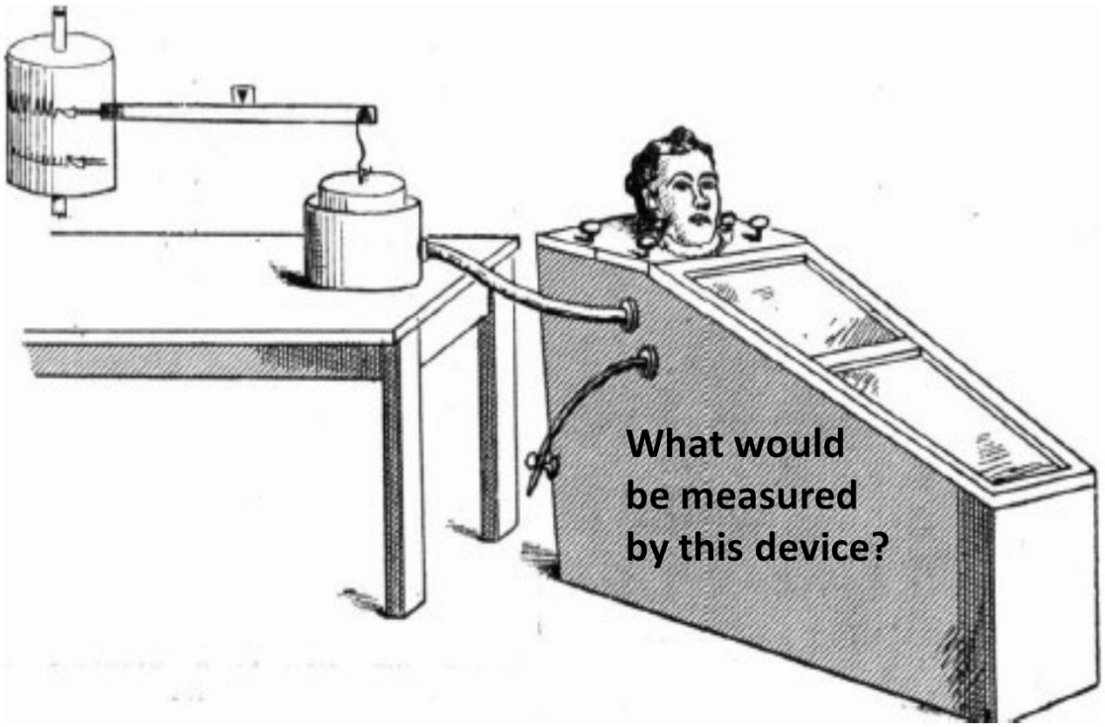
Physiology of Respiration



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Physiology of Respiration
Dr. HN Mayrovitz
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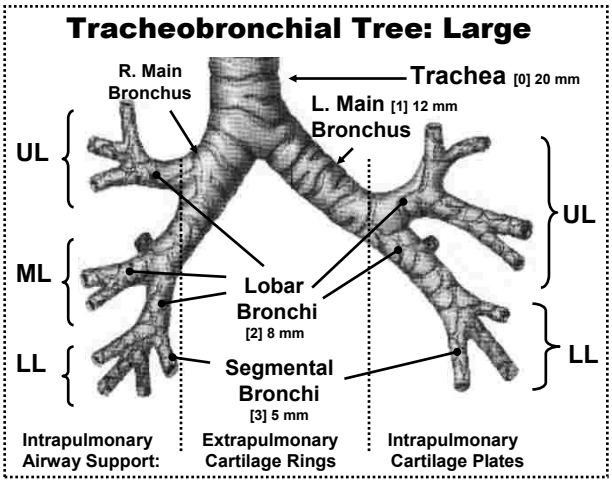
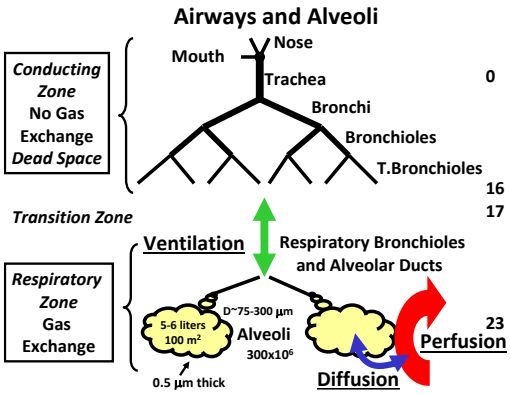
1.0 MAIN RESPIRATORY COMPONENTS TOC

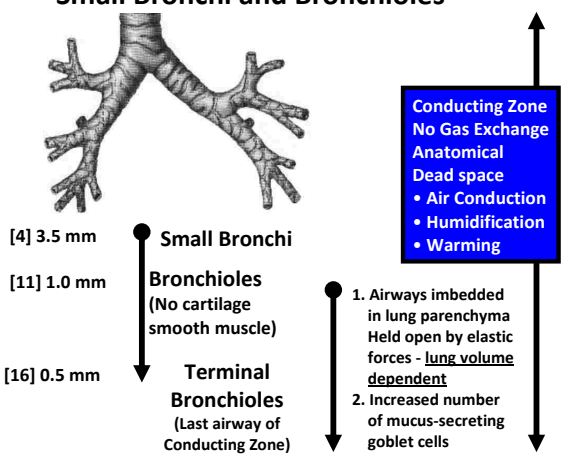
- ***Lungs***: Left and Right divided into lobes and segments
- ***Alveoli:*** small air sacs (~300 million) where gas exchange occurs; O_2 into blood; CO_2 out of blood
- ***Airways***: Series of interconnected branching tubes that carry air to and from the alveoli
- ***Thorax*** (chest wall): Expansion of the thorax pulls lungs further open (inspiration)
- ***Respiratory Muscles***: Control expansion and contraction of thorax thereby drive respiration

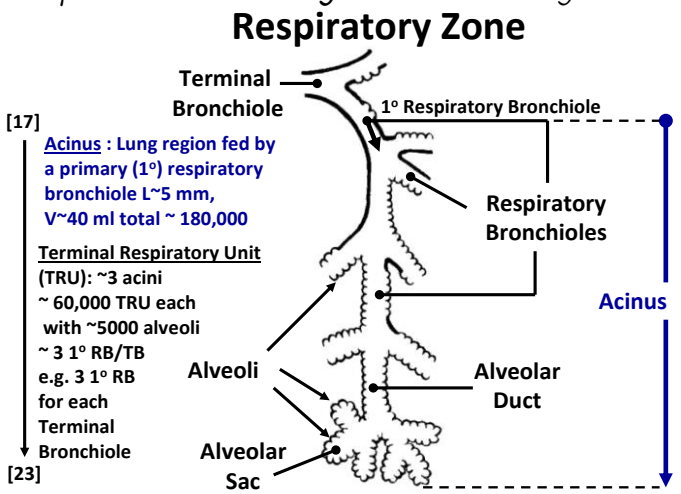
Airways and Alveoli: Functional Features



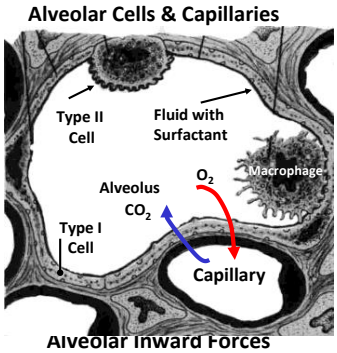
Airways: Fresh air is brought to the alveoli via many bifurcating air tubes that increase in number and decrease in diameter and length as they penetrate deeper. Air enters the nose passing through the external nares (nostrils), then through the nasal cavity and the pharynx, a muscular tube that carries both food and air throughout most of its length. Air then enters the larynx and trachea, which is held open by incomplete cartilage rings. The trachea divides into the left and right main bronchi. Bronchi divide into lobar bronchi, then segmental bronchi (also called secondary and tertiary bronchi), which distribute air to lung lobes and segments. Bronchioles are branches of bronchi; they lack cartilage and have smooth muscle. Bronchioles branch into terminal bronchioles and then to respiratory bronchioles. Upper airways (trachea, bronchi, bronchioles, and terminal bronchioles) are part of the ***conducting zone*** in which no gas is exchanged (anatomical dead space). The ***respiratory zone*** comprises the distal airways, where gas exchange occurs. Respiratory bronchioles that are fed by terminal bronchioles are the 1st airways of the respiratory zone. These give rise to alveolar ducts that conduct air to and from alveoli. The region that is fed by a 1° respiratory bronchiole is termed acinus. Acini are the largest units in which all airways participate to some degree in gas exchange. A **Terminal Respiratory Unit** (TRU) has ~ 3 acini from a single terminal bronchiole.

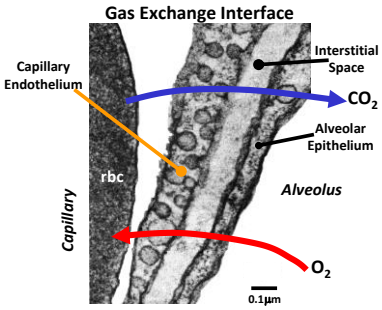




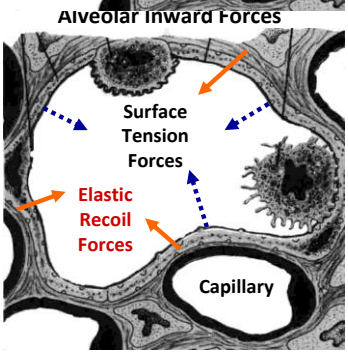


Alveoli: **Alveolar Cells (pneumocytes) Type I** squamous epithelial cells: 95% of wall area – thin. **Type II** cuboidal clusters: surfactant-secreting. Macrophages remove debris/microbes. O_2/CO_2 diffuse through 0.2-0.5 µm alveolar wall.



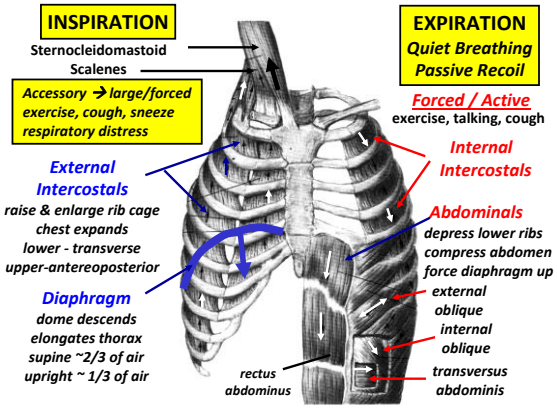


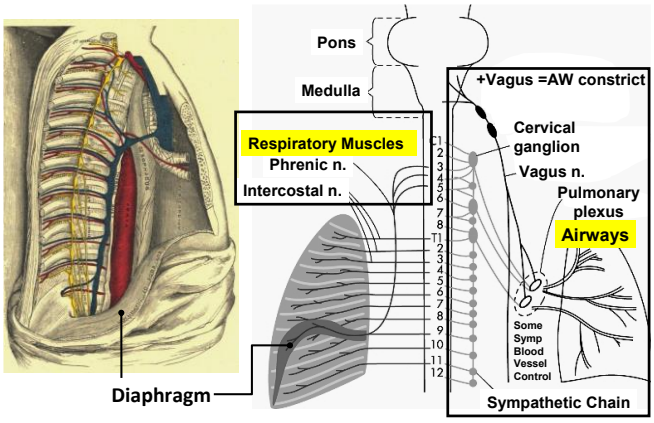
Alveolar Forces: Inside surface is wet. Fluid-gas interface creates ***surface tension.*** Surface tension tends to pull alveoli inward and close. ***Surfactant*** is a mixture of phospholipids and lipoproteins that lowers surface tension by interfering with attraction between H_2O molecules and preventing alveolar collapse (***atelectasis***). Without surfactant, alveoli would need to be completely re-inflated between breaths. ***Elastic tissue Recoil Forces*** also tend to close alveoli. These arise from tissue stretch - much like a stretched spring. Two layers of simple squamous epithelium and basement membranes separate alveolar gas from blood. Membranes average ~0.5 µm, so O2/CO2 can diffuse easily across this thin membrane of capillary endothelial & alveolar epithelial cells.



Respiratory Muscles

For *quiet normal breathing* (eupnea), contraction of primary inspiration muscles (diaphragm and external intercostals) are induced via nerve impulses in phrenic (C3-C5) and segmented spinal nerves (T1-T11) respectively. Contractions translate into thoracic cavity enlargement in all dimensions. The diaphragm (main chest wall muscle) descends caudally, displacing abdominal contents, thereby elongating the thorax. For a deep inspiration, greater caudal diaphragm displacement results in a push force that elevates the lower ribs. The external intercostals rotate the rib cage upward and outward, increasing the chest cavity's anterior-posterior dimension. Since the lung and chest wall are held together via a visceral-parietal pleurae seal, chest wall (thorax) expansion pulls the lung with it & expands lung volume. This volume expansion causes a relative pressure decrease within lung alveoli, which causes airflow into the airways and adds fresh air to the alveolar volume. When respiratory muscles relax, passive recoil forces reverse the process, and airflow is directed out of alveoli. For deeper inspiration & forced expiration, additional muscles are used.





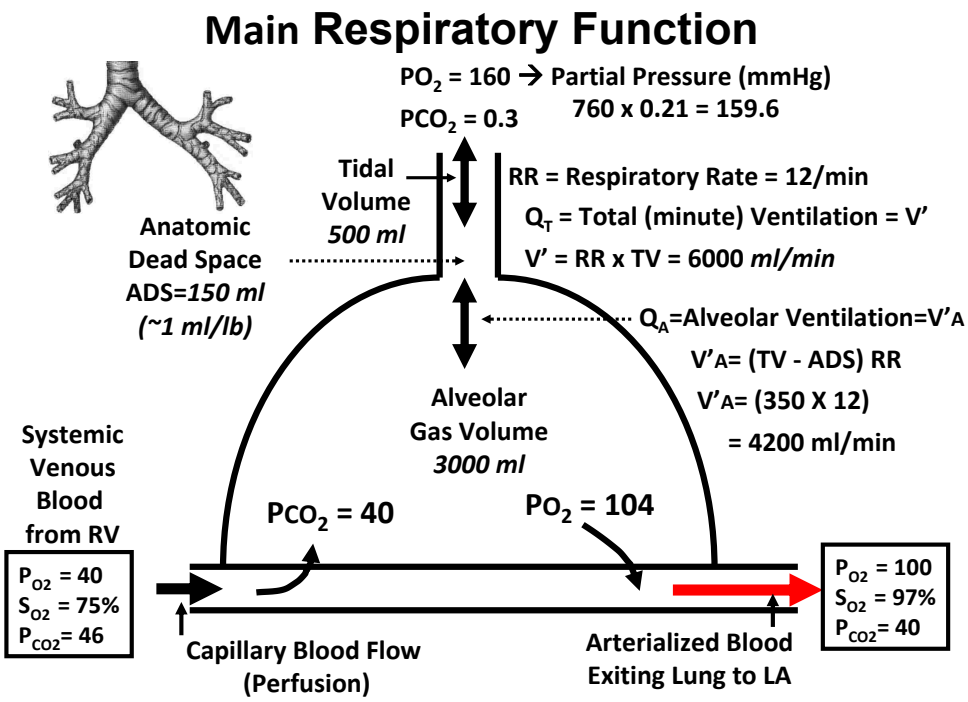
Breathing and Neural Aspects.

Air is drawn into the lungs by the actions of the inspiratory muscles (diaphragm, external intercostals, neck, and back). These actions enlarge the thorax, which pulls the lung further open. For "quiet" breathing at rest, inspiration is an active process, but expiration is passive via recoil that pulls the diaphragm up and chest inwards 3. Forced or labored breathing: Abdominal & internal intercostal m. contract

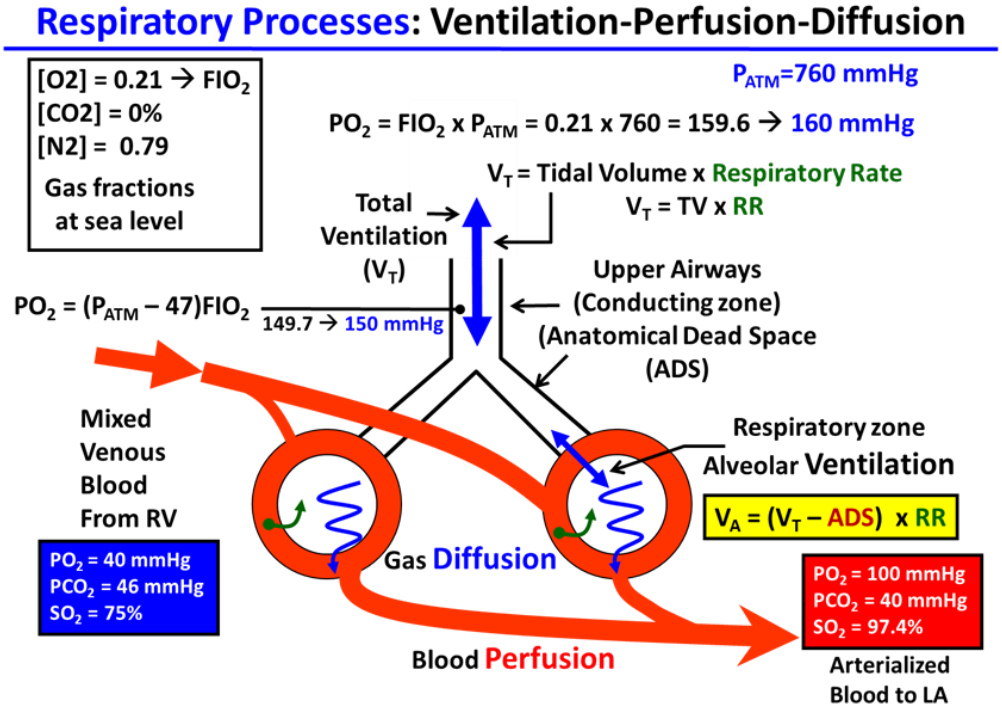
2.0 RESPIRATION: OVERVIEW OF FUNCTION and FEATURES TOC

Main Function - Arterialize blood flowing through lung capillaries

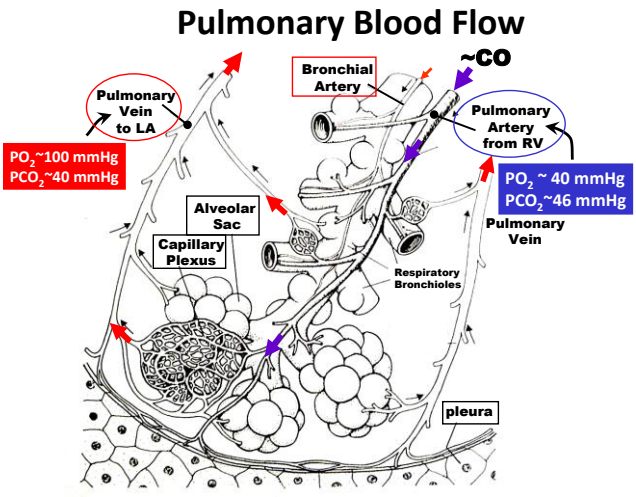
*Blood returning from the systemic circulation is pumped into the lung by the RV. Blood that enters pulmonary capillaries has a partial pressure of oxygen (P_{O2}) of ~40 Torr and a partial pressure of carbon dioxide (P_{CO2}) of ~46 Torr (1 Torr = 1 mmHg). Blood exits at '**arterialized**' values of ~100 and 40 Torr.*



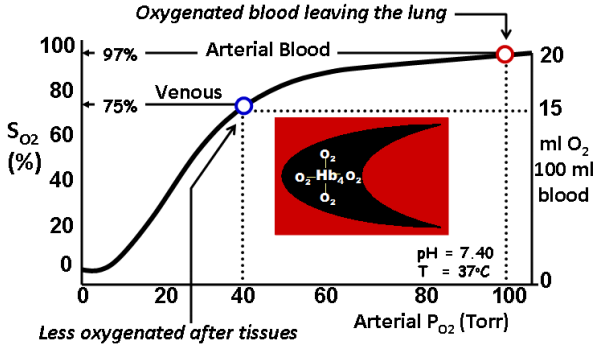
*Arterialization is achieved by (1) adequate air flow in and out of alveoli (**alveolar ventilation**); (2) adequate **diffusion** of O_2 and CO_2 across alveolar-capillary interfaces and O_2 uptake by blood and CO_2 removal and (3) adequate capillary blood **perfusion** (blood flow) to match ventilation. Total ventilation (Q_T) depends on amount of gas entering the lung with each breath (**tidal volume, TV**) and the number of breaths per minute (**respiration rate, RR**). Ventilation available for gas exchange in alveoli is called **alveolar ventilation** (Q_A). NOTE: The symbol V' is used to represent airflow: V'T is total (minute) ventilation, and V'_A is alveolar ventilation. The adjacent figure amplifies some of the above topics and provides basic equations used to calculate key parameters, such as PO2 in atmospheric air and in the trachea. The term FIO_2 is the fraction of O_2 in the inspired air, and ADS is the anatomical dead space. Note the three major functions —ventilation-perfusion-diffusion — that provide for effective respiration. Ventilation aspects will be discussed more fully in other sections.*



Pulmonary blood flow carries the blood gases



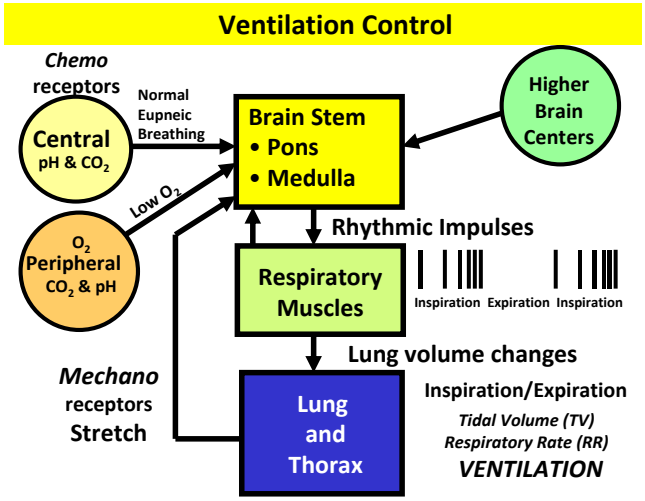
Pulmonary arteries carry blood (less O2, increased CO2) from the right ventricle to the lungs. Repeated branching of pulmonary arteries eventually forms dense capillary networks surrounding each alveolus. A rich blood supply, close proximity of capillaries to alveoli and thin gas-blood interface allow efficient O_2 and CO_2 exchange between alveoli air and capillary blood. Blood leaves capillaries via pulmonary veins that transport "arterialized" blood to the LA. Arterialized blood is distributed to the systemic circulation. The bronchial artery supplies airways and lung tissues via the systemic circulation. Blood perfusing pulmonary capillaries must match alveolar ventilation by facilitating the necessary CO_2 removal from capillaries to alveoli and O_2 entry into capillaries. This process of ventilation-perfusion matching is important to insure proper blood gas. As shown in the adjacent graphic, oxygenated blood that leaves the lungs contains slightly less than about 20 mL of O2 per 100 mL of blood at a nearly fully saturated state. The blood moves around the vascular circuit, supplying O_2 to tissues and picking up CO_2. When blood has passed through the systemic vasculature, the O2 saturation (SO2) has decreased to about 75%, and the blood has given up about 5 mL of O2 per 100 mL of blood.



An important aspect about the O_2 association-disassociation property is that over a wide range of changes in blood oxygen partial pressure (PO_2) the SO_2 does not change much. The significance of this fact is that if PO_2 drops moderately, there is still adequate O_2 being carried to the tissues.

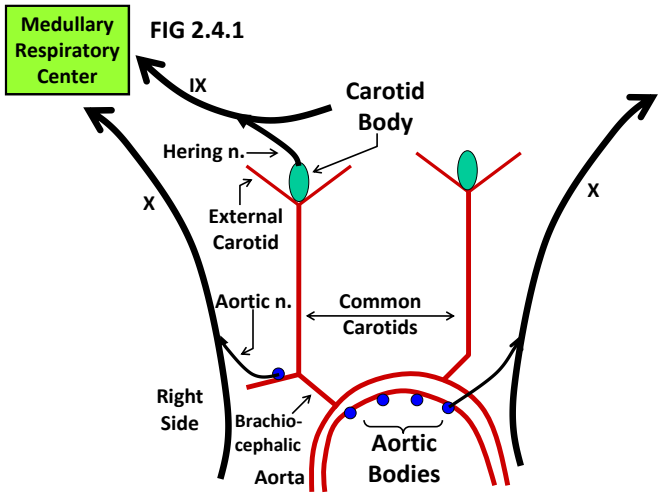
Ventilation is controlled by neural modulation of the respiratory muscles TOC

TV and RR depend on neural impulse patterns that excite respiratory muscles. More impulses during an inspiration phase cause greater muscle contraction and thus a greater TV. Shorter time intervals between impulse-bursts occur with increased RR. The basic rhythmic impulse pattern that impinges on the respiratory muscles originates from the medullary region of the brain stem. However, the pattern is very dependent on neural inputs from other brain areas (pons and cortex) and, importantly, on afferent feedback signals from both chemo- and mechano-receptors. Feedback signals from chemoreceptors attempt to alter ventilation in a direction consistent with the principle of "arterialization". Feedback from mechanoreceptors alters ventilation in accordance with various conditions. Ventilation is a process driven by a basic central pattern generation that is continually modified by neural signals, which modulate TV, RR, or both, to meet the demand for minute ventilation.

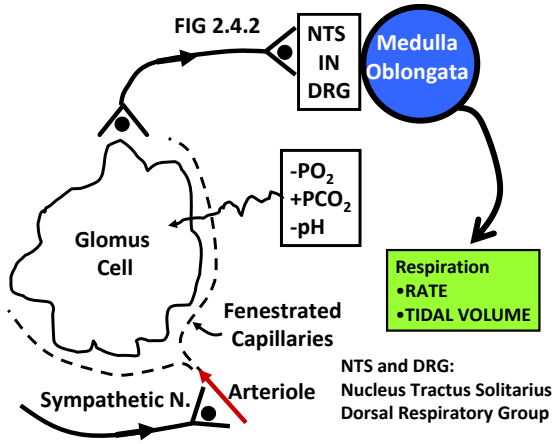


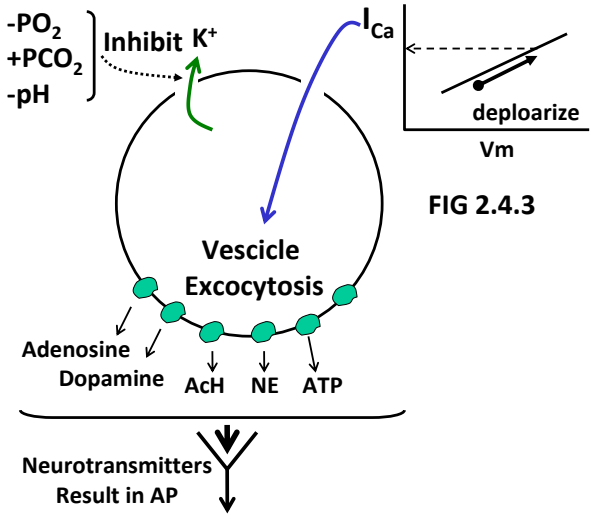
Chemical control: Mediated by Peripheral (PCR) & Central chemoreceptors (CCR)

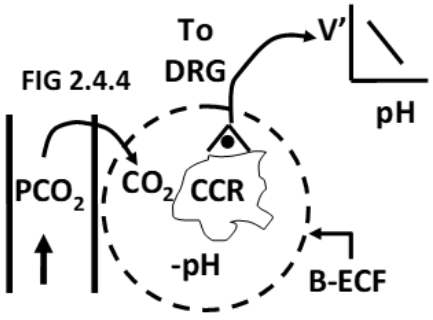
Carotid and aortic bodies are the main sensory components of the peripheral chemoreceptors (PCR) and are conceptually shown in **FIG 2.4.1. They** are located near the bifurcation of the common carotid into external and internal carotid arteries. The size is about 6 x 3 mm on average. Also, there are chemoreceptors in the aortic walls (aortic bodies) that function similarly to carotid bodies. Afferent nerve traffic from carotid bodies passes to the medullary respiratory center by way of cranial IX nerve (glossopharyngeal), and afferent nerve traffic from aortic bodies via the X cranial nerve (vagus).



An expanded summary is provided in FIG. 2 .4.2. Glomus type 1 cells are the main cell type responsible for transducing decreases in PO_2, pH, and increases in PCO_2 into increased neural traffic. Details of the process are as yet unclear. However, transduction causes increased nerve traffic towards the medullary respiratory center with afferent traffic entering through the NTS (Nucleus Tractus Solitarius). Changes in arriving nerve traffic impact the DRG (Dorsal Respiratory Group) and other cells that cause changes in respiration via efferent nerve traffic to respiratory muscles and airways. Ventilation changes are due to changes in respiratory rate (RATE) and tidal volume, which is the amount of air inhaled and exhaled per breath. Much is not known about the transduction mechanism; however, the initiating events are summarized in FIG. 2 .4.3. In FIG. 2.4.3, outward flux of K+ is reduced by decreased PO2 and pH and elevated PCO2, causing the membrane potential to become more positive (depolarize). As a result, more Ca^{++} enters through Ca^{++} voltage-gated channels, causing the release of neurotransmitters that collectively cause increased nerve traffic back toward the respiratory center.

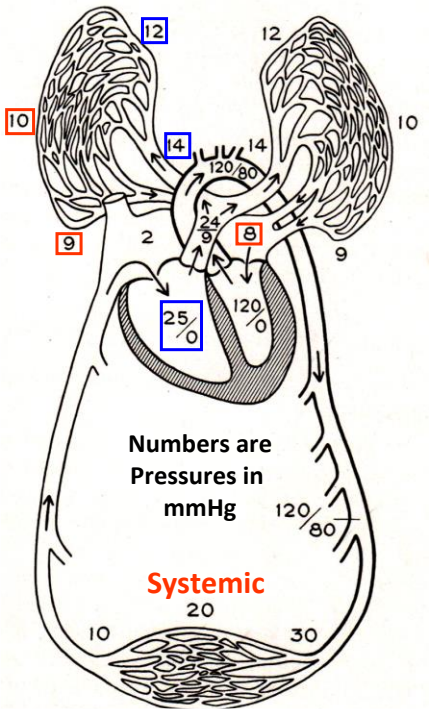






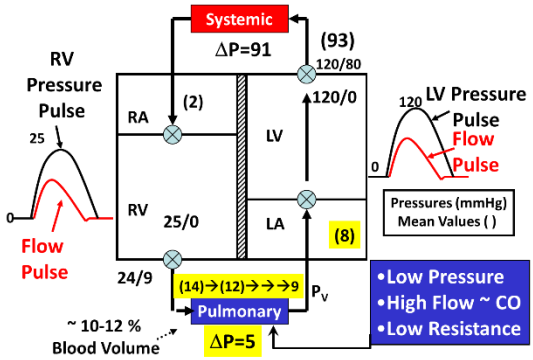
The basic function of CCR is illustrated in FIG. 2 .4.4. The CCRs are bathed in brain extracellular fluid, which, if subject to a decrease in pH, results in increased afferent nerve traffic to the respiratory center, causing increased ventilation (V').

