5. RESPIRATORY PHYSIOLOGY

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STATIC PULMONARY MECHANICS

1. What is the primary function of the lung?

To maintain optimal levels of blood gases (i.e., oxygen and carbon dioxide) to meet metabolic demands.

2. Define static pulmonary mechanics.

Static refers to those properties of the lung (e.g., volume) that do not change acutely. **Mechanics** deals with the motions and forces acting on a body (i.e., the lung in this case). Thus, **static pulmonary mechanics** refers to the mechanical forces acting on the lung and chest wall that determine volume.

3. Name and define the various static lung volumes.

- **Vital capacity (VC)**—the amount of air that can be exhaled slowly and completely after a maximal inspiration. The VC is measured in liters and expressed at body temperature, pressure, saturated (BTPS).
- **Inspiratory capacity (IC)**—the amount of air that can be inhaled from the resting end-expiratory level expressed in liters at BTPS.
- **Inspiratory reserve volume (IRV)**—the amount of air that can be inhaled from the resting end-inspiratory level expressed in liters at BTPS.
- **Expiratory reserve volume (ERV)**—the amount of air that can be exhaled from the resting end-expiratory level expressed in liters at BTPS.
- **Tidal volume (V_t)**—the amount of air inhaled or exhaled during normal quiescent breathing expressed in milliliters at BTPS.
- **Residual volume (RV)**—the amount of air remaining in the lungs after a maximal expiration expressed in liters at BTPS.
- **Functional residual capacity (FRC)**—the amount of air in the lungs at resting end-expiratory level expressed in liters at BTPS.
- **Total lung capacity (TLC)**—the amount of air in the lungs at maximal inspiration expressed in liters at BTPS.

4. What is meant by the terms lung volumes or capacities?

Volumes are air-containing compartments of the lung that, although not visible on a chest radiograph, can be measured by various techniques. Lung **capacities** are two or more volumes added together:

$$TLC = VC + RV$$

$$FRC = ERV + RV$$

5. Define ATPS, BTPS, and STPD.

- **ATPS**—*a*mbient *t*emperature, *p*ressure, *s*aturated with water vapor (surrounding temperature, barometric pressure, and water vapor at that ambient temperature).
- **BTPS**—*b*ody *t*emperature, *p*ressure, *s*aturated with water vapor (37°C, current barometric pressure, 47 mmHg water vapor pressure).
- **STPD**—*s*tandard *t*emperature, *p*ressure, *d*ry (0°C, 760 mmHg, 0 mmHg water vapor pressure).

6. How does a person's age, height, sex, and ethnicity affect lung volumes or capacities?

A person's lung increases in size from birth to the late teens or early 20s, plateaus, then declines throughout life. With the **aging** process, there are natural lung tissue degenerative processes that reduce some of the lung volumes and increase others.

- RV increases with age (about 1% per year).
- VC decreases with age (about 0.5% per year).
- TLC decreases (about 0.2% per year).
- ERV decreases with age.
- FRC has no significant change.

Lung volumes are directly related to the **height** of an individual, and studies have demonstrated a 1–2% increase per centimeter in lung volumes when comparing age-matched and sex-matched subjects.

A **female** compared against her **male** counterpart (i.e., same age and height) has lung volumes 10–15% less, owing to differences in thorax-to-trunk ratios.

Different **ethnic groups** (e.g., African-Americans and Native-Americans) have been shown to be approximately 10–15% less than their white counterparts, again, apparently owing to differences in thorax-to-trunk ratio (i.e., longer legs, smaller trunk, and hence smaller lungs).

7. How is the RV measured?

The RV is not measured directly but determined mathematically by subtracting the ERV from the FRC:

$$\mathbf{RV = FRC - ERV}$$

8. What is the physiologic function of the FRC?

Breathing is **cyclic,** whereas blood flow through the pulmonary capillary bed is **continuous.** During the respiratory cycle, there are short periods of apnea (at end-inspiration and end-expiration) at which times there is no ventilation but continued blood flow. Without the FRC acting as a buffer for continued gas exchange during these apneic periods, this would, in effect, constitute an intrapulmonary shunt. This would lead to deoxygenated blood from the pulmonary capillaries emptying into the pulmonary veins (ordinarily rich in oxygen) and as a consequence lower arterial oxygen tension.

9. What are air trapping and hyperinflation?

Enlargement of the air spaces distal to the terminal bronchioles, as seen in the early stages of emphysema, is termed **air trapping.** With air trapping, there is an increase in the residual volume (RV) and functional residual capacity (FRC). As the emphysematous process worsens, there is further lung tissue and alveolar wall destruction as well as loss of elastic recoil, resulting in airway collapse and additional trapping and is now termed **hyperinflation**. With hyperinflation, there are increases not only in RV and FRC but also in the total lung capacity (TLC).

10. What is an obstructive ventilatory impairment?

The prolongation or impairment of airflow during expiration with concomitant air trapping and hyperinflation.

11. What is a restrictive ventilatory impairment?

The inability to expand the lung fully, the hallmark of which is a decrease in TLC.

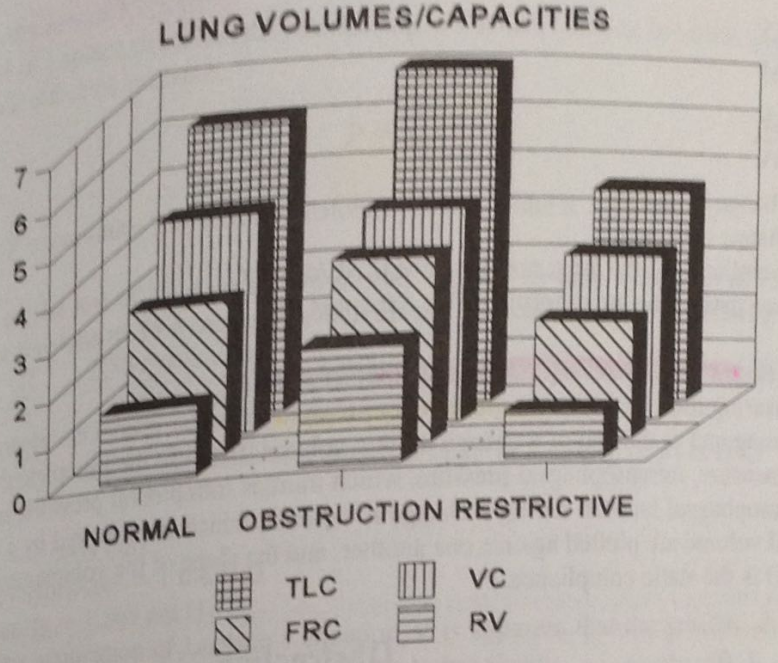
12. List examples of conditions that result in a restrictive ventilatory impairment.

- Lung resection
- Thoracic cage deformities
- Scleroderma (progressive, leathery, induration of the skin of unknown etiology unknown; eventually, the skin becomes taut)

- Idiopathic pulmonary fibrosis (interstitial lung disease of unknown origin)
- Morbid obesity
- Asbestosis
- Third trimester of pregnancy

13. In a restrictive ventilatory impairment, which of the lung volumes or capacities are decreased?

Typically all volumes or capacities are proportionately decreased (see figure).



Relationship of the static lung volumes and capacities in normal, obstructive, and restrictive ventilatory impairments.

14. What determines the FRC?

The counterbalancing forces between the lung and the chest wall. The lung has a tendency to move inward and the chest wall outward.

15. Is there a disadvantage to a small FRC?

Too small of an FRC can cause wide fluctuations in the alveolar partial pressure of oxygen and lead to uneven distribution of ventilation.

16. Is there a disadvantage to a large FRC?

Although, at rest, a large FRC may buffer against wide fluctuations in alveolar oxygen levels, it is deleterious at increased minute volumes (e.g., during exercise). This is due to the need for rapid turnover of alveolar gases with increasing minute volumes, which cannot be achieved if the FRC is too large.

17. Does hyperinflation produce pulmonary disability?

Although hyperinflation indicates disease, it, in and of itself, does not produce disability. The major determinant is the amount of alveolar ventilation and gas exchange, which can be normal in patients with hyperinflation as evidenced by an increase in their FRC.

18. What factors give rise to an increase in the FRC resulting in hyperinflation?

- Increase in pulmonary compliance

- Expiratory airway obstruction
- Enlargement of the thorax

19. Define static pulmonary compliance and elastance.

Static pulmonary compliance is a measure of the elasticity of the lung expressed in liters per centimeter of water (L/cm H_2O). A high compliance infers increased elasticity and hence distensibility, whereas a low compliance implies a stiff lung. **Elastance** is the reciprocal of compliance and is therefore expressed as centimeters of water per liter (cm H_2O/L). Thus, a low elastance implies a high compliance or, in this case, an easily distensible lung:

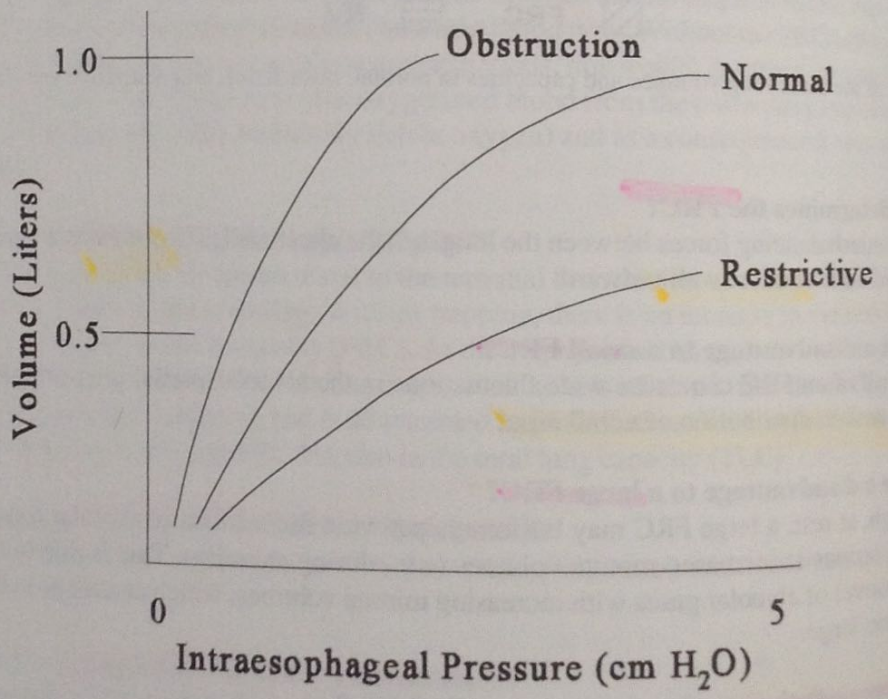
$$C_L = \frac{\Delta V}{\Delta P}$$

$$E_L = \frac{\Delta P}{\Delta V}$$

ΔV = change in volume
ΔP = change in pressure
C_L = compliance of the lung; normal value 0.2 L/cm H_2O
E_L = elastance of the lung: normal value 5.0 cm H_2O/L

20. How is the static pulmonary compliance determined?

By measuring the change in transpulmonary pressure (alveolar pressure – pleural pressure) at the beginning and at the end of a change in lung volume. Because the intrapleural pressure is difficult to measure, intraesophageal pressure, which mimics intrapleural pressure, is monitored via an intraesophageal balloon during a change in volume, which is measured by a spirometer. Pressure and volume are plotted against one another, and the slope of the volume-pressure curve in L/cm H_2O is the static compliance.



Static pulmonary compliance curves of normal, obstructive, and restrictive lungs.

21. A patient undergoing a static volume-pressure study showed an 8 cm H_2O intraesophageal pressure change during an inspiratory volume of 1.0 L. Determine the static pulmonary compliance and elastance.

$$C_L = \frac{\Delta V}{\Delta P} = \frac{1.0\ L}{8\ cm\ H_2O} = 0.12\ L/cm\ H_2O$$

$$E_L = \frac{\Delta P}{\Delta V} = \frac{8\ cm\ H_2O}{1.0\ L} = 8\ cm\ H_2O/L$$

The reduced compliance (normal 0.20 L/cm H_2O) and increased elastance (normal 5.0 cm H_2O/L) are consistent with a **stiff lung** (e.g., pulmonary fibrosis).

