonstrate an understanding of the use of the simplified version of the *alveolar air equation* in calculating alveolar PO_2 when given values for inspired PO_2, the respiratory exchange ratio, and arterial or alveolar PCO_2 in a real or simulated patient case, as described by the following expression:

$$P_A O_2 = P_I O_2 - \frac{P_a CO_2}{R}$$

16. Given information about the results of pulmonary function tests in a real or simulated patient case, indicate whether the patient most likely has an *obstructive disorder*, a *restrictive disorder*, or both, and support this position with specific and appropriate data from the case.

Ventilation

The purpose of ventilation, a form of convective transport, is to bring ambient air and its supply of oxygen into the respiratory system and into close contact with pulmonary capillary blood to facilitate gas exchange. The structure of the discussion of ventilation in this handout is based on the following deceptively simple questions:

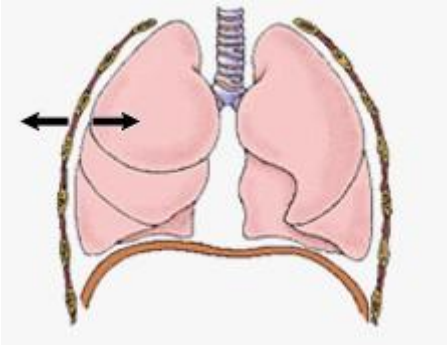
- How does air move?
- How much air moves?
- How fast does air move?
- Where does the air go?

A full discussion of these questions will lead the student through the mechanics of ventilation, the actions of the muscles of ventilation, the work of breathing, and the quantification of airflow within the respiratory system. The following discussion is only an attempt to provide the student with a framework for understanding and integrating facts and concepts related to ventilation, and *the information in this handout is not meant to substitute for attendance in class or completion of the assigned reading in the required textbook*.

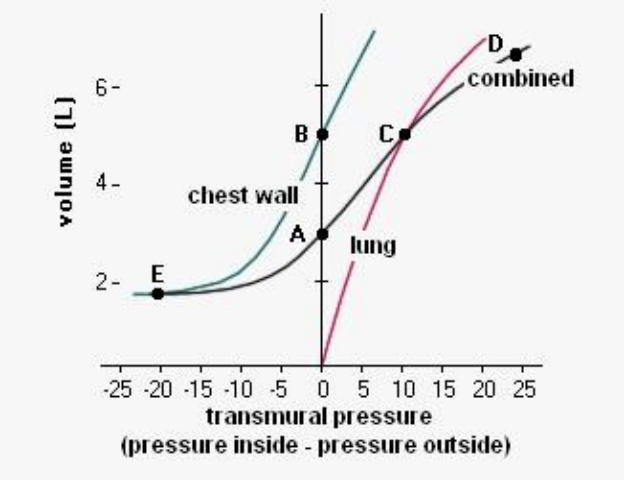
How does air move?

Ironically, the discussion of how air moves during ventilation begins with consideration of a healthy human at rest, with no ventilatory muscle activity. The resting thorax, in a typical 70-kg standard human subject, contains about 2200-2300 ml of air within the airways and alveoli. The lung is inflated, not collapsed, and is held against the inside of the thoracic wall by a layer of slippery fluid within the pleural space. The lung can be simplistically visualized as a balloon, which can only be inflated if the pressure inside the balloon, P_i, exceeds the pressure outside the balloon, P_o. One way that this could be accomplished is blowing air into the balloon to inflate it, and then pinching off or tying off the neck of the balloon, trapping air inside. If air is subsequently allowed to leave the balloon through the neck, P_i approaches P_o – *i.e.*, the transmural pressure (P_i-P_o) approaches zero [0] – and the balloon collapses due to the elastic forces with its wall. In contrast to blowing up a balloon, in a resting human subject with an open glottis, the lung remains inflated, even though the pressure inside the lung is equal to the atmospheric pressure outside the body. This is possible because the true transmural pressure for the lung in an intact chest is the difference between the pressure within the lung – the *intrapulmonary* pressure – and the pressure immediately outside the lung – the *intrapleural* pressure. The latter pressure is usually subatmospheric, or negative, meaning that the transmural pressure for the lung is a positive value and the lung is inflated.