Pulmonary Blood Vessels, Pressures, and Flow Features TOC



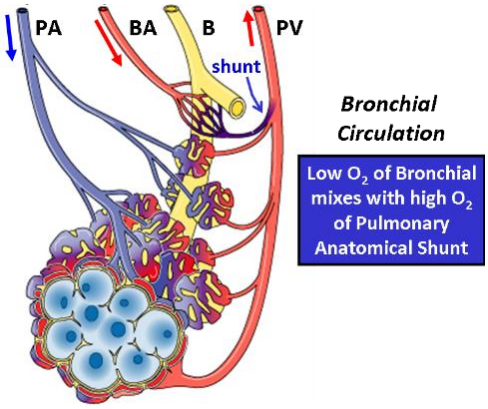
Pulmonary: *Blood flow = RV output ~ CO. Pulmonary arteries bring blood, low in O_2 and high in CO_2, to alveolar capillaries where gas exchange occurs. The pulmonary vascular bed is characterized by low pressure and low resistance compared to systemic circulation.*

Pulmonary Pressure and Flow Features



Pressures and Volumes: *Perfusion pressure is the mean PA pressure – the mean LA pressure. The figure shows systolic/diastolic and (mean) pressures. RBC transit times: pulmonary ~ 5 sec; capillary ~ 3/4 sec. Capillary pressure is less dependent on arteriole activity than in systemic circulation since arteriole control is limited. Capillary vascular resistance accounts for approximately half of the total pulmonary resistance.*

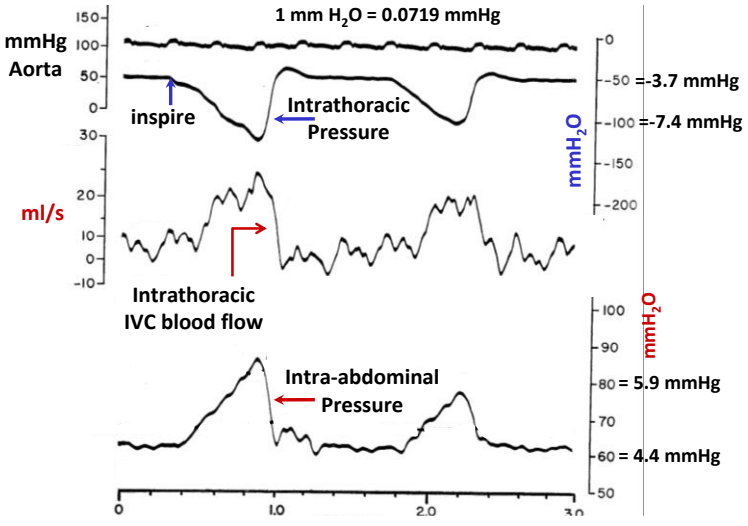
Bronchial: *Bronchial arteries (BA) branch from the thoracic aorta to supply blood (~1% of CO) to bronchioles (B) and the tracheobronchial tree down to and including the terminal bronchioles and provide circulation to supporting lung tissues, visceral pleura, nerves, airway glands, and outer walls of pulmonary arteries (PA). BA does not supply walls of alveoli, alveolar ducts, or respiratory bronchi; alveolar capillaries supply these. Approximately 50% of the bronchial circulation drainage is via the azygos or hemiazygos veins, and ~50% is directed into the pulmonary veins (PV). Blood emptying into PV is de-arterialized and causes a slight P_{O2} reduction in arterialized PV blood. Capillary blood to the conducting zones and parenchyma is from the BA. Flow from both is collected in the PV; the result is a blood shunt (S).*



Arteries/Arterioles/Capillaries: *PA divides to a diameter of ~50 μm at the alveolar duct. Blood vessel walls are thin with little VSM. Vasomotor control of pulmonary vascular resistance is much less than systemic control.*

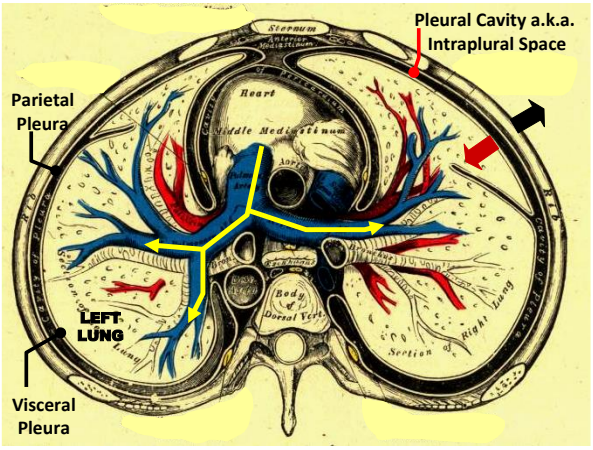
Respiration Effect on Blood Flow

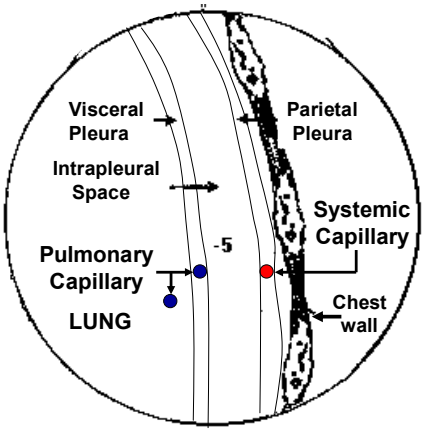
The adjacent figure shows the effects of an inspiration on intrathoracic pressure (ITP), IVC blood flow, and intra-abdominal pressure. Inspiration causes the ITP to fall, abdominal pressure to rise, and IVC blood flow to return to the RA and thence to the RV to increase. Note the two scales for the pressures.



Fluid Balance in Lung Capillaries and Intrapleural Space TOC

Intrapleural Space: Visceral pleura surrounds and is connected to the lung surface. Parietal pleura line the thoracic cage. The fluid-containing space between these is the intrapleural space. The total fluid volume in the very narrow intrapleural space is only about ¼ ml/Kg, but it is sufficient to provide a lubricating layer that allows the lung to slide easily during respiration and to provide a cohesive seal between the lung and the chest wall. The seal is similar to that between two glass cover slips with a drop of water between. Due to the seal, if the chest wall expands, so do the lungs!





Fluid Balance: The Parietal pleura has systemic capillaries, and the visceral pleura has lung capillaries at a lower pressure than systemic. As with other tissues fluid balance depends on hydrostatic-oncotic pressures and lymphatic function. Fluid entering the pleural space is termed transudative (**FIG 2.6.1**) and fluid entering the space from parietal or visceral pleural cells is termed exudative.

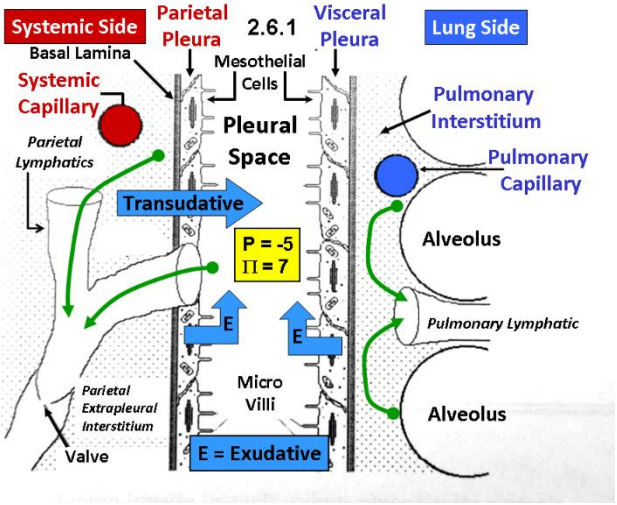


FIG 2.6.2 Pulmonary Fluid Balance

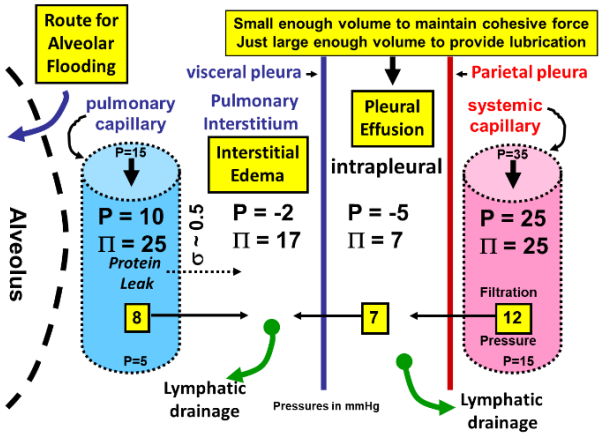


FIG 2.6.2 shows examples of effective filtration pressures determined by pulmonary interstitial and intrapleural hydrostatic (P) and oncotic (Π) pressures. The pulmonary capillaries have a lower reflection coefficient (σ=0.5) than systemic capillaries, resulting in more protein flux into interstitial spaces to be removed by lymphatics. The intrapleural space volume should be sufficient to lubricate, but excess will disrupt the cohesive forces holding the two pleurae together. Excess intrapleural fluid is "pleural effusion," and excess interstitial fluid is "edema". High interstitial compliance allows for large volume increases without significant pressure increases. But once a critical threshold is reached, fluid enters alveoli ("*alveolar flooding*"). A delicate balance Exists to maintain the intrapleural space sufficiently hydrated for lubrication but not so hydrated as to break the cohesive seal

FIG 2.6.3 summarizes aspects of "when things go wrong" with respect to types and causes of pleural effusion, interstitial edema, and alveolar flooding. Note that alveolar flooding can occur with alveolar cell injury that increases its membrane permeability without the necessity for interstitial edema.

FIG 2.64 is a clinical correlation depicting (in cartoon fashion) the presence of a pleural effusion and its drainage. The accumulation of fluid is shown in blue in the cartoon, whereas the x-ray of the lung shows the effusion as an opaque whiteness in the lower right part of the lung.

FIG 2.63 "When things go Wrong"

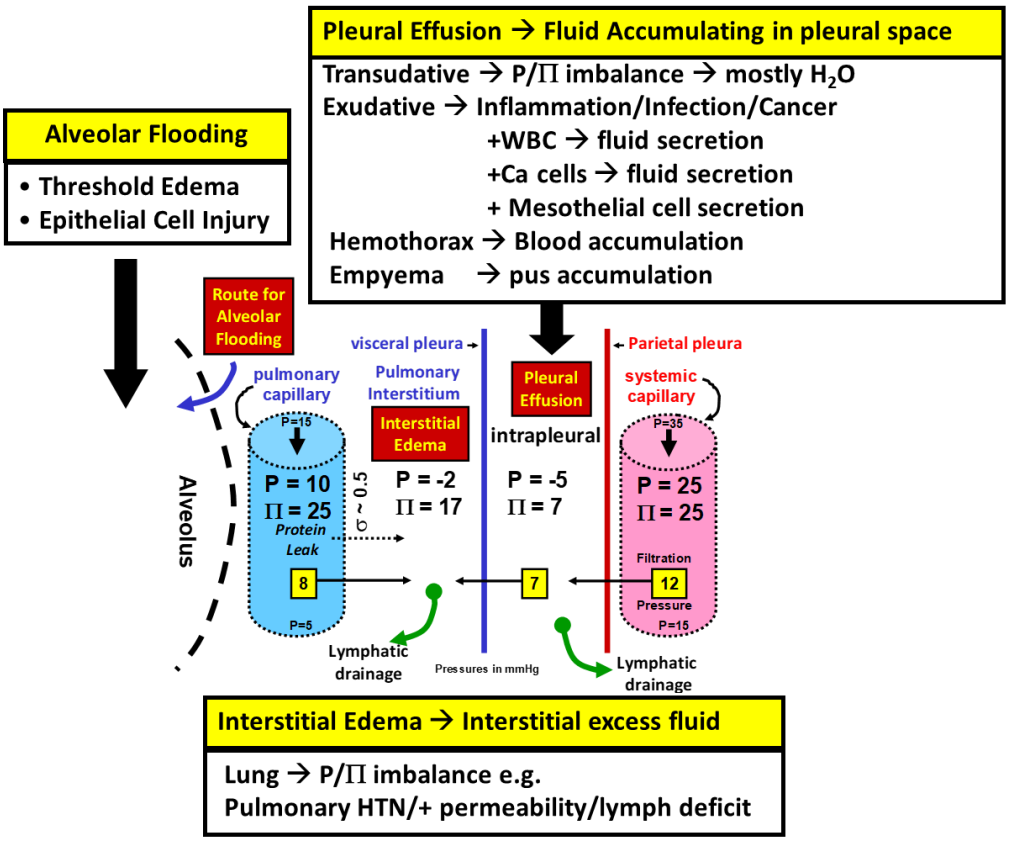
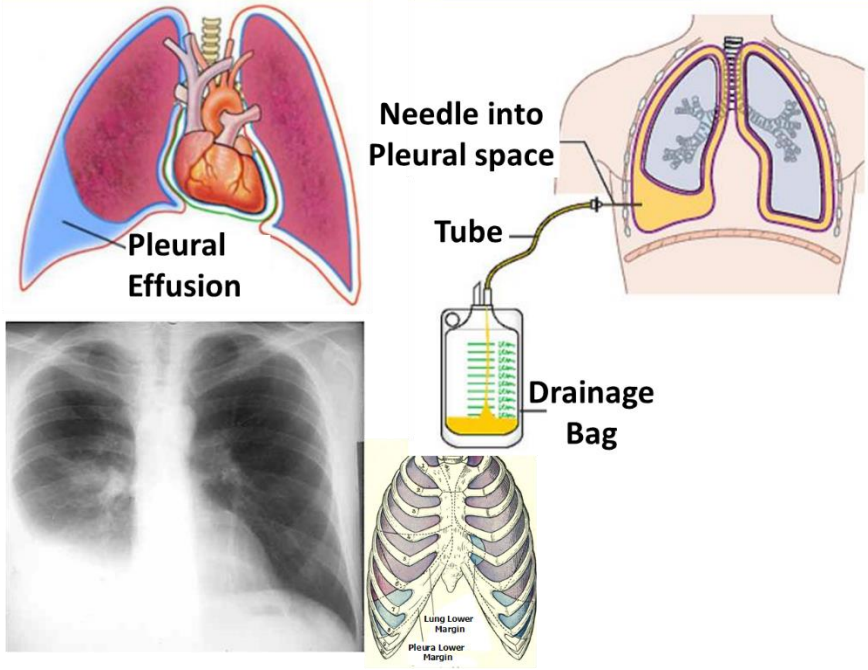
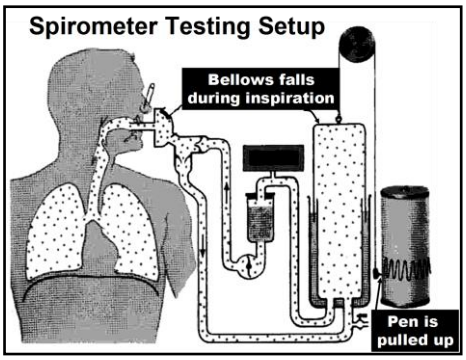


Fig 2.64 Clin Correlation: Pleural Effusion → Drainage



3.0 RESPIRATORY VOLUMES AND PRESSURES TOC

Lung Volumes and Capacities



*There are four lung volumes and four lung capacities. Most can be determined by spirometry. Volume in and out of the lung is measured and recorded using a **spirometer** with mouth breathing. Most volumes and capacities can be determined this way, but **neither FRC nor RV** can be determined by simple spirometry; Gas dilution or body plethysmography techniques are needed.*

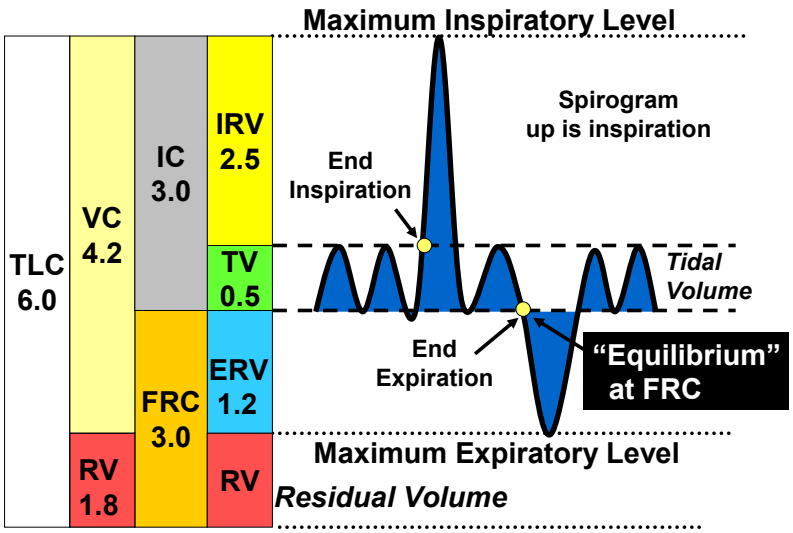
Volumes

1. ***Tidal Volume** (TV): gas volume inspired or expired during each "quiet" respiratory cycle*
2. ***Inspiratory Reserve Volume** (IRV): maximum additional gas volume that can be **inspired** above that present at the end of a normal inspiration*
3. ***Expiratory Reserve Volume** (ERV): maximal additional gas volume that can be **expelled** after reaching normal end-expiration volume*
4. ***Residual Volume** (RV): gas volume **remaining** in lungs at the end of maximal expiration*

Capacities

(Capacities have two or more lung volumes)

1. ***Total Lung Capacity** (TLC): maximum potential lung gas volume = RV+ERV+TV+IRV*
2. ***Vital Capacity** (VC): maximum **useful** potential lung gas volume range = TLC-RV*
3. ***Inspiratory Capacity** (IC): max potential volume inspired after a "quiet" expiration IC = TV+IRV*
4. ***Functional Residual Capacity** (FRC): residual gas volume remaining in the lungs after a "quiet" expiration. **FRC** = RV+ERV. Normally, inspiration begins when lung volume is at FRC.*



"Typical" values (shown in the above figure) vary with height, age, gender, condition and training

*Approximate changes in lung and ribs at different lung volumes is shown in **FIG 3.1.1.** The ribs (7 through 10) are indicated as a pair of dashed lines as they would be seen during maximum inhalation (inspiration) corresponding to TLC.*

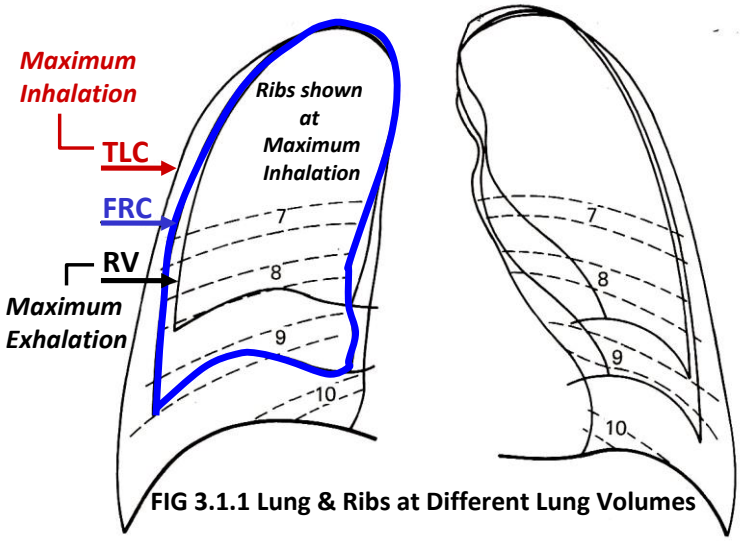
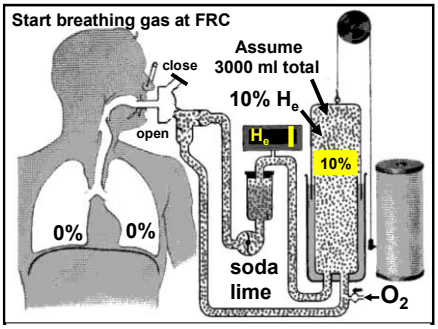


FIG 3.1.1 Lung & Ribs at Different Lung Volumes

Helium Dilution Measurement of FRC and RV TOC

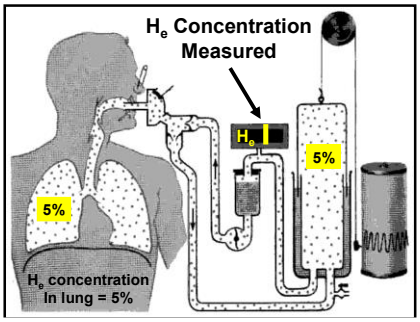
A spirometer is loaded with 3,000 mL of gas that initially contains 10% Helium. A valve is opened at the end of a quiet expiration (FRC), and Bill starts breathing gas from the spirometer. O_2 is added via a valve, and CO_2 is removed by soda lime. Before breathing starts, the concentration of He in the lungs is zero. After some time, equilibrium is reached and the concentration of He in the lungs equals that in the spirometer. In this example, equilibrium is established at 5% in the lungs (an increase from zero) and in the spirometer (a decrease from 10%). Determining FRC and then RV is by calculation. The procedure is based on the indicator dilution principle. Since the initial and final He volumes are equal, the volume of dilution (lung) can be determined as shown. This volume is FRC since that was lung volume when breathing started. Once FRC is known, RV is determined as FRC-ERV, where ERV is determined by simple spirometry.

FRC via Helium Dilution→ Start



Before start He concentration in spirometer = 10%

At Equilibrium→End



H_e concentration in lung & spirometer = 5%

Initial H_e volume = Final H_e volume

Start	End
H_e in lungs + H_e in spiro	= H_e in combined (lung + spiro)
0 + 0.10x3000	= 0.05 (FRC + 3000)

FRC = 3000

Calculated → RV = FRC - ERV ← Measured by SS

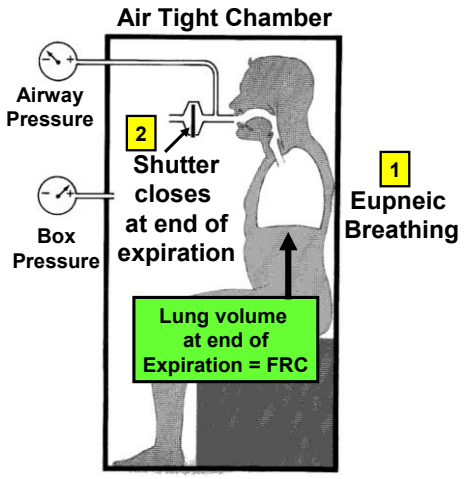
$$V_L \times F_{L\_start} + V_{sp} \times F_{sp\_start} = (V_L + V_{sp})\, F_{L\_end}$$

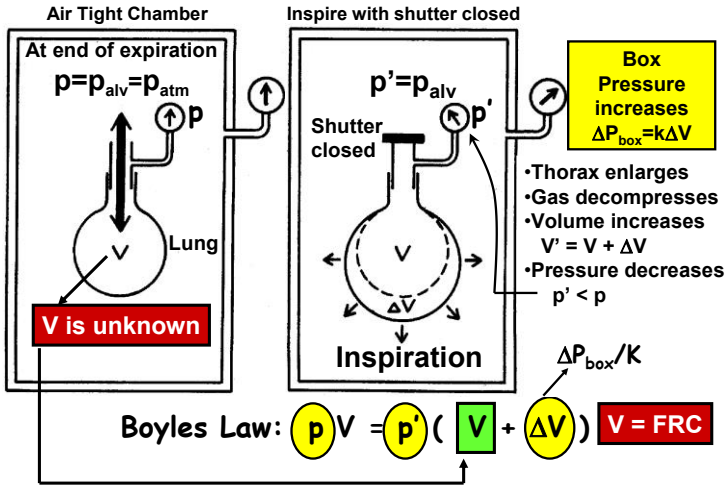
$$F_{L\_end} = F_{sp\_end}$$

V_L & F_L are Volume & Fractional Lung concentration
V_{sp} & F_{sp} are Volume & concentration in Spirometer

Whole Body plethysmography (WBP) to determine FRC and RV TOC

The Whole Body Plethysmography (WBP) method allows determining FRC based on Boyle's gas law. The unknown initial volume (FRC) is determined from changes in box pressure.





Methods Comparison

He dilution (& N_2 washout) methods measure COMMUNICATING GAS VOLUME; Lung gas that can mix with the breathing mixture. WBP method measures TOTAL gas volume - gas that is or is not in direct communication with alveoli. Differences in values if a significant amount of "trapped" air.

Respiratory Pressures: Introduction TOC

- ***Alveolar (P_{ALV}) and Recoil (P_{REC}) Pressures***

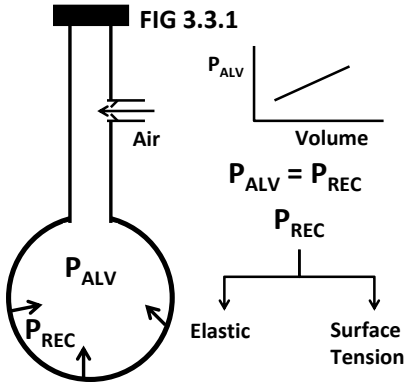


FIG 3.3.1 is an alveolus with trachea blocked and air entry through the valve-inlet. A certain volume has entered at which volume the alveolar pressure (P_{ALV}) is balanced by an oppositely directed recoil pressure (P_{REC}). P_{REC} has two components; one is elastic, similar to that of a stretched spring. The other is due to surface tension that arises because alveoli epithelial cells are moist and alveolar content is gas. Both pressures (forces) are directed inward, and $P_{ALV} = P_{REC}$.

- ***Intrapleural (P_{PL}) Pressure***

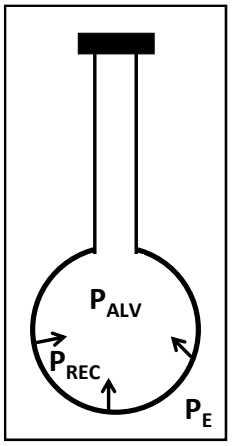


FIG 3.3.2

To maintain the same size P_{ALV} must change by P_E

$P_{ALV} - P_E = P_{REC}$

$P_{ALV} = P_{REC} + P_E$

If P_E is intrapleural Pressure P_{PL} then

$P_{ALV} = P_{REC} + P_{PL}$

FIG 3.3.2 is the alveolus now in a box that has a uniform external pressure P_E. If alveolus volume remains the same, then its pressure must change by a value equal to P_E. One way to see this is to consider the transmural pressure (TMP) to achieve balance. Equilibrium volume occurs when the TMP = the recoil pressure or ($P_{ALV} - P_E$) = P_{REC}. Rearranging shows that at equilibrium $P_{ALV} = P_{REC} + P_E$. If we view P_E as intrapleural pressure (P_{PL}) that surrounds the alveolus, we get $P_{ALV} = P_{REC} + P_{PL}$. This is a steady state relationship and is changed if there is air flow.

- ***Pressure Changes Linked to Air Flow***

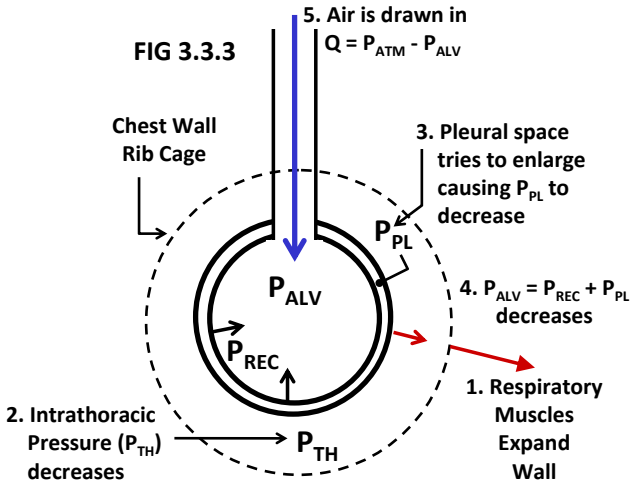


FIG 3.3.3 shows basic processes of inhalation as related to pressures. We take as the 1st event (1) activation of respiratory muscles, e.g., diaphragm contraction, causing chest wall expansion. This causes the intrathoracic pressure (P_{TH}) to decrease (2) as a consequence of Boyle's Law. The wall expansion tends to enlarge the intrapleural space, causing its pressure to decrease (3) by the same amount as the decrease in PTH. Since P_{PL} falls, so does PALV (4), which is now less than atmospheric pressure (PATM), creating a favorable pressure gradient to cause air to flow into the alveolus (5).

- ***Intrathoracic Pressure – Intrapleural Pressure Relationship***

P_{PL} is defined as pressure in the intrapleural space but is close to the value everywhere in the thorax (chest cavity) except inside blood vessels, lymphatics, and airways. So, this includes interstitial space surrounding airways inside lung, around heart and great vessels and around and inside esophagus. Esophageal pressure is a very good estimate of P_{TH} and is often used clinically for that purpose.