22. Define the law of Laplace.

The law of Laplace describes the relationship in a sphere between its radius and surface tension and their effect on pressure.

$$P = \frac{2T}{R}$$

Where P = pressure; T= surface tension (dynes/cm); and R = radius (cm).

23. Based on the law of Laplace, if two alveoli are side-by-side with radii of 75 and 150 m and surface tensions of 50 dynes/cm, which alveoli will collapse into the other?

$$P = \frac{2T}{R} = \frac{2(50\ dynes/cm)}{0.0075\ cm} = 13{,}333\ dynes/cm^2 \text{ or } 10\ mmHg \text{ or } 14\ cm\ H_2O$$

$$P = \frac{2T}{R} = \frac{2(50\ dynes/cm)}{0.0150\ cm} = 6{,}666\ dynes/cm^2 \text{ or } 5\ mmHg \text{ or } 7\ cm\ H_2O$$

(1 μ = 0.0001 cm)
(1333 dynes/cm^2 = 1 mmHg)
(1 mmHg = 1.369 cm H_2O)

From this application of Laplace's equation, it is apparent that the smaller alveoli have a greater **collapse pressure** and will empty into the larger alveoli.

24. How is it possible that alveoli of varying sizes (i.e., diameters) can coexist without emptying into one another, based on the law of Laplace?

Type II alveolar epithelial cells secrete a substance called **pulmonary surfactant,** which has the unique ability not only to lower surface tension, but also to lower surface tension to a greater degree as the alveoli get smaller. The surface tension of pure water is about 72 dynes/cm, whereas the surface tension of alveoli with surfactant is lowered to between 5 and 30 dynes/cm.

Example: Alveolus 1 is 75 μ in diameter with a surface tension of 15 dynes/cm.
Alveolus 2 is 150 μ in diameter with a surface tension of 30 dynes/cm.

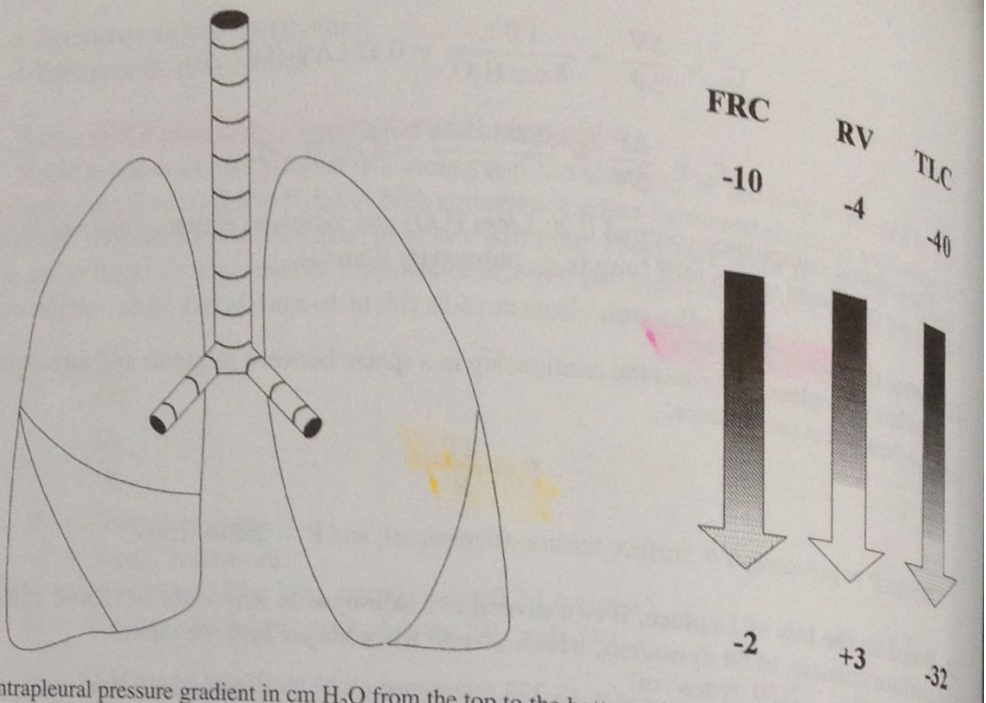
Alveolus 1: $P = \frac{2T}{R} = \frac{2(15\ dynes/cm)}{0.0075\ cm} = 4000\ dynes/cm^2$ or 3 mmHg or 4 cm H_2O

Alveolus 2: $P = \frac{2T}{R} = \frac{2(30\ dynes/cm)}{0.0150\ cm} = 4000\ dynes/cm^2$ or 3 mmHg or 4 cm H_2O

Thus, alveoli of different diameters can coexist because pulmonary surfactant lowers surface tension thereby equalizing collapse pressures among the alveoli.

25. Does the entire lung work on the same pressure-volume curve?

In the upright lung, there is an intrapleural pressure gradient from the top to the bottom owing to the effects of gravity. (See figure for example.) Thus, during an inspiration, although the change in transpulmonary pressure is the same from the top to the bottom, more air is directed toward the basilar alveoli as they are on different parts of the pressure-volume curve. This gives rise to regional differences in ventilation.



Intrapleural pressure gradient in cm H_2O from the top to the bottom of an upright lung at different lung volumes. This gradient accounts for differences in regional ventilation during inspiration owing to regional static lung compliance differences.

DYNAMIC PULMONARY MECHANICS

26. Define dynamic pulmonary mechanics.

Those properties of the lung (e.g., flow) that can vary from moment to moment and those mechanical forces that affect them.

27. Describe laminar and turbulent air flow.

In **laminar** or stream-lined **flow,** although the air moves faster in the center of the airway as compared with the sides, it moves parallel to the sides. In **turbulent flow,** eddies and vortices disrupt the air flow pattern, and as a result a higher driving pressure is required. Somewhere between laminar and turbulent is **transitional flow,** which has both laminar and turbulent flow patterns. For the most part, air flow in the tracheobronchial tree is laminar; however, there are turbulent flow patterns at the bifurcation of the airways.

28. What is the difference between ventilation and respiration?

Ventilation is a dynamic process that involves contraction of the respiratory muscles with subsequent changes in the size of the thorax and movement of air through the airways and into the alveoli.

Respiration, also a dynamic process, involves gas exchange (e.g., carbon dioxide and oxygen) either at the alveolar-capillary level or at the tissue-cellular level.

29. What is the difference between hyperventilation and hypoventilation?

Hyperventilation is ventilation in excess of metabolic needs and leads to an increase in arterial oxygen tension (PaO_2), a decrease in arterial carbon dioxide tension ($PaCO_2$), with a concomitant increase in the arterial pH (pHa). **Hypoventilation** is ventilation less than metabolic needs and results in a decrease in PaO_2, an increase in $PaCO_2$, with a concomitant decrease in the pHa:

Hyperventilation:	$PaCO_2 < 35$ mmHg	pHa > 7.45
Hypoventilation:	$PaCO_2 > 45$ mmHg	pHa < 7.35

Chronic hyperventilation or hypoventilation associated with abnormal $PaCO_2$ has near-normal pH.

30. Name the possible causes of hyperventilation.

Infections
Drugs
Hormones (e.g., progesterone)
Anxiety
Exercise

Increase in ventilation seen in infections and exercise may be appropriate to keep pace with the increased metabolic demands.

31. Name the possible causes of hypoventilation.

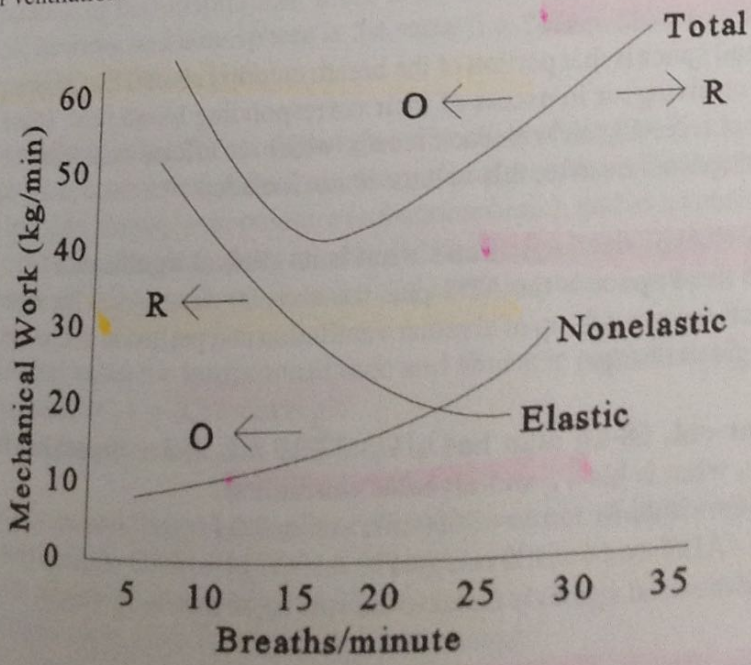
- Depression of the central nervous system (e.g., anesthesia, drugs, head trauma)
- Respiratory muscle disease
- Thoracic cage deformities
- Scleroderma
- Obstructive or restrictive ventilatory impairments

32. Which of the following have more of an effect on dynamic rather than static pulmonary mechanics: emphysema, pulmonary fibrosis, asbestosis, scleroderma, asthma, lung resection, bronchitis, morbid obesity, third trimester of pregnancy, and thoracic cage deformities?

Emphysema, asthma, and bronchitis are all classified as obstructive airways disease because they exhibit decreases in airway flow rates (**dynamic mechanics**) owing to loss of the structural integrity of the airway, decrease in airway patency, and as a consequence decrease in air flow. As these disease states worsen, there may also be changes in static pulmonary mechanics.

33. Why do individuals with emphysema tend to breathe slower with larger tidal volumes?

The mechanical work of breathing comprises an elastic component (lung tissue) and a nonelastic component (airway). To maintain their alveolar ventilation, emphysematous patients breathe at a slower respiratory rate to reduce air flow and hence the nonelastic (flow-resistive) component of mechanical work (see figure). They, however, need to increase their tidal volume to maintain normal alveolar ventilation.



The effect of elastic and nonelastic work on total mechanical work and consequently the breaths/minute. The arrows indicate in which direction these curves are shifted from the normals in persons with either an obstruction (O) or a restriction (R).

34. What is the difference between alveolar volume and alveolar ventilation?

Alveolar (effective) **volume** is the amount of fresh inspired air that reaches the alveoli with each breath, whereas **alveolar ventilation** ($\dot{V}_A$) is the amount that reaches the alveoli per minute.

35. What is the difference between the tidal volume and minute ventilation?

Tidal volume (V_t) is the amount of air that is either inspired or expired during the respiratory cycle, whereas minute ventilation ($\dot{V}_E$) is the amount of air either inspired or expired each minute.

36. How are the V_t and $\dot{V}_E$ determined?

The subject is instructed to breathe quiescently through a mouthpiece/filter assembly with a nose clip attached into a spirometer for at least 1 minute, during which time the expired air is collected and respiratory rate measured. The V_t is determined by dividing the volume of air collected over the minute by the respiratory rate (i.e., frequency). The $\dot{V}_E$ is the total amount of expired air collected during the minute.

37. Calculate the V_t of a subject breathing with a respiratory rate of 12 and an exhaled $\dot{V}_E$ of 6 L.

$$V_t = \frac{\dot{V}_E}{f} = \frac{6\ L}{12} = 0.5\ L\ (or\ 500\ mL)$$

38. Why is the expired volume not equal to the inspired volume during the respiratory cycle?

The expired volume is normally a little less than the previous inspired volume because at rest carbon dioxide production is normally a little less than oxygen consumption. Expired minute volume is about 60 mL less than inspired minute volume because oxygen **uptake** by the blood is greater than carbon dioxide **output** by the blood.

39. What is the anatomic dead space?

Anatomic dead space (ADS) refers to that portion of the breath that remains in the airways. The ADS does not contribute to gas exchange and is washed out on the next breath. This is also referred to as **wasted, ineffective,** or **useless** ventilation and typically is equal to 2.2 mL/kg of lean body weight. Surgical procedures such as a pneumonectomy or tracheostomy will reduce the ADS as will hyperextension of the neck or hypoextension of the jaw.

40. What is alveolar dead space?

Alveolar dead space is that portion of the breath entering alveoli that are not perfused as well as those alveoli receiving air in excess of their corresponding blood flow. (*Note:* There may be alveoli that are not receiving air with each breath, which, in effect, would also be contributing to the alveolar dead space; however, this volume is not included.)