The negative pressure in the intrapleural space arises from the elastic properties of the lung and chest wall. As described above for a balloon, the elasticity of the lung would cause it to collapse if the transmural pressure were reduced to zero. The elastic forces within the lung in a healthy human subject, therefore, pull the chest inward. The chest wall alone, on the other hand, has a resting volume that is larger than the resting volume of the intact thorax of a human subject. For the chest wall, the transmural pressure would be the difference between the pressure inside, the intrapleural pressure, and the pressure outside, the atmospheric pressure. Since the intrapleural pressure is negative, P_i-P_o for the chest wall alone is a negative number, which means that the chest wall is being pulled inward, toward a smaller volume than its resting volume. If the transmural pressure for the chest was were reduced to zero [0], the chest wall would spring outward toward its resting volume. The resting volume of the chest, therefore, can be considered to represent the point at which the tendency of the lung to collapse and pull the chest wall inward is matched by the tendency of the chest wall to expand and pull the lung outward, as shown in the figure below.



A graphical representation of this concept is shown in the figure below. In this diagram, the vertical axis represents the volume in liters of the lungs alone, the chest wall alone, or the intact thorax. The horizontal axis in this figure is labeled "transmural pressure", meaning the pressure gradient across the wall (the pressure inside minus the pressure outside, or P_i-P_o). Compliance curves are drawn on this set of axes for the lung alone, the chest wall alone, and the combined lung-chest wall unit.



A positive transmural pressure for the lung alone indicates that the pressure inside the lung is higher than the pressure outside, causing the lung to increase in volume. A positive value for transmural pressure could occur either by an increase in the pressure within the lung (as in positive pressure ventilation), or by a decrease in the pressure outside the lung, which is what happens during normal inspiration. Similarly, a negative value for transmural pressure could occur either by reducing the pressure inside the lung, or by increasing the pressure outside the lung, which is what happens during a forceful expiratory effort.

Consider first the compliance curve for the lung alone. For the lung, the transmural pressure equals the difference between the intrapulmonary pressure within the lung and the intrapleural pressure outside the lung (but within the chest). At a transmural pressure of zero [0], indicated by the vertical line in the center of the graph, there is no difference between the pressure inside the lung and outside the lung – no pressure gradient tending to keep the lung open. Under this condition, the lung is collapsed to a very small volume due to its inherent elastic recoil. In order for the lung to expand, there must be a higher pressure inside the lung than outside, and the compliance curve for the lung alone represents the increase in volume that occurs with increasingly positive transmural pressure.

Consider next the compliance curve for the chest wall. For the chest wall alone, the transmural pressure equals the difference between the intrapleural pressure and the atmospheric pressure. At a transmural pressure of zero [0], the chest wall is not collapsed, but has a relatively large volume of about five liters (point "B" on the diagram above). Increasing the transmural pressure will cause the chest wall to expand to a larger volume, decreasing the transmural pressure will cause the chest wall volume to decrease. There is a minimum value for chest wall volume (point "E" on the diagram above) that is determined by the bony structure of the chest wall, in particular the ribs.

Consider last the compliance curve for the intact thorax, with the lungs encased within the chest cavity. For the intact thorax, the transmural pressure equals the difference in pressure between the intrapulmonary pressure inside the lung and the atmospheric pressure outside the body. Point "A", located on the vertical line representing a transmural pressure of zero [0] (no net force tending to increase or decrease thoracic volume), represents the normal stable resting volume of the thorax. This resting volume is determined the balance between the tendency of the chest wall to expand to its resting volume (point "B") and the tendency of the lung to collapse to a very low volume.

Moving the thorax away from its resting volume, in either direction, requires the use of force in the form of ventilatory muscle contraction. As inspiration occurs, and thoracic volume increases away from the resting value along the combined compliance curve, the inspiratory muscles must overcome the elastic forces tending to make the lung collapse. On the other hand, the elastic properties of the chest wall assist inspiration, at least at first. However, a point is reached (point "C" on the diagram) when further inspiratory effort must overcome the elastic forces in both the lung and the chest wall, the compliance curve for the intact thorax becomes flatter as thoracic volume approaches its maximum (point "D" on the diagram).