Respiratory Pressures: Comments and Summary TOC

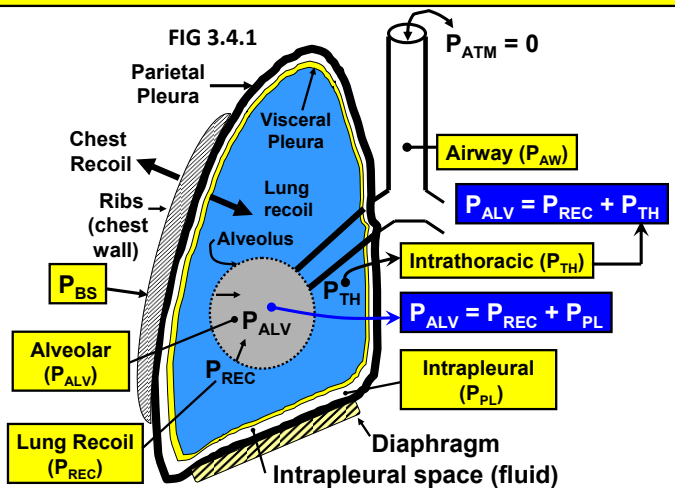
Summary of Basic Pressures

Alveolar	$P_{ALV} = P_{PL} + P_{REC}$
Intrapleural	P_{PL}
Atmospheric	P_{ATM}
Body surface	P_{BS}
Intrathoracic	$P_{TH} \rightarrow P_{PL}$
Lung recoil	P_{REC}
Wall recoil	P_{RECW}

Pressure Differences (Transmural)

Translung	$P_{TL} = P_{ALV} - P_{PL} = P_{REC}$
Transpulmonary = Translung	
Transwall	$P_{TW} = P_{PL} - P_{BS}$
Total Respiratory	$P_{RS} = P_{TL} + P_{TW} = P_{ALV} - P_{BS}$

Pressures Illustrated



"NEGATIVE PRESSURE": *Oppositely directed forces (lung recoil vs. chest wall) act to separate pleurae. Virtual expansion of this very narrow space with a fixed volume makes* $P_{PL} < P_{ATM}$ *during inspiration (Boyles' law). This sub-atmospheric pressure is called a "negative" pressure. If* P_{ATM} *=760 mmHg and* P_{PL}*=752 mmHg then* P_{PL} *is -8 mmHg relative* P_{ATM}*.*

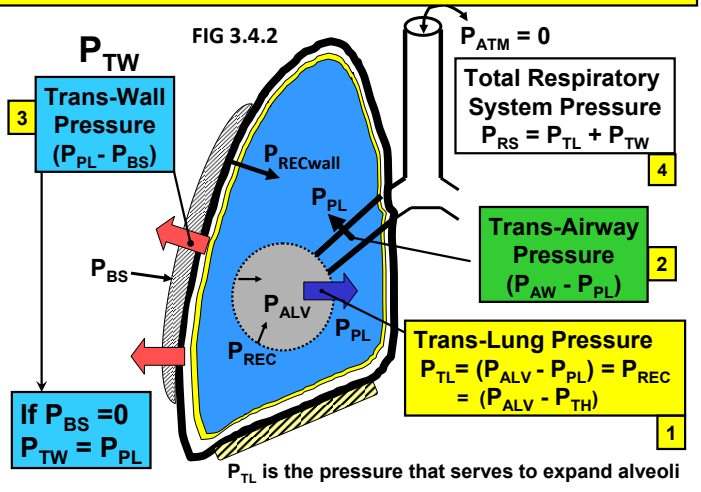
INTRAPLEURAL PRESSURE: *In eupneic quiet breathing,* P_{PL} *is <* P_{ATM}*. It is determined by oppositely directed lung vs. chest recoil forces acting to expand intrapleural space.* P_{PL} *is + in forced expiration.*

LUNG RECOIL PRESSURE *is due to alveoli elastic recoil and surface tension. Elastic recoil forces arise because lung is stretched beyond its zero-stress size. The pleural seal causes lung to stretch above its zero-stress state as is illustrated subsequently. If the seal breaks the lung collapses (pneumothorax).*

CHEST WALL RECOIL PRESSURE *arises when thorax is not at its equilibrium zero stress state. This is because it is pulled inward by lung recoil via the pleural seal. Chest wall recoil force is to restore the chest wall to its unstressed length. For static relaxed conditions, FRC is determined by the volume at which the two opposing forces (inward lung-outward chest) balance each other.*

TRANSLUNG (TRANSPULMONARY) PRESSURE **(P_{TL})** *is the difference between alveolar and pleural pressures:* $P_{TL} = P_{ALV} - P_{PL}$*.* P_{TL} *increases during inspiration and decreases during expiration but is always positive; e.g. if* P_{PL} *= -8 cm*H_2O *and* P_{ALV} *= -3, then* P_{TL} *= -3 - (-8) = + 5 cm* H_2O*.*

Transmural Pressures



TRANSWALL PRESSURE (P_{TW}) *is the difference between* P_{PL} *and body surface pressure (*P_{BS}*).* P_{BS} *differs from* P_{ATM} *if an external pressure on the chest (e.g. large weight on chest or upper-body negative pressure). Transwall pressure determines chest wall expansion during inspiration - if inadequate to expand the thoracic cage - breathing stops!*

TRANSMURAL & RECOIL PRESSURE RELATIONSHIP

For relaxed static conditions, absolute values of lung and chest wall transmural pressures (P_{TL} and P_{TW}) are equal to the absolute values of their corresponding recoil pressures. By convention, recoil pressures that act in a direction to reduce volumes are taken as positive.

TRANS-AIRWAY PRESSURE **(P_{TA})** is the difference between inside (P_{AW}) and external pressure (P_{PL}) surrounding airways. P_{TA} is a main factor keeping small airways open when positive. If TMP reverses airways tend to collapse. This occurs during forced expiration as P_{PL} becomes positive and exceeds P_{AW}. The position in the airway system where this occurs is called the Equal Pressure Point (EPP).

TOTAL RESPIRATORY SYSTEM PRESSURE (P_{RS}) is the algebraic sum of translung and transwall pressures. When considering Volume-Pressure relations of the combined lung-chest wall system, P_{RS} is often used. Numerically $P_{RS} = P_{TL} + P_{TW}$ which, for static conditions (no airflow), is the same as $P_{ALV} - P_{BS}$. So, under most circumstances, total respiratory system pressure can be viewed as simply alveolar pressure as shown in the adjacent figure.

Transmural Pressures: Total Respiratory Pressure

Transwall: $P_{TW} = P_{PL} - P_{BS}$

Translung: $P_{TL} = P_{ALV} - P_{PL}$ FIG 3.4.3

$P_{TW} + P_{TL} = P_{RS} = P_{ALV} - \cancel{P_{BS}}$

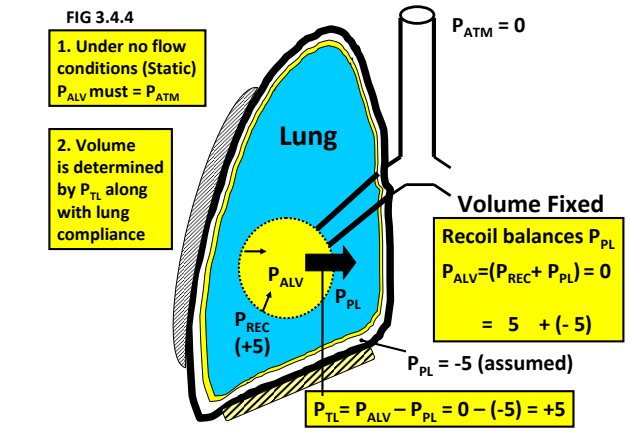
$P_{RS} = P_{ALV}$

Relationships depend on whether air is flowing or not

With reference to FIG.ures 3.4.4 and 3.4.5, which illustrate the conditions for zero airflow (Q) that occur at the end of inspiration and also at the end of expiration. When Q is zero and the glottis is open, P_{ALV} must equal P_{ATM}. For this to be true, P_{REC} must equal P_{PL} in magnitude. Two examples with zero airflow are shown below. <u>During</u> inspiration/expiration Q is not zero so P_{ALV} is determined by two conditions: (1) $P_{ALV} = P_{ATM} \pm QR_{AW}$ (R_{AW} is airway resistance) and (2) $P_{ALV} = P_{REC} + P_{PL}$. These relations are discussed in the following section. Note that translung pressure, along with compliance, determines *lung volume* under both static (no airflow) and dynamic (airflow) conditions. This state of affairs is to be contrasted with events that occur during airflow, as discussed in section 4.0

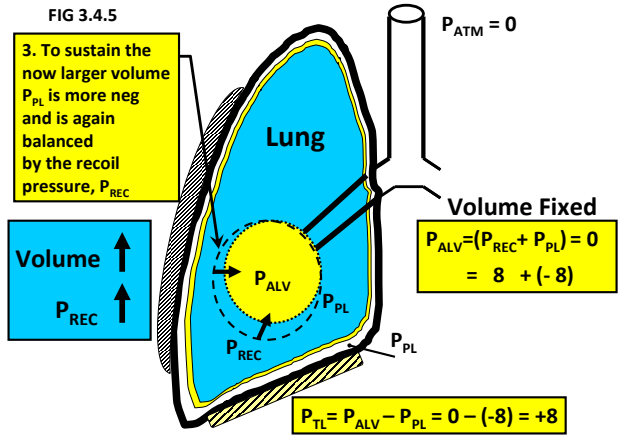
Pressure Relations: NO AIRFLOW: *End Expiration*

FIG 3.4.4



Pressure Relations: NO AIRFLOW: *End Inspiration*

FIG 3.4.5



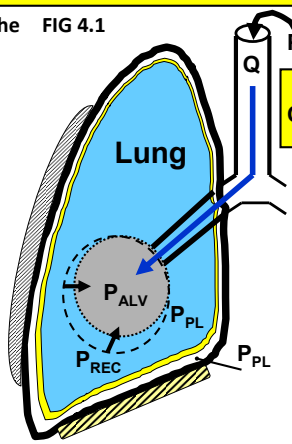
4.0 AIR FLOW GENERATION AND PRESSURE RELATIONS TOC

Thorax expansion during inspiration decreases P_{PL}, causing the alveoli to expand at a fixed gas volume (FIG.. 4 .1), and PALV decreases (Boyle's Law). A reduced PALV creates a favorable pressure difference for airflow (Q) into the lungs ($Q \sim P_{ATM} - P_{ALV}$). As air enters alveoli, the condition of a fixed volume is no longer true, and P_{ALV} begins to return toward P_{ATM} (FIG 4.2) despite the now larger alveolar volume. A more negative PPL supports the larger volume and thus a greater P_{TL}. Q reduces as P_{ALV} returns toward zero (P_{ATM}). At the end, inspiration Q is again zero.

DURING Inspiration - Dynamic

1. In response to the decrease in P_{PL} alveoli expand at initially fixed gas amount
2. P_{ALV} decreases (Boyles Law) and air flow begins
3. As more air enters alveoli, P_{ALV} becomes *less reduced*
4. At end of inspiration P_{ALV} again = P_{ATM}

FIG 4.1



$$Q = \frac{P_{ATM} - P_{ALV}}{R_{AW}}$$

This relationship conceptually determines amount of air flow

Dynamic Pressure and Flow Changes

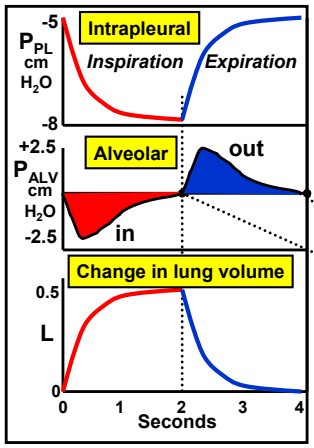


FIG 4.2

Air Flow depends on the difference between alveolar pressure and atmospheric pressure
$Q \sim P_{ATM} - P_{ALV}$

Q (l/sec) has same form as P_{ALV}

Air flow is zero twice during cycle
If Q=0 $P_{ALV} = P_{ATM}$

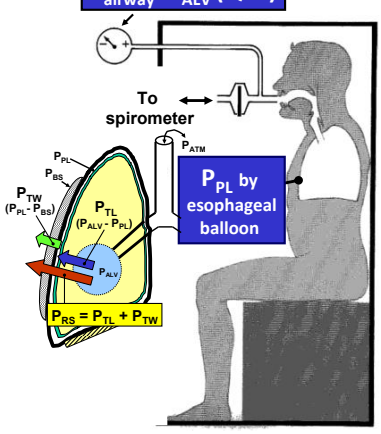
The reverse occurs during expiration since a greater lung recoil force compresses the larger end-inspiratory volume. So, P_{ALV} varies during a breathing cycle (FIG.. 4 .2), being zero when there is no airflow, negative during inspiration, and positive during expiration.

5.0 RESPIRATORY COMPLIANCE AND PRESSURES TOC

Pressure-Volume Relationships – Static: Compliance is evaluated on the deflation limb of a static P-V curve. Static means that P-V relationships apply when airflow = 0. This is achieved by having a person change their lung volume in increments and hold their breath with relaxed respiratory muscles (FIG. 5.1). For each volume, pressure is measured, and a P-V graph is created.

Measuring Passive/Relaxed Pressure-Volume

FIG 5.1 $P_{airway} = P_{ALV}$ (Q=0)



Measurements lead to Respiratory System P-V

- Take in/out a certain volume
- Close stopcock
- Relax respiratory muscles
- Measure P_{ALV} and P_{PL}
- Repeat for different volumes

$$P_{ALV} = P_{TW} + P_{TL} = P_{RS}$$

(P_{ALV} measured; $P_{TW} + P_{TL}$ = Recoil)

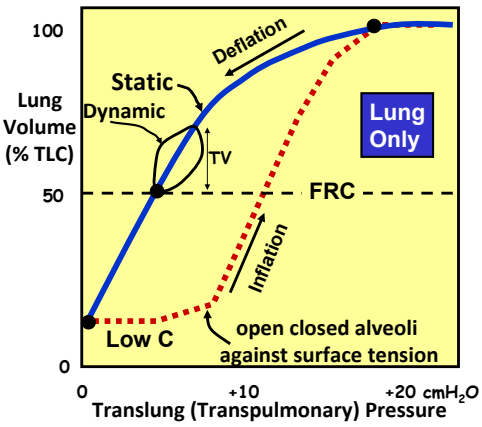
Individual components

Chest: $P_{TW} = P_{PL}$ ← measured

Lung: $P_{TL} = P_{RS} - P_{TW}$

Lung Pressure-Volume Relations

FIG 5.2



(FIG. 5 .2).

Since muscles are relaxed (FIG.. 5.1), a passive or relaxed P-V relation is generated. From the measurement, the lung, chest, and overall respiratory compliances can be determined. Lung (alone) compliance is determined as the slope of the P-V curve at any point, but the full P-V curve shown (FIG 5.2) extends over a much wider range than occurs during a normal breathing cycle, shown as a dynamic P-V loop. The area of the TV loop (FIG.. 5 .5) is a measure of the energy lost in overcoming airway and tissue resistances during the breathing cycle.

Pressure-Volume Loop – Dynamic

Normal quiet breathing occurs in the near-linear portion of the P-V curve (FIG.. 5.3, 5.4, and 5.5) with inspiration starting at FRC. For a "typical" TV of 500 mL and FRC of 2500 mL, lung compliance, calculated as $\Delta V/\Delta P$ is~ 0.2 L/ cmH_2O. Purely elastic work to expand the lung during inspiration is 1/2 ΔV x ΔP (triangle area). If there were no losses it would be fully recoverable during expiration. Inflation and deflation would occur along the straight-line path A-B in FIG.. 5.5. But losses due to airway and tissue resistances mean that additional energy is needed during inspiration, with some energy also lost during expiration. The area of the closed loop represents these energy components. In **restrictive** lung disorders, the needed elastic work to expand the lung increases, requiring the respiratory muscles to generate more force than normal. In **obstructive** lung disorders, there is increased airway resistance (R_{AW}), so both inspiratory and expiratory portions of the loop area increase. Normally, ~ 4/5 of irrecoverable energy (inelastic work) is due to R_{AW} and ~ 1/5 due to tissue viscosity. The normal volume change during eupneic breathing is only about 8% of TLC (**FIG 5.3**).

FIG 5.3 Lung "Typical" Values

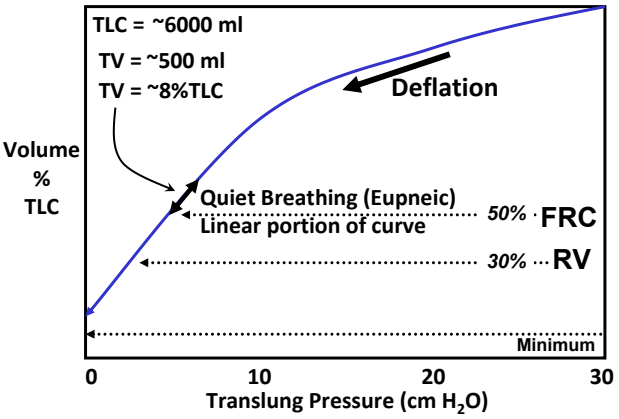


FIG 5.4 Lung Compliance

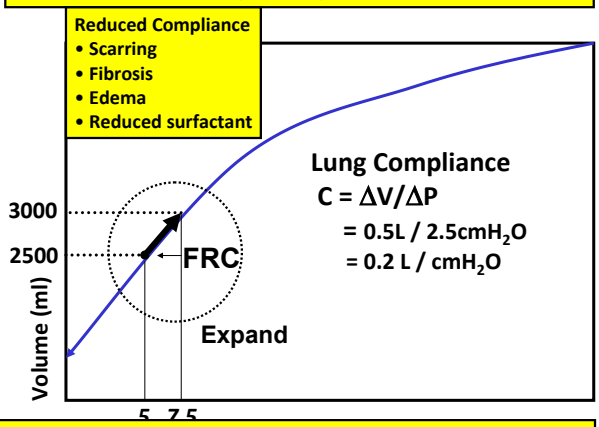
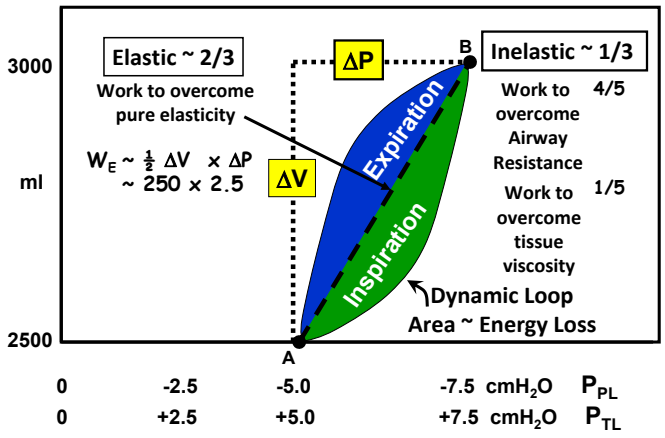


FIG 5.5 Elastic vs. Inelastic Work



Respiratory System Compliance/Pressures TOC

Lung inflation/deflation depends on lung and chest wall forces that in turn depend on lung volume.

FIG 5.7 Lung and Thorax as Springs

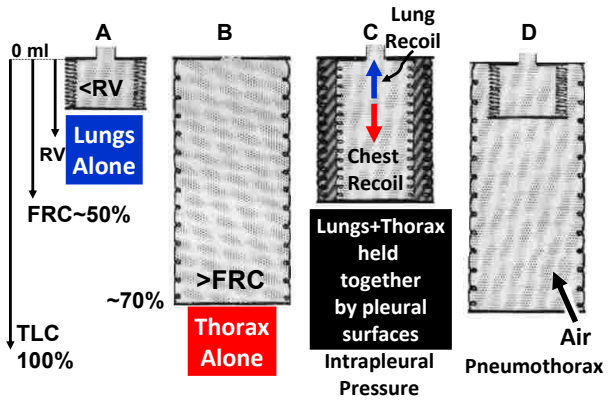


FIG 5.6 Lung and Chest Wall Forces

Lung + Thorax Interactions Determine Respiratory System P-V and Compliance

- **Lung Elastic Forces:** *tend to close the lung at any lung volume*
- **Chest Wall Elastic Forces:** *tend to expand lung for most lung volumes*

At FRC: Forces are equal but oppositely directed

Inspiration: Lung force ↑ Chest force ↓

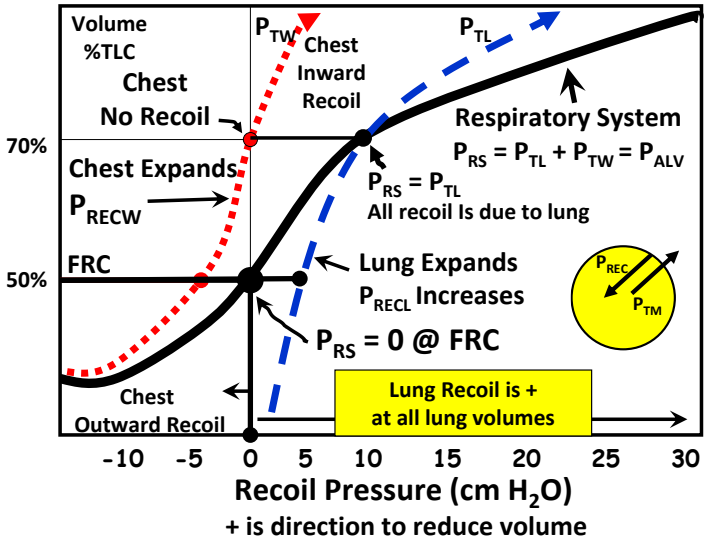
At ~70% TLC: Chest force = 0 (at 0 stress position)

> ~60-70% TLC: Lung & Chest forces tend to close lung

FIG. 5.7 shows a model that can be used to examine the overall interactions between the lung and thorax and their associated forces. FIG. 5.6 summarizes some main points that are elaborated on in FIG. 5.8.

At any lung volume, $P_{RS} = P_{TL} + P_W$. At FRC, the tendency for the chest wall to expand is balanced by oppositely directed lung recoil forces. P_{RS} is thus zero at FRC (FIG. 5.8). At a lung volume of ~70% TLC, the chest wall force is zero, and PRS is due solely to the lung. For volumes greater than this, lung and wall recoil forces are in the same direction. P_{RS} is positive if lung volume is greater than FRC and negative if volume is less. At FRC, transwall pressure (P_{TW}) is negative, which means that the chest cage still tends to "spring out". Not until a lung volume of ~ 70% of TLC does it reach its "unstressed" length; this corresponds to zero transwall pressure and zero recoil force. In contrast, translung pressure (P_{TL}) is always positive – meaning that it tends to recoil. In a relaxed lung at any volume, P_{RS} is the sum of pressures due to the chest wall and the lung acting separately. The slope of the respiratory system P-V curve is less than that of the lung or chest wall because total compliance is due to wall and lung compliance in series, and thus overall compliance is less than either individual compliance; 1/CRS= 1/CL + 1/CW; for normal lung volumes, CL ~ C_W ~ 0.2 L/cmH_2O.

FIG 5.8 Respiratory System P-V relations

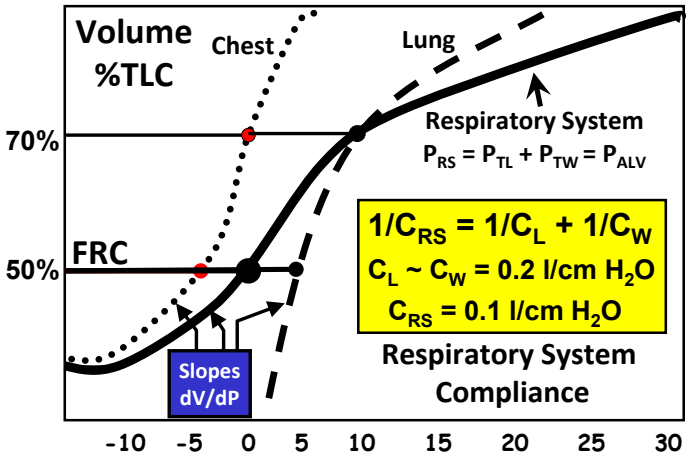


Determinants of Compliance TOC

FIG. 5.9 illustrates some of the attributes associated with respiratory system compliance that depend on both lung and chest wall properties.

Chest Wall Properties: Since overall respiratory compliance depends on both the lung and chest wall compliance, any condition or process that alters chest wall compliance affects overall respiratory system compliance.

FIG 5.9 Respiratory System Compliance



Lung Tissue Properties and thickness: Lung changes that cause its tissue to be less "stretchable," e.g., scarring, fibrosis, and edema, decrease lung compliance. This makes it more difficult to inflate the lung because of the increased P_{REC}.

Lung Surfactant (LS): Produced by type II alveolar cells; acts to reduce surface tension and thus reduce the effective recoil force of the lung. If surfactant levels are low, the forces tending to close alveoli are greater, and compliance is reduced. This makes it more difficult to inflate the lungs and increases the work associated with inspiration

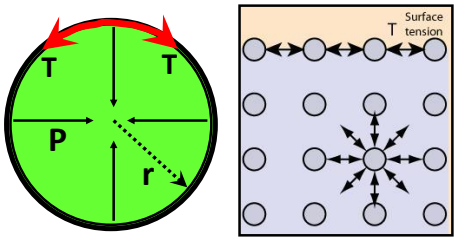
Lung Surface Tension: TOC

Because of interactions between air and fluid molecules at alveoli surfaces (**FIG 5.10**), there is an interface ***Surface Tension*** (T) that tends to contract the interface inwards. T tends to keep fluid molecules within the fluid and shrink the surface to the smallest possible surface area. Surface-active agents (surfactants) can reduce T by accumulating at an interface, thereby reducing fluid-air interaction forces.

FIG 5.10 Surface Tension-Surfactant Effects

- **Surface Tension = T causes inward pressure P = 2T/r**
- **T is reduced by presence of lung surfactant (LS)**

Alveolus pictured as a Soap Bubble



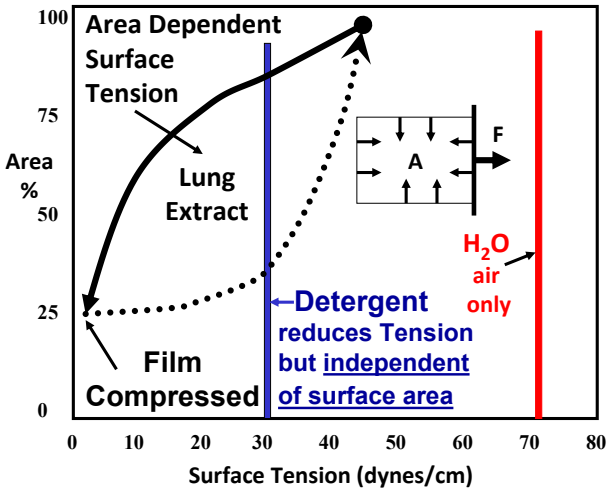
Effects of Lung Surfactant

1. **Increases Compliance**
2. **Reduces tendency for closure (atelectasis)**
3. **Reduces tendency for alveolar capture**
4. **Reduces tendency for fluid transudation**

Property of Lung Surfactant (LS)

A unique LS property is that its surface tension-reducing action increases as the surface area decreases. For a thin film of lung extract in a frame with a movable end (FIG 5.11), the force (F) measured as the frame area (A) is changed is surface tension. If this is done with normal lung extract, surface tension is lower when the film is at a lower surface area. Detergents reduce surface tension, but none exhibit a change in surface tension with area, unlike lung surfactant.

FIG 5.11 Lung Surfactant: Special Features

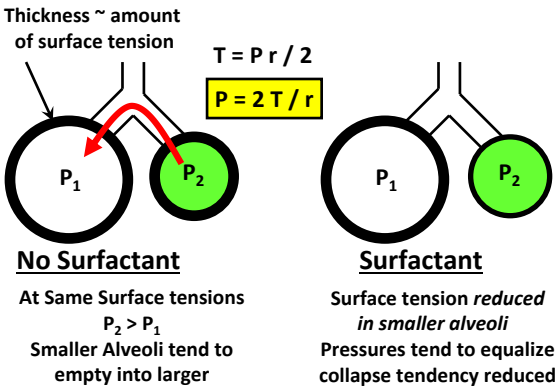


Lung Surface Tension: Tends to close Alveoli

About 1/2 of total recoil force of normal lungs is due to surface tension with pressure to overcome tension given by Laplace's law; $T = (P_{TM} \times r) / 2$. Surfactant infiltrates air-fluid interface *more during inflation* as surfactant molecules spread out over a larger area. A "sigh" promotes this process. During deflation, beneficial surfactant effects increase since a smaller surface area has a greater density of surfactant molecules at the interface. *Surface tension is less at low volumes.*

General Effects of Lung Surfactant

FIG 5.12 Surfactant Stabilizes Alveoli



- Compliance is increased, and the work of inspiration is reduced
- Helps keep alveoli 'dry'; lowered tension draws less fluid into alveoli
- Helps promote alveoli stability since LS causes T to be less at lower alveoli volume. So, the pressure needed to keep smaller alveoli from collapsing is less, and this reduces the tendency for alveoli to collapse at the end of expiration. This would require a large energy expenditure to reopen with each breath. LS also reduces the tendency of small alveoli connected to larger ones to be absorbed by the larger ones.
- LS also helps stabilize the rates of alveoli deflation. Without LS, faster deflating alveoli would tend to have lower recoil forces since their volume would be less than alveoli that started at the same volume but deflated more slowly. Since LS reduces T more at lower alveoli volumes, faster deflating alveoli are slowed by their reduced recoil force, allowing more slowly deflating alveoli to "catch up.

Inadequate Surfactant Effects

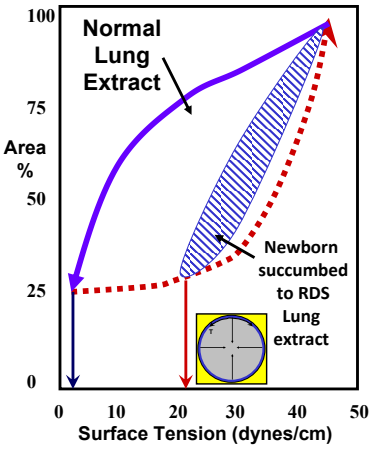
a) Stiffer lungs (lower compliance)

b) **Atelectasis** (collapsed alveoli) – low lung capillary blood flow (e.g., pulmonary embolism) may cause atelectasis due to less substrate supply for LS production; reversible if blood flow is restored

c) Alveoli partially filled with fluid

d) Newborns - **respiratory distress syndrome** (RDS) Absence or inadequate levels of LS is more prevalent in pre-term babies since the fetal lung's ability to synthesize adequate amounts of material occurs during the third trimester. This normally occurs in anticipation of the pending transition from fluid-filled lungs to air-breathing, an event heralded by the newborn's first cry.

FIG 5.13 Respiratory Distress Syndrome



Deflation: Low surfactant
- Normal decrease in surface tension not present
- Greater force at any alveolar volume acts to close alveoli

Inflation: Once closed:
- Big work/breath needed to re-inflate lungs
- Increased muscular work fatigues diaphragm

Pressures induced by Muller and Valsalva Maneuvers TOC

The solid curve in FIG. 5.13a shows total respiratory P-V relations as developed previously (FIG. 5.8). Dashed lines are maximum active pressures developed at various lung volumes. Muller's maneuver is an inspiratory effort against a closed airway or glottis. This effort decreases intrathoracic (and alveolar) pressure but expands pulmonary gas volume. Valsalva's maneuver is an expiratory effort against a closed glottis. It increases intrathoracic (and alveolar) pressures. The developed pressures and their potential effects depend on lung volumes when the maneuvers are initiated. Greater (positive) expiratory pressures occur when starting from greater lung volumes and doing the Valsalva maneuver. Greater (negative) inspiratory pressures occur if forced inspiration starts at low volumes, during the Muller maneuver. Possible dangers of each are shown above in FIG 5.13b, and hemodynamic changes with the Valsalva maneuver are shown in FIG 5.14.