41. What is physiologic dead space and what is its clinical significance?

Physiologic dead space is the ADS plus the alveolar dead space. Increases in physiologic dead space reflects poor match-up of alveolar ventilation and perfusion and as a consequence contributes to poor gas exchange.

42. If a 39-year-old, 68-kg man has a V_t of 500 mL and a breathing frequency of 14 breaths/minute, what is his $\dot{V}_E$ and alveolar ventilation?

$\dot{V}_E = V_t \times f = 500\ mL \times 14 = 7000\ mL/min$ or $7.0\ L/min$

$\dot{V}_A = (V_t - ADS) \times f = (500\ mL - 150\ mL) \times 14 = 4900\ mL/min$ or $4.9\ L/min$

ADS (anatomic dead space) is equal to 2.2 mL/kg of lean body weight.

43. Define transpulmonary pressure.

Transpulmonary pressure (P_{tp}) is the pressure difference across the lung (alveolar pressure minus the pleural pressure). The net pressure difference determines whether the lung has a ten-

dency to inflate or deflate. If P_{tp} is positive, the lungs tend to inflate, whereas a negative value results in a tendency for the lungs to collapse.

44. Define work in terms of the respiratory system.

Mechanical **work** is the product of the force applied to a body and the movement of that body in the line of force generally expressed in dynes per centimeter (dynes/cm). In the respiratory system, work is the product of pressure and volume also expressed as dynes/cm. The work of breathing includes compliance work, tissue resistance work, and airway resistance work (see figure in question 33).

45. What factors are important when considering the work of breathing?

- Total mechanical work
- Amount of alveolar ventilation
- Oxygen consumption by the respiratory muscles

46. What is meant by the term cost of ventilation (COV)?

That portion of total oxygen consumption used to drive the ventilatory muscles.

47. What portion of total oxygen consumption is used by the respiratory muscles?

Generally the COV in a normal subject at rest is approximately 2–5% of the total oxygen consumption up to minute volumes of about 50 L/min. It has been estimated that at minute volumes greater than 70 L/min (e.g., during severe exercise), the COV can exceed 30% of the total oxygen consumption. At rest, normal oxygen consumption is approximately 3.5 mL/min/kg of body weight or about 250 mL/min in a 70-kg person. Thus, the COV at rest is approximately 0.07–0.17 mL/min/kg or 5–12 mL/min in a 70-kg person.

48. Is the COV increased at rest in patients with emphysema?

At rest, the COV in patients with emphysema may be 4–10 times that of a normal. This increase in the COV is due to the increased work of the respiratory muscles to overcome the resistance to airflow seen in individuals with emphysema.

49. When is alveolar pressure equal to atmospheric pressure?

At end-expiration or end-inspiration, there is no air flow, and consequently the pressure within the alveoli, airways, and atmosphere is the same (i.e., 760 mmHg or 1034 cm H_2O at sea level). (*Note:* 1 mmHg = 1.36 cm H_2O.)

50. During V_t breathing, what forces determine direction of air flow?

During inspiration, contraction of the inspiratory muscles enlarges the thorax, lowering alveolar pressure to less than atmospheric pressure (subatmospheric), and as a consequence air flows inward. During expiration, the inspiratory muscles relax, and the thorax and lung recoil, increasing alveolar pressure above atmospheric pressure (supra-atmospheric), causing outward air flow.

51. What is a normal value for lung compliance and thoracic compliance?

Lung compliance (C_L) = 0.2 L/cm H_2O.

Thoracic cage compliance (C_T) = 0.2 L/cm H_2O.

52. Why is total (lungs and thorax) compliance less than either of its components alone?

Total compliance (C_{LT}) = 0.1 L/cm H_2O. As a single unit, the lungs have a tendency to pull inward, whereas the thorax has a tendency to pull outward. As a result, when acting together as a single unit, they require more force for a given volume change:

$$\frac{1}{C_{LT}} = \frac{1}{C_L} + \frac{1}{C_T} = \frac{1}{0.2} + \frac{1}{0.2} = \frac{2}{0.2} = \frac{1}{0.1} \text{ reciprocal} = 0.1 \text{ L/cm } H_2O$$

53. What determines the resting expiratory volume (i.e., the FRC)?

The resting expiratory level is determined by the counterbalance of the forces acting on the lung to pull it inward and those forces acting to distend the thoracic cage. The volume of air in the lung at resting end-expiratory level is the FRC.

54. Describe the phenomenon called lung hysteresis.

Hysteresis is a lag effect that occurs after the forces on a body are changed. In the lung, after a change in transpulmonary pressure, the volume change depends on the previous volume. As a result, when inflating or deflating the lung in 500-mL increments, the inspiratory and expiratory limbs of the volume-pressure curves are not the same.

55. If an emphysematous lung is more compliant than a normal lung, why does the individual have a more difficult time breathing?

Work of breathing (work of the respiratory musculature to overcome the elastic recoil of the lung and chest wall) studies have shown that although less work is required to inflate a more compliant lung, more work is required during the subsequent deflation (i.e., the lungs are much more distensible during inspiration but consequently much more collapsible during expiration, requiring a greater driving pressure). Therefore, the net effect is an increase in the work of breathing. Individuals with emphysema have an easier time getting air into the lung as compared with the normal; however, they have a much greater difficulty exhaling the air such that they have an increase in their work of breathing, which is manifested as shortness of breath (dyspnea).

56. Distinguish among pulmonary, airway, and tissue resistance.

Airway resistance is the impedance of air flow through the tracheal bronchial tree as a result of the friction of gas molecules:

$$\text{Airway resistance} = \frac{\text{change in pressure}}{\text{change in flow}}$$

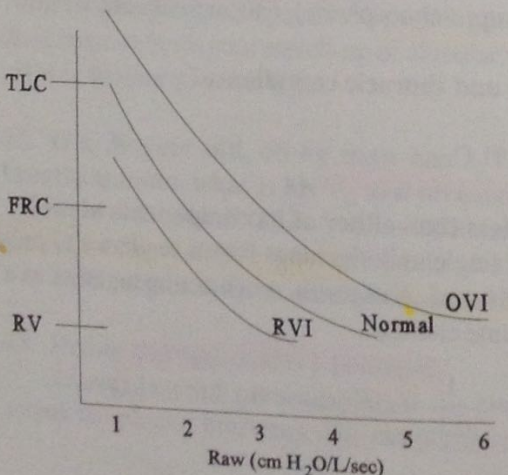
$$R_{aw} = \frac{\Delta P}{\Delta \dot{V}} \quad \text{normal range: 0.6 to 2.4 cm } H_2O/L/s$$

Larger airways (> 2-mm inside diameter) account for about 80% and smaller airways (< 2-mm inside diameter) about 20% of total airway resistance.

Tissue resistance is the impedance to overcome the viscous forces within the lung parenchyma as they move during inspiration and expiration.

Pulmonary resistance is equal to the sum of airway and tissue resistance and is sometimes called total resistance. **Tissue resistance** comprises about 20% and airway resistance about 80% of total pulmonary resistance.

57. Show airway resistance curves for normal, obstructive ventilatory impairments, and restrictive ventilatory impairments.



Airway resistance (R_{aw}) curves at various lung volumes for normal, obstructive ventilatory impairments (OVI), and restrictive ventilatory impairments (RVI).

58. Does nasal breathing contribute significantly to total airway resistance?

The upper airways (above the larynx) can contribute from 20% to 50% of total airway resistance. The nose can contribute as much as 50% of upper airway resistance in normal subjects.

59. Why is the airway resistance highest at low lung volumes (i.e., at or near RV) and lowest at high lung volumes (i.e., at or near TLC)?

Volume dependence of airway resistance is a result of two factors:

1. Alveolar wall tension
2. Airway caliber

At low lung volumes there is less tension in the alveolar walls and therefore a reduced parenchymal tethering (mechanical) effect on the airways. Also, there is less stretch in the airways, thereby decreasing the firing rate of airway stretch receptors with a subsequent increase in parasympathetic tone. Both of these lead to bronchial constriction and as a result an increase in airway resistance. At or near TLC, the reverse description is true, leading to a greater degree of airway patency (dilation) and consequently a reduction in airway resistance.

60. What is airway conductance?

Airway conductance (G_{aw}) is the reciprocal of airway resistance (R_{aw}) and is recorded in L/s/cm H_2O. A normal G_{aw}, inversely linear to lung volume, is between 0.42 and 1.67 L/s/cm H_2O.

61. During an inspiration, why is air flow turbulent in the trachea and not the terminal bronchioles, which have much smaller diameters?

Although the diameters of terminal bronchioles are much smaller than the trachea, less than 2 mm versus 20 mm, the total number of airways increases dramatically, and as a result the cross-sectional area also increases. Consequently the air is divided up among thousands of airways, velocity decreases, and air flow becomes laminar. As a matter of fact, air flow is almost never turbulent in the smaller airways of the lung, whereas it is turbulent in the larger airways (i.e., > 2 mm in diameter).

62. What is the Bernoulli effect?

The **Bernoulli effect** is seen as air passes into airways of smaller diameter with a concomitant increase in velocity or when air passes through a larger total cross-sectional area with a decrease in velocity. Thus, during exhalation, as air moves from many smaller airways with a combined larger total cross-sectional area toward fewer larger airways with a combined smaller cross-sectional area, there is an increase in velocity (i.e., air flow). Conversely, during inhalation, air moves from larger airways toward smaller airways with a concomitant pressure drop and deceleration of air flow.

63. What is a time constant?

A **time constant** = compliance × resistance within a given lung unit. Uneven distribution of ventilation in a lung unit can be accounted for by an increase (long) in the time constant. Thus, increasing compliance or resistance of a lung unit yields a long time constant and is consistent with maldistribution of air to that unit.

64. Define pendelluft.

Pendelluft is a phenomenon that occurs in the lung when there is uneven ventilation such that at end-tidal expiration, although there is no air flow at the mouth, there may still be flow within the lung. This is especially true in lung units that have long time constants (compliance × resistance) wherein gas moves from one unit to an adjoining unit.

65. In a normal subject, what limits exercise, the heart or the lungs?

A normal individual, trained or untrained, reaches maximal predicted heart rate long before

maximal ventilatory capacity (resting minute ventilation 6–8 L/min can increase to 90–120 L/min during severe exercise) is reached. At maximal exercise, the minute ventilation is about 70% of its maximal capacity.

66. What are the various transmural pressures within the thorax?

Airway:

Airway transmural pressure = bronchial pressure – pleural (intrapleural) pressure

$$P_{aw} = P_{br} - P_{pl}$$

Transpulmonary:

Lung transmural pressure = alveolar pressure — pleural pressure

$$P_l = P_A - P_{pl}$$

Chest wall:

Chest wall transmural pressure = pleural pressure — atmospheric pressure

$$P_{cw} = P_{pl} - P_{atm}$$

Transthoracic:

Thoracic transmural pressure = alveolar pressure — atmospheric pressure

$$P_{thoracic} = P_A - P_{atm}$$

67. A decrease in forced expiratory flow is consistent with an underlying obstruction (e.g., emphysema). What limits air flow during a forced expiratory maneuver assuming maximal effort?

During a forced expiratory effort, intrathoracic pressures are increased 5–10 times above resting levels. These high intrathoracic pressures place the airway under considerable pressure, and if the airway is intact it remains patent. If, however, there has been loss of structural integrity because of a disease process, the airway undergoes dynamic compression reducing its caliber and consequently air flow as well. In extreme cases, the airway may actually collapse during the forced expiration trapping air distal to the point of airway collapse, resulting in not only a severe reduction in air flow, but also an apparent loss of volume.

GAS EXCHANGE

68. What is the percent of oxygen at sea level and at 18,000 feet (5486 m)?

Sea level: 21% (20.93%)
18,000 Feet: 21%

69. If the percent oxygen is 21% both at sea level and at 18,000 feet, why do we become short of breath at high altitudes?