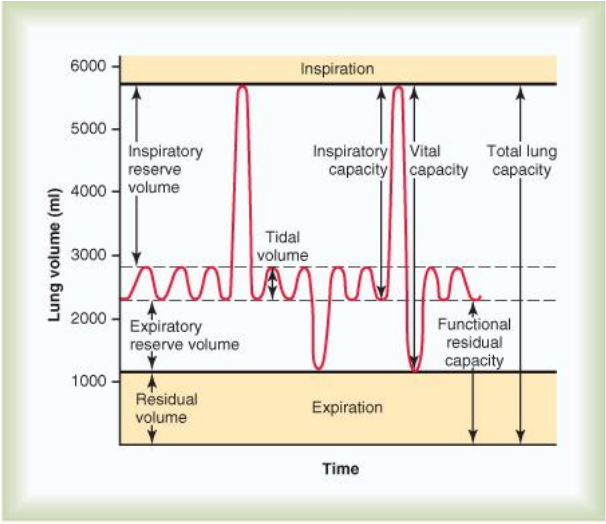
As forceful expiration occurs, and thoracic volume decreases away from the resting value, the expiratory muscles are assisted by the tendency of the lung to collapse but are opposed by the chest wall. Even with a very forceful expiratory effort, the bony structure of the thorax prevents all the air from being expelled, and there is still a residual volume of air left in the lung (point "E" in the diagram).

The air within the lung communicates with the air outside the body through the airways that terminate at the openings of the nose and mouth. The answer to the question "*How does air move*?" can now finally be addressed directly. According to Boyle's Law, increasing the thoracic volume during inspiration will transiently decrease the pressure with the lung, producing a pressure gradient that promotes air movement from the region of higher pressure, the atmosphere, through the nose and mouth into the region of lower pressure, the interior of the lung. Conversely, decreasing the volume of the thorax during expiration will transiently increase the pressure within the lung, and create a pressure gradient that tends to move air from the region of high pressure within the lung out through the nose and mouth into the region of lower pressure, the atmosphere outside the body. Air will flow into or out of the lung as long as there is a pressure gradient promoting movement. Once the pressure within the lung becomes equal to the pressure outside the body, no more air will flow.

Using the ventilatory muscles to increase or decrease thoracic volume therefore requires energy to overcome the elastic forces of the lung and chest wall. A major component of the *work of breathing*, therefore, resides in the *elastic properties* of the structures comprising the thorax. Air must move through the conducting system, which offers resistance to air flow related to the size and length of the airways. Another component of the work of breathing resides in *airway resistance*, although in a healthy human subject airway resistance is very low. A third component of the work of breathing is due to the *viscoelastic properties of tissues*, which means that a force applied suddenly to the thorax will not result in an instantaneous change in its dimensions, but rather a somewhat delayed response. A final component of the work of breathing is alveolar *surface tension*. The walls of the alveoli are moist, covered with a thin film of water exposed to the air within the alveoli. This air-water interface generates surface tension, a strong force that contributes, along with the inherent elasticity of the lung, to the tendency of the lung to collapse. The surface tension within the alveoli is reduced by surfactant, a mixture of lipids synthesized by type II alveolar cells. These lipids naturally move to the surface of the liquid, breaking up the attractive forces between the water molecules and reducing surface tension.

How much air moves? How fast does air move?

These two questions can both be answered using spirometry. In a typical procedure, a patient is provided with a noseclip and is asked to breath in and out through a mouthpiece connected to a recording device, which can measure flow rates and volumes during inspiration and expiration. The patient is asked to breath quietly, then take in a maximum inspiration, and follow it with a maximum expiratory effort. At the completion of the maximum expiratory effort, the patient is asked to breath quietly again. . The result is a tracing similar to that shown below, taken from the required text.