FIG 5.13a Muller and Valsalva Maneuvers Large Pressures Associated with Active/Forced Inspiration/Expiration

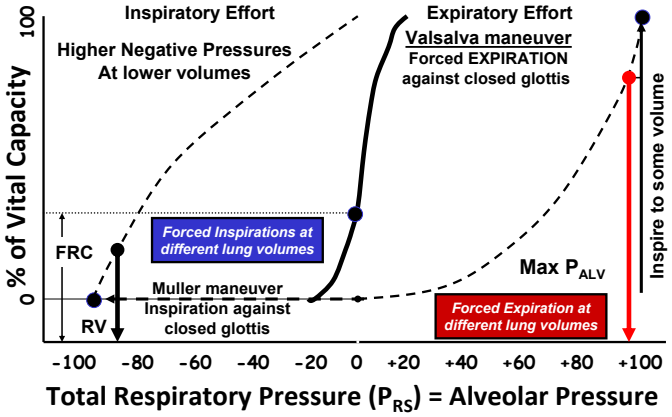
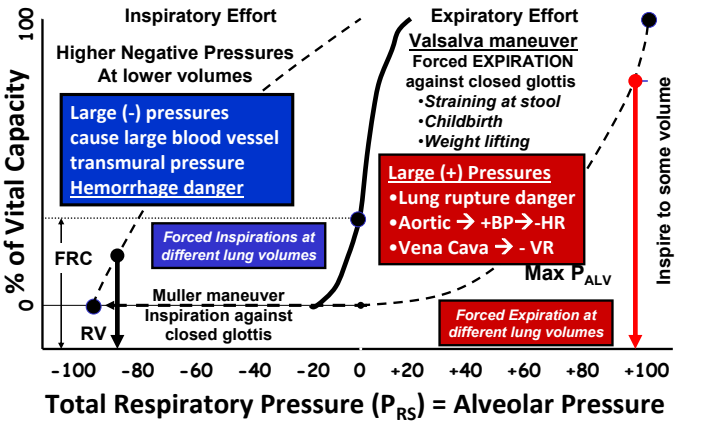


FIG 5.13b Muller and Valsalva Maneuvers Large Pressures Associated with Active/Forced Inspiration/Expiration



Muller and Valsalva Maneuvers: Hemodynamic and Intrathoracic Effects TOC

FIG 5.14 Valsalva Maneuver: Normal CV Effects

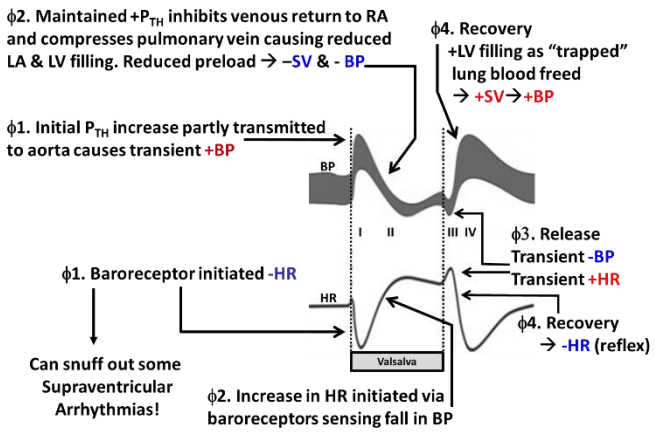
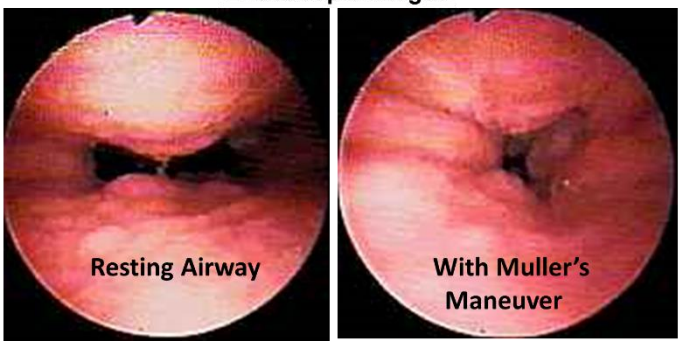


FIG 5.15 Muller Maneuver Use

Observe site of upper airway collapse in obstructive sleep apnea

Endoscopic Images

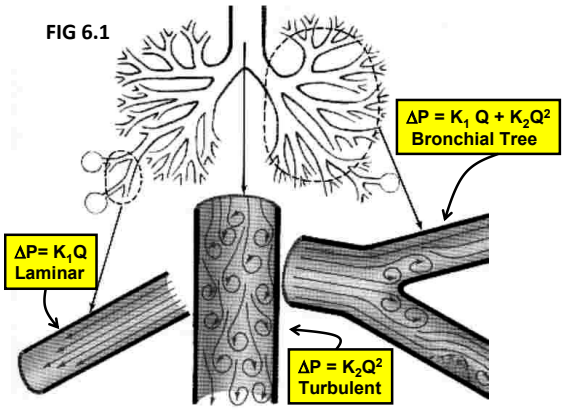


6.0 AIRWAY RESISTANCE (R_{AW}), AIR FLOW (Q) AND LUNG VOLUME TOC

Airway Resistance and Air Flow Features

*For non-collapsed airways, $Q = (P_{ATM} - P_{ALV})/R_{AW}$ with R_{AW} = total airway resistance. Since Q is turbulent in the trachea (**FIG 6.1**) a greater pressure difference is*

FIG 6.1



*required to produce the same amount of flow ($Q \sim \Delta P^{1/2}$) rather than $Q \sim \Delta P$. So R_{AW} is greater than for laminar flow. In part due to the 'upstream' turbulence, and in part due to large numbers of parallel smaller airways, most R_{AW} is in upper airways. About 40% of R_{AW} is in the pharynx-larynx (**FIG 6.2**), about 40% in airways greater than 2 mm, and only 20% in airways less than 2 mm. However, in conditions such as chronic obstructive pulmonary disease (COPD), where airway resistance increases, the increase is primarily in the lower airways, so the percentages cited for normal lungs are reversed. For example, total airway resistance may triple, with virtually all the increase occurring in airways with diameters < 2 mm. Normal AWR at end inspiration is ~1-1.5 $cmH_2O/L/sec$. If airways collapse, then conditions for flow in collapsible vessels apply as in FIG 6.3.*

FIG 6.2 Airway Flow Features and Resistance

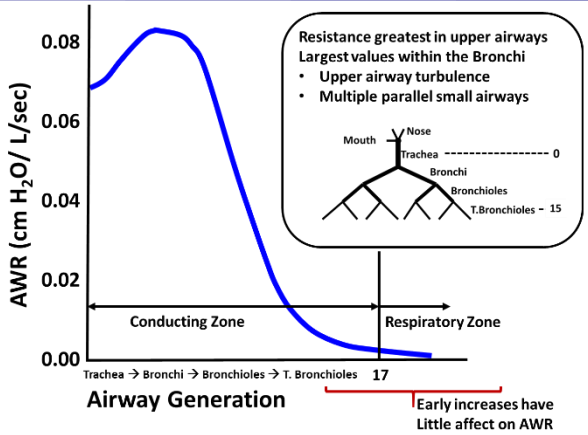
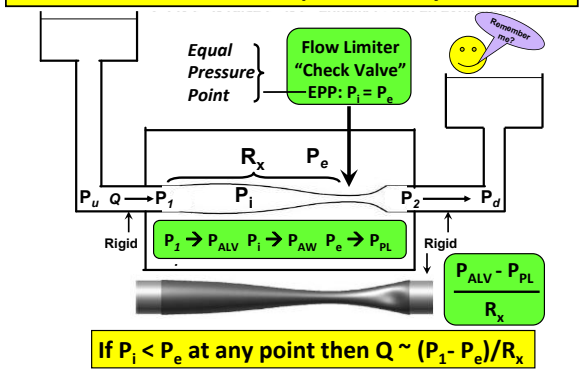


FIG 6.3 **Air Flow in Collapsible Airways**



Lung Volume Effects: Airways lengthen with inspiration but the diameter increase dominates and R_{AW} decreases as shown in **FIG 6.4**. Diameters increase because (1) airways are tethered to lung parenchyma and alveoli septa and (2) TMP increases due to a more negative P_{PL}. If lung volume increases from an FRC of ~ 2300 ml to 2800 ml, R_{AW} decreases by half from about 2.8 to ~ 1.4 cm H_2O/l/sec as summarized in **FIG 6.5**.

FIG 6.4 Airways widen with increasing volume

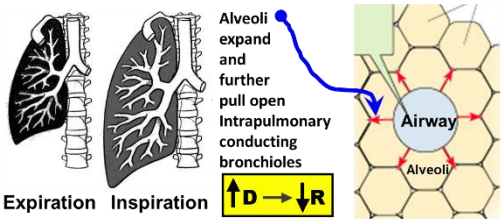
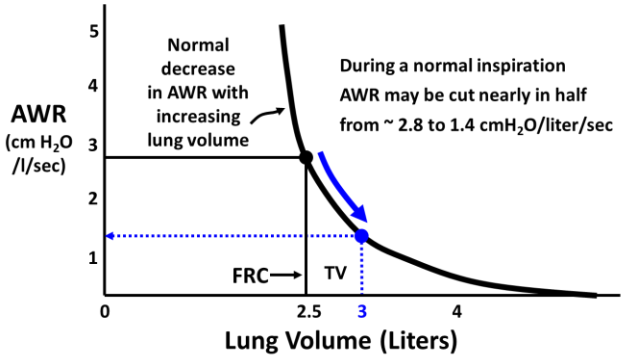


FIG 6.5 Airway resistance decreases with increasing volume

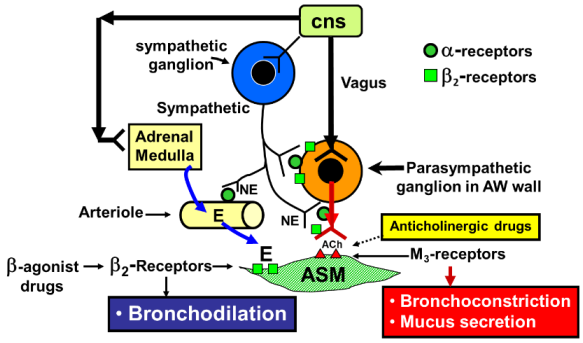


Persons with airway resistance issues tend to breathe at increased volumes (FRC is increased → Tends to lower already elevated AWR)

Neural Impacts on Airways

FIG 6.6 summarizes some main neural effects on airway smooth muscle (ASM) that have both β and M_3 receptors. Activation of β-receptors either by epinephrine (E) or norepinephrine (NE) causes bronchodilation. Conversely, activation of M_3-receptors via acetylcholine (Ach) released from parasympathetic nerves or other sources causes bronchoconstriction.

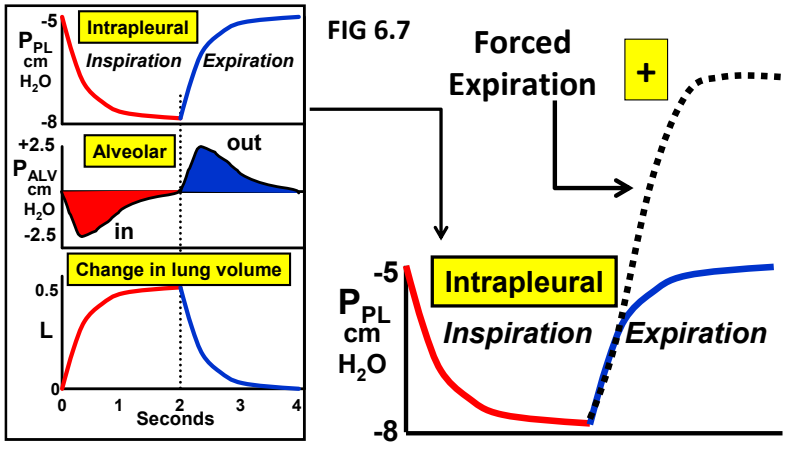
FIG 6.6 Airways - Neural Mechanism (In Brief)



Forced Expiration

FIG. 6.7 emphasizes the point that a forced expiration is associated with a positive intrapleural pressure. This is important since this positive pressure causes a reduction in the airway TMP that facilitates airway buckling or collapse.

Forced Expiration causes a Positive P_{PL} that impacts airways



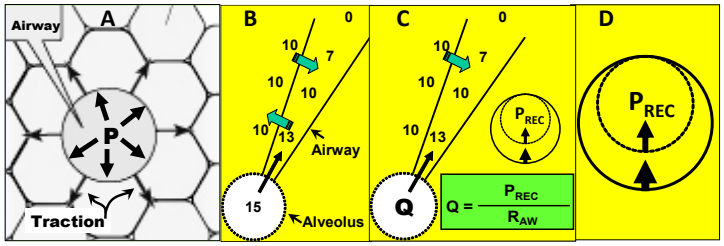
7.0 DYNAMIC COMPRESSION AND FLOW LIMITATION TOC

Main Causes and Features

During expiration, airflow (Q) moves from the alveoli to the airways and into the atmosphere, where the pressure is ~ 760 mmHg. For eupneic breathing alveolar pressure needed to support Q is low since $Q = \Delta P/R_{AW}$ and R_{AW} is low. During ***forced*** expiration, P_{PL} and P_{ALV} achieve positive values. If the pressure surrounding an airway equals or exceeds the pressure in the airway, then at that point, the airway tends to collapse. This is known as dynamic compression, and the collapse point is called the ***equal pressure point (EPP)***. For this condition, outflow through airways connected to this point is determined by the difference between P_{ALV} and the ***surrounding pressure*** (P_{PL}). But, since $P_{ALV} = P_{PL} + P_{REC}$, the pressure forcing air out is just P_{REC}. Trying to force more air out with greater effort will not work since any increase in P_{PL} is also experienced by the alveolus and adds nothing to the driving pressure.

Fig 7.1 Dynamic Compression-Airway Closure: Basic Concept

A. Small intrapulmonary airways are distensible and compressible. Held open by combination of: (1) Airway transmural pressure (2) Tethering or traction by attachments to surrounding tissue.
B. During a forced expiration, PPL becomes + causing pressure surrounding some airways to become greater than pressure inside.
C. This collapsible condition causes airflow to be determined mainly by P_{REC} alone which itself decreases with lung volume.
D. As volume falls so does P_{REC} ultimately causing airway closure. Net result: No further volume can be expelled. This occurs in normal lungs at low volumes. In obstructive lung conditions the volume at which closure occurs is larger.



The location of the EPP in the vast pulmonary airway system changes during a forced expiration since it depends on both inside airway pressure and surrounding pressure, which are both changing with time. As noted, as EPP enters small, easily collapsible airways, a collapsible state exists, and flow becomes ***independent of effort*** since driving pressure (P_{REC}) is itself independent of effort. P_{REC} decreases with lung volume, and at some low lung volume, no further air can be moved out of the alveoli: the result of this process is trapped volume = ***residual volume***. These aspects are illustrated in **FIG. 7.2** TMP holds airways open, aided by tethering traction from surrounding tissue and alveoli. Neglecting tethering, airway collapse occurs if TMP =0. If, at a fixed lung volume, PALV is +15 and PPL is +8 cm H2O, as shown, then if PAW at any point is also +8 cm H2O, a "collapse state" occurs, and Q depends only on P_{REC} and R_2. As volume continues to decrease, P_{REC} decreases, and R_2 increases since airway diameters upstream from EPP are decreasing. Reduced recoil pressures result in greater RV. For example, persons with emphysema have reduced lung recoil with resultant abnormally increased RV.

Fig 7.2 Equal Pressure Point (EPP) Concept

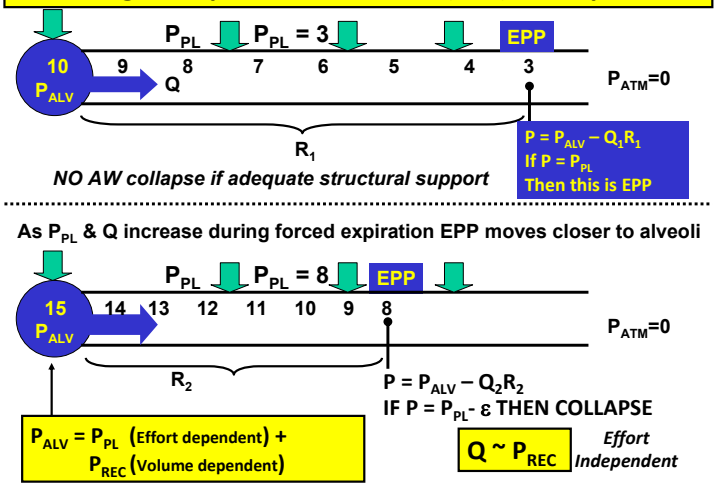
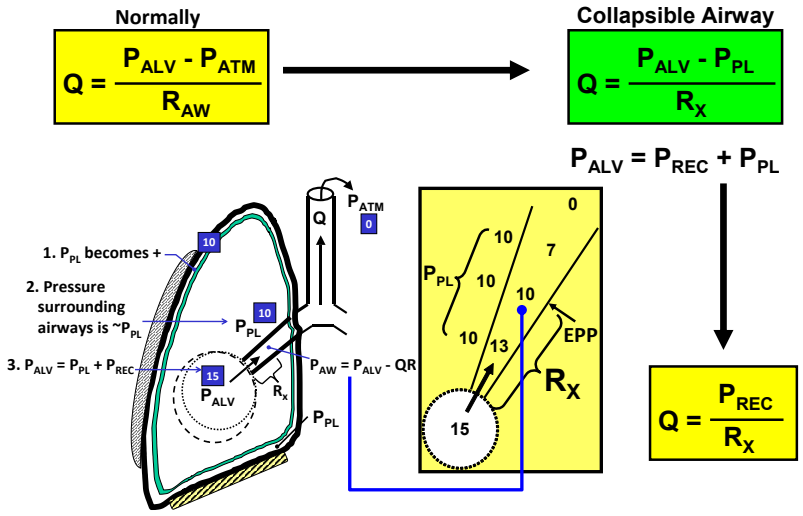


Fig 7.3 Dynamic Compression Summary and Example

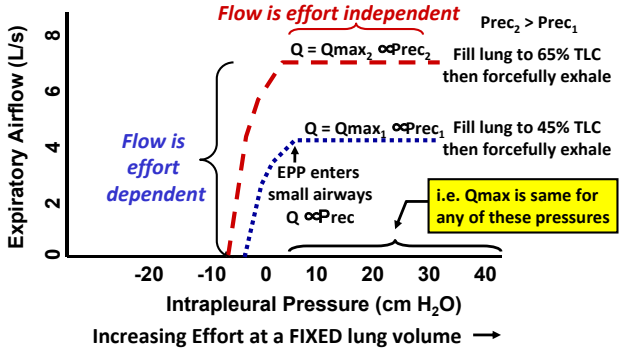


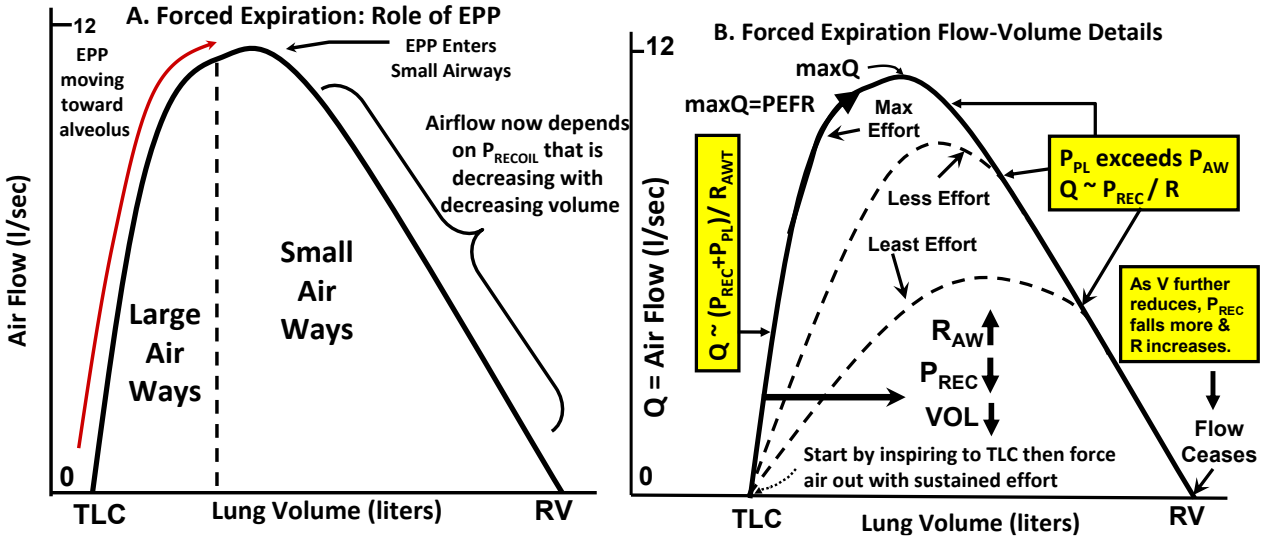
Airflow Limitation and Airflow Independence of Muscular Effort TOC

FIG. 7.4 shows Q at fixed lung volumes. Curves result from repeated expiratory maneuvers at different effort levels. Since lung volume is fixed for each curve, P_{REC} is constant. Increased effort, measured by increased P_{PL}, initially causes Q to increase. But, at a certain effort level, P_{PL} reaches a value that causes dynamic compression. For this condition, the pressure available to force airflow is now P_{REC}. Thus, no amount of added effort will cause an increase in flow (Effort Independent). Also, since P_{REC} decreases as lung (alveolar) volume decreases, the maximum achievable flow at a lower lung volume is less for the same amount of effort used than if at a larger volume. These details are shown below in A and B.

Fig 7.4 Max flow *at any effort* level depends on P_{REC} which in turn depends on lung volume

When P_{PL} reaches a certain + value no amount of added muscular effort will increase expiratory air flow





8.0 OBSTRUCTIVE AND RESTRICTIVE LUNG DISEASES TOC

Basic Concepts

Obstructive = Abnormal Increase in Airway Resistance (R)

Restrictive = Abnormal Decrease in Respiratory Compliance (C)
→ More difficult to expand
→ Greater recoil force

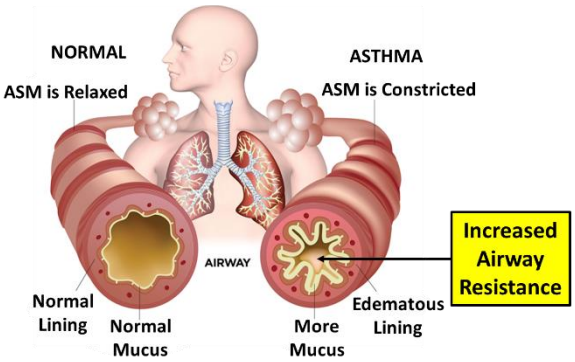
Could have combinations – Mixed Disease

OBSTRUCTIVE → Increased airway resistance

Major types of obstructive lung disease are summarized in the four images below. Asthma is characterized by increased resistance due to either or a combination of airway mucus, wall edema, and constriction of airway smooth muscle. A variety of stimuli can trigger it. Bronchiectasis is also characterized by mucus plugging but may be associated with somewhat dilated bronchi. The mucus may be present due to infection and the reduced ability of ciliary action to remove secreted mucus. The condition may have various origins, including genetic components and/or autoimmune aspects. Airway generalized inflammation and edema may be present in this condition, as well as in chronic bronchitis with an associated hypertrophy of mucus glands. In emphysema, the walls of the lung parenchyma and alveoli are destroyed, causing enlarged airspaces (increased compliance) with a decreased recoil force. Decreased airway traction causes increased airway resistance. Individuals with this condition typically exhibit increased residual volume and total lung capacity. These features are related to a reduced alveolar recoil force, which diminishes the lung's ability to empty during expiration and leads to the occurrence of trapped air as a consequence.

Obstructive Pulmonary Disease Features: Asthma

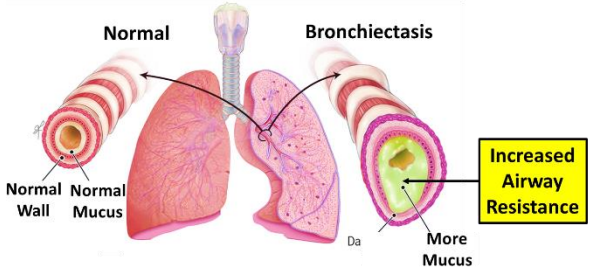
Asthma → Airways swell → Narrow → Mucus
Allergic - Non-allergic - Exercise-Induced



Obstructive Pulmonary Disease: Bronchiectasis

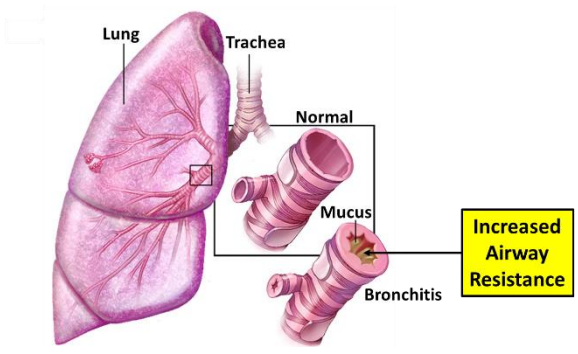
Bronchiectasis → Dilated bronchi with Mucus
→ ineffective secretion removal → infection

- Genetic → Cystic fibrosis and Ciliary dyskinesia
- Immune related → Autoimmune
- Infection
- Unknown



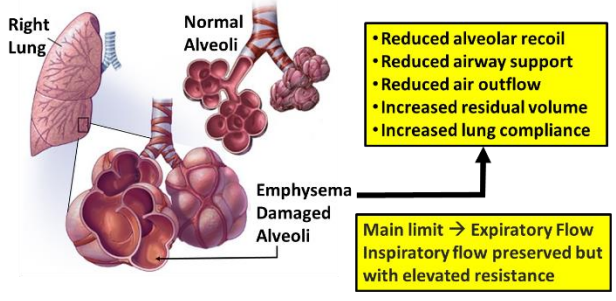
Obstructive Pulmonary Disease: Chronic Bronchitis

Chronic Obstructive Pulmonary Disease (COPD)
Chronic Bronchitis → Bronchi lining inflammation → Mucus



Obstructive Pulmonary Disease: Emphysema

Chronic Obstructive Pulmonary Disease (COPD)
Emphysema → Alveolar destruction
Abnormal permanent enlargement of airspaces distal to terminal bronchioles (Assini) with alveolar wall destruction



Restrictive Diseases: *Restricts Lung Expansion*

"PAINT"

SITE → CAUSES

Pleural → Scarring or Effusion or fibrosis etc

Alveolar → Edema or Hemorrhage

Interstitial → Interstitial Lung Disease or Fibrosis

Neuromuscular → ALS or Myopathy

Thoracic/Extra-thoracic → Obesity or Ascites

- **Interstitial Fibrosis**
  + alveolar fibrous tissue
  Lung becomes stiffer
  (-) compliance
  Inspiration more difficult
- **Allergic Alveolitis**
  Alvoli Wall Thickens
  (-) compliance
- **Pleural Effusion**
  Intrapleural Fluid buildup:
  (-) compliance
  Pleural fibrosis & + rigidity:
  (-) compliance

RESTRICTIVE DISEASE

Characterized by restricted lung expansion and increased recoil. Causes include interstitial fibrosis, pleural effusion, pleural fibrosis, lung edema, and thickened alveolus wall and neuromuscular abnormalities that make chest wall stiffer.