Although the concentration of oxygen is the same at both sea level and 18,000 feet, the differences in partial pressure are responsible for hypoxemia at higher altitudes.

$$P_{O_2} = F_{O_2} \times P_B$$

P_{O_2} = partial pressure of oxygen in mmHg or torr (1 torr = 1 mmHg)
F_{O_2} = fractional concentration of oxygen; 0.2093

P_B = barometric pressure; 760 torr at sea level and 380 torr at 18,000 feet

$PO_2 = 0.2093 \times 760$ torr = 159 torr at sea level

$PO_2 = 0.2093 \times 380$ torr = 79 torr at 18,000 feet

Thus, at higher elevations (e.g., 18,000 feet), an individual is breathing lower partial pressures of oxygen (e.g., 79 torr). Normal arterial oxygen (PaO_2) levels are greater than 80 torr, which can be achieved while breathing at sea level where the PO_2 is about 159 torr but not at higher elevations where the PO_2 is much lower and in some cases less than a normal PaO_2.

70. State the gas composition and concentration of ambient, inspired, and expired air at sea level.

GAS	AMBIENT AIR (DRY)			INSPIRED AIR	EXPIRED AIR
	%	Fractional Concentration	Partial Pressure (mmHg)	Partial Pressure (mmHg)	Partial Pressure (mmHg)
Nitrogen	78.10	0.7810	593.5	556.8	566.3
Oxygen	20.93	0.2093	159.1	149.2	100.0
Carbon dioxide	0.03	0.0003	0.2	0.2	40.0
Trace gases*	0.95	0.0095	7.2	6.7	6.7
Water vapor	0.00	0.00	0.0	47.0	47.0

*Inert gases (e.g., argon, neon, helium).

71. What is the difference between hypoxemia and hypoxia?

Hypoxemia is below normal arterial oxygen tension, whereas **hypoxia** is the state of tissue oxygen deficiency. Hypoxemia does not necessarily imply hypoxia and vice versa.

72. What is the difference between external, internal, and cellular respiration?

- **External respiration** involves the exchange of gases (oxygen and carbon dioxide) between the alveoli and the pulmonary circulation at the level of the alveolar/capillary membrane.
- **Internal respiration** involves the exchange of oxygen and carbon dioxide between the systemic circulation and the tissues.
- **Cellular respiration** involves the process of oxygen exchange between the cell and its mitochondria to be used as an oxidizing agent resulting in the production of high-energy bonds.

73. What is a shunt?

There are two types of shunts: **venous-to-arterial** (V-A) and **arterial-to-venous** (A-V).

- In a V-A shunt, blood bypasses ventilated regions of the lung and is dumped back into the arterial system, thereby lowering the oxygen level.
- In an A-V shunt, arterialized blood is dumped into the venous system (e.g., atrial-septal defect).

74. What is a normal shunt fraction?

Approximately 2–5% of the cardiac output is shunted through the pulmonary circulation via the thebesian veins of the heart and branches of the bronchial circulation.

75. Define $C(a-v)O_2$ and give a normal range.

$C(a-v)O_2$ is the difference between the arterial oxygen content and venous oxygen content,

which reflects the amount of oxygen extracted. The normal range is about 4.5–6.0 mL/100 mL of blood. This means on average that about 5.0 mL of oxygen is extracted for every 100 mL of blood passing through the tissues.

76. What are the causes of hypoxemia?

Hypoventilation
Gas diffusion defects
Pulmonary shunts
Ventilation/perfusion mismatching
High altitude

77. What is the normal oxygen consumption ($\dot{V}O_2$) of a person at rest?

Approximately 3.5 mL/min/kg body weight. Thus, a 70-kg person would have a $\dot{V}O_2$ of 245 mL/min (3.5 mL/min × 70 kg) at rest.

78. What is the normal carbon dioxide production ($\dot{V}CO_2$) of a person at rest?

Approximately 3.0 mL/min/kg body weight. Thus, a 70-kg person would have a $\dot{V}CO_2$ of 210 mL/min (3.0 mL/min × 70 kg) at rest.

79. What is the difference between RQ and the respiratory exchange ratio (RER)?

The **RQ** is the ratio between carbon dioxide production and oxygen consumption occurring at the cellular level, whereas the **RER** is the ratio of carbon dioxide output and oxygen uptake occurring in the lung. In steady state, the RQ and RER are equal.

80. Given a $\dot{V}O_2$ of 300 mL/min and a $\dot{V}CO_2$ of 250 mL/min, determine the RQ.

$$RQ = \frac{\dot{V}CO_2}{\dot{V}O_2}$$

$$RQ = \frac{250 \text{ mL/min}}{300 \text{ mL/min}} = 0.83$$

81. During transient hyperventilation, why does the RER increase and not the RQ?

The RER is determined by measuring oxygen uptake and carbon dioxide output from the lung. If an individual is transiently hyperventilating, there is an increase in carbon dioxide output from the lung, and as a result the RER increases. Transient hyperventilation does not affect cellular metabolism; therefore, carbon dioxide production does not change, and subsequently there is no change in the RQ.

82. What happens to the RER when an individual transiently hypoventilates?

During transient hypoventilation, there is a decrease in carbon dioxide output at the level of the lung, and as a result the RER decreases.

83. What is the difference between P_AO_2 and PaO_2?

- **P_AO_2** is the partial pressure of alveolar oxygen expressed in mmHg or torr. The normal value is about 100 mmHg or torr.
- **PaO_2** is the partial pressure of arterial oxygen expressed in mmHg or torr. The normal adult value is > 80 mmHg or torr.

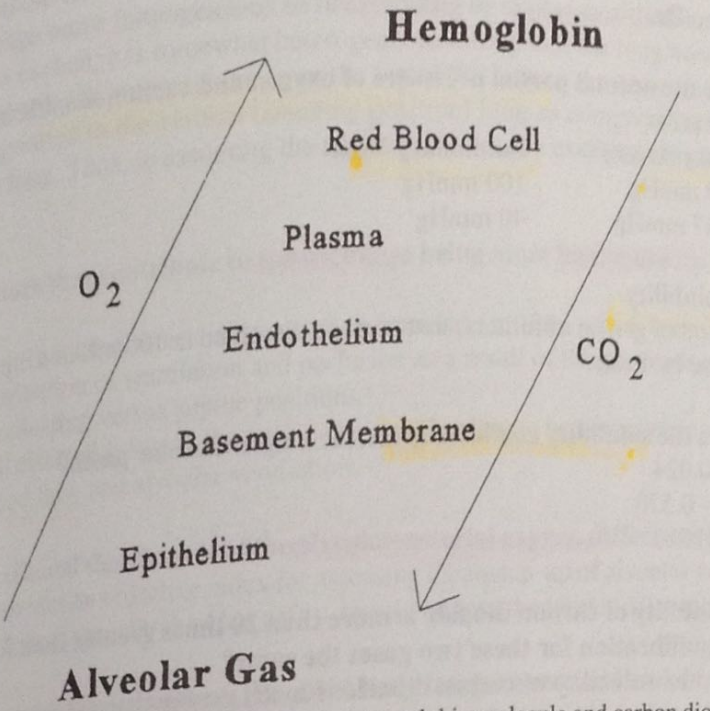
84. What is diffusion?

Diffusion is a process whereby a gas moves from an area of higher concentration to an area of lower concentration across a semipermeable membrane. In the lung, diffusion involves the

movement of oxygen and carbon dioxide between the alveoli and the pulmonary capillary bed along their respective gradients across the alveolar-capillary membrane.

85. Describe the pathway for diffusion of oxygen from the alveolus to the red blood cell.

On reaching the alveolar-capillary membrane, an oxygen molecule must cross through the epithelium of a type I alveolar cell, basement membrane, and endothelium; into the plasma; and then into the red blood cell.



Pathway for diffusion of oxygen from the alveolus to the hemoglobin molecule and carbon dioxide in the opposite direction.

86. How thick is the diffusion pathway (i.e., from the alveolar surface to the surface of the red blood cell)?

About 0.1–0.3 μ (1 μ = 0.003 mm).

87. What factors increase the pathway for diffusion?

- Intra-alveolar edema
- Thickening of the alveolar wall
- Interstitial edema
- Thickened capillary endothelium
- Increased intracapillary path (capillary dilation)

88. How large is the surface area for diffusion in the lung?

The surface area available for gas exchange in the lung is approximately 70–90 m^2, about the size of one side of the playing surface of a tennis court (singles court is 189 m^2; doubles court is 252 m^2). In comparison, the skin has a surface area of about 1.5–2.0 m^2, and as such the lung has been referred to as the **environmental organ** because it has a surface area some 40 times larger than the skin.

89. What factors determine the rate of gas transfer across the alveolar-capillary membrane?

- Pressure difference of the gas between the alveoli and the blood

- Surface area available
- Membrane thickness
- Solubility of the gas
- Diffusion coefficient

90. How long is the transit time in the pulmonary capillary bed?

Under resting conditions, red blood cells move through the pulmonary capillary bed in approximately 0.75 seconds, although equilibration of oxygen and carbon dioxide takes place in about 0.25 seconds.

91. What are the normal partial pressures of oxygen and carbon dioxide in the pulmonary artery and vein?

Pulmonary Artery	Pulmonary Vein
P_{O_2} = 40 mmHg	100 mmHg
P_{CO_2} = 47 mmHg	40 mmHg

92. Define solubility.

The amount of gas (in milliliters) that must be dissolved in 100 mL of a liquid to increase the partial pressure by 1 torr.

93. What are the solubility coefficients for the major alveolar gases?

$O_2 = 0.024$
$CO_2 = 0.570$
$N_2 = 0.012$

94. If the solubility of carbon dioxide is more than 20 times greater than for oxygen, why is the rate of equilibration for these two gases the same?

Although the solubility of carbon dioxide is much greater than for oxygen, its larger diffusion coefficient offsets this, and the net effect is nearly the same equilibration.

95. What is the difference between diffusion limited and perfusion limited?

In a **diffusion-limited** gas exchange situation, the alveolar gas is still equilibrating with the blood cell at the end of its transit time. In a **perfusion-limited** gas exchange situation, the blood cell has reached equilibration with alveolar gas during its transit time. Carbon monoxide represents a diffusion-limited exchange, whereas oxygen and carbon dioxide are perfusion limited.

96. In the systemic circulation are oxygen and carbon dioxide diffusion or perfusion limited?

In contrast to the situation in the lung in which both oxygen and carbon dioxide reach equilibration during the transit time (i.e., perfusion limited), in the systemic capillaries, a longer transit time sees greater oxygen extraction and greater carbon dioxide unloading. Therefore, in the systemic circulation, oxygen and carbon dioxide are diffusion limited.

97. Describe Fick's law as it applies to the diffusion of gases across the alveolar-capillary membrane of the lung.

Fick's law states that the diffusion of a gas (e.g., oxygen or carbon dioxide) across a tissue (e.g., the alveolar-capillary membrane) is proportional to the surface area of the tissue and the pressure difference of the gas on either side of the membrane but inversely proportional to the thickness of the tissue:

$$D_{gas} = A \times D_C/T \times (P_1 - P_2)$$

D_{gas} = diffusion of a gas

A = surface area of the membrane (cm^2)

T = thickness of the membrane (cm)
D_C = diffusion constant of the gas (related to its solubility and molecular weight) (cm^2/mmHg/min)
$P_1 - P_2$ = pressure gradient of the gas between the two sides (mmHg)

98. The ability of the lungs to transport gas is dependent on what two primary factors?
Distribution of alveolar ventilation and perfusion, and the pulmonary diffusing capacity.

99. Is gas exchange more homogeneous in the standing or supine position?
Although gas exchange is somewhat heterogeneous throughout the lung because of differences in ventilation-perfusion match-up from the top of the lung to the bottom, the mismatching is more exaggerated in the vertical (standing position) lung as compared to the horizontal (supine position) lung. Thus, in assuming the supine position, gas exchange becomes more homogeneous.

100. List the factors that contribute to gas exchange being more homogeneous in the supine position.
- The apical-to-basilar distance is greater than from side-to-side, which contributes to more uneven distribution of ventilation and perfusion as a result of the gravitational pull on the lung in the standing versus supine positions.
- The vertical distance is less in the supine position, leading to better match-up between pulmonary blood flow and alveolar ventilation.

101. What is the clinical significance of the alveolar-arterial oxygen difference [$(A - a)Do_2$]?
$(A - a)DO_2$ provides an objective index for assessing the match-up of alveolar ventilation and pulmonary blood flow. Typically the $(A - a)DO_2$ should be less than about 10 mmHg.