Spirometry and other associated techniques can identify the various lung volumes and capacities indicated on the diagram above. The four lung volumes that can be identified by spirometry and other related tests are:

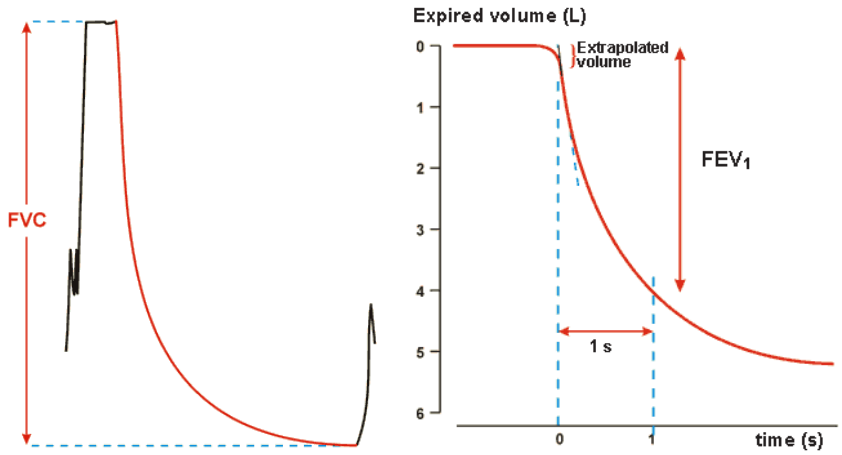
- *Tidal volume* (**V_T**), the volume of air breathed in and out during one respiratory cycle, or one breath;
- *Inspiratory reserve volume* (**IRV**), the additional volume of air that could be inspired above and beyond the normal resting tidal volume;
- *Expiratory reserve volume* (**ERV**), the additional volume of air that could be expired after a normal quiet expiration;
- *Residual volume* (**RV**), the volume of air left in the lung after a maximal expiratory effort.

The four pulmonary capacities are:

- *Functional residual capacity* (**FRC**), the resting volume of the lung, with no ventilatory muscle activity;
- *Inspiratory capacity* (**IC**), the maximum volume of air that can be inspired starting from the FRC;
- *Vital capacity* (**VC**), the maximum volume of air that can be forcefully expired after a maximal inspiratory effort, or, the largest tidal volume possible;
- *Total lung capacity* (**TLC**), the volume of air in the lung at the end of a maximum inspiratory effort.

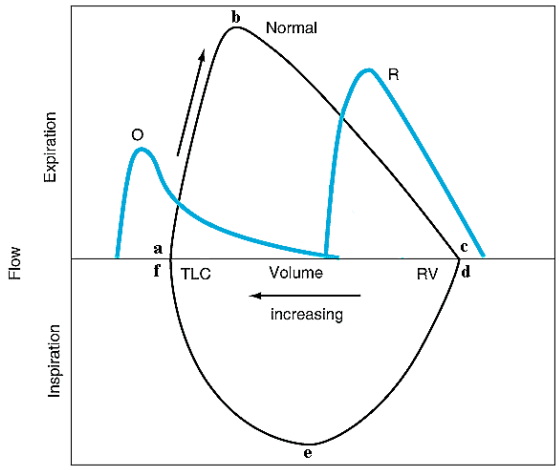
Of the above pulmonary volumes and capacities, only the following can be directly measured by spirometry – V_T, IRV, ERV, VC, and IC. The remaining quantities – FRC, RV, and TLC – require the use of an inert gas and are calculated based on the dilution of the gas throughout the entire lung volume.

The answer to the question "*How much air moves*" is best answered by the spirometric measurement of forced vital capacity, or FVC. The FVC represents the largest tidal volume an individual can generate, by calling upon the accessory muscles of inspiration and expiration to utilize the full inspiratory and expiratory reserve volumes, respectively. Expected or predicted values for FVC are related to the age, sex, and body size of the individual being tested. A measured value for FVC that is less than the expected value indicates that the individual is somewhat restricted in his or her ability to generate thoracic volume changes. Diseases or disorders that result in a reduction in FVC are therefore called *restrictive* disorders. Restrictive disorders can result from a variety of disturbances, including neural, muscular, skeletal, and lung disorders. A graphical description of the FVC is provided in the left panel of the figure below, showing a maximum expiratory effort following a maximum inspiration.