Abnormal Compliances TOC

Although emphysema is an obstructive disease, a major feature is the loss of alveoli, resulting in large airspaces and less lung recoil, causing increased compliance, TLC, and RV, as illustrated in ***FIG. 8.1****. FRC is increased since the lung-chest wall force balance (equilibrium) shifts to a higher volume. Contrastingly in restrictive lung conditions, compliance is reduced and recoil is increased. TLC is reduced because a greater inspiratory force is needed, and RV is reduced because of the greater recoil pressure during expiration. Vascular engorgement in heart failure, atelectasis in surfactant deficiency, and lung edema all cause reduced compliance. The impacts of restrictive and obstructive disease on the dynamic volume-pressure loops are illustrated in* ***FIG. 8.2****. The loop areas are related to the work required of the respiratory muscles. For pure restrictive disease, the main effect is a reduced volume-pressure line slope; for obstructive disease, there is a larger increase in loop area.*

FIG 8.1 Compliance Abnormalities

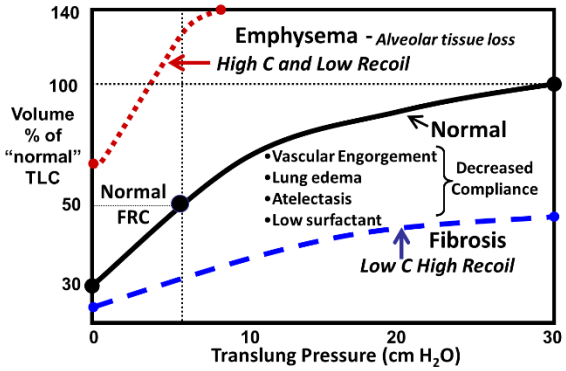
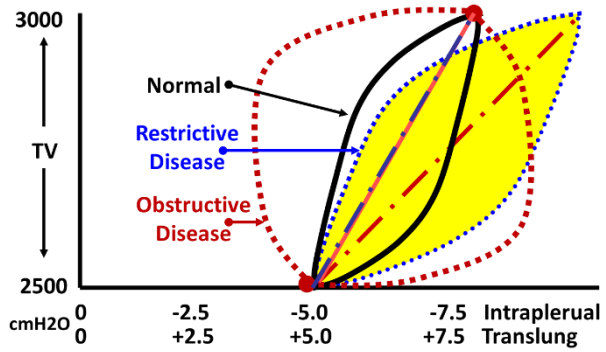


FIG 8.2 Differential Effects on Lung Dynamic Work



Forced Expiratory Flow-Volume Curves (One of several pulmonary function tests)

Forced expiratory flow-volume curves illustrating obstructive and restrictive diseases are shown on the following page. In ***FIG. 8.3****, a comparison is shown between normal, obstructive, and restrictive lung disease. A completely normal full flow-volume loop is shown in* ***FIG. 8.4****. In emphysema, the peak expiratory flow rate (PEFR) is reduced due to increased airway resistance (RAW) and decreased lung recoil pressure (P_{REC}). The larger total lung capacity in emphysema (TLC_E) as compared to normal (TLC_N) is due to increased compliance in emphysema. In obstructive disease (emphysema and asthma as illustrated) the residual volume (RV_E and RV_A) is increased as compared to normal (RV_N) due to reduced recoil (P_{REC}) in emphysema and increased resistance in both asthma and emphysema. In restrictive diseases, both TLC and RV are reduced.*

FIG 8.3 Differential Forced Expiratory Flow-Volume

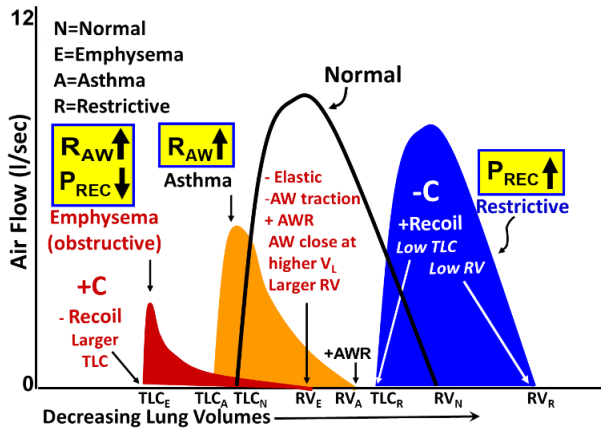
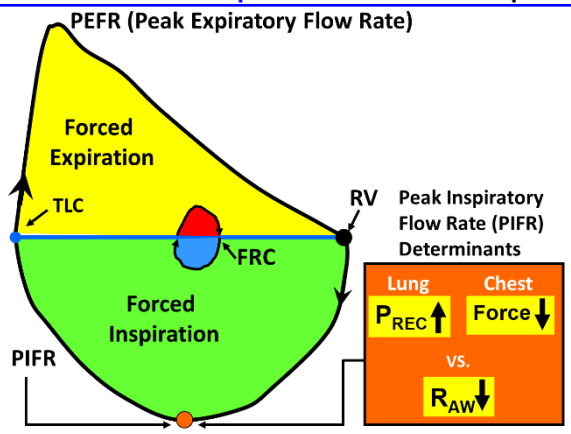


FIG 8.4 Normal Complete Flow-Volume Loop



*The complete flow-volume loop in **FIG. 8.4** includes the factors that impact the determination of the peak inspiratory flow rate (PIFR). As air is inspired starting from residual volume, the lung volume increases, and as such, there is an increase in lung recoil pressure and a reduction in chest wall force as the chest gets closer to its equilibrium zero-stress condition that occurs between 65-75% of TLC. Both of these changes favor reducing inflow. Contrastingly, as volume increases, the airway resistance decreases, which tends to facilitate air entry for the same muscular work. Thus, at some volume, these tendencies balance, and the PIFR results.*

Forced Expiratory Volume-Time Curves (Another pulmonary function test) TOC

*After an interval of eupneic breathing, a maximal inspiration to TLC is taken as shown in **FIG. 8.5**. Air is then expelled as forcefully as possible. The volume expelled after 1 second is known as the forced expiratory volume (FEV1). The maximum volume forced out is the forced vital capacity (FVC). The ratio (FEV_1/FVC) is a good index of obstructive disease presence and its degree. A normal value for this ratio is about 0.8, with lower values indicating small airway obstruction. Although several factors affect PIFR and PEFR (box in **FIG. 8.5**), the FEV1/FVC ratio tends to remain at about 0.8. **FIG. 8.6** shows FEV1 and FVC for a standard forced expiratory air flow-volume test format. It is important to note that the early part of this curve, which is within the effort-dependent part, is largely determined by medium and large airways. Contrastingly, once a collapsible condition becomes present, which occurs when the equal pressure point (EPP) enters small airways, this effort-independent part assesses mainly small airways, with the indicated shape change with increasing R.*

FIG 8.5 Forced Expiratory *Volume-Time* Test

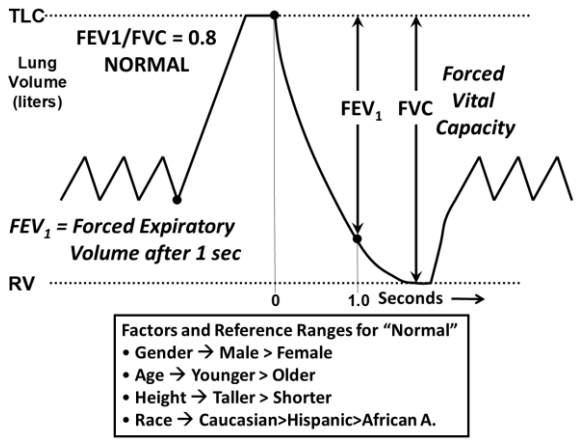


FIG 8.6 Forced Expiratory Flow-volume Test

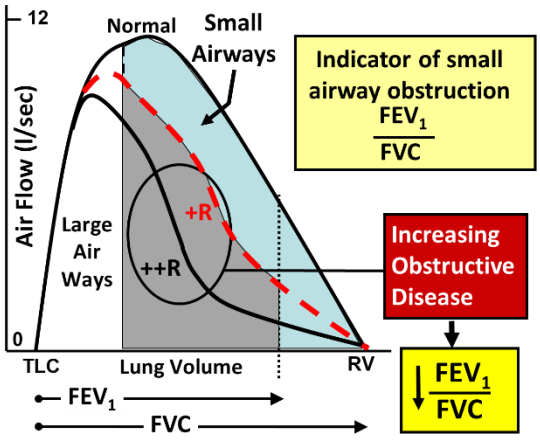


***FIG.ure* 8.7** compares the generalized test results for the forced-expiratory volume-time test for the cases of a normal lung, obstructive lung disease, and restrictive lung disease. To emphasize that lung parameters depend on multiple factors, the dependency of PEFR on gender, age, and height is shown in ***FIG.* 8.8** along with the predicted values and range for FVC, FEV1, and their ratio for a Caucasian male age 25 with a height of 70", along with the lower limits of normal for these parameters.

FIG 8.7 Forced Expiratory *Volume-Time* Test
Normal-Obstructive-Restrictive

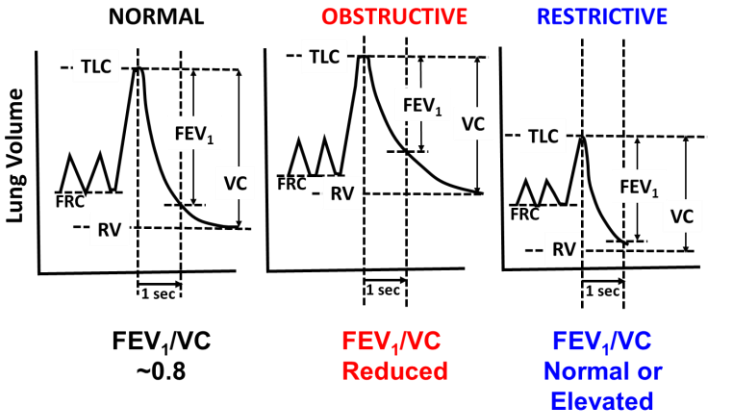
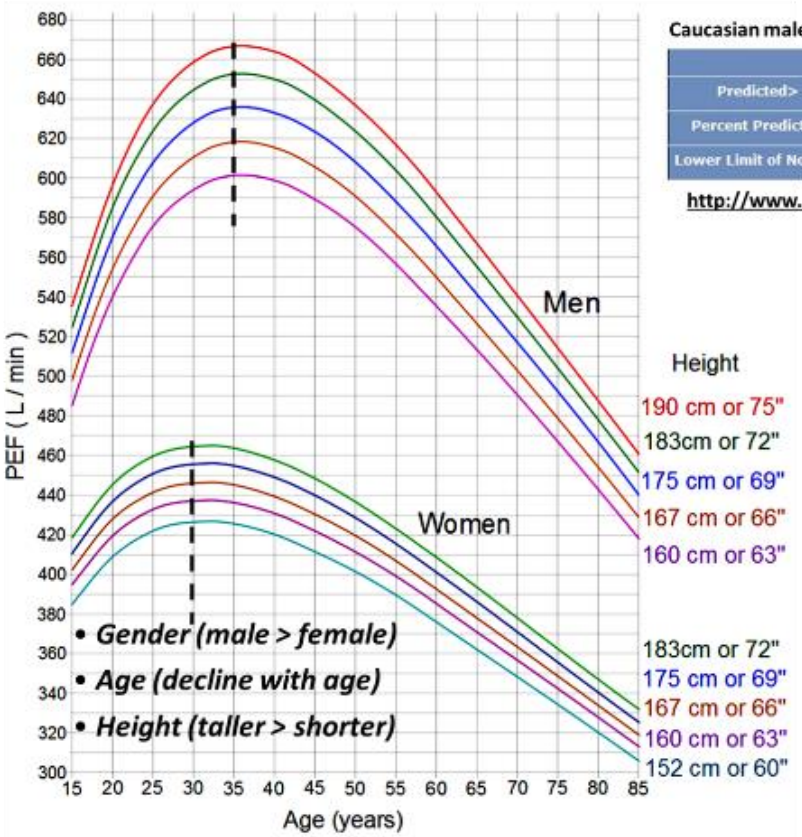


FIG 8.8 PEFR 'Normal' and Predicted Ranges



Caucasian male age 25 with height of 70" according to Hankinson-1999

	FVC (L)*	FEV1 (L)*	FEV1/FVC%	FEF25-75% (L/s)*
Predicted>	5.55	4.58	82.9%	4.72
Percent Predicted	Blank	Blank	98.3%	Blank
Lower Limit of Normal	4.62	3.79	73.2%	3.13

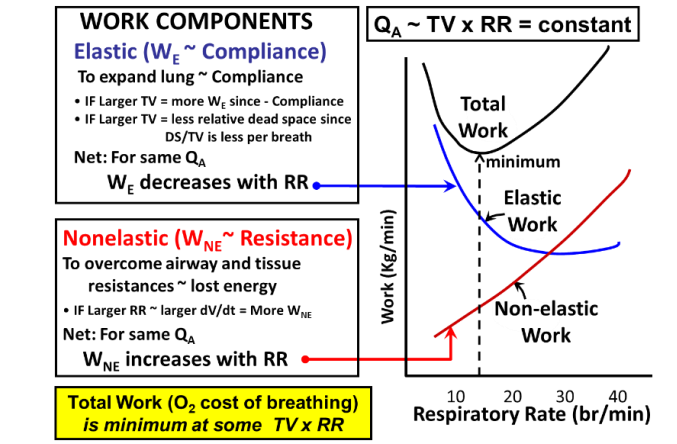
http://www.cdc.gov/niosh/topics/spirometry/RefCalculator.html

The above graphics emphasize the need to consider the "normal" values for lung parameters that takes into consideration the various demographic factors affecting them.

Adaptive Breathing Patterns and the Work of Breathing TOC

Normal Adaptations

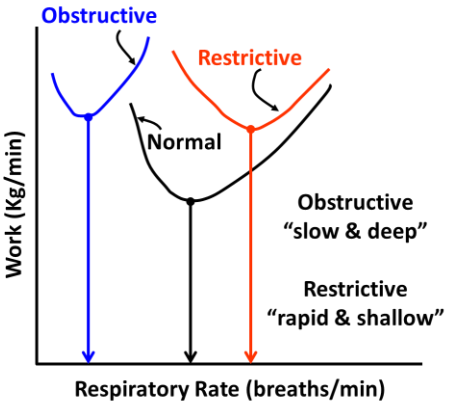
FIG 8.9 Optimum Combination of TV and RR



Alveolar ventilation (Q_A) is proportional to TV x RR, so the same Q_A can be achieved for various combinations of TV and RR. Values of TV and RR that minimize breathing work depend on four factors: airway resistance (R_{AW}), tissue resistance and viscosity, respiratory compliance (C), and dead space (DS). As summarized in ***FIG. 8.9****, a larger TV increases elastic work (recoverable) since C is less at a greater lung volume. Contrastingly, a larger TV results in less relative dead space ventilation. The net result is that less total ventilation is needed to have the same Q_A. Further, since non-elastic work (energy loss) increases with air flow rate and since Q_A = rate of change of alveolar volume (dV/dt), non-elastic work increases with RR, and work decreases as TV increases. These facts set a minimum work at a specific TV and RR, which for many folks is between 10-14 breaths/minute.*

Disease-Related Adaptations

FIG 8.10 Disease Related Adaptations



The location of the optimum respiratory rate for a given alveolar ventilation will change if lung disease is present, as shown in ***FIG. 8.10****. The location of the minimum work shifts left (lower RR) in obstructive disease and to the right (higher RR) in restrictive disease. Patients with obstructive disease tend to breathe more slowly and deeply, while those with restrictive disease tend to breathe more rapidly and shallowly.*

Emphysema Special Problem

A problem in this condition is getting adequate air out. This is made difficult due to premature small airway closure by dynamic compression. For any R_{AW} and alveolar pressure, airway pressure loss is directly related to the amount of airflow. One adaptation that persons with this condition do to forestall airway closure is to exhale slowly. A 2nd adaptation is to breathe at higher-than-normal lung volumes. This forestalls airway closure since airway tethering is greater at higher lung volumes. A maneuver called "puffing", in which expiration is through pursed lips, artificially increases outflow resistance, thereby elevating small airway pressures and forestalling airway collapse.

Obstructive Disease Adaptation Summary: Inspiratory and expiratory aspects are affected by increased R_{AW}. During inspiration, more energy (muscular effort) is needed to overcome increased R_{AW}. The required energy can be lessened by breathing more deeply (+TV) and slowly (-RR). Reason: energy loss is proportional to Q^2, but to maintain the needed total ventilation, TV must be increased – hence breathing is slow and deep.

Restrictive Disease Adaptation Summary: The Primary factor is reduced compliance, resulting in increased energy needed to expand the lungs. Energy to expand the lung by a volume (ΔV) is proportional to $(\Delta V/C)^2$. This required energy can be reduced by reducing ΔV (reducing TV). To maintain adequate ventilation, breathing rate (RR) must be increased. This is observed in patients with restrictive dysfunction: Breathing tends to be shallow and rapid.

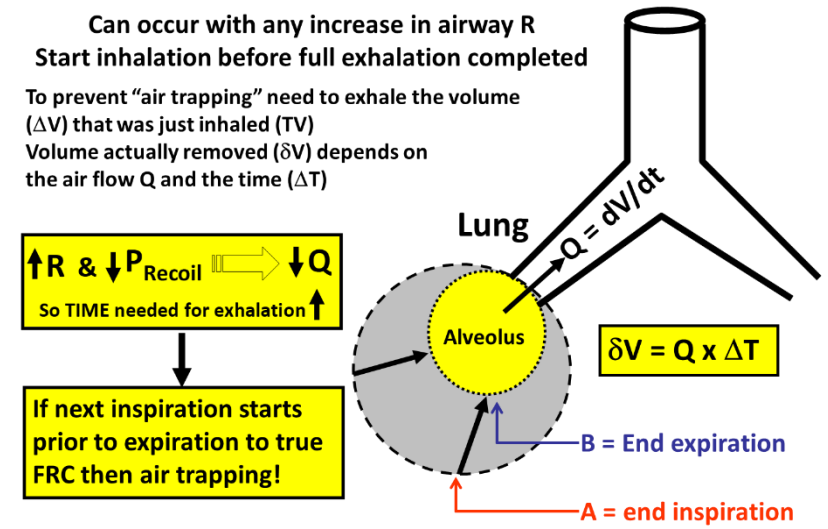
9.0 HYPERINFLATION TOC

Hyperinflation may occur when inhalation is started prior to a full exhalation being completed:

(1) Potentially all levels of COPD, including ASTHMA
(2) Temporary and Variable in extent
(3) Can occur with no increase in TLC
(4) May occur at rest but often manifests if increased ventilation demand
(5) Increased respiratory rate (RR) further shortens available exp time
    Further air trapping results and TV begins to be limited by now
    diminishing inspiratory capacity (IC) due to rising FRC
(6) Load on inspiratory muscles increases since recoil is greater than if full exhalation were allowed
(7) Increased FRC reduces the mechanical advantage of inspiratory muscles
(8) Increased work of inspiration and oxygen cost of breathing
(9) Increasing amounts of dyspnea

The main factors determining the extent of hyperinflation are summarized in **FIG. 9.1.** These include the extent of the airflow limitation and the time available for exhalation, which depends on the respiratory rate.

FIG 9.1 Hyperinflation: "Air Trapping"



10.0 GAS PRESSURES TOC

Gas partial pressure is the pressure of one gas when multiple gases contribute to the total pressure: The sum of all partial pressures = total gas pressure. Partial pressure depends on **(Fractional Volume Concentration of that Gas) x (Total Gas Pressure).** At sea level, atmospheric (barometric) pressure is 760 mmHg and the fractional volume concentration of oxygen (O_2) is about 0.21 (21%). The partial pressure of O_2 is its fractional concentration (0.21) x 760 = 159.6 mmHg. N_2 is about 78% of air and its partial pressure is 0.78 x 760 = 592.8; all other gases comprise the remainder. Dry air entering the trachea becomes humidified due to water vapor pressure. At 37°C, water vapor pressure P_{H2O} is 47 Torr and its value is *independent of* P_{ATM}. When determining gas partial pressure, water vapor pressure must first be subtracted from total gas pressure. ***FIG. 10.1*** shows the partial pressures of the respiratory-related gasses at different sites with all values expressed in Torr.

10.1 Respiratory Gas Partial Pressures

	Dry Air	Moist Tracheal Air	Alveolar Gas	Arterial Blood	Mixed Venous Blood
P_{O2}	160	150	104	100 →	40
P_{CO2}	0.0	0.0	40	40 →	46
P_{H2O}	0.0	47	47	47	47
P_{N2}	600	563	569	573	573
P_{total}	760	760	760	760	706

Mixed Venous Blood = Pulmonary Artery Blood

Solubility and Partial pressure: If a liquid is exposed to gas, gas molecules diffuse into the liquid until gas pressure in both are equal (equilibrium). The gas amount (e.g. ml) in a liquid and its partial pressure (e.g. Torr) depend on the gas solubility. If solubility is high, much gas can dissolve at a low partial pressure. If solubility is low, small amounts of gas dissolve, even at high pressures.

11.0 VENTILATION TOC

Total ventilation: Q_T = volume of air entering and leaving each minute (minute ventilation).

Alveolar ventilation: Q_A = the part of Q_T that brings O_2 to, and O_2 and CO_2 out of alveoli.

Anatomic Dead Space (ADS): Inspired air doesn't directly enter alveoli – it first enters conducting zone airways. Since there are no gas exchanges in this zone, the volume of these airways is considered dead space: no O2 reaches the alveoli, so

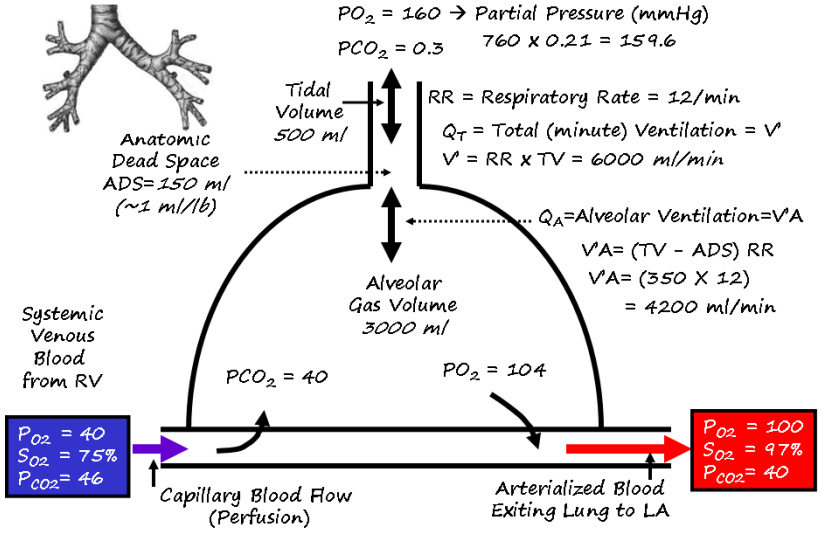
QA = (TV-ADS) x RR.

Alveolar Dead Space (ALDS) is the alveolar volume that is ventilated but not perfused or is over-ventilated relative to their blood perfusion. Both of these represent wasted ventilation.

Physiological Dead Space:

PDS = ADS + ALDS

Fig 11.1 Ventilation Related Processes



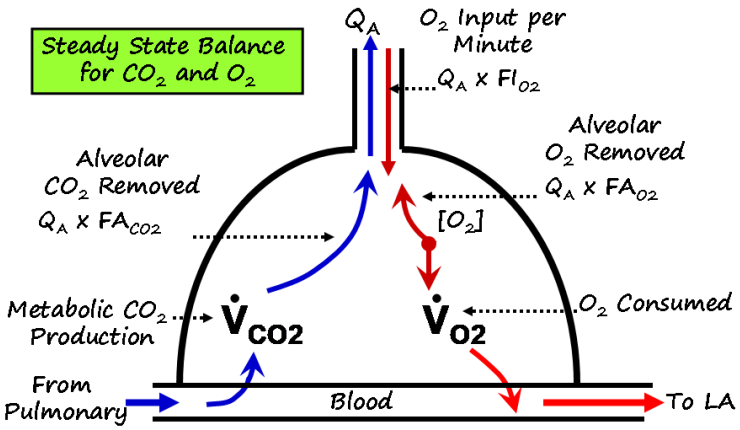
ADS Wasted Gas Volume

During inspiration, the 1st air to the alveoli comes from ADS. ADS gas composition at end-expiration is that of the alveoli. P_{O2} is ~ 104, not 160 torr, as in fresh air, and PCO2 is ~ 40, not 0.3 Torr in fresh air. If the next breath's TV is 500 mL, the alveoli receive 500 mL of gas; however, the first 150 mL is drawn from ADS and does not raise the *alveolar* P_{O2}. A useful "rule-of- humb" is ADS (ml) = ideal weight in lbs. (if within 25% of ideal weight).

Overview of Gas Movement and Some Further Definitions TOC

Gas fractional concentrations are represented as FI_{O2}, FI_{CO2}, FA_{O2} and FA_{CO2} where the letter I denotes inspired gas and A denotes alveolar gas. For a steady state situation, alveolar ventilation will result in gas movements (fluxes or flows) that match CO_2 production to CO_2 removed and O_2 supplied to blood to replenish O_2 consumed on a minute basis. **FIG. 11.2** shows various gas fluxes. In a steady state, the metabolic CO2 produced is equal to the CO_2 removed from the alveoli. At rest, an "average" whole body CO_2 production is 250 ml/min. Also, at steady state, O2 input equals O2 output, which is the sum of the O2 supplied to blood (O2 consumed) and the amount removed from the alveolus during expiration. At rest, the average whole-body O2 consumption is approximately 250 ml/min. The ratio of CO_2 produced to O_2 consumed is the respiratory quotient (RQ), which depends on the substrates metabolized. For glucose, it is ~1.0, and for fats, it is ~ 0.7. A typical mixed value is usually taken as ~0.8 (1 mol O_2 produces 0.8 mol of CO_2).

Fig 11.2 Alveolar Gas Movements



The Alveolar Ventilation Equation TOC

Maintaining alveolar P_{CO2} at 40 Torr requires that alveolar ventilation (Q_A) adjust to meet changing CO_2 loads and be sufficient to remove added amounts of CO_2 being produced. The ***alveolar ventilation equation*** defines the relationship between alveolar P_{CO2}, alveolar ventilation and CO_2 production, summarized in **FIG. 11.3**

Fig 11.3 Alveolar Ventilation Equation Basic Concept

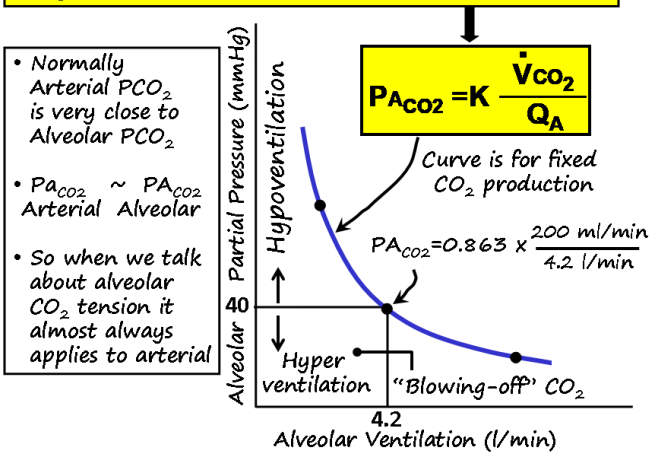
$$P_{ACO2} \sim \frac{CO_2 \text{ Production}}{\text{Alveolar Ventilation}} = K\frac{\dot{V}_{CO_2}}{Q_A}$$

K = 0.863 with $\dot{V}_{CO_2}$ in ml/min and Q_A in L/minute

- Hypoventilation if ratio high: PA_{CO2} rises
- Hyperventilation if ratio is low: PA_{CO2} falls

Accordingly, PA_{CO2} is inversely proportional to alveolar ventilation. Alveolar P_{CO2} is tightly regulated by respiratory controls (peripheral and central chemoreceptors) that sense blood levels of CO_2 and adjust ventilation as needed. The difference between alveolar carbon dioxide tension (PA_{CO2}) and arterial PCO_2 (Pa_{CO2}) is normally very small so that $PA_{CO2} \sim Pa_{CO2}$. The ratio of CO_2 production to alveolar ventilation is a key to determining hypoventilation and hyperventilation. **As shown in FIG. 11.4**

Fig 11.4 Alveolar Ventilation Equation



Hypoventilation: V/Q ratio is low, causing PA_{CO2} to rise above the normal limit

Hyperventilation: V/Q ratio is high, causing PA_{CO2} to fall below the normal limit

The Alveolar Gas Equation – Relates alveolar PA_{O2} to PA_{CO2} TOC

Basic Concept

PA_{O2} depends on:

- **Composition of inspired air (F_{IO2})**
- **Atmospheric pressure (P_{ATM})**
- **Respiratory Quotient ($R = CO_2/O_2$)**
- **PA_{CO2}**

Alveolar oxygen tension (PA_{O2}) depends on: 1) atmospheric pressure (P_{ATM}), O_2 fraction in inspired air (FI_{O2}), alveolar CO_2 partial pressure (PA_{CO2}), water vapor partial pressure (P_{H2O}), and the respiratory exchange ratio (R). The alveolar gas equation expresses the relationship between the factors as

$$PA_{O2} = (P_{ATM} - P_{H2O}) \times FI_{O2} - PA_{CO2}[FI_{O2} + \{(1 - FI_{O2})/R\}]$$

Although this is a fearsome-looking equation, its essence is to describe quantitatively the fact that changes in alveolar O_2 are associated with inverse changes in alveolar CO_2. Fortunately, simplifications can be used to appreciate the significance of this relationship. At sea level, P_{ATM} = 760, FI_{O2} = 0.21, and R ~ 0.8, so $PA_{O2} \cong 150 - 1.2PA_{CO2}$. The equation shows that alveolar O_2 and CO_2 pressures move in opposite directions.

Caution: this is an approximate relationship with assumptions! If P_{ATM} or FI_{O2} were to change, so would the constants (150 and 1.2). Example: If a patient receives 50% O_2 at 2 atmospheres then by calculation $PA_{O2} \cong 736.5 - 1.125PA_{CO2}$.

ALVEOLAR GAS EQUATION

$$PA_{O2} = (P_{ATM} - 47) \times F_{IO2} - PA_{CO2}[F_{IO2} + (1-F_{IO2})/R]$$

R = respiratory exchange ratio
= CO_2 produced/O_2 consumed

PA_{O2} = (760-47) x .21 - 40 [.21 + (1-.21)/.8]

PA_{O2} = (713) x .21 - 40 [1.2]

PA_{O2} ~ = 150 - 40 [1.2] = 102 torr

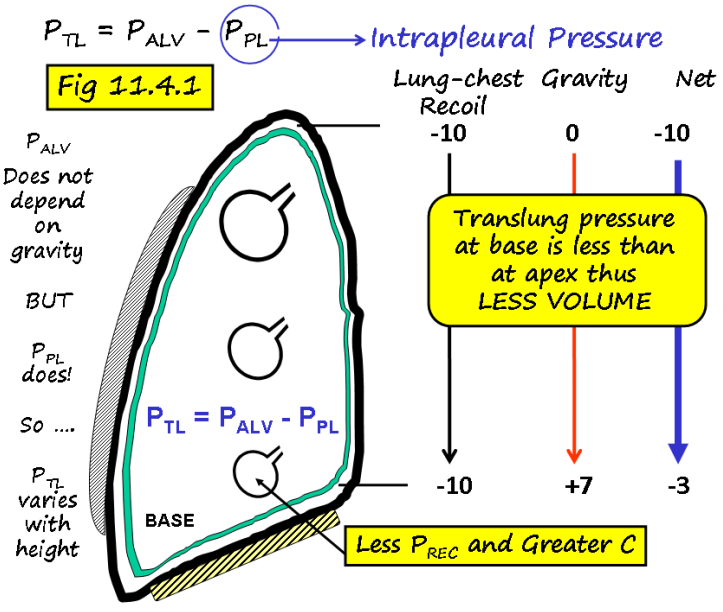
$PA_{O2} \sim 150 - 1.2\ PA_{CO2}$ for room air at sea level

Not All Alveoli are ventilated the same: The Uneven Ventilation Concept

Gravity Main Effects

- **Alveoli at base have less volume but greater compliance**
- **Result is a better ventilation of base alveoli during normal TV**

The vertical lung acts like a fluid column with a density about 1/4 that of water. Hydrostatic pressure at the base, relative to the apex, is higher (+7 cm H2O in **FIG. 11.4.1**). This pressure adds to base P_{PL}, making it less negative, thereby decreasing P_{TL}. The result is that the base alveoli are smaller than the alveoli at the apex. **Base Alveoli Have Greater Compliance at FRC.** This is because base alveoli are less stretched and recoil forces are less, so it is easier to increase their volume. So, at FRC, base alveoli are better ventilated than apical alveoli. At FRC, most alveolar air is in the upper alveoli, which therefore contain most of the lung's ERV. During a tidal breath initiated at FRC, most of the inspired air enters the dependent (lower) alveoli, as they have greater compliance compared to the upper alveoli. But, during a tidal breath started near RV (e.g., after a forceful expiration), it is the upper alveoli that fill first. Reason: lower alveoli, having a lower translung pressure, are more likely to close during a forced expiration. During the next inspiration, they must be reopened and operate on the low compliance region of the P-V inflation limb.