102. What is the water vapor pressure (PH_2O) at body temperature and at the boiling point?
Body temperature (37°C): 47 mmHg
Boiling point (100°C): 760 mmHg

103. During strenuous exercise, the rate of gas diffusion can increase by a factor of three. What factors can account for this marked increase?
- Increase in the number of functional alveolar/capillary units, hence an increase in surface area
- Increase in ventilation/perfusion ratio (i.e., a better match-up of ventilation and perfusion) of alveolar/capillary units

PULMONARY CIRCULATION

104. Where does the pulmonary circulation start and end?
The pulmonary circulation encompasses those blood vessels (arteries, capillaries, and veins) that conduct blood from the right side of the heart (right ventricle) through the lungs and then return it to the left side of the heart (left atrium). The pulmonary circulation begins at the pulmonic valve and ends at the junction of the pulmonary veins with the left atrium.

105. Describe the three-compartment model of the lung as it relates to ventilation and perfusion.
The three-compartment model describes three types of lung units (alveolar/capillary) and their ventilation/perfusion ($\dot{V}_A/\dot{Q}$) relationships:
- **Compartment 1**—alveolar/capillary units receiving little to no ventilation but normal blood flow; $\dot{V}_A/\dot{Q} = 0$

- **Compartment 2**—alveolar/capillary units receiving normal ventilation and normal blood flow; $\dot{V}_A/\dot{Q} = 0.1$ to 10
- **Compartment 3**—alveolar/capillary units receiving normal ventilation but little to no blood flow; $\dot{V}_A/\dot{Q} =$ infinity

106. What are the blood flow characteristics through compartments 1, 2, and 3 of the three-compartment model of ventilation/perfusion?

It has been estimated that 90% of pulmonary capillary blood flow is through compartment 2, and the remaining 10% is split between compartments 1 and 3.

107. Describe West's zones of the lung.

- **Zone 1** is found at the top or apical area of the lung, a region where alveolar pressure exceeds pulmonary arterial and venous pressures:

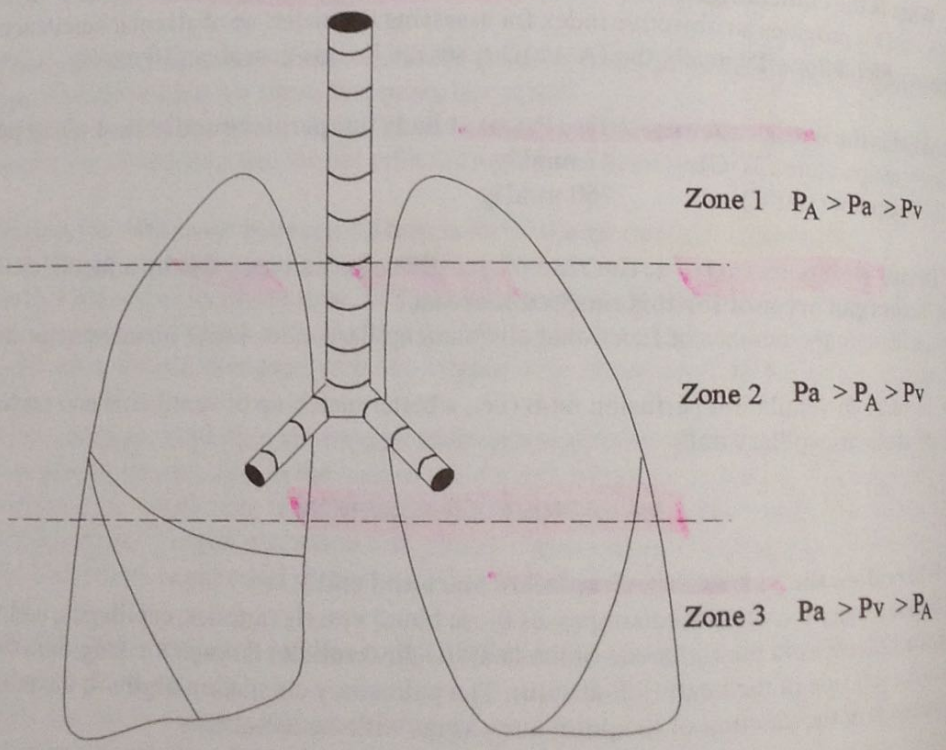
$$P_A > P_a > P_v$$

- **Zone 2** is found midway in the lung, a region where pulmonary arterial pressure is greater than alveolar pressure owing to the hydrostatic effect:

$$P_a > P_A > P_v$$

- **Zone 3** is found near the bottom or basilar area of the lung, a region where both pulmonary arterial and venous pressures exceed alveolar pressure owing to increased patency of the capillaries, which subsequently compresses the alveoli:

$$P_a > P_v > P_A$$



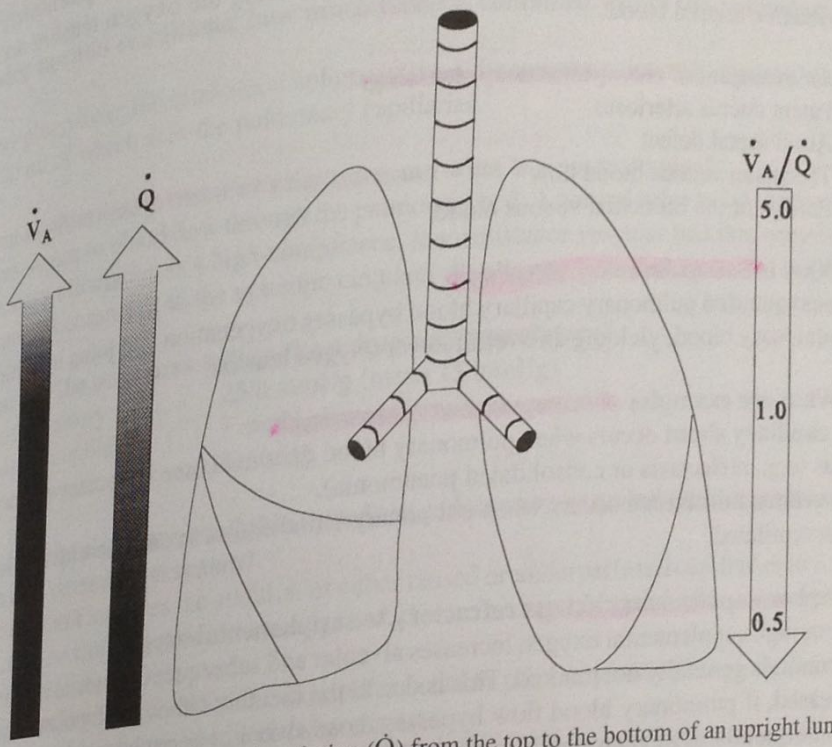
The alveolar (P_A), arterial (P_a), and venous (P_v) pressure gradients in the upright lung. In zone 1, there would be no flow; zone 2, intermittent blood flow; and zone 3, continuous blood flow through the pulmonary capillary bed.

108. What is the normal ventilation/perfusion ratio in healthy lungs?

Although a ventilation/perfusion ratio of 1.0 reflects equal distribution of ventilation and perfusion, there are, in fact, widely different ratios throughout the lung. This is due to both a venti-

lation and a perfusion gradient from the top of the lung to the bottom of the lung in the upright individual as a result of the effects of gravity on intrathoracic pressures. Not only does this gradient contribute to varying ratios, but also there are disproportionate ventilation and perfusion patterns to the lung units. Theoretically the ventilation/perfusion ratios can vary on a continuum from zero to infinity; however, the range is from 0.1 to 10. Approximately 90% of the pulmonary blood flow is to those areas with ventilation/perfusion ratios of about 1.0, and the remaining 10% is divided between ratios of 0.1 to 1.0 and 1.0 to 10.0 equally.

109. Show the relationship of ventilation and perfusion of an upright lung.



Relationship of ventilation ($\dot{V}_A$) and perfusion ($\dot{Q}$) from the top to the bottom of an upright lung.

110. Does the ventilation/perfusion ratio tell you anything about gas exchange?

The ventilation/perfusion ratio describes the relationship between ventilation and blood flow for the lung but provides no direct indication as to the gas exchange characteristics across the alveolar-capillary membrane.

111. Describe the ventilation/perfusion relationships of a ventilation/perfusion ratio of 0.6 versus a ratio of 8.0.

A ventilation/perfusion ratio of 0.6 implies poorly ventilated alveoli in relation to blood flow and as a result low arterial oxygen tension. A high ventilation/perfusion ratio of 8.0 implies overventilation in relation to blood flow and as a result normal arterial oxygen tension. Overventilation of alveoli does not make up for underventilated alveoli, and a ventilation/perfusion mismatch results.

112. What would be the ventilation/perfusion ratio of a single alveolus if the oxygen tension were equal to mixed venous oxygen tension?

The $\dot{V}_A/\dot{Q}$ ratio of the alveolar capillary unit would be approaching zero (e.g., in obstruction of a bronchus by a mucus plug).

113. Under what circumstances would mixed venous oxygen tension be equal to inspired oxygen tension?

As the ventilation/perfusion ratio approaches infinity, the capillary P_{O_2} approaches the inspired P_{O_2} (e.g., in hyperventilation).

114. What is extrapulmonary shunting?

Virtually all of the blood passes through the pulmonary circulation and hence participates in gas exchange. There are, however, several potential sites whereby blood bypasses the pulmonary circulation, and as a consequence mixed venous blood dumps back into the systemic circulation. Ultimately, extrapulmonary shunts dump **desaturated** venous blood into the pulmonary circulation downstream from the alveoli (arterialized blood), reducing the oxygen tension and content of the systemic arterial blood.

115. List examples of extrapulmonary shunting.

- Patent ductus arteriosus
- Atrial septal defect
- Thebesian venous blood flow
- Portion of the bronchial venous blood

116. What is intrapulmonary shunting?

Deoxygenated pulmonary capillary blood bypasses oxygenation and joins up with **arterialized** pulmonary blood, yielding an overall lower oxygen tension.

117. What are examples of intrapulmonary shunting?

A **capillary shunt** occurs when pulmonary blood does not come in contact with a ventilated alveolus (e.g., atelectasis or consolidated pneumonia).

A **venous admixture** occurs when pulmonary blood comes in contact with an alveolus that is underventilated.

118. Are extrapulmonary shunts refractory to supplemental oxygen?

Although supplemental oxygen increases alveolar and subsequently arterial oxygen tensions, the increase is generally not marked. This is due to the fact that although alveolar oxygen tension is increased, if pulmonary blood flow bypasses those alveoli, gas exchange does not take place, and consequently **deoxygenated** blood is still being dumped back into the **oxygenated** or **arterialized** blood, diluting it and rendering low arterial oxygen tensions.

119. Is supplemental oxygen of benefit in treating ventilation/perfusion mismatching?

In ventilation/perfusion mismatching, the pulmonary blood does come in contact with alveoli, and as such if alveolar oxygen is improved, so also are arterial oxygen tensions.

120. What is the difference between pulmonary and bronchial circulations?

The **pulmonary circulation** includes arteries, capillaries, and veins that function in gas exchange between the blood and the environment via the alveolar-capillary membrane. Pulmonary arteries are carrying mixed venous blood from the right side of the heart to the pulmonary capillaries where gas exchange takes place. The pulmonary veins carry **arterialized** blood back to the left side of the heart to be pumped out into the systemic circulation.

The **bronchial circulation** provides oxygenated blood to the tissues of the lung (parenchyma) and removes carbon dioxide. In contrast to the pulmonary arteries and veins, bronchial arteries are carrying **arterialized** blood, and bronchial veins are carrying **deoxygenated** blood.

Almost the entire cardiac output traverses the pulmonary circulation, whereas only about 1–2% of the cardiac output is directed through the bronchial circulation.

121. What is a bronchopulmonary arterial anastomosis?

A direct vascular connection between a pulmonary artery and a bronchial artery.

122. Define venous-admixture–like perfusion.

When poorly ventilated alveoli are well perfused, giving rise to a low ventilation/perfusion ratio, a venous-admixture–like perfusion occurs. The pulmonary capillary blood remains relatively poorly oxygenated and somewhat hypercapnic and subsequently mixes with arterialized blood, the net effect of which is lowering of arterial oxygen tension.

123. What is a true venous admixture?

When pulmonary blood flow bypasses ventilated alveoli, a true venous admixture occurs. In the healthy lung, about 2–3% of pulmonary blood flow is mixed directly with arterialized blood having not taken part in gas exchange.