The question "*How fast does air move?*" can also be answered by spirometry, as shown in the right panel of the figure above. The volume of air expired in the first second of a forced expiratory effort, the FEV_1, can be compared to the FVC using the $\frac{FEV_1}{FVC}$ ratio. Normally, more than 80% of the eventual FVC can be expired in the first second. A $\frac{FEV_1}{FVC}$ ratio that is less than normal suggests the presence of an *obstructive* lung disease that decreases the rate of expiratory flow. Obstructive lung disorders can be caused by reversible processes such as reactive bronchoconstriction, or more permanent conditions such as chronic bronchitis, emphysema, or masses that reduce airway diameter.

Another approach to the evaluation of airflow through the tracheobronchial tree is the generation of *flow-volume loops*. The diagram below is an illustration of normal and abnormal flow-volume loops, similar to Figure 42-02 in the required text. Note that the axes are somewhat unusual. The vertical axis represents flow, with the horizontal line across the middle of the diagram indicating zero [0] flow. Positive outward flows (expiration) are located above the horizontal line; negative inward flows (inspiration) are located below the horizontal line. The horizontal axis represents lung volume, but the magnitude of lung volume increases from right to left.



Consider first the normal flow-volume loop in the center of the diagram. Recording of a flow-volume loop begins at the end of a maximal inspiratory effort (*i.e.*, at the total lung capacity), and this point is indicated by "**a**" on the normal curve in the diagram above. The patient then forcefully exhales, and flow velocity reaches a maximum expiratory flow rate at point "**b**", relatively early in the expiratory effort. Expiration then continues until the subject or patient has reached the residual volume and cannot expire any more air, point "**c**" in the diagram. A maximum inspiratory effort follows immediately, beginning at point "**d**". Maximum inspiratory flow is achieved at point "**e**", about midway through the inspiratory effort, and the subject or patient returns to the maximum inspiratory volume (or total lung capacity) at point "**f**".

The inspiratory portions of the curves for the patients with obstructive lung disease (O) and restrictive lung disease (R) are not shown for the sake of clarity, but the student should notice the differences between the abnormal expiratory flow-volume patterns and the normal expiratory pattern. The patient with the obstructive lung disorder (O) has higher lung volumes than the normal subject at the end of both inspiration and expiration, and has a lower peak expiratory flow rate. The patient with the restrictive disorder (R) has end-inspiratory and end-expiratory volumes that are lower than those of the normal subject, and has a smaller tidal volume (on the diagram above, the horizontal distance between the end-inspiratory and end-expiratory volumes).

The generation of pulmonary volumes and capacities and pressure-volume loops are a normal part of pulmonary function testing in a patient suspected of having respiratory disease. The student should become very familiar with the definitions of pulmonary volumes and capacities, and with the concepts behind the pressure-volume loop, since these will be encountered again in respiratory pathophysiology and in the clinical segments of the curriculum.

Where does the air go?

Inspired air moves into the respiratory system at the nose and mouth, passes through the tracheobronchial tree, and enters the alveoli. A portion of the air in each inspiration that enters the conducting system never reaches the alveoli, and, because of this, represents the first portion of the air that leaves the body in the subsequent expiration. Since the conducting system does not participate in gas exchange, it is considered to be *dead space*, in contrast to the *alveolar space*, where gas exchange occurs. Each tidal volume (V_T), therefore, consists of air that remains in the dead space (V_D) and air that reaches the alveolar space (V_A), according to the following relationship:

$$V_T = V_D + V_A$$

The minute ventilation, $\dot{V}_E$ (expressed either as L/min or ml/min), represents the product of tidal volume and

respiratory frequency. According to the standard terminology used in respiratory physiology, the dot over the "V" indicates a rate (volume per unit time) and the subscript "E" represents the historical method of measuring minute ventilation by collecting expired air. Minute ventilation can therefore be described by multiplying each of the terms in the above expression for tidal volume by the respiratory frequency, f, yielding the following:

$$\dot{V}_E = f \cdot V_T = f \cdot V_D + f \cdot V_A$$

or

$$\dot{V}_E = \dot{V}_D + \dot{V}_A$$

where $\dot{V}_D$ and $\dot{V}_A$ represent *dead space ventilation* and *alveolar ventilation*, respectively, in L/min. Total minute ventilation, therefore, consists of ventilating both the dead space (conducting system) and the alveolar space where gas exchange occurs.