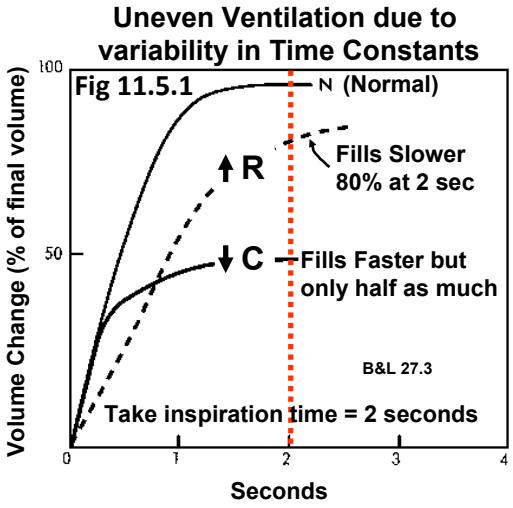


Time Constants Also Contribute to Uneven Ventilation [TOC]

The time constant (τ =RC) with R=resistance of airways filling and emptying alveoli and C = alveoli compliance. R and C are nonuniformly distributed throughout the lung. Time to fill and empty alveoli (typically 2 and 3 seconds respectively) depends on τ. Since τ varies among the many lung regions there is also variability in rates of filling and emptying causing uneven ventilation. Effects of τ differences are shown in ***FIG. 11.5.1****.*

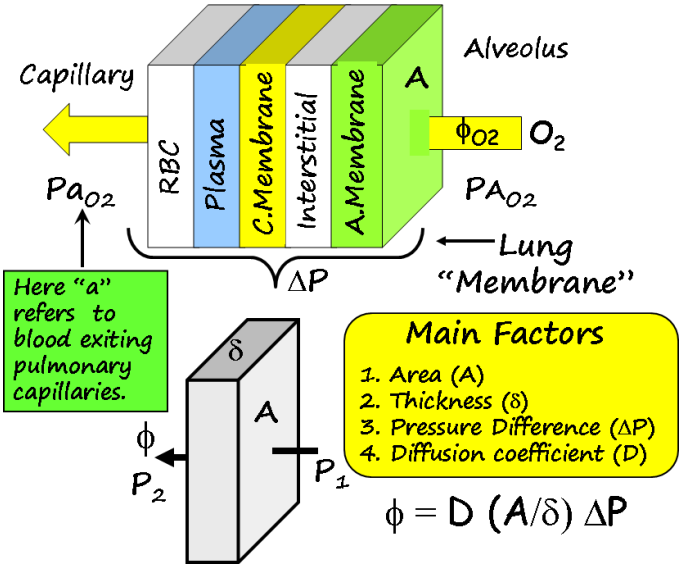
Time Constant Effects

- **Time Constant = R x C = τ**
- **Time to fill/empty ~ R x C**
- **Variability in RC causes uneven alveolar ventilation within lung**



12.0 GAS EXCHANGE [TOC]

Alveolar-Capillary gas exchange occurs by passive diffusion of O_2 from the alveolus to the pulmonary capillary and diffusion of CO2 from the capillary to the alveolus. The diffusion path traverses the alveolar membrane, interstitial fluid, capillary membrane, plasma, and red blood cell. Gas transfer rate (ϕ) is directly proportional to tissue cross-sectional area (A), difference in gas partial pressure across the tissue (ΔP), and gas diffusion coefficient (D); it is inversely proportional to thickness (δ). Since CO_2 diffuses ~20x faster than O_2 in tissues, CO_2 diffusion is rarely a clinical problem.



O_2 Diffusion decreased in several ways

(1) Low alveolar-capillary O_2 pressure difference due to:

- *hypoventilation*
- *low atmospheric pressure*
- *low alveolar PO_2*

(2) Increased path-length between the O_2 source and its tissue targets. May be caused by;

- *alveolar wall thickening due to fibrous tissue growth or additional alveolar cells*
- *capillary membrane thickening*
- *increased interstitial fluid*
- *fibrosis.*

(3) Decreased surface area for O_2 exchange.

This depends on the number of functioning alveoli in contact with functioning capillaries. The disruption of alveolar architecture decreases total surface area. Examples include: emphysema that destroys alveolar walls and their contained capillaries; pulmonary embolism that decreases the number of capillaries; loss of functioning alveoli due to airway blockages → decreased surface area for exchange.

Lung Diffusion Capacity (D_L)

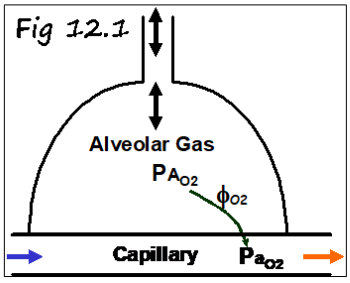
The diffusion equation $\phi = D(A/\delta)\,\Delta P$ is conceptually useful, but impractical for the complex total lung. Instead, the effective diffusing capacity of the whole lung is used to measure the lung's gas transfer rate as $\phi_L = D_L \times \Delta P$. D_L is the lung diffusing capacity and is a measure of the amount of gas transfer produced per unit difference between alveolar and capillary partial pressures (**FIG. 12.1.**) Although called lung diffusion capacity, D_L is actually a conductance since it is a measure of the ease with which the gas moves between alveolus and capillary i.e. flow/ΔP

Lung Diffusing Capacity

D_L takes into account all factors that effect <u>whole lung diffusion</u>

$$D_L = \frac{\text{ml } O_2/\text{min from alveoli to blood}}{\text{(alveolar) } PA_{O2} - Pa_{O2} \text{ (capillary)}}$$

Fig 12.1



$$D_L = \frac{\phi_{O2}}{PA_{O2} - Pa_{O2}}$$

D_L is a form of "conductance" i.e. flow/ΔP

Effects of Diffusion Abnormalities

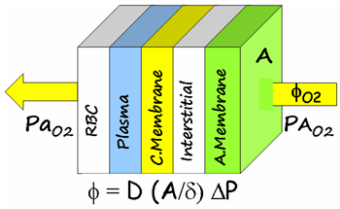
As blood moves through pulmonary capillaries, oxygen passes from the alveoli to the blood by diffusing through the alveolar-capillary membranes and into the red blood cells. (RBC) The amount of oxygen that a red cell can 'pick up' in its transit through the capillary depends on the factors described in FIG.. **12.4.1.** Although the lung's diffusing capacity (D_L) is a global property of all lung alveoli-capillary-blood units taken together, the impacts of impaired diffusion can be understood with reference to **FIG. 12.2.**

Fig 12.2 Factors Decreasing D_L

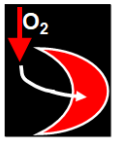
<u>Diffusion Distance</u>
- Alveolar Wall Thickening
- Alveoli-Capillary separation by: edema, exudate or fibrous tissue

<u>Surface Area</u>
- Fewer functioning capillaries
- Fewer functioning alveoli
- Disrupt normal alveolar architecture

<u>Red Blood Cells and Diffusion Resistance</u>
- Decreased rbc membrane permeability
- Decreased Hb O_2 affinity
- Decreased total amount of Hb available

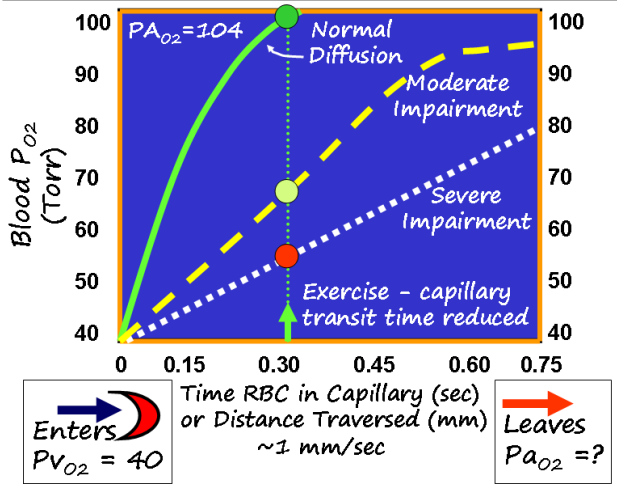


$$D_L = \frac{\phi_{O2}}{PA_{O2} - Pa_{O2}}$$



Normal diffusion: Under resting cardiac output conditions, RBC are fully oxygenated after traversing about 1/3 of a capillary's length. Since RBC speed is about 1 mm/sec and capillary length is about 3/4 mm (**FIG. 12.3**), transit from the pulmonary to the arterial end of the capillary takes about 3/4 of a second. Even during heavy exercise, when RBC speed may triple, RBC uptake of O_2 is sufficient to nearly fully saturate the capillary blood and bring blood PaO2 levels to arterialized levels.

Fig 12.3 Capillary Blood Oxygenation



Moderate Impairment

Blood exiting capillaries has near-normal PO2 levels at rest, but this decreases with exercise, as reduced transit time prevents adequate RBC O_2 uptake.

Severe impairment

There is low arterial P_{O2} even at rest.

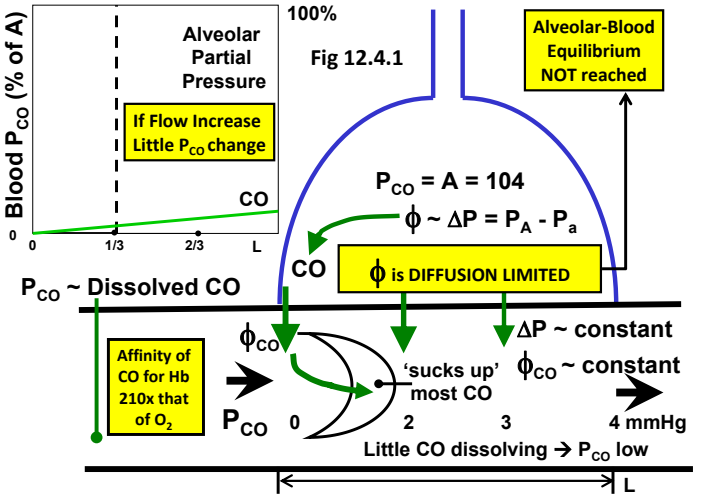
Concepts of Diffusion and Perfusion Limits TOC

The partial pressure of a gas in a fluid is proportional to the amount dissolved in the fluid

Diffusion Limited

*Gas entering pulmonary capillaries from alveoli depends on diffusion forces and pathway properties. Carbon monoxide (CO) has an affinity for Hb that is ~210 times > O_2. Partial pressure of CO in capillaries (P_{CO}) depends on CO dissolved in plasma, and since most is bound to Hb, little dissolves and PCO remains low throughout the capillary (**FIG. 12.4.1**). CO flux into capillaries does not depend on capillary perfusion since more in perfusion will not change capillary CO, since the Alveolar-capillary CO gradient does not change.*

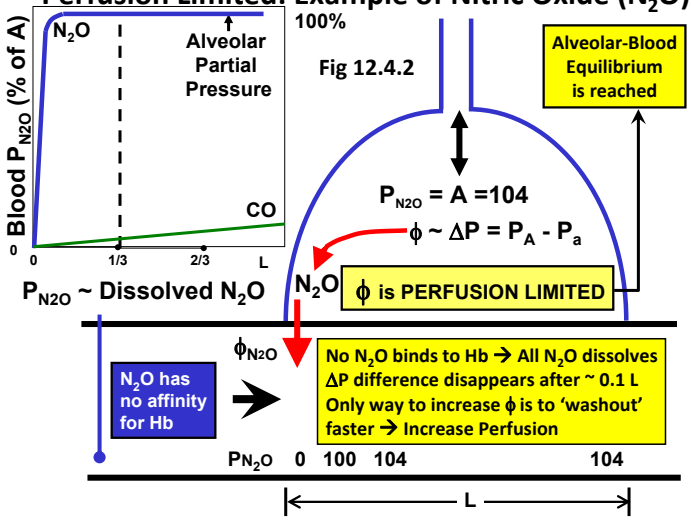
Diffusion Limited: Example of Carbon Monoxide (CO)



Perfusion Limited

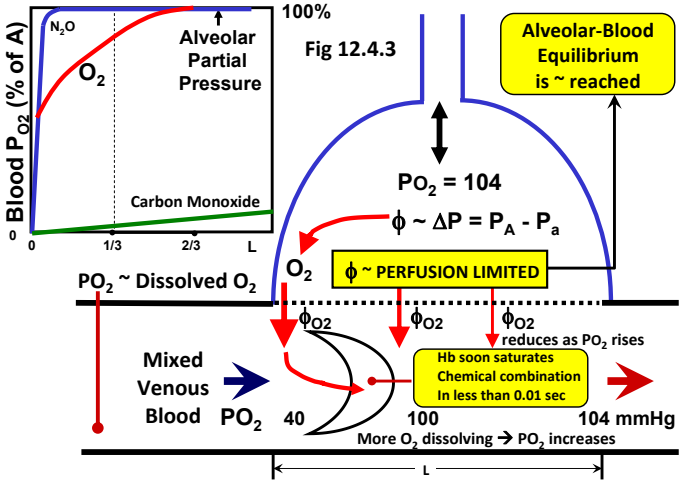
If the amount of gas entering the pulmonary capillary from the alveoli depends mainly on capillary perfusion, then it is perfusion limited. An example is nitric oxide (N_2O), which has no affinity for Hb, so the gas dissolves in plasma and rapidly causes P_{N2O} in capillary blood to rise to the level in the alveolus. This process reduces the driving force (ΔP_{N2O}) for further N_2O entry and thus reduces its entry to near zero after a very short distance. So, continued entry of N_2O into capillaries from alveoli depends on blood perfusion that is sufficient to 'wash out' N_2O to bring the blood's P_{N2O} down, allowing Alveolar-capillary flux.

Perfusion Limited: Example of Nitric Oxide (N_2O)



Oxygen Transfer *The Hemoglobin binding affinity for O_2 is much less than for CO, so more dissolves in plasma, causing its PO2 to rise much more rapidly than for CO, but somewhat less rapidly than for N_2O. This process is illustrated in **FIG. 12.4.3**. It turns out that normal O_2 transfer from alveoli into capillaries is closer to perfusion-limited than to diffusion-limited. This is demonstrated in **FIG. 12.4.3** by comparing the pattern of gas tension increase with capillary distance between the red O_2 curve in the inset diagram in comparison to the N_2O curve.*

Oxygen Transfer: Closer to Perfusion Limited



13.0 GAS TRANSPORT TOC

Oxygen

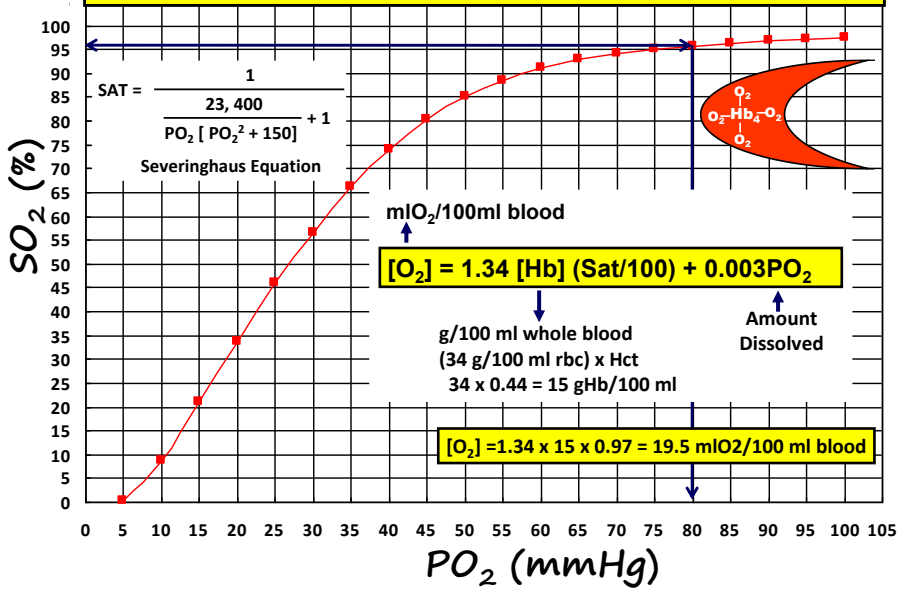
Dissolved O_2

Most O_2 is bound to Hemoglobin (Hb) with a small amount dissolved in plasma (0.3 ml O_2/100 ml at 100 Torr). If 100% O_2 is breathed (alveolar P_{O2} = 760-47-40 =673 Torr), then ~2 ml of O_2 /100 ml is dissolved (673 x 0.003), but is still only 10% of O_2 normally bound to Hemoglobin (Hb).

Bound O_2

Hb allows whole blood to take up ~ 65 times as much O_2 as plasma at a P_{O2} of 100 Torr. If tissues extract all O_2 in blood, resting O_2 needs are met with a CO of only ~ 1.3 L/min. The fact that CO ~ 4-5 times this indicates that average O_2 extraction is ~20%-25%. As shown by the calculation of **FIG. 13.1**, O_2 content of 97% saturated blood is about 19.5 ml per 100 ml of blood at a Hb concentration of 34 g Hb/ 100 ml. Approximating the 19.5 as ~ 20 ml O2/100 ml blood indicates that in a total whole-body blood volume of 5 liters there is ~ 50 x 20 = 1000 ml of O_2.

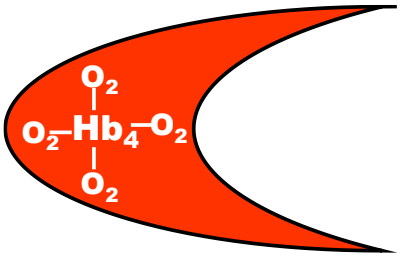
Fig 13.1 Blood Oxygen Content Equation



Note that the O2 saturation curve shown in **FIG. 13.1** can be generated using the Severinghaus equation to a very close approximation to what is measured. The equation for the O_2 concentration in blood given as $[O_2]$ = 1.34 [Hb] (SAT/100) + 0.003PO_2 with concentration as mlO_2/dl is extremely important clinically.

Hemoglobin Summary Review

Hb has 4 O_2-binding heme molecules (iron-containing porphyrin rings). Each heme group combines with one globin (protein) chain. Neither heme alone, globin alone or iron alone can take up O_2 - only the 3 together in proper spatial relation have this property. Hb features include:



1. Hb combines reversibly with O_2 forming oxyhemoglobin (HbO_2). The deoxygenated form of Hb is called deoxyhemoglobin.
2. O_2 associates (binds to Hb) and dissociates (is released from HbO_2) very quickly – in milliseconds
3. The HbO_2 equilibrium curve is sigmoidal in shape due to heme-group interactions
   (a) If O_2 is bound to 3 groups, 4th group's O_2-binding affinity greatly increased
   (b) Similarly, release of O_2 from any 3 groups, enhances O_2 release from 4th
   (c) Interaction tends to cause a hemoglobin molecule to carry either 4 molecules of O_2 or none.
4. Oxygen carried by RBCs depends directly on hemoglobin concentration [Hb] and on the degree to which Hb is saturated with O_2. At 100% saturation, all four heme molecules would be occupied by O_2 molecules. If blood is 100% saturated, it carries about ~20 ml O_2 for each 100 ml of blood

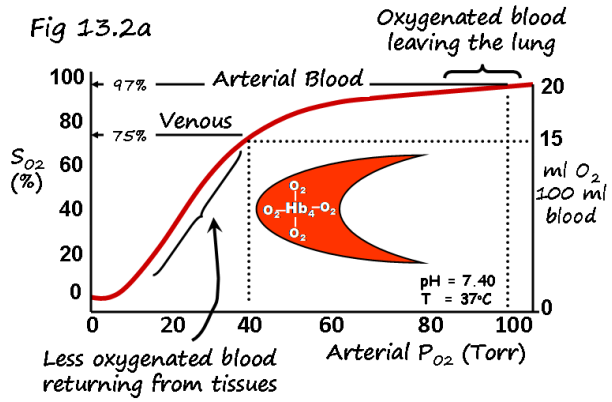
O_2 Uptake in Lung & Delivery to Tissues

Uptake in lung is facilitated by near-flat part of curve in the *association range* (**FIG. 13.2a**). Saturation % (S_{O2}) is nearly independent of P_{O2}. This is a "buffer range" that allows good blood oxygenation despite decreases in PO_2

Delivery is facilitated by the steeper part of curve (**FIG. 13.2a**). The amount of bound O2 and thus SO2 is determined by blood PO2, which itself depends on O_2 dissolved in plasma. Low tissue P_{O2} facilitates O_2 release to tissue. This is the *dissociation range*. At a P_{O2} of ~40 Torr, Hb is ~75% saturated.

In **FIG. 13.2b,** an example is shown for an anemic person who has an abnormally low Hb level. The calculation for blood oxygen content is illustrated using an O_2-Sat curve.

O_2- Uptake & Delivery – Normal

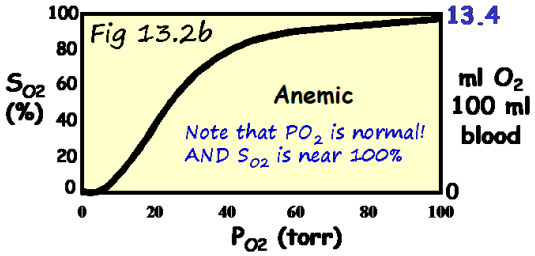


O_2- Uptake & Delivery – Example

An SO_2 measurement reveals that a patient's blood is near 100% saturated, but that her hemoglobin is only 10 g/100 ml blood. What is her blood oxygen CONTENT?

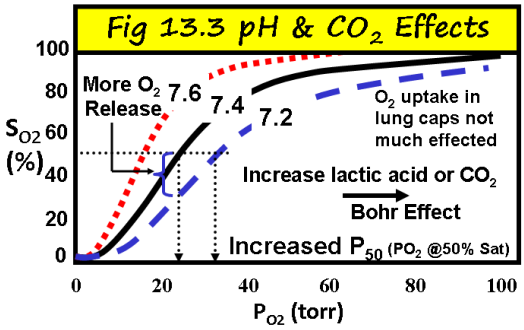
$[O_2] = 1.34\ [Hb]\ (Sat/100) + 0.003PO_2$

$1.34 \times 10 = 13.4$ mlO_2/100 ml blood



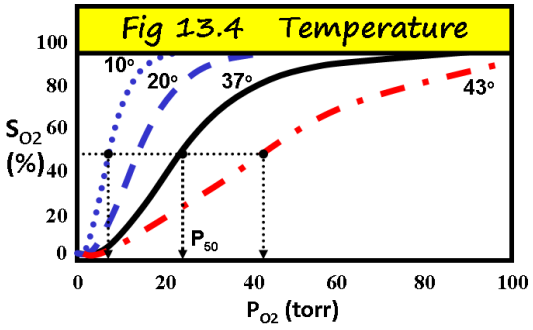
Factors Affecting SO_2 Curve Shape

Increases in CO_2 and H^+ (**FIG. 13.3**) and temperature (**FIG. 13.4**) both decrease affinity of Hb for O_2. This shifts curves to the right whereas an increase in affinity shifts curves left.

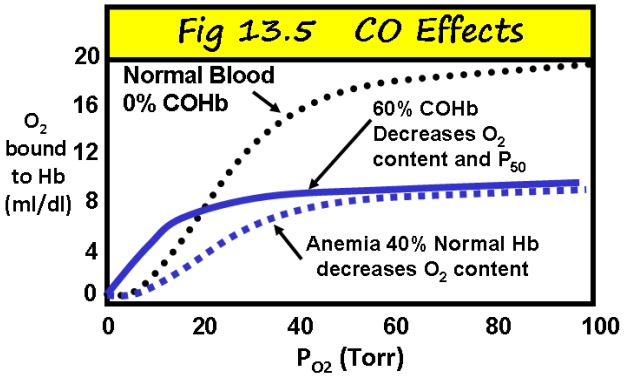


pH decrease or CO_2 increase
H^+ or CO_2 binds to Hb; Facilitates O_2 Release
P_{50} is increased

The P_{50} value (P_{O2} at which S_{O2} is 50%) is also a measure of shift. Increased P_{50} facilitates O_2 release from HbO_2 to tissue. Decreased P_{50} favors O_2 binding. So, a lower P_{50} causes a left shift. P_{50} shifts have small effects on the association region. The right-shift caused by CO_2 increase is the Bohr Effect. Since affinity of CO for Hb is ~ 210x O_2 and O_2 is ~ 21% of air, blood equilibrated with air having [CO] of only 0.1% contains 1/2 HbO_2 and 1/2 HbCO. One effect of CO is similar to severe anemia (**FIG. 13.5**). Both reduce blood O_2 content. But, CO is more life threatening since it also decreases P_{50}. So, O_2 is even less available for tissues. The low partial pressure of CO in blood requires a long time to unload the CO even if exposed to 100% O2.



Hotter: Facilitates O_2 Release
•Less Saturation for same P_{O2}
•More P_{O2} for same saturation



2.3-diphosphoglycerate (DPG) Regulates RBC's Affinity for O_2

DPG binds to Hb → More DPG → Less affinity, so more DPG facilitates O_2 release→ P50 shift to right, easier to deliver O_2 to tissue. Less DPG is the opposite.

Increased DPG Concentrations with:

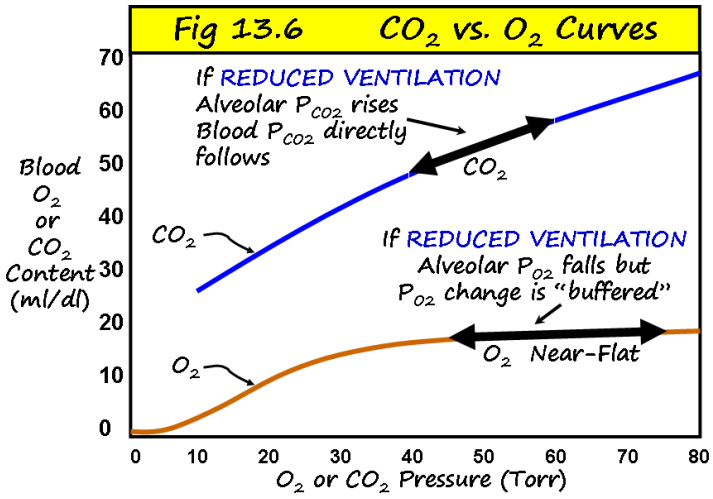
- residence at high altitude
- hypoxia due to cardiopulmonary disease or anemia
- sickle cell anemia (sickle cells have increased DPG)
- pyruvate kinase deficiency (leads to increased DPG)
- exercise.

Carbon Dioxide (CO_2) and Acid Base Issues TOC

Carbon Dioxide

Main product of cellular metabolism; carried to lung; excess eliminated in expired gas. Because of CO_2 + H_2O reaction to H_2CO_2, CO_2 transport and elimination of its excess are important in acid-base. Lung excretes about 13,000 mEq/day of volatile acid (CO_2) and kidney excretes about 40-80 mEq/day of nonvolatile acid. CO_2 is carried in blood (50 ml/100 ml) in 3 forms:

1. Dissolved in plasma as carbonic acid (5%)
2. Bound to Hb (carbaminohemoglobin) (5%)
3. As bicarbonate ($HCO3^-$) in rbc's ~ 90%



Changes in alveolar PCO_2 influence arterial CO_2 much more than alveolar PO_2 influences arterial O_2 (**FIG. 13.6**). This is due to shape differences between CO_2 and O_2 curves. Hypoventilation or hyperventilation cause direct changes in CO_2 but O_2 effects are "buffered" over a wide range of alveolar PO_2 due to near flatness of the $[O_2]$-PO_2 relationship. This is important since it allows respiratory control of P_{CO2} without significant O_2 content effects. Note that in FIG. 13.4 the vertical axis is blood content of either O_2 or CO_2 not % saturation.

Acid-Base Issues TOC

CO_2 transport affects blood acid-base status. Many effects can be understood based on the Henderson-Hasselbalch eq.

$pH = pK_A + log\ \{[HCO_3^-] / [CO_2]\}$

$pH = pK_A + log\ \{[HCO_3^-] / (0.03P_{CO2})\}$ in which, pK_A is 6.1 and the normal $HCO3^-$ concentration of arterial blood is ~24 mmol/liter which, if substituted yields

pH = 6.1 + log (2) = pH of 7.4.

As long as the ratio remains at 20, blood pH remains at 7.4.

Acid Base Issues: Henderson Hasselbalch

$$pH = \underset{6.1}{pK_A} + \log\left[\underbrace{(HCO_3^-)/(0.03P_{CO2})}_{\text{Normal Ratio} = 20}\right] = 7.4$$

Deviations in the ratio from 20 alter pH

- **Respiratory Acidosis**
- **Respiratory Alkalosis**
- **Metabolic Acidosis**
- **Metabolic Alkalosis**

Respiratory Acidosis

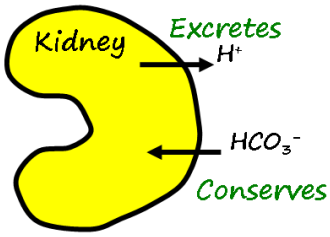
As noted in **FIG. 13.2.1.**, CO_2 retention due to hypoventilation or ventilation-perfusion mismatch increases P_{CO2} and decreases (HCO_3^- / P_{CO2}). Sustained respiratory acidosis causes the kidneys to conserve HCO3- tending to normalize the ratio. This pH normalization tendency is termed *compensated* respiratory acidosis, although renal compensation is rarely complete. Such compensation may take 3-6 days to complete.

Fig 13.2.1 Respiratory Acidosis

Increased P_{CO2} → decreases (HCO_3^- / P_{CO2}) ratio → -pH

Cause: Hypoventilation or Ventilation-Perfusion Mismatch

Renal COMPENSATION to Respiratory and/or non-Renal ACIDOSIS



Respiratory Alkalosis

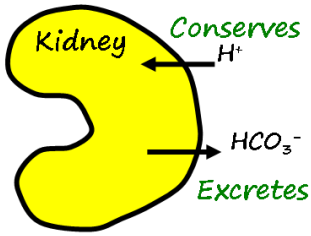
If P_{CO2} decreases, the ratio (HCO_3^- / P_{CO2}) increases, and blood pH increases. One cause is excessive ventilation, which may occur prior to adaptation to high-altitude living (FIG. 13.2.2). Renal compensation is mainly achieved through increased excretion of bicarbonate, thereby tending to normalize the ratio. There are also metabolic causes of alkalosis.

Fig 13.2.2 Respiratory Alkalosis

Decreased P_{CO2} → increases (HCO_3^- / P_{CO2}) ratio → +pH

Cause: Hyperventilation e.g. At High Altitude

Renal COMPENSATION to Respiratory and/or non-Renal ALCALOSIS



Metabolic Acidosis (non-respiratory)

Cause is decreased plasma HCO_3^- or increased H^+. As HCO_3^- falls, the ratio falls, causing a decrease in pH. Respiratory compensation occurs through increased ventilation, which reduces PCO2 and tends to normalize the ratio. Ventilation increase is driven mainly by the action of H^+ on peripheral (PCR) and central (CCR) chemoreceptors as summarized in **FIG. 13.23**.