124. Under normal conditions, how much blood is contained within the pulmonary capillary bed?

At any given time, the total blood volume of the pulmonary circulation is approximately 900 ml, 75–100 ml of which is in the pulmonary capillaries.

125. What is pulmonary vascular resistance and what is a normal value?

The resistance to blood flow through the pulmonary bed. A normal value is 1.5 mmHg/L/min. The pulmonary circulation is a high-compliance, low-resistance vascular bed that contributes to low pressures as compared to the systemic circulation.

126. What are the pressures within the pulmonary vasculature?

Pulmonary artery	25/8 mmHg (mean 15 mmHg)
Pulmonary capillaries	7 mmHg
Pulmonary veins	5 mmHg

127. What mechanisms are available to reduce pulmonary vascular resistance when pulmonary artery pressure increases?

- **Recruitment** involves the addition of either closed or underperfused capillaries to increase the cross-sectional area of the vascular bed, thus reducing the burden of increased pressure in the rest of the system.
- **Distention** involves the increase in capillary caliber primarily via a change in their shape (i.e., from a near-flattened to a circular shape).

128. Define hypoxic pulmonary vasoconstriction.

When the **alveolar** oxygen tension is reduced (< 70 mmHg), there is active vascular smooth muscle contraction in the precapillary pulmonary blood vessels. This shifts blood flow away from the area(s) of reduced oxygen tension to area(s) of normal oxygen tension. The underlying mechanism is not clearly understood but appears to be a local effect mediated by the alveolar epithelial cells. The hypoxic vasoconstriction seen in the lungs is unique, in that systemic hypoxia results in vasodilation.

129. What is the net mean filtration pressure at the pulmonary capillary membrane?

The balance of forces tending to cause movement of fluid outward is approximately +29 mmHg, whereas the balance of forces tending to cause absorption of fluid is approximately –28 mmHg. Thus, the **net mean filtration pressure** is +1 mmHg, which leads to a continuous flow of fluid out of the pulmonary capillaries and into the interstitial space.

	mmHg
Outward forces	
Mean capillary pressure	+7
Interstitial fluid colloid osmotic pressure	+14

(Table continued on following page.)

	mmHg
Outward forces (*cont.*)	
Negative interstitial fluid pressure	+8
Total	+29
Inward force	
Plasma fluid osmotic pressure	−28
Total	−28
Net force	+1

130. What happens to the fluid that is continually leaking from the pulmonary capillaries?

Under normal circumstances, the capillary fluid is picked up by the pulmonary lymphatic system and returned to the systemic circulation. (Lymph flow in the lung is only a few milliliters per hour.)

131. State Starling's equation for transvascular fluid movement.

$$\text{Flux} = K_{fc}[(P_{iv} - P_{is}) - r_c(C_{iv} - C_{is})]$$

Flux = flow (mL/min)
K_{fc} = capillary filtration coefficient (1/resistance)
P_{iv} = intravascular hydrostatic pressure
P_{is} = interstitial hydrostatic pressure
r_c = reflection coefficient (permeability of the membrane to the proteins exerting the oncotic pressure, averages about 0.75)
C_{iv} = intravascular colloid osmotic pressure
C_{is} = interstitial colloid osmotic pressure

132. What is the significance of negative flux and positive flux?

From Starling's equation, it becomes apparent that P_{iv} and P_{is} are tending to force fluids out of the capillary, and C_{iv} and C_{is} are tending to pull fluids into the capillary. Thus, a **negative flux** indicates fluid reabsorption, and a **positive flux** indicates fluid movement out of the capillary.

133. What is the pulmonary edema safety factor?

Because the net filtration pressure is positive in the pulmonary circulation, there is the tendency for fluid accumulation in the pulmonary interstitium as well as the potential for alveolar edema. In addition to the pulmonary lymphatics, there is a **pulmonary edema safety factor** that guards against the aforementioned. This safety factor requires the pulmonary capillary pressure to increase from 7 to 28 mmHg before pulmonary edema would occur.

134. What is the difference between high-pressure pulmonary edema and high-permeability pulmonary edema?

In **high-pressure** pulmonary edema, there is an increase in pulmonary hydrostatic pressure and as a result an increase in fluid leaking into the interstitial space and alveoli. This can occur in left heart failure.

In **high-permeability** pulmonary edema, there is an increase in capillary permeability to protein and as a result an increase in alveolar fluid. This can occur as a result of damage to the capillary endothelium by chemicals, drugs, or bacterial toxins.

135. What role does nitric oxide play in the control of pulmonary circulation?

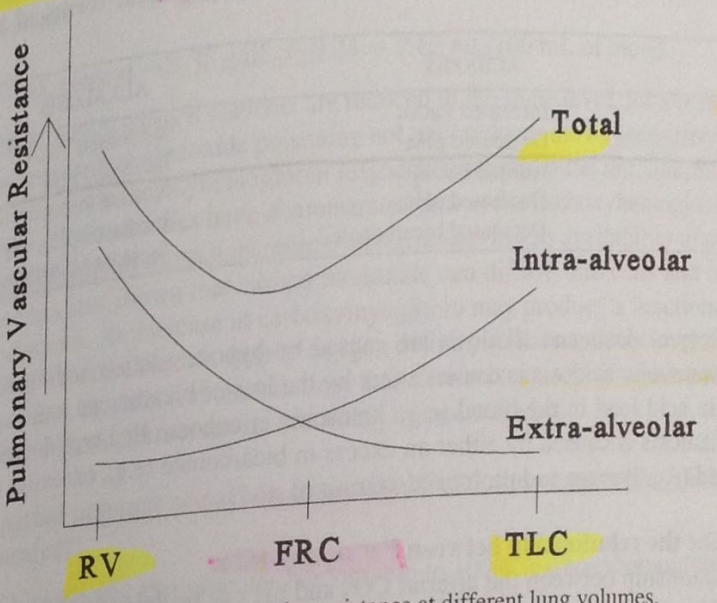
Nitric oxide, derived from the endothelium, causes relaxation of vascular smooth muscle. The effects of nitric oxide are modulated via activation of guanylate cyclase and the subsequent production of cyclic guanosine monophosphate. Inhalation of 20 ppm nitric oxide attenuates the hypoxic pulmonary vasoconstriction.

136. Discuss metabolic functions of the lung and pulmonary circulation.

The pulmonary circulation is involved with activation and inactivation of many substances. For example, angiotensin I is converted to angiotensin II by angiotensin-converting enzyme during its passage through the pulmonary circulation. Angiotensin-converting enzyme is found on the surface of the pulmonary capillary endothelial cells. Angiotensin-converting enzyme has also been shown to inactivate bradykinin partially, whereas other substances (e.g., serotonin) are inactivated by uptake and storage. The lung can also secrete immunoglobulins (e.g., IgA) and heparin.

137. How does a deep inspiration affect pulmonary vascular resistance?

As an individual inhales from RV to TLC, there are changes in both alveolar and intrapleural pressures (see figure). The resistance in the extra-alveolar and corner vessels progressively decreases owing to the aforementioned pressure changes, whereas the resistance of intra-alveolar vessels increases as the lung volume increases. Overall the pulmonary vascular resistance decreases from RV to FRC, then increases to TLC as the volume in the lung is progressively increased.



Changes in pulmonary vascular resistance at different lung volumes.

138. What are the neural controls of pulmonary vascular resistance?

- **α-Adrenergic stimulation** causes vascular constriction and hence an increase in PVR.
- **Stimulation of the β-adrenergic receptors** causes dilation and hence a decrease in PVR.
- **Increased sympathetic nerve activity** results in pulmonary vasculature constriction.

GAS TRANSPORT IN BLOOD

139. How are O_2 and CO_2 carried in the blood?

Oxygen is carried in the blood either dissolved (0.003 ml O_2/torr P_{O_2}) or bound to hemoglobin (1.34 ml O_2/g Hb).

Carbon dioxide is carried in three ways

1. Dissolved (2.4 ml/100 ml of blood)
2. As carbamino compounds (5–10%), which are chemical combinations of carbon dioxide to the terminal amine groups of blood proteins (e.g., hemoglobin)
3. As bicarbonate ions (80–90%)

140. What is the function of carbonic anhydrase?

In the red blood cell and on the vascular endothelial surface of the lung, carbonic anhydrase

(CA) is involved in the CO_2 hydration reaction that converts CO_2 to carbonic acid, which subsequently dissociates into hydrogen and bicarbonate ions. Inhibition of CA would require a significant increase in cardiac output to ensure adequate CO_2 exchange.

$$CO_2 + H_2O \xleftrightarrow{CA} H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

141. Describe the Bohr and Haldane effects.

The **Bohr effect** states that increasing PCO_2 reduces the affinity of hemoglobin for oxygen, thus facilitating the release of oxygen. The Bohr effect aids in the unloading of O_2 from the blood at the level of the tissues.

The **Haldane effect** states that decreasing the O_2 saturation causes a leftward shift in the CO_2 dissociation curve thus facilitating the uptake of CO_2. The Haldane effect helps the loading of CO_2 into the blood at the level of the tissues as the blood gives up O_2 to the tissues.

142. Define respiratory and metabolic acidosis and alkalosis in terms of arterial blood gases.

	ACIDOSIS	ALKALOSIS
Respiratory	Increased $PaCO_2$ Decreased pHa	Decreased $PaCO_2$ Increased pHa
Metabolic	Normal $PaCO_2$ Decreased pHa Decreased bicarbonate	Normal $PaCO_2$ Increased pHa Increased bicarbonate

Respiratory acidosis and alkalosis are caused by hypoventilation and hyperventilation respectively. Metabolic acidosis is caused either by the loss of bicarbonate ions (e.g., diarrhea) or an increase in acid load in the blood (e.g., ketoacids in uncontrolled type 1 diabetes mellitus). Metabolic alkalosis is caused by either an excess in bicarbonate (e.g., excessive antacid intake) or loss of acid (e.g., severe and prolonged vomiting).

143. Describe the relationship between $PaCO_2$ and pHa.

The relationship between the arterial CO_2 and pH can be described by a derivation of the Henderson-Hasselbalch equation.

$$pHa = pk + \log \frac{[HCO_3^-]}{s \times PaCO_2}$$

pk = pH value at which the solute is 50% dissociated (6.1)
s = solubility coefficient (0.0301)

The ratio of the bicarbonate ion to CO_2 determines the pHa. If the $PaCO_2$ increases, then the pHa decreases and, conversely, if the $PaCO_2$ decreases, then the pHa increases. Starting with a normal $PaCO_2$ of 40 mmHg, for every 20 mmHg increase, the pHa will decrease by 0.10, and for every 10 mmHg decrease, the pHa will increase by 0.10. Thus, there is an inverse relationship between $PaCO_2$ and pHa.

144. How much oxygen can hemoglobin carry?

Each molecule of hemoglobin can bind four oxygen atoms. Thus, each gram of hemoglobin can carry 1.39 mL of oxygen (1 mmol of hemoglobin can carry 14 mmol of oxygen).

1mmol of hemoglobin = 64.5 g
1mmol of O_2 = 22.4 mL

$$\frac{4 \times 22.4 \text{ mL/mmol } O_2}{64.5 \text{ g of Hb}} = \frac{89.6 \text{ mL/mmol}}{64.5 \text{ g Hb}} = 1.39^* \text{ mL } O_2\text{/gram of Hb}$$

*Typically, 1.34 is used because 1.39 represents chemically pure hemoglobin.

145. John suffered acute carbon monoxide poisoning, which resulted in a carboxyhemoglobin level of 50%. Frank, diagnosed with an anemia, had a hemoglobin of 7 g/dL. In terms of oxygenation, which of the patients is in a more critical situation?