Dead space ventilation serves the very useful purposes of warming, humidifying, and cleaning the inspired air before it reaches the alveoli. Heat and moisture is added to the incoming air by the tissues lining the nose, mouth, pharynx, larynx, trachea, and bronchi, so that the inspired air entering the alveoli is at body temperature and is 100% humidified. A significant fraction of the heat and moisture is re-deposited on the surface of the conducting system during expiration, minimizing heat and water loss during breathing. (In some mammals with thick, furry coats, such as dogs, increased dead space ventilation [panting] serves the purpose of cooling the body by evaporative heat loss from the respiratory system.) The inspired air is cleaned by trapping air particles in the thin mucus layer lining the tracheobronchial tree, which in turn is swept by ciliary action toward the nasopharynx.

Quantification of alveolar ventilation:

The rate of alveolar ventilation can be quantified using the *alveolar ventilation equation,* which relates the rate of carbon dioxide production ($\dot{V}_{CO_2}$, L/min), the rate of alveolar ventilation ($\dot{V}_A$, L/min), and the fractional concentration of carbon dioxide in the alveolar air (F_ACO_2 , %) as follows:

$$\dot{V}_{CO_2} = \dot{V}_A \cdot F_ACO_2$$

The basis for this relationship is the assumption that all of the carbon dioxide in the expired air comes from carbon dioxide that has diffused from the pulmonary capillary blood into the alveolar gas. The rate of carbon dioxide production can be measured by analyzing the carbon dioxide concentration in expired air, the fractional concentration carbon dioxide in alveolar gas can be measured in an end-tidal air sample, and alveolar ventilation can therefore be calculated. The expression can also be re-arranged algebraically into the following form:

$$P_ACO_2 = \frac{\dot{V}CO_2}{\dot{V}_A} \cdot K$$

In the equation above, the rate of CO_2 production is expressed as ml/min (STPD); the rate of alveolar ventilation is expressed as L/min (BTPS), and alveolar PCO_2, is expressed as mm Hg. K is a constant (0.863) that corrects for differences among these units. In the form shown above, the alveolar ventilation equation correctly places the two independent determinants of alveolar PCO_2 – alveolar ventilation ($\dot{V}_A$) and the rate of CO_2 production ($\dot{V}_{CO_2}$) – correctly together on the right-hand side of the equation, where independent variables usually reside. According to these relationships, alveolar PCO_2 (and therefore arterial PCO_2) can be increased only by increasing the rate of CO_2 production or by decreasing the rate of alveolar ventilation. Under most conditions, a measurement of arterial PCO_2 can be substituted for alveolar PCO_2, since the two are very similar. Similarly, alveolar PCO_2 (and therefore arterial PCO_2) can be decreased only by decreasing the rate of CO_2 production or by increasing the rate of alveolar ventilation.

Once alveolar PCO_2 has been calculated using the alveolar ventilation equation, the *alveolar air equation* is used to calculate a value for alveolar PO_2 given knowledge of the barometric pressure, the arterial PCO_2 (P_aCO_2,

substituting for the alveolar PCO_2, or P_ACO_2), and the respiratory exchange ratio, R. The full form of the alveolar air equation is the following:

$$P_AO_2 = P_IO_2 - \frac{P_aCO_2}{R} + \left[P_ACO_2 \cdot F_IO_2 \cdot \frac{1-R}{R} \right]$$

The equation above can be simplified greatly, however, since the magnitude of the last term in brackets is only a few mm Hg. The simplified form of the alveolar air equation that students should use in this course and in next year's Respiratory System is the following:

$$P_AO_2 = P_IO_2 - \frac{P_aCO_2}{R}$$

where

$$P_IO_2 = (P_B - P_{H_2O}) \cdot F_IO_2$$

In the expression immediately above, F_IO_2 represents the fractional concentration of oxygen in the ambient air, or 21%. For completely humidified air at body temperature (100% saturated with water vapor), P_{H_2O} is 47 mm Hg. At sea level, with a normal barometric pressure of 760 mm Hg, P_IO_2 becomes (760-47)·0.21, or about 150 mm Hg.