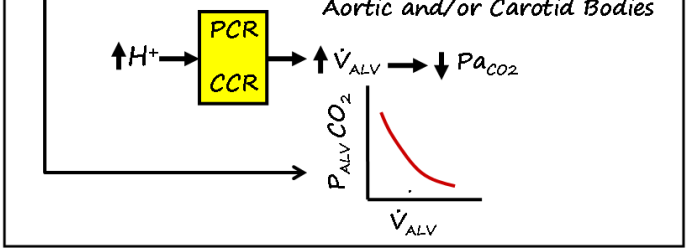
Fig 13.2.3 Metabolic Acidosis

Less HCO3- → decreases (HCO_3^- / P_{CO2}) ratio → -pH

Respiratory Compensation = Increased ventilation reduces P_{CO2} to normalize ratio

Respiratory COMPENSATION to Non-respiratory Acidosis

Aortic and/or Carotid Bodies



Metabolic Alkalosis (non-respiratory)

This condition is associated with an increase in HCO_3^- that raises HCO_3^-./ P_{CO2} causes an increase in pH. Sources of excess HCO_3^- include the ingestion of alkali and the loss of gastric acid secretions. Respiratory compensation is small or absent.

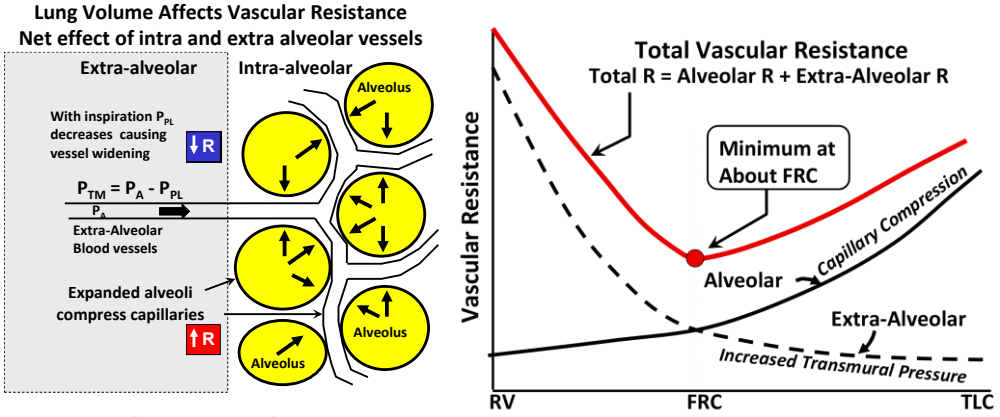
14.0 PULMONARY BLOOD FLOW (PERFUSION) TOC

Normal vascular resistance is low, allowing for the entire cardiac output to pass through the lung at a relatively low pulmonary artery pressure. Normal values for mean PA range between 8 to 20 mmHg.

Factors Influencing NORMAL Lung Blood Perfusion TOC

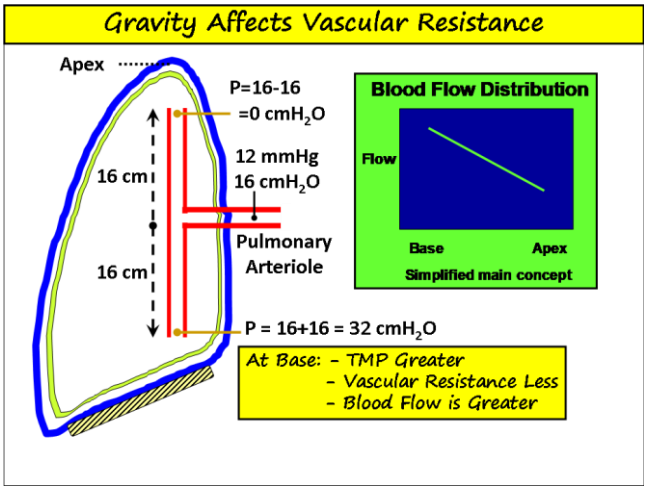
A. Lung Volume

Alveoli expand as lung volume increases, causing intra-alveolar capillaries to stretch & narrow; Capillary resistance increases. Extra-alveolar vessels widen due to traction and increased transmural pressure resulting from a more negative PPL; extra-alveolar resistance decreases. Above FRC, capillaries dominate and total resistance increases. At ~FRC total resistance is minimum (flow is maximum).



B. Gravity: Affects Resistance and Flow

In an upright position, blood flow is greater at the base of the lungs than at the apex. Reason: vascular TMP at base is greater. Result: Vessel diameters are larger, resulting in less vascular resistance and increased flow. Due to normal low pulmonary pressures, a person with abnormally low pressures may cause the TMP in the upper lung regions to fall below that needed to keep these blood vessels open. Although they are ventilated, the absence of blood flow results in alveolar dead space.

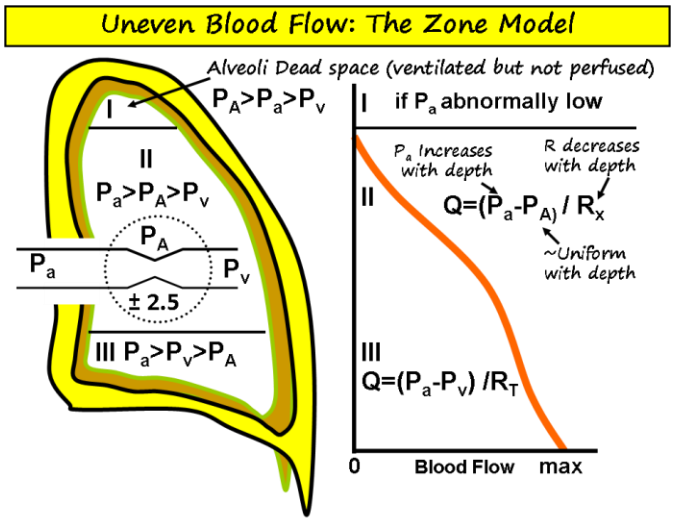


C. Blood Flow Distribution: Zone Model

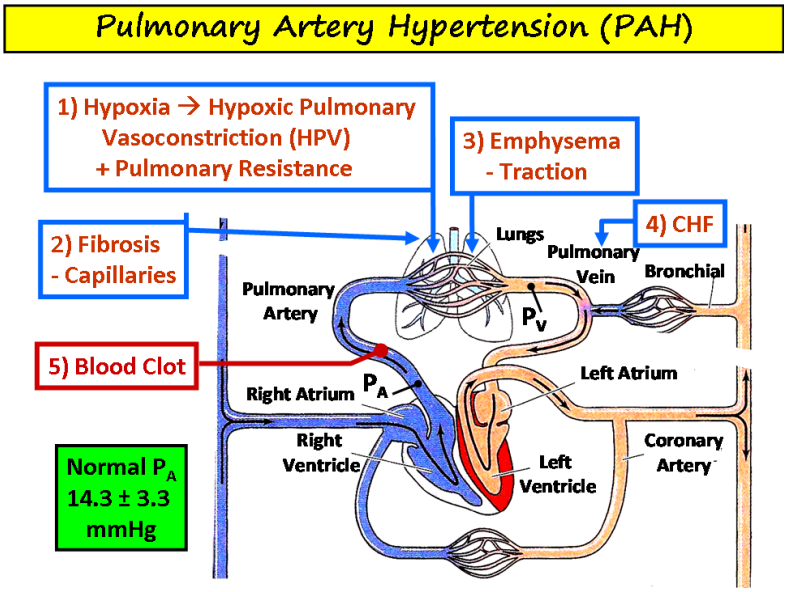
Apex-to-base blood flow distribution depends on variations in arterial, alveolar, and venous pressures. From apex to base, pressure & flow vary as shown in in the adjacent figure. ***Zone I***: Intravascular pressure may be too low to keep vessels open, resulting in no blood flow. This is known as ventilation without perfusion, which is equivalent to alveolar dead space. Zone I can become important in cases of low Pa.

Zone II Alveolar pressure during part of the respiratory cycle may be greater than venous pressure, creating a collapsible vessel situation. So, Q is determined by collapsible P-Q relations.

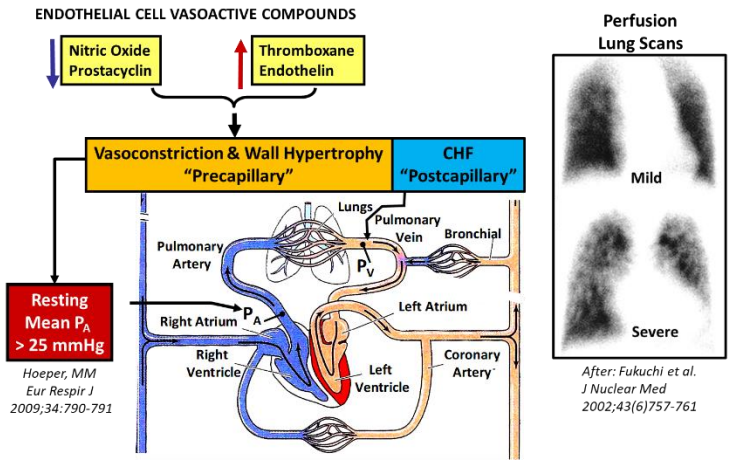
Zone III Arterial and venous pressures exceed any possible value of alveolar pressure and no vessel collapse. "Normal" P-Q relation is operative.



Pulmonary Artery Hypertension



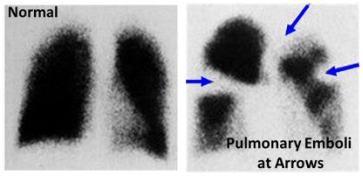
Some conditions cause PA to rise significantly above normal, resulting in pulmonary artery hypertension (PAH). These include (1) hypoxic pulmonary vasoconstriction (HPV) that causes abnormal constriction of lung arterioles in regions of reduced alveolar ventilation, (2) Congestive heart failure (CHF) that causes increased pressure due to increased pulmonary intravascular volume, (3) lung fibrosis that causes loss of capillaries, (4) emphysema that diminishes the tissue traction that helps hold open blood vessels and the (5) formation of blood clots that elevate vascular resistance. These increases in PA have defined and potentially treatable causes.



In addition to these PAH causes, there is a type of PAH called primary or idiopathic pulmonary artery hypertension (iPAH) that has no confirmed mechanism. It is believed that at least in part it is caused by dysfunction of endothelial cell-related vasoactive substances. Specifically, within small pulmonary vessels, there is a decrease in the vasodilators nitric oxide and prostaglandin and an increase in the vasoconstrictors endothelin and thromboxane. This combination leads to increased vascular resistance and vessel wall hypertrophy. iPAH is defined as a mean P_A > 25 mmHg and is a diagnosis of exclusion. These features are shown in the adjacent **figure**. Note that causes of PAH may be classed as "precapillary" or "postcapillary" depending on the nature of causative factors with postcapillary mainly referring to effects of CHF.

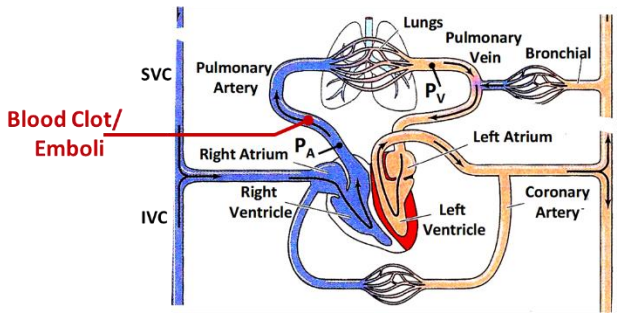
Clinical Correlation: Pulmonary Embolism

- Inject radiolabeled albumin (^{99m}Tc-labeled macroaggregated albumin)
- Detect distribution of radiation (Gamma-camera)



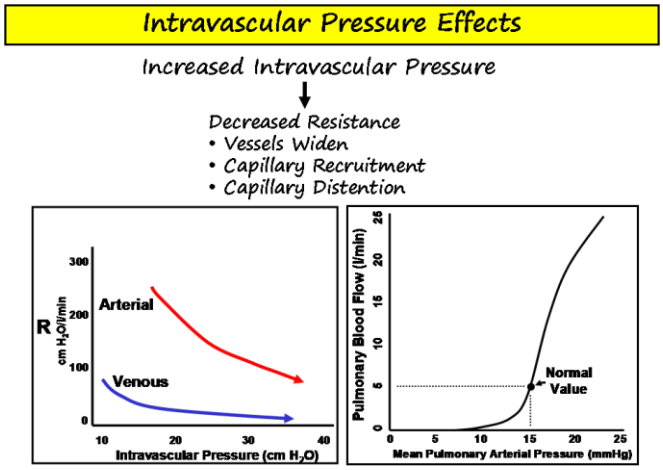
Pulmonary Embolism

Blood flow is also adversely affected by pulmonary emboli, as summarized in the adjacent **figure**. The radiographs with the overlying arrows indicate regions that were affected by pulmonary emboli in both lungs of the patient.



Other Factors Affecting Pulmonary Hemodynamics

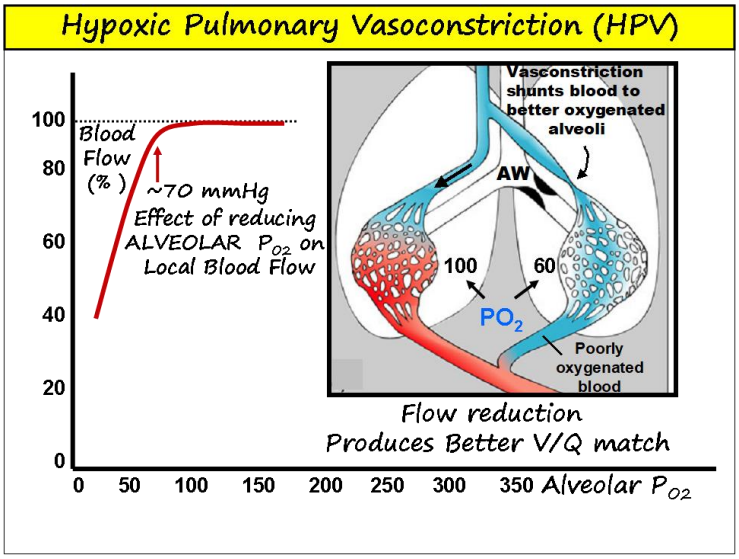
A. *Intravascular Pressures*



Observations show that if pulmonary blood flow increases, there is not a proportional increase in pulmonary pressure. This is explained by reduced vascular resistance due to blood vessel distension (capillaries and extra-alveolar vessels) and capillary recruitment caused by increased TMP that distends most of these thin-walled vessels.

B. *Hypoxia and Other Flow Reducers*

Local or systemic hypoxia is the most important active process for vasoconstriction



- ***Local hypoxia***

Causes constriction in the hypoxic region; shifts blood flow to the alveoli with higher P_{O2}. This is Hypoxic Pulmonary Vasoconstriction (HPV).

- ***Systemic hypoxemia***

Causes generalized pulmonary constriction; leads to pressure increases in RV and pulmonary A.

- ***LA and PA Pressure Increase***

(e.g., mitral stenosis) causes reflex constriction; protects against pulmonary edema but may result in pulmonary HTN

- ***Intravascular obstructions***

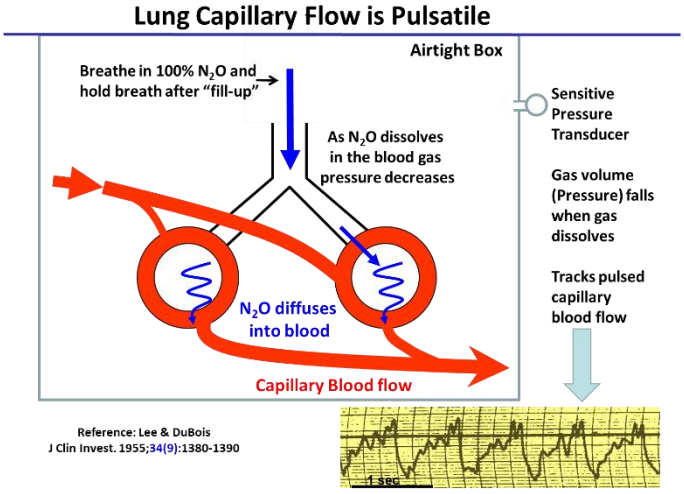
(thrombi, emboli, blood clots, parasites, fat cells, tumor cells, WBCs) can block flow pathways

- ***Obliterative or obstructive lung diseases***

*Emphysema: Tissue loss with loss of capillaries. Interstitial pulmonary fibrosis: vascular tissue replaced by fibrous scar tissue. **Critical closure** of small vessels due to hypotension*

- ***Compression** of blood vessels by masses or lesions*

C. *Lung Capillary Blood Flow is Pulsatile*



*Measurements of pulmonary capillary blood flow patterns show it to be pulsatile, as shown in the adjacent **figure**. Breathing 100% N2O and then holding breath allows the N2O to dissolve into the blood and exit via the capillaries. This dynamic is tracked, demonstrating the pulsatile nature of the pulmonary capillary blood flow as shown.*

15.0 VENTILATION-PERFUSION (V/Q) MATCHING TOC

Basic Concept
It is neither ventilation nor perfusion alone that determines arterial blood gases. It is the ratio of ventilation to perfusion that is the determinant!

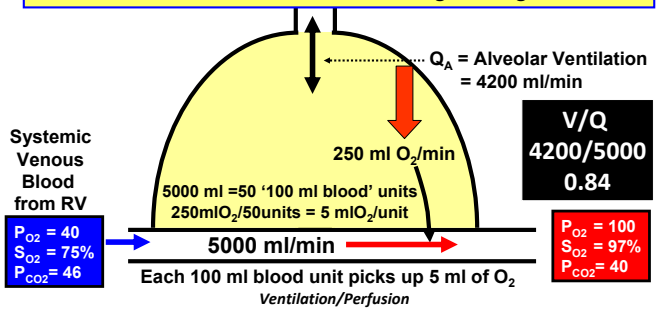
Ventilation/Perfusion = V/Q ratio

Arterialization of blood as it passes through the lung requires that alveolar ventilation is matched to pulmonary capillary blood flow. Since neither ventilation nor blood flow is uniform throughout a lung, there are regions in which the match is less than optimal. The impact of mismatching is to cause arterial gases to be less than optimal. When lung dysfunction or disease is superimposed, the effect on arterial gases is increased. Most clinical problems have their basis in V/Q mismatching.

A. Ventilation-Perfusion Concept

Assume that an alveolar ventilation of 4200 ml/min will deliver 250 ml O_2/min to capillary blood.

If blood flow is 5000 ml/min then each of the (50) 100 ml of blood must pick up 5 ml of O_2. This results in a proper "arterialization" of blood exiting the lung.

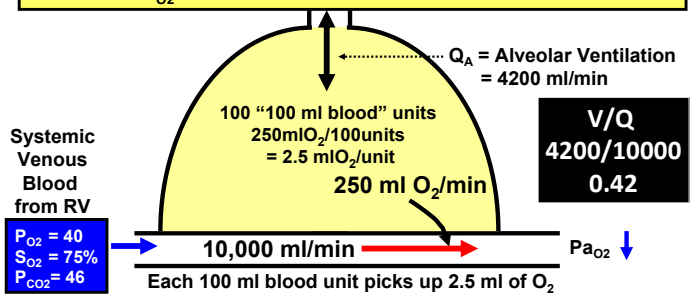


To maintain arterial PO_2 at 100 Torr for a total body O_2 utilization of 250 ml/min, alveolar ventilation must add 5 ml of O_2 to each 100 ml of blood. For example (A), blood flow is 5000 ml/min, so there are 50 "100 ml units" passing through the lung each minute, and each "100 ml unit" picks-up 5 ml of O_2. Suppose both O_2 utilization and alveolar ventilation remained the same, but blood flow increases to 10,000 ml/min (B). Now, 10,000 ml/min corresponds to 100 "100 ml units" passing each minute, so each picks-up only 25 ml O_2. As a result, arterial PO_2 decreases. The same decrease in PO_2 occurs if blood flow remained the same (at 5000 ml/min), but alveolar ventilation was cut in half; each 100 ml of blood would again only pick up 25 ml of O_2. Now, suppose that both ventilation and blood flow were halved (C). Since 2500 ml/min is 25 "100 ml units", each "100 ml unit" picks-up the proper 5 ml of O_2 and proper arterial gas tensions are achieved.

B. Ventilation-Perfusion Concept

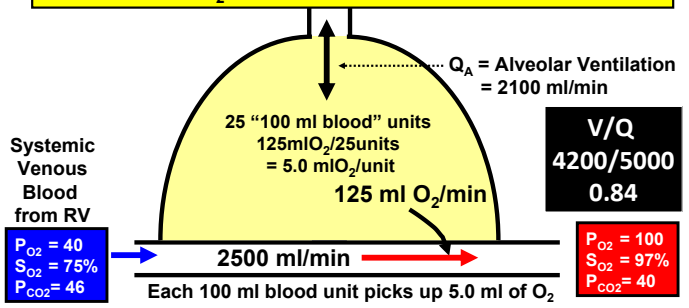
Now suppose ventilation stays constant but blood flow increases to 10,000 ml/min.

Now, 100 "100 ml units" pass each minute.
Soooo..... each will pick up only 2.5 ml of O_2 since Q_A is constant.
Since this is 1/2 as much as needed to properly saturate the blood,
Sooo ..... Pa_{O2} will fall!



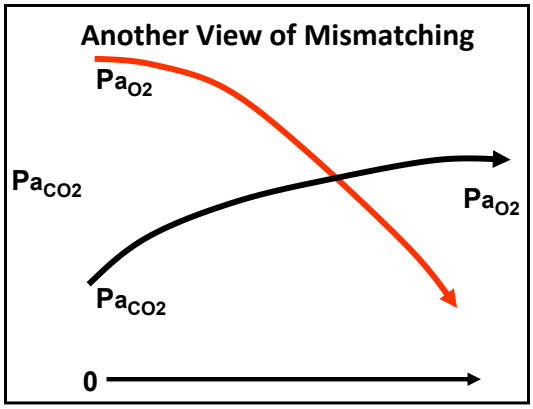
C. Ventilation-Perfusion Concept

Now suppose ventilation and perfusion become 1/2 of what they originally were. Now each 100 ml of blood again picks up 5.0 ml of O_2. Thus Ventilation is again optimally matched to perfusion to properly cause the needed blood O_2 saturation.



The take home message you ask? It is neither blood flow (perfusion) nor ventilation alone that determines arterial gas tensions, it is their ratio. Proper blood gas partial pressures depend on a proper match between alveolar ventilation (Q_A) and lung capillary perfusion (Q_C). The (Q_A / Q_C) ratio is expressed as the V/Q ratio.

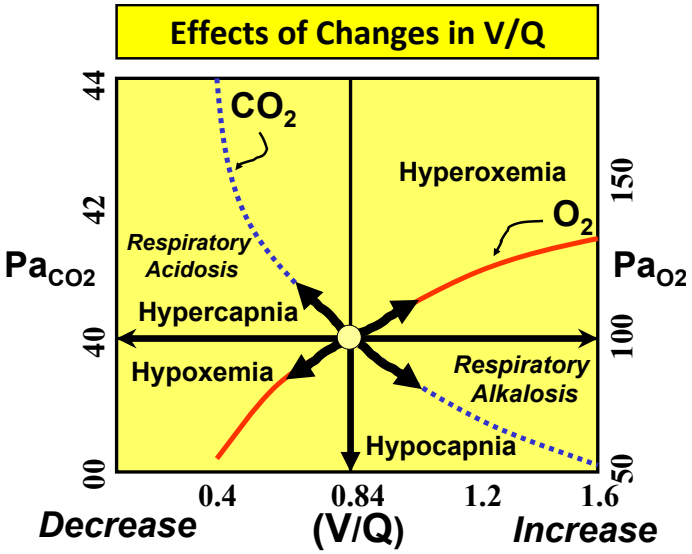
Another way of viewing mismatching is based on number of lung units having a low V/Q ratio. As shown below, if there are more low V/Q units then there is a lower is Pa_{O2} and a higher Pa_{CO2}.



the

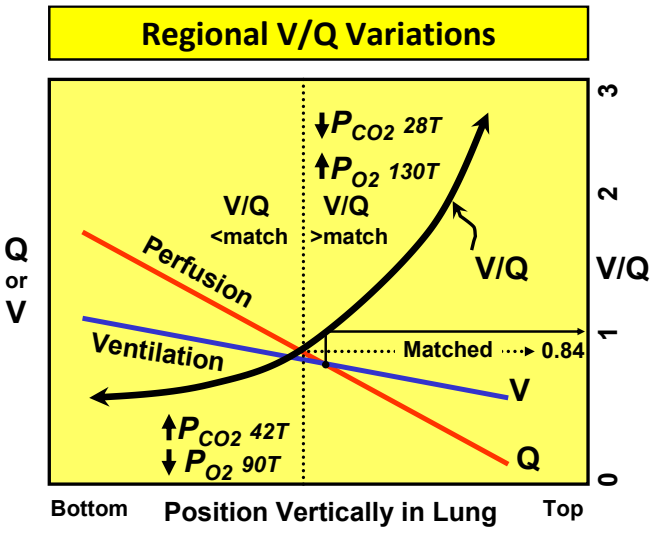
Arterial Gas Dependence on Ventilation/Perfusion (V/Q) Ratio

A useful qualitative way of visualizing the effects of changes in V/Q is via the adjacent graphic. A normal whole lung V/Q ratio is ~0.80-0.84, and arterial gases are near their "optimal" values of 40 and 100 Torr for CO2 and O2, respectively. But, if V/Q decreases, either by less V or more Q, Pa_{CO2} increases and Pa_{O2} decreases. The opposite occurs if V/Q increases. Note that O_2 and CO_2 changes are inversely related to each other. This is due to the alveolar gas and ventilation equations.



Factors Affecting the V/Q Ratio

Blood flow and ventilation decrease from base to apex, but flow decreases more than does ventilation. Result is that V/Q increases from base to apex causing uneven arterial blood gases. Thus, blood coming from upper lung areas that have high PO_2 combines with blood coming from capillaries in lower areas with low PO_2 to become the arterial blood that perfuses the systemic circulation. High and low P_{CO2} capillary blood combines in a similar way. From this, it is clear that ***arterial P_{O2} and P_{CO2} ultimately depend on how well ALL lung terminal units are matched!***



Summary of Some Causes of Hypoxic Processes and Effects TOC

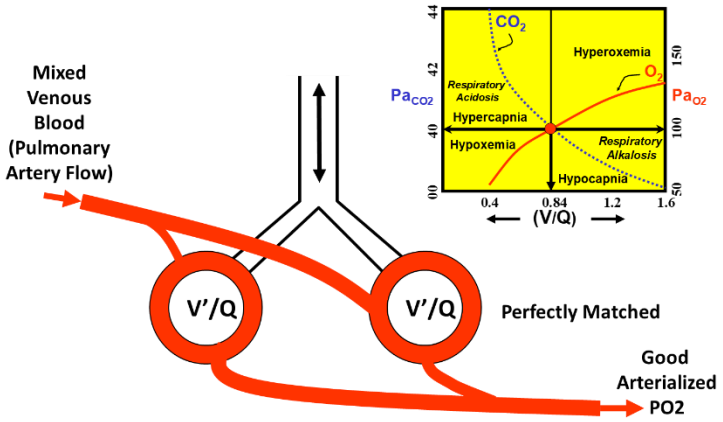
V/Q: *Non-uniform V/Q arises from mechanical factors that cause non-uniformity of R and C throughout the lung. Present in normal lungs but they are exacerbated in clinical conditions.*

Uneven R: *Regional airway obstruction (e.g., bronchospasm in asthma, exposure to irritants, airway closure (e.g., emphysema), narrowing of airways (e.g., bronchitis or bronchiolitis), compression of airways (e.g., tumor).*

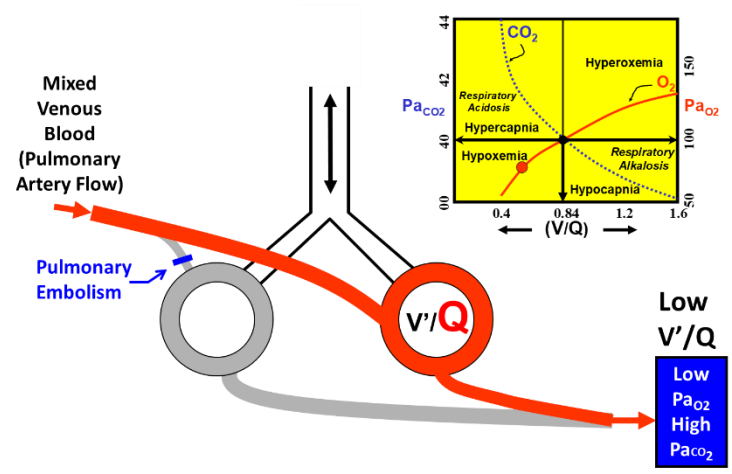
Uneven C: *Fibrosis, elastic recoil loss (emphysema), uneven surfactant distribution, pleural thickening, pulmonary congestion or edema, compression (tumors, abscesses or cysts) or uneven intrapleural pressures*

Perfusion: *Mechanisms causing uneven blood flow to different parts of the lungs fall into four main categories: 1) effects of gravity on columns of blood in upper and lower parts of the lung, 2) Regional differences in intrapleural pressure, 3) Regional differences in alveolar pressure, and 4) Constriction, blockage or compression of parts of the circulation that include; (a) Regional vessel congestion (heart failure). (b) Pulmonary blood vessel closure due to low blood pressure (severe hypotension), (c) embolization or thrombosis of parts of the pulmonary circulation, (d) lung vascular tissue destruction (emphysema or fibrotic obliteration of some pulmonary vessels).*

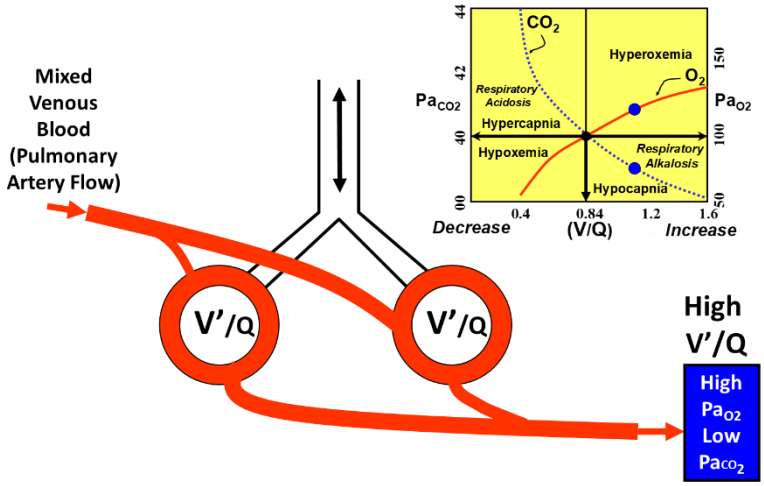
Clinical Correlation: Ventilation matched to Perfusion