In both cases, the hemoglobin available for oxygen transport is in effect reduced by one-half. In the case of the acute carbon monoxide poisoning, one-half of John's hemoglobin is bound to carbon monoxide (COHb = 50%), thereby reducing his arterial oxygen content:

$$\text{Oxygen content} = 1.34 \text{ (hemoglobin} \times Sa_{O_2}) + (Pa_{O_2} \times 0.003)$$

$$O_2 \text{ content} = 1.34(14 \text{ g/dL} \times 50\%) + (80 \text{ mmHg} \times 0.003)$$

$$O_2 \text{ content} = 9.38 \text{ g/dL} + 0.24 = 9.62 \text{ mL/100 mL of blood}$$

Likewise, because Frank's hemoglobin is reduced by one-half of normal, if we assume a normal hemoglobin of about 14 g/dL, his oxygen content is reduced to the same level as John's:

$$O_2 \text{ content} = 1.34(7 \text{ g/dL} \times 100\% \ O_2 \text{ saturation}) + (80 \text{ mmHg} \times 0.003)$$

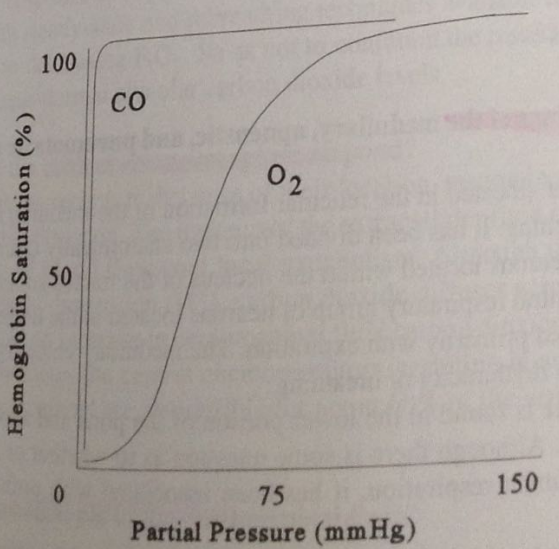
$$O_2 \text{ content} = 9.38 \text{ g/dL} + 0.24 = 9.62 \text{ mL/100 mL of blood}$$

Although their arterial oxygen contents are reduced to the same level, John is in a more critical situation because carbon monoxide poisoning not only reduces the oxygen-carrying capacity of the blood but also shifts the oxyhemoglobin dissociation curve to the left, altering the affinity of hemoglobin for oxygen. Studies have demonstrated that as the carboxyhemoglobin increases, the affinity of hemoglobin for oxygen increases, which results in less availability of oxygen to the tissues. Evidence has also shown that carbon monoxide can diffuse into cells and bind to myoglobin and cytochromes. An increase in carboxymyoglobin may produce a functionally hypoxic state at the level of the mitochondria despite oxygen delivery at the capillary level. Inhibition of cytochrome C oxidase by carbon monoxide may interfere with transport of adenosine triphosphate across the mitochondrial membrane according to recent studies.

146. At what partial pressure of carbon monoxide (P_{CO}) and oxygen (P_{O_2}) is hemoglobin maximally saturated?

P_{CO} of 1 mmHg (0.14%) saturates hemoglobin to 100% (carboxyhemoglobin).

P_{O_2} of > 150 mmHg (> 21%) saturates hemoglobin to 100% (oxyhemoglobin).

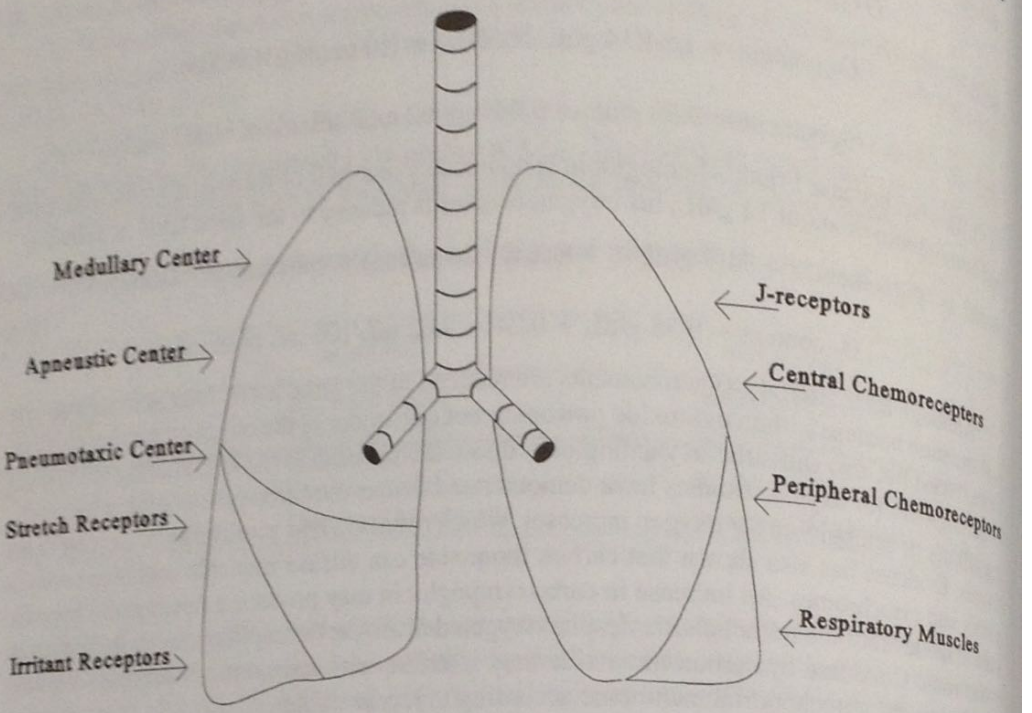


The dissociation curves for oxyhemoglobin and carboxyhemoglobin.

CONTROL OF BREATHING

147. Define control of breathing.

The control of breathing involves mechanisms that work together to generate, regulate, and adjust ventilation to match metabolic needs, whether it be during quiet breathing, sleep, or severe exercise (see figure).



Schematic overview of the functional (not anatomic) control of breathing.

148. What are the mechanisms that control breathing?

- Neural medullary and pontine centers
- Central and peripheral chemosensors
- Lung receptors
- Respiratory muscles

149. What are the functions of the medullary, apneustic, and pneumotaxic respiratory centers?

The **medullary center** (located in the reticular formation of the medulla) is responsible for the coarse control of breathing. It has been divided into two anatomically discrete areas: A dorsal respiratory group of neurons located within the nucleus of the tractus solitarius is associated with inspiration, and a ventral respiratory group of neurons located in the nucleus ambiguus and retroambiguus is associated primarily with expiration. The medullary center has been identified as the site for the inherent rhythmicity of breathing.

The **apneustic center** is found in the lower portion of the pons and appears to retard the switch-off of inspiration. Although there is some question as to whether or not the apneustic center plays a role in human respiration, it has been associated with prolonged inspiratory gasps.

The **pneumotaxic center,** located in the nucleus parabrachialis of the upper pons, is respon-

sible for switching off inspiration (i.e., it limits inspiration). A strong signal from the pneumotaxic center causes a short inspiration (0.5 seconds) and increases breathing frequency up to 30–40 breaths/min, whereas a weak stimulus prolongs inspiratory effort for 5 seconds or more, decreasing the breathing rate to just a couple of breaths per minute. The pneumotaxic center does contribute to regulation of inspiratory volume.

150. What is meant by the term inspiratory ramp signal?

During normal breathing, the nerve impulse pattern sent to the inspiratory muscles exhibits a weak signal followed by a progressively stronger signal (i.e., a ramp signal) over a 2-second duration and then a 3-second termination. The pattern of the inspiratory ramp signal allows for a smooth inspiration rather than an abrupt inspiration.

151. Where are the central and peripheral chemoreceptors located?

- Central chemoreceptors—within the ventrolateral surface of the medulla
- Peripheral chemoreceptors—in the carotid bodies (located at the bifurcation of the common carotid arteries) and in the arch of the aorta

152. To what do the peripheral chemoreceptors respond?

The peripheral chemoreceptors respond to changes in PaO_2, $PaCO_2$, and the arterial pH by changing their rate of nerve firing to the central nervous system. Specifically, either a decrease in PaO_2 or arterial pH or an increase in the $PaCO_2$ alters the rate of firing. For example, a change in the rate of nerve firing in response to PaO_2 begins at about 500 mmHg and reaches its maximum when the arterial oxygen drops below 50–60 mmHg. The increase in response to hypoxemia is largely as a result of the peripheral chemoreceptors.

153. Outline the nerve pathway of the peripheral chemoreceptor system.

From the carotid bodies, afferent nerve fibers pass through Hering's nerve to the glossopharyngeal nerves and then to the dorsal respiratory neurons of the medulla. From the aortic bodies, afferent nerve fibers pass through the vagi and then to the dorsal respiratory neurons.

154. What is the normal response to breathing increasing F_ICO_2?

Normal individuals increase their ventilation by a factor of four when breathing 5% carbon dioxide or approximately 1.5–2.5 L/min per mmHg increase in $PaCO_2$. (See figure, top of next page.)

155. How is the response to oxygen measured?

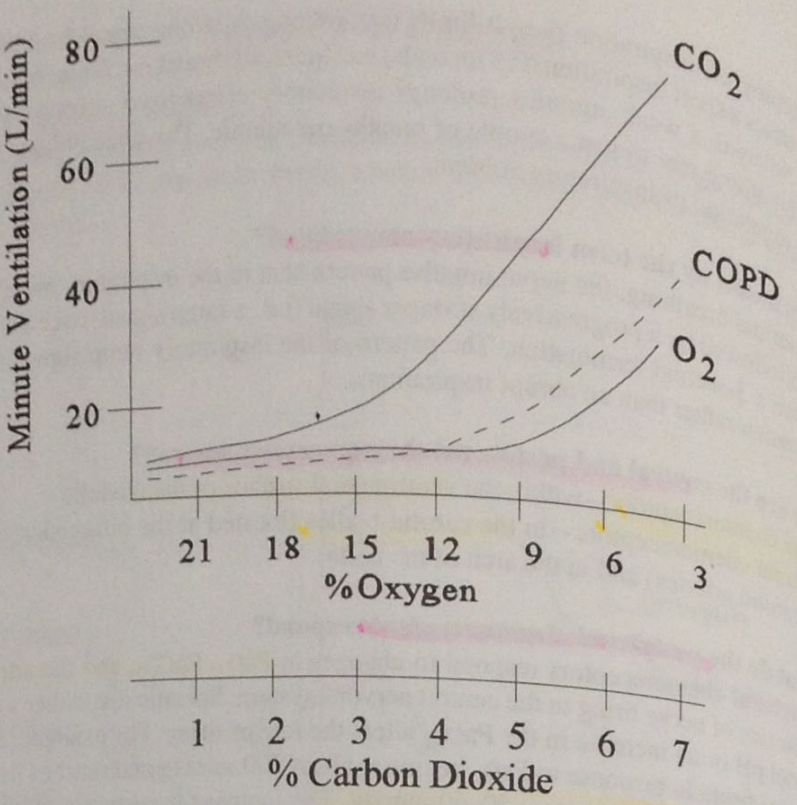
There are both steady-state and rebreathing techniques available to test an individual's ventilatory response to decreasing F_IO_2. So as not to confound the results, the gas mixture must be maintained with near-normal alveolar carbon dioxide levels.

156. To what do the central chemoreceptors respond?

The central chemoreceptors, because of their location, respond to changes in the pH of the extracellular fluid of the brain. The makeup of the extracellular fluid is determined by the cerebrospinal fluid, local blood flow, and local metabolism. Although the blood-brain barrier is impermeable to the hydrogen ion (H^+), carbon dioxide diffuses across it easily. An increase in the $PaCO_2$ leads to an increase in cerebrospinal fluid carbon dioxide, thereby increasing H^+, which, in turn, stimulates the central chemoreceptors, resulting in an increase in ventilation. The central chemoreceptors are responsible for about 60% of the ventilatory response to carbon dioxide.

157. What is the normal pH of the cerebrospinal fluid?

7.32.



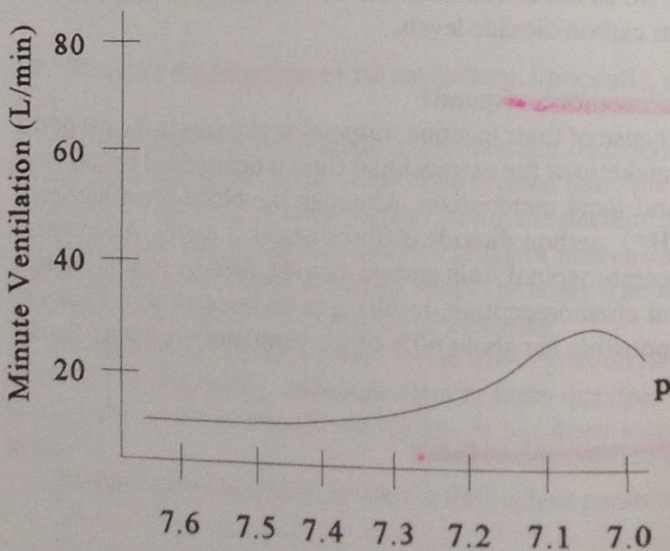
The normal ventilatory responses to decreasing inspired oxygen (O_2) and increasing inspired carbon dioxide (CO_2). The chronic obstructive pulmonary disease (COPD) curve represents the blunted CO_2 response in a person with emphysema.