The logic behind the alveolar air equation is the following: as inspired air enters the alveoli, oxygen is removed from it and carbon dioxide is added to it. The alveolar PO_2 is therefore lower than the inspired PO_2, and the alveolar PCO_2 is higher than the inspired PCO_2. If we know the ratio of oxygen and carbon dioxide exchange (the respiratory exchange ratio, R), we can predict the magnitude of the drop in PO_2 between inspired air and alveolar gas from the corresponding increase in alveolar PCO_2 by using the term PCO_2/R. Subtracting this calculated change in PO_2 from the actual inspired PO_2 will yield a very good approximation of the alveolar PO_2.

For example, arterial blood gas values obtained from a patient breathing room air at sea level (barometric pressure, 756 mm Hg) include the following: arterial PO_2, 86 mm Hg; arterial PCO_2, 42 mm Hg; pH, 7.38; bicarbonate, 24 mEq/L. Inspired PO2 would be calculated as (756-47)·0.21, or 149 mm Hg. Alveolar PO_2, calculated from the simplified version of the alveolar gas equation above, assuming a respiratory exchange ratio of 0.8, would be $149 - \frac{42}{0.8}$, or 96.5 mm Hg.

Quantification of Dead Space Ventilation:

Physiological dead space represents all the regions of the respiratory tree that do not participate in gas exchange. Physiological dead space includes the *anatomical dead space*, defined as all the portions of the conducting system down to the level of the terminal bronchioles, and *alveolar dead space*, consisting of any alveoli that do not participate in gas exchange due to pathology. The calculation of physiological dead space is an application of the dilution principle. Expired air contains a mixture of air from the dead space (where PCO_2 is negligible) and alveolar gas (where PCO_2 is relatively high). The mixed expired air therefore has a PCO_2 (designated P_ECO_2) that falls between that of inspired air (P_ICO_2) and alveolar gas (P_ACO_2). The greater the dead space volume in relation to the alveolar volume, the more the carbon dioxide from the alveolar gas will be diluted in the expired air, and P_ECO_2 will be farther away from P_ACO_2. The smaller the dead space volume compared to alveolar volume, the less the carbon dioxide from the alveolar gas will be diluted in the expired air, and P_ECO_2 will be closer to P_ACO_2.

The ratio of dead space volume to tidal volume (V_D/V_T), and ultimately the absolute volume of the physiological dead space ($V_{D[phys]}$), can be calculated using the following expression:

$$\frac{V_{D[phys]}}{V_T} = \frac{P_ACO_2 - P_ECO_2}{P_ACO_2 - P_ICO_2}$$

Since P_ICO_2 is usually negligible, the Bohr equation for calculating physiological dead space is often written as the following:

$$\frac{V_{D[phys]}}{V_T} = \frac{P_A CO_2 - P_E CO_2}{P_A CO_2}$$

or, rearranging and multiplying tidal volume and dead space volume by respiratory frequency,

$$\dot{V}_{D[phys]} = \dot{V}_T \cdot \frac{P_A CO_2 - P_E CO_2}{P_A CO_2}$$

The *anatomical dead space* can be measured using Fowler's method, in which the partial pressure of nitrogen (PN_2) is measured at the mouth following an inhalation of 100% oxygen. During the early part of the expiration, the PN_2 will be zero [0] because the dead space has been filled with 100% oxygen. During the latter part of the exhalation, the PN_2 measured at the mouth will suddenly rise and reach a "plateau" value, as expired alveolar gas containing a mixture of oxygen, nitrogen, and carbon dioxide reaches the nitrogen sensor. The expired volume achieved at the midpoint of the rising PN_2 is usually considered to represent the anatomical dead space.