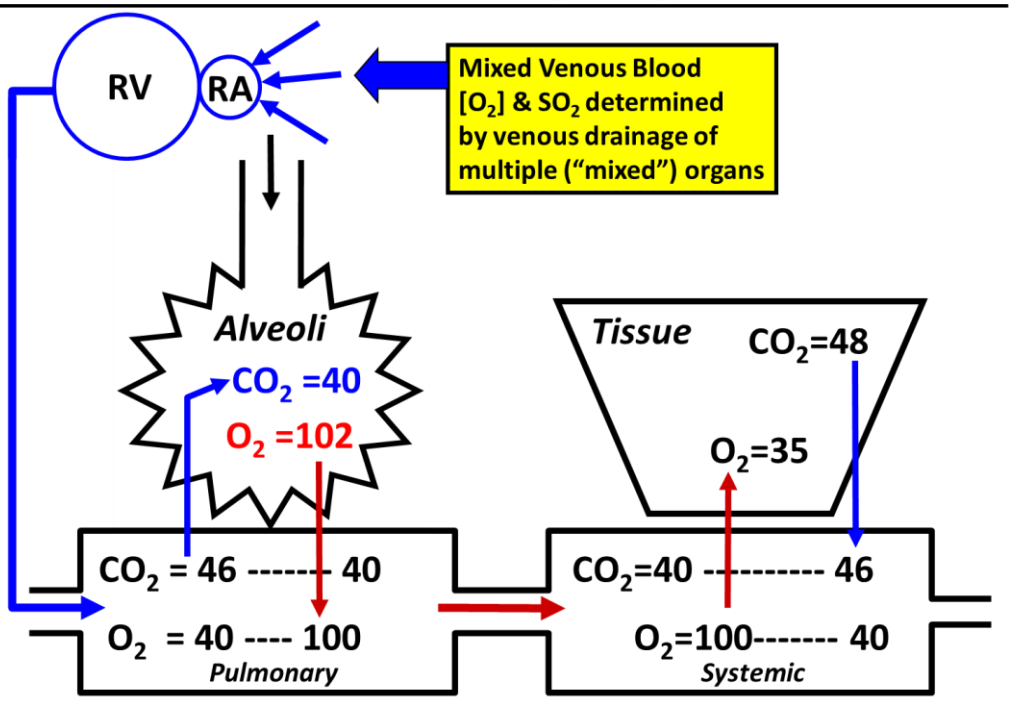
Clinical Correlation: Pulmonary Embolism



Clinical Correlation: Hyperventilation



Review of Normal O_2 –CO_2 Process



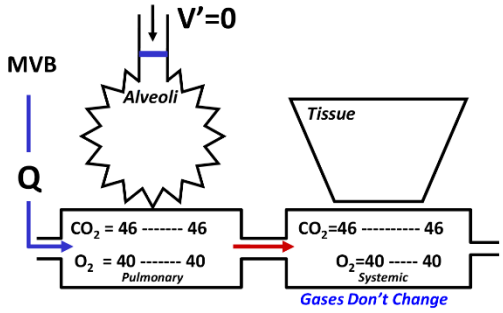
Review: V'/Q Low Limit

Alveoli can be PERFUSED but NOT ventilated

e.g. Airway Obstruction

V/Q → 0 this is an absolute intrapulmonary shunt

Mixed venous blood (MVB) passes "untouched" into arterial blood

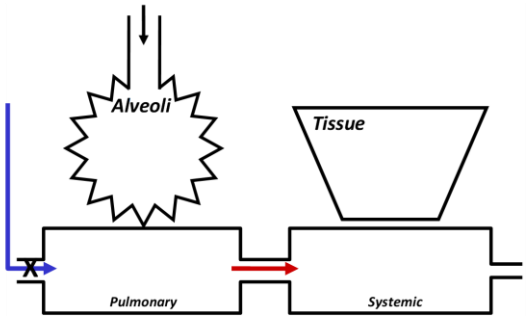


Review: V'/Q High Limit

Alveoli can be VENTILATED but NOT perfused

V/Q → ∞ this is ALVEOLAR DEAD SPACE

Example would be ZONE I



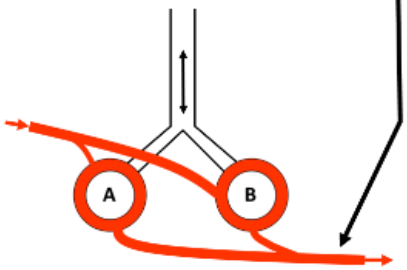
Hypoxic Mechanisms

1. Low levels of inspired O_2
2. Hypoventilation per se
3. Lung diffusion abnormalities
4. V/Q mismatching
5. Shunts

Hypoxic Mechanisms: Definitions and Examples TOC

Mechanisms – Hypoxemia – Low O_2 in Blood

PROCESS	EXAMPLE
Reduced O_2 in inspired air ------>	Altitude Fires
Inadequate Ventilation ---------->	CNS depression (anesthesia) Neural deficit Muscle deficit
Diffusion Abnormality ---------->	Edema, Fibrosis
Shunts ---------->	Anatomical → Bronchial artery drainage Functional → Perfusion with no ventilation
V/Q mismatching ---------->	Airway block → low V' → low v'/Q Embolus → increased Q to remaining area → Low v'/Q Alveolar DS → V' with no perfusion → Zone I



Oxygen Deficiency -Terms

ANOXIA = No O_2

HYPOXEMIA = Hypoxic Hypoxia
= Low arterial blood PO_2

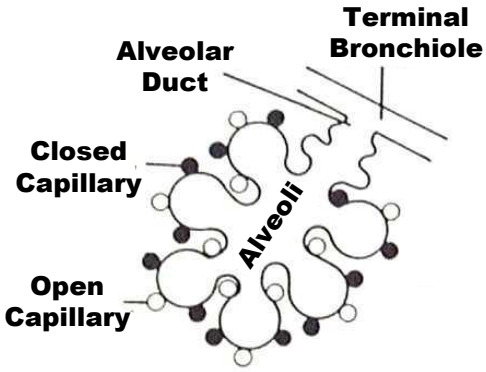
HYPOXIA = Inadequate O_2 Available for Tissue Needs

Hematological Hypoxia
Low Hb to bind/carry O_2 but normal PO_2
e.g. Anemia or Carbon Monoxide Poisoning

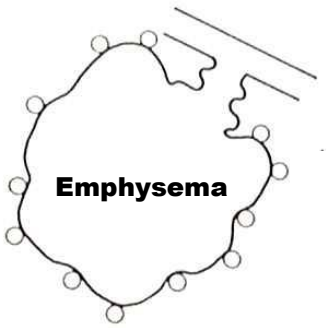
Ischemic Hypoxia
Low tissue O_2 due to low flow (blood PO_2 is normal)

Histotoxic Hypoxia
Normal O_2 supplied but can't be utilized by tissue;
e.g. Cyanide Poisoning

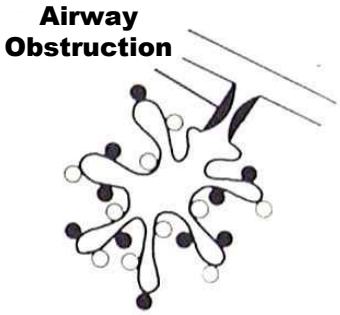
Alterations in Effective Gas Exchange



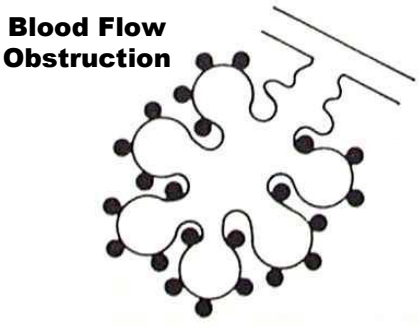
Normal



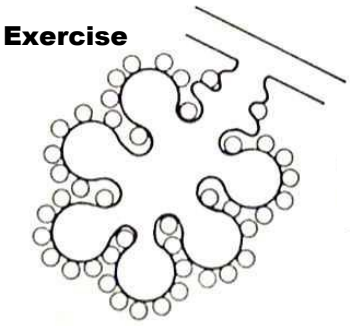
Destroyed alveolar walls
and some capillaries



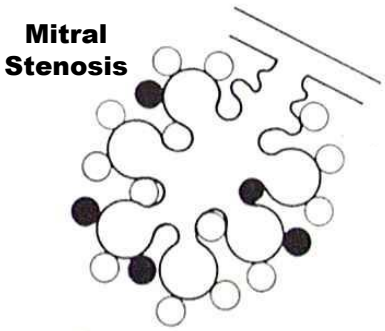
Reduced Alveolar ventilation
Functional Deadspace



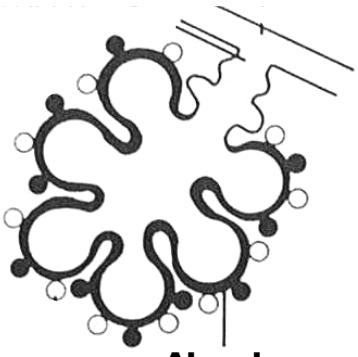
Reduced Capillary Flow
Functional Deadspace



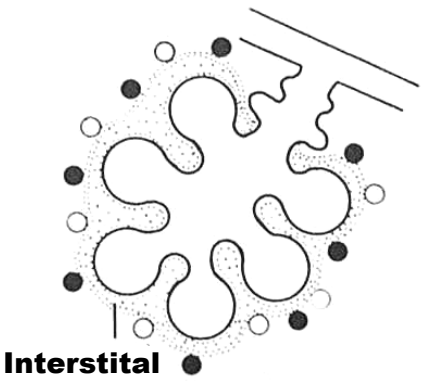
Capillary Recruitment
Gas-Blood Flow match



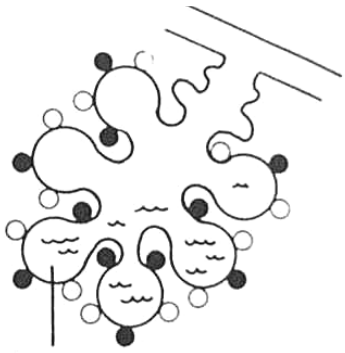
Enlarged Capillaries
Exchange Area increased



Thickening of
Alveolar Epithelium



Widening of space
increases distance
from alveolus to capillary



Edema or exudates
causes alveoli to be
non - ventilated

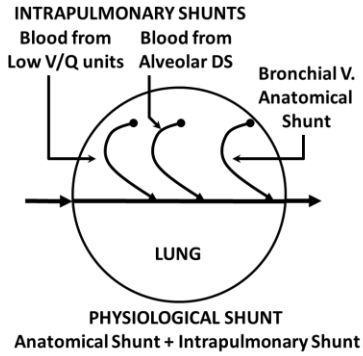
Shunts TOC

A shunt is a condition in which deoxygenated blood enters systemic arterial blood without having been adequately "arterialized" in the lung. This can occur through an anatomical shunt, in which blood completely bypasses the lung oxygenation process (e.g., blood exiting the bronchial circulation or blood returning directly to the left ventricle through the Thebesian vein). It can also occur due to inadequate oxygenation of blood passing through the lung (e.g., V/Q mismatch). Blood with a low P_{O2} that exits from lung units with low V/Q ratios or from blood draining from alveolar dead space mixes with other capillary blood returning to the left atrium. Arterial O2 tension of this blood is diminished as a consequence of mixing of some adequately oxygenated blood with some partially or poorly oxygenated blood.

Shunts: Mixing Low O_2 Blood with Arterial Blood

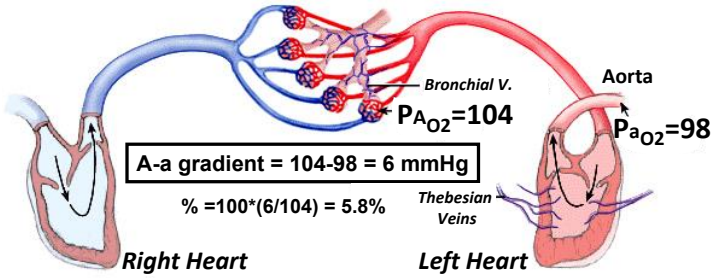
Anatomical Shunts: systemic venous blood
- Bronchial veins
- Thebesian veins
- Pleural veins

Intrapulmonary Shunts:
- Mixed venous blood has zero alveolar gas exchange (e.g. airway obstruction)
- Low V/Q → low O_2 mixes with all oxygenated blood

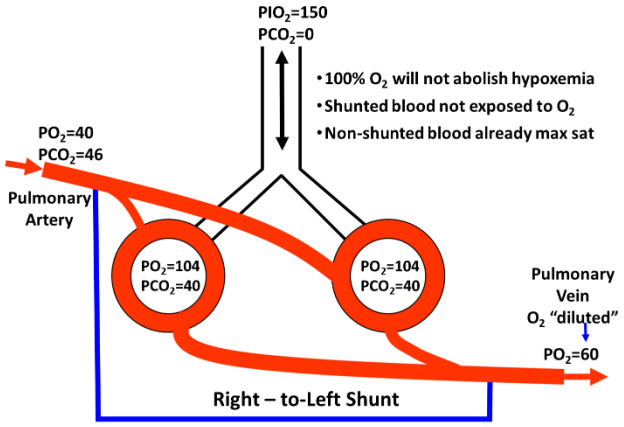


Some shunting is normal, with a resulting difference between alveolar and arterial PO_2 known as the A-a gradient. The magnitude of this gradient is an index of the amount of shunting. In the example below, the gradient is 6 mmHg, well within the normal range. Shunting tends to increase arterial CO_2, but such CO_2 elevations are usually not sustained, even if shunted blood has a high level of CO_2. This is because the action of chemoreceptors tightly controls arterial CO2; if CO_2 increases so does ventilation. The CO_2 level of unshunted blood decreases, and when mixed with shunted high CO2 blood, it will decrease the arterial CO_2 tension. Treating a shunt that is causing significant hypoxemia depends on whether the shunt is anatomical or physiological as with the intrapulmonary shunt shown below. For an anatomical shunt, 100% O_2 won't alter the shunt effects since shunted blood is not exposed to the O_2. In contrast, high levels of O_2 in inspired air will produce improvement in arterial P_{O2} for intrapulmonary shunts.

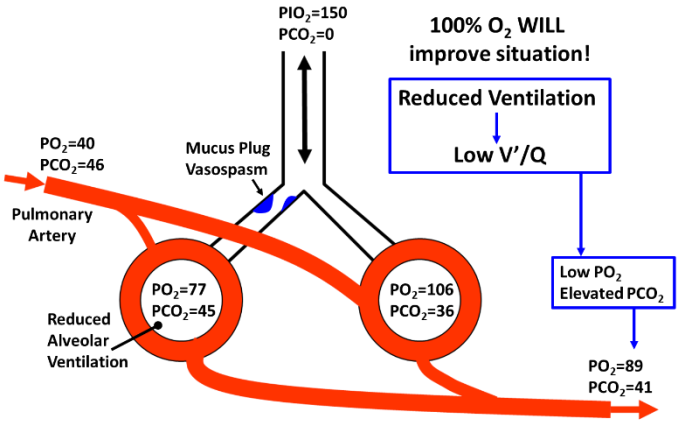
Normal Physiological Shunt Values ~ 5-15% (A – a Gradient)



Anatomical Shunt (Right-to-Left)



Intrapulmonary Shunt

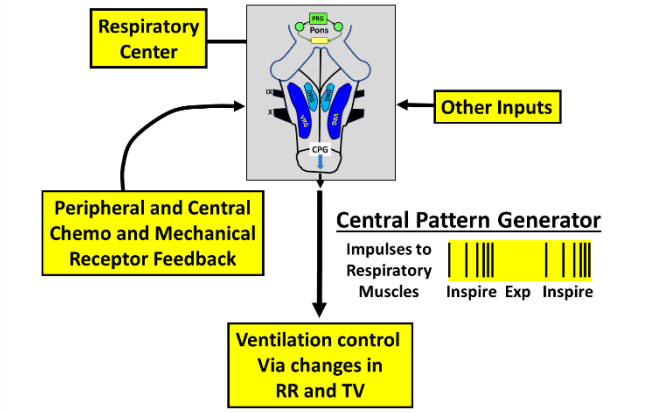


Numbers are illustrative only

16.0 CONTROL OF RESPIRATION [TOC]

Rhythms, Interactions, and Feedback Determine the Breathing Pattern

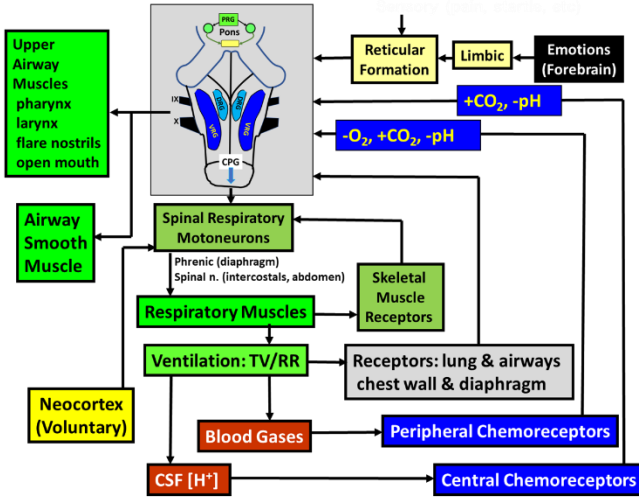
FIG 16.1 Basic Respiratory Control



*The heart beats rhythmically since it has a pacemaker. Muscles that drive respiration have no known pacemaker. If the motor nerves of these muscles are disconnected from CNS input, contraction ceases and respiration stops. Eupneic breathing is rhythmic and involuntary. It occurs due to a nerve discharge from a respiratory center (**central pattern generator**, CPG) that drives the respiratory muscles. The pattern is modified by many afferent signals that impinge on medullary (DRG and VRG) and pontine (PPG) cell groups that serve to adjust ventilation to body demands. The automatic pattern can be overridden consciously within limits by higher centers. Voluntary forced hyperventilation can cut arterial P[illegible] forced hypoventilation (e.g. breath-holding) is limited in duration by CO_2 buildup and O_2 decrease that ultimately terminate the action. The limbic system & hypothalamus can alter breathing in states of rage, fear and other emotions. These concepts are summarized in **FIG. 16.1**.*

Respiratory rate (RR) and depth (TV) are regulated to keep Pa_{CO2} close to 40 mmHg

FIG 16.2 Feedback Control



*Regulation is on a breath-by-breath basis due to **CO_2 sensitive controls** that adjust RR and TV. These controls require actions of **central chemoreceptors** (CCR) in the brain stem and **peripheral chemoreceptors** (PCR) in carotid and aortic bodies. CCR are sensitive to local pH changes in cerebral spinal fluid and PCR are sensitive to arterial hypoxia, hypercapnia and acidosis. If hypoxemia occurs, the O_2 sensitive PCR overrides CO_2 controls. Mechanoreceptors in airways, lung and chest provide feedback to the **respiratory center** in response to mechanical events associated with breathing..*

Ventilation (TV x RR) Depends on Efferent Impulses to Muscle

FIG 16.3 Central Pattern Generator Drive inspiration

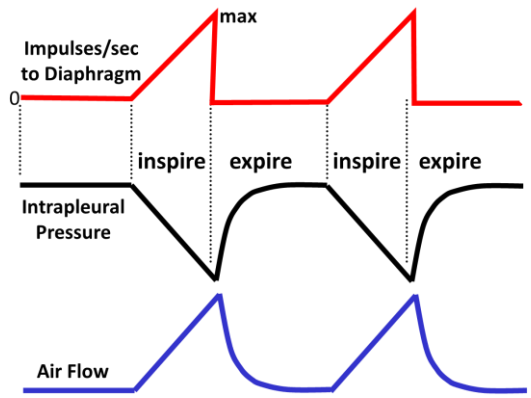


***FIG. 16.3** shows the efferent nerve traffic to respiratory muscles and the impact on air flow. There is an increase in impulses to the muscles during inspiration (ramping up) and an absence of impulses during expiration which is a passive process during eupneic breathing.*

Respiratory Centers

*Brain stem sectioning experiments provided initial insight into the locations and effects of major groups of neurons involved in breathing control (**FIGs. 16.4-16.6**). These are medullary respiratory cell groups (DRG and VRG), a pontine respiratory cell group (PRG or pneumotaxic center), and an apneustic center in the lower pons. The combined activities of these cell groups control respiratory rhythm. Feedback from mechanical and chemical receptors modulates this process, resulting in impulse rates to respiratory muscles in accordance with need. There is debate if the fundamental rhythm is driven by pacemaker-like activity or via complex neural network interactions or perhaps both. The term "central pattern generator" describes the process responsible for the rhythmical ventilatory pattern. Changes in this pattern are how breathing is adjusted to meet the array of changing physiological and pathophysiological needs.*

Respiratory Cell Groups

*As shown in **FIG. 16.6**, the VRG contain inspiratory (I) and expiratory (E) cells i.e. some fire during inspiration and some during expiration. Most VRG cells are inactive during eupneic breathing, but are active during forced or labored breathing. The neurons of the DRG are mostly inspiratory (active during inspiration) and of at least three types (see Herring-Breuer section); Iα (inhibited by lung inflation), Iβ (excited by lung inflation) and a P-type that receive afferent information from pulmonary receptors. A region located in the VRG called the pre-Botzinger complex has 'pacemaker-like' activity and may serve either alone or in combination with other processes as the source of the central pattern generation.*

FIG 16.4 Respiratory Center Actions: Summary

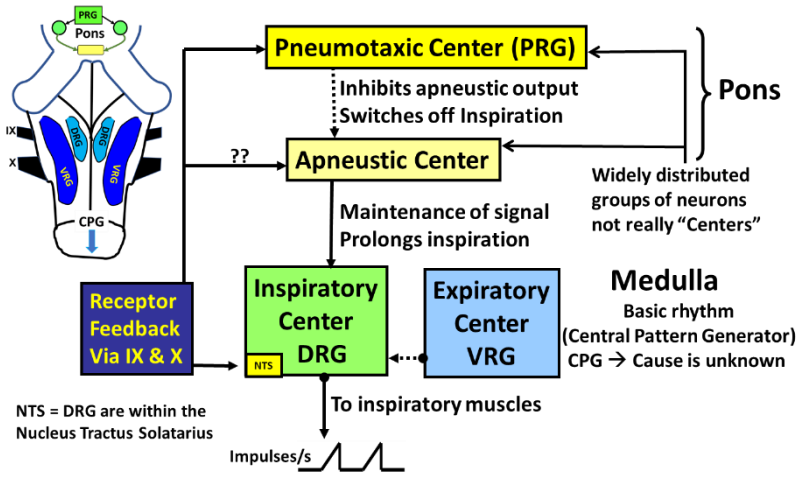


FIG 16.5 Respiratory Cell Groups

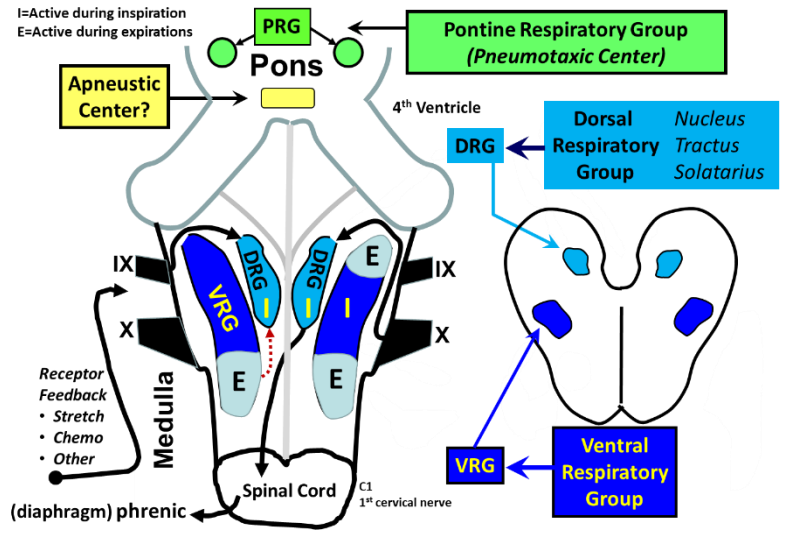
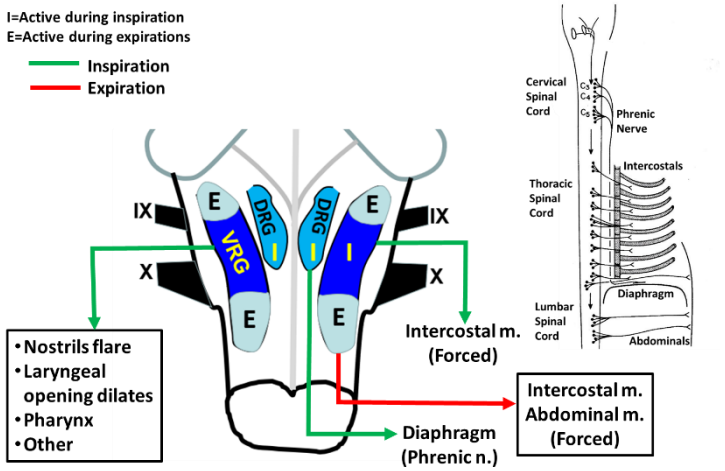
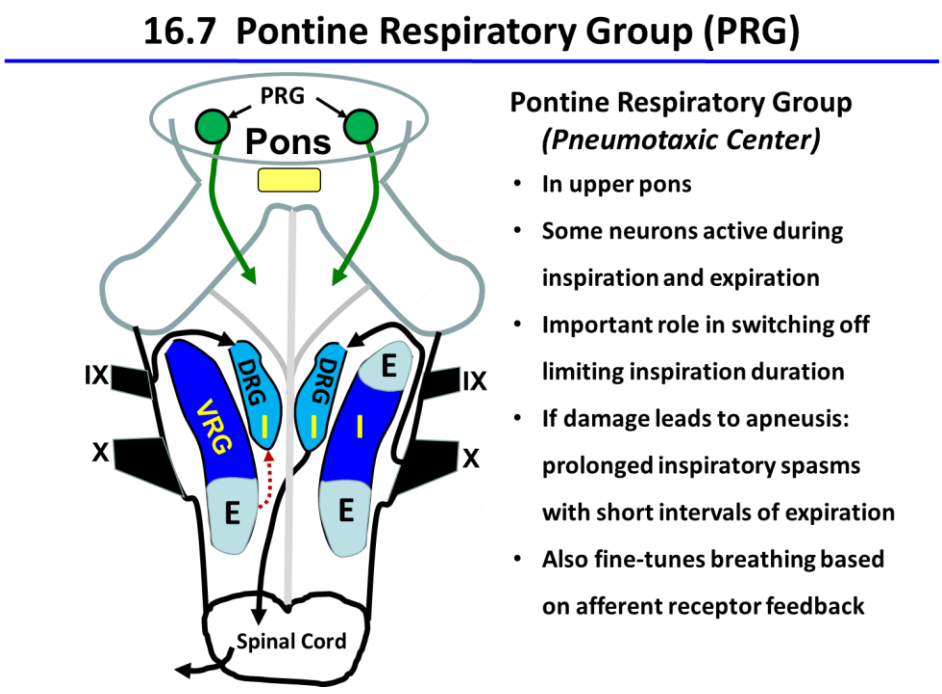


FIG 16.6 Medullary Cell Groups: Motor Outputs



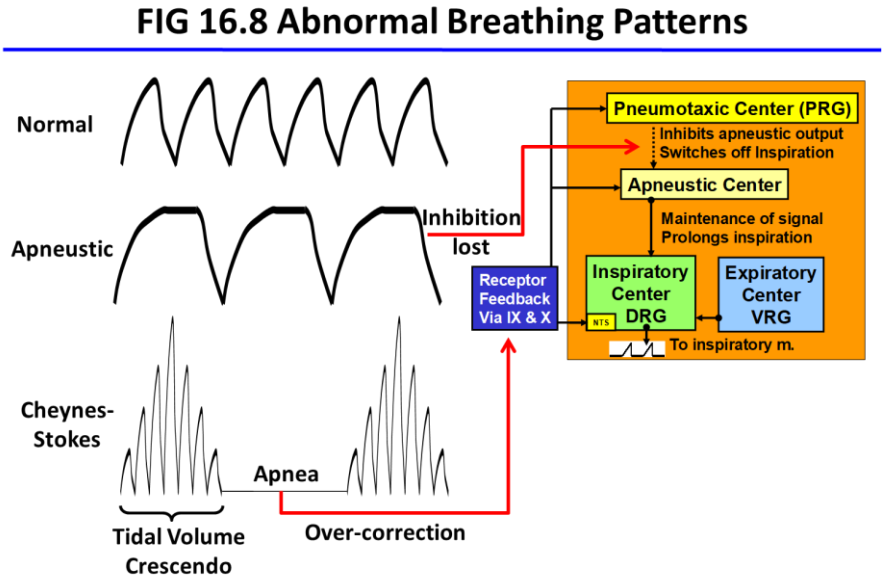
Pneumotaxic and Apneustic Centers

The pneumotaxic center provides input to the apneustic center, which in turn provides input to the medullary cell groups. The apneustic center input to the medullary groups helps drive inspiration as modulated by feedback from the peripheral and central receptors. Pneumotaxic center inputs inhibit the apneustic center output. So, the PRG play a vital role in the process of switching between inspiration and expiration.



The net output from the respiratory control center is impulses that travel to the respiratory muscles, causing contraction of the inspiratory muscles. During quiet expiration, efferent nerve traffic to the respiratory muscles is normally absent. But, during inspiration, the impulse rate "ramps" up, reaches a maximum, and then returns to zero, as was shown in ***FIG. 16.3****. This pattern causes an increasing contraction intensity of inspiratory muscles, and an associated decrease in intrapleural pressure and increase in lung volume.*

Examples of two abnormal breathing patterns are shown in ***FIG. 16.8****.*



Apneustic breathing can result from a lesion or other pathology that reduces or eliminates inhibitory input to the apneustic center from the pneumotaxic center. This pathway interruption is indicated by the red line in ***FIG. 16.8****.*

For Cheyne-Stokes breathing shown in ***FIG. 16.8*** *there may be multiple possibilities