158. How does a change in $PaCO_2$ affect cerebrospinal fluid pH as compared with arterial pH?

Because it has less protein than arterial blood, the cerebrospinal fluid pH has lower buffering capacity than the arterial blood. Therefore, a small change in $PaCO_2$ results in a larger change in cerebrospinal fluid pH as compared with arterial pH.

159. Can a reduction in arterial pH without a concomitant increase in $PaCO_2$ stimulate a change in ventilation?

In the face of a decrease in arterial pH alone, ventilation increases under isocapnic conditions (see figure). The increase in ventilation seen in response to a decrease in arterial pH (e.g., meta-



The normal ventilatory response to decreasing blood pH (increasing H^+ ion concentration) under isocapnic conditions.

bolic acidosis) is less than under hypercapnic conditions. The peripheral chemoreceptors have been implicated in the primary response, although a secondary effect from the central chemoreceptors may also play a role.

160. Identify the different types of lung receptors and discuss their function.

1. **Pulmonary stretch receptors** are located in the smooth muscle of the airway and respond to lung distention, subsequently increasing expiratory time and thereby decreasing respiratory rate. Two types of pulmonary stretch receptors have been identified, slowly adapting (SAR) and rapidly adapting (RAR) receptors. The SARs lie in the smooth muscle of both intrathoracic and extrathoracic airways and are activated by increases in V_t. The SARs may be responsible for increased expiratory time (T_E). Although the SARs are mechanoreceptors, evidence has demonstrated that they may also respond to changes in carbon dioxide. Airway hypercarbia decreases SAR discharge and subsequently increases respiratory drive to reduce airway levels of carbon dioxide. The RARs are associated with airway epithelial cells near the carina and large bronchi of the lung and respond to both mechanical and chemical stimuli. Both hyperinflation and hypoinflation stimulate the RARs and may be responsible for the deflation reflex. Reports have also demonstrated response of the RARs to smoke and ammonia.

2. **Juxtacapillary or juxta-alveolar receptors** are located in the capillary or alveolar walls. They respond to pulmonary capillary congestion and increases in interstitial fluid, thereby resulting in tachypnea and dyspnea. There is also an associated reflex bradycardia and hypotension.

3. **Irritant receptors** are located in the epithelial cells of the nose and upper airways. They respond to smoke, dust, cold air, and noxious gases, resulting in hyperpnea and bronchoconstriction.

4. **Upper airway receptors** are located in the nose, larynx, nasopharynx, and trachea. They respond to both mechanical and chemical stimuli, causing coughing, sneezing, and bronchospasm.

161. What is the short-term response to breathing at high altitudes?

On ascending to a high altitude (e.g., 10,000 feet [3048 m]), the resulting decrease in PaO_2 is sensed by the peripheral chemoreceptors with a concomitant increase in alveolar ventilation. As a result of this hyperventilation, there is a decrease in arterial and cerebrospinal fluid CO_2. This reduction in cerebrospinal fluid PCO_2 leads to an increase in pH, which inhibits the central chemoreceptors.

162. What happens after several days at high altitude?

Although the bicarbonate (HCO_3^-) level is decreased, restoring the cerebrospinal fluid pH and eliminating the alkalemia, hyperventilation continues.

163. What are the mechanisms involved in high-altitude acclimatization?

With high-altitude acclimatization, there is observed an increase in alveolar ventilation, capillarity, gas diffusion, and oxygen extraction (i.e., wider arteriovenous oxygen content difference). Concomitant increases in red blood cell content (hematocrit may rise to 60%) and hemoglobin (may rise to 20 g/dL) will result in an increase in the oxygen-carrying capacity. There is also a leftward shift in the oxyhemoglobin dissociation curve, which increases the affinity of hemoglobin for oxygen.

164. During the normal course of the day, what factor is the most important in the control of breathing?

Under normal circumstances, the $PaCO_2$ is the major determinant of breathing being held to within ± 3 mmHg. A 1–2 mmHg increase in the $PaCO_2$ evokes a 30–40% increase in minute ventilation.

165. What is the hypoxic drive?

Because of chronic carbon dioxide retention, patients with chronic obstructive pulmonary

disease have lost their sensitivity to pH changes in the cerebrospinal fluid and remain dependent on the response of peripheral chemoreceptors to arterial oxygen changes. Thus, arterial hypoxemia and not hypercapnia provides their stimulus to breathe (i.e., the hypoxic drive or low oxygen stimulus). This drive can be dampened by supplemental oxygen, and thus, when titrating oxygen it is best to monitor the $PaCO_2$ as well as the PaO_2.

166. In carbon monoxide poisoning, will the hypoxic drive be triggered?

Although the oxygen content and saturation are low, the PaO_2 is within normal limits and thus the hypoxic drive will not be triggered.

167. What is Kussmaul breathing?

In diabetic ketoacidosis, there is a decrease in arterial pH, which leads to an increase in V_t and $\dot{V}_E$ that has been termed **Kussmaul breathing**. Kussmaul breathing leads to hypocapnia and a subsequent decrease in the extracellular bicarbonate content.

168. What is the difference between apnea and apneustic breathing?

- **Apnea** is the cessation of breathing with or without a concomitant decrease in arterial oxygen
- **Apneustic breathing** is characterized by prolonged inspirations followed by brief periods of expiration.

169. What is Cheyne-Stokes breathing?

Cheyne-Stokes breathing is a form of periodic breathing characterized by a waxing-waning tidal volume with interspersed periods of apnea lasting 10–20 seconds. The underlying mechanism of Cheyne-Stokes breathing is a lag time between hyperventilation, which increases PaO_2 and decreases $PaCO_2$ and chemosensor detection. The respiratory center responds by decreasing ventilation, and consequently the PaO_2 decreases and $PaCO_2$ increases. This results in a cycle that repeats itself about every 40–60 seconds.

170. Describe the Hering-Breuer reflex.

The Hering-Breuer reflex, also referred to as the **inspiratory-inhibitory** or **inflation reflex**, is triggered by large inspiratory efforts. The subsequent increase in lung volume causes increased rate of firing from the airway stretch receptors and switching off of the inspiration. It is thought that the Hering-Breuer reflex becomes active when the V_t is greater than 1.5–2.0 L.

171. What is the deflation or excito-inspiratory reflex?

The deflation reflex is initiated by collapse of areas of the lung, which elicits a rapid inspiration and an increase in frequency of breathing.

172. At what level of respiratory muscle force does fatigue set in?

The respiratory muscles can work at about 40% of their maximal force for indefinite periods. Above this level, respiratory muscle fatigue becomes a major factor and can contribute to ventilatory failure.

173. What is the duty cycle?

A **duty cycle** is not a list of jobs a worker is to complete by the end of his or her shift that repeats itself every day. The duty cycle is an objective measurement to assess respiratory muscle function. It is the ratio of inspiratory time to the duration of the respiratory cycle (both inspiratory and expiratory times) and is seen to increase in respiratory muscle fatigue:

$$\text{Duty cycle} = \frac{T_I}{T_I + T_E} = \frac{T_I}{T_{tot}}$$

T_I = inspiratory time
T_E = expiratory time
T_{tot} = total duration of one respiratory cycle

174. What is meant by the term air hunger?

As the $PaCO_2$ increases above 50–60 mmHg, the individual's minute ventilation is nearing maximum, and he or she experiences a sensation of labored breathing or **air hunger**. If the $PaCO_2$ exceeds 80–100 mmHg, the individual can become semicomatose, and at levels greater than 120 mmHg, death occurs. Air hunger is also referred to as **dyspnea**.

175. What is the gamma system?

The **gamma system** has been implicated in the sensation of dyspnea that occurs when there is an increase in respiratory effort as a result of respiratory disease. The intercostal muscles and the diaphragm contain receptors in their muscle spindles, innervated by gamma motoneurons, which are stimulated by muscle elongation and hence control the strength of contraction.

176. What factors account for the sensation of dyspnea?

Dyspnea, or labored breathing, is a subjective feeling experienced by an individual who is having a difficult time breathing deep or fast enough to keep up with the increasing metabolic demands of oxygen consumption and carbon dioxide production. The primary factors associated with the feeling of dyspnea include:

- Hypercapnia
- Hypoxia
- Increase in the mechanical work of breathing
- A psychogenic component

177. During exercise, there is an increased metabolic demand that is met by a concomitant increase in ventilation. This increase in ventilation is as a result of changes in V_t and respiratory rate. What is the appropriate response in terms of V_t and respiratory rate?

Changes in ventilation can be accomplished by increasing V_t, respiratory rate, frequency, or a combination. The normal response is a linear increase in both $\dot{V}_E$ and V_t until about half the individual's VC. Beyond that, increases in $\dot{V}_E$ are accomplished by significant increases in respiratory rate. Up to about twice the V_t, T_I (inspiratory time) remains constant with concomitant decreases in T_E. Further increases in V_t are inversely related to T_I. Thus, increases in $\dot{V}_E$ are now a result of decreases in both T_I and T_E.

178. What is the pre-Botzinger complex?

A region located in the ventrolateral medulla model that contains a group of pacemaker neurons responsible for respiratory rhythmogenesis.

179. Discuss the model of respiratory rhythm generation.

Evidence has suggested that the respiratory cycle is made up of three phases, which has been proposed as a model for respiratory rhythm:

- **Phase 1**—inspiratory phase, which is terminated by late-inspiratory inhibitory interneurons
- **Phase 2**—postinspiratory phase, which inhibits inspiratory neurons
- **Phase 3**—expiratory phase, which promotes active expiration

180. What is the mechanism of chemotransduction by the cells of the carotid body in response to decreased PaO_2?

Although the mechanism has not been clearly elucidated, it has been suggested that in response to low arterial oxygen (below 50–60 mmHg), there is a reduction in potassium (K^+) channel activity and an increase in calcium (Ca^{++}) from intracellular stores. A reduction in cell mem-

brane bound K^+ channel activity would lead to depolarization and subsequent propagation of action potentials. This would lead to opening of voltage-gated Ca^{++} channels, allowing Ca^{++} to enter the cell and subsequent release of neurotransmitter.

181. A reduction in cerebrospinal fluid pH results in an increase in ventilation. Is the hydrogen ion itself a unique chemical stimulus to the observed change in ventilation?

There is a greater increase in ventilation owing to reduction in cerebrospinal fluid pH as a result of hypercapnia than isocapnic acidemia. These results suggest that a reduction in cerebrospinal fluid pH, although a stimulus to increased ventilation, is not the unique stimulus because there is a difference in the ventilatory response to a metabolic acidosis or a respiratory acidosis.

182. What limits how long you can hold your breath?

The break point for breath hold occurs at about a $PaCO_2$ of 50 mmHg. At this point, the stimulus to breathe overwhelms any voluntary effort to hold your breath.

183. What is the synergistic effect between carbon dioxide and oxygen?

It has been shown that the ventilatory response to an increased $Paco_2$ combined with a decreased PaO_2 is augmented. The combined effect is a greater stimulus to an increased ventilation than the sum of each separately (i.e., synergism).

184. Is the inspired oxygen tension less in a commercial airplane than at sea level?

The cabins of commercial aircraft are pressurized to about 5000–6000 feet above sea level. As a result, although the fractional concentration of oxygen is the same as at sea level, the barometric pressure is less, yielding a lower oxygen tension.

Example: Given the following data, calculate the inspired oxygen tension (P_IO_2) in the cabin of an airplane:

$$P_B = 600 \text{ mmHg}$$
$$P_{H2O} = 47 \text{ mmHg}$$
$$F_IO_2 = 0.2093 \ (21\%)$$
$$P_IO_2 = F_IO_2 \times (P_B - P_{H_2O}) = 0.2093(600 \text{ mmHg} - 47 \text{ mmHg}) = 116 \text{ mmHg}$$

This translates to a lower arterial oxygen tension in the passenger owing to a lower inspired oxygen tension. At sea level, the inspired oxygen tension is 149 mmHg.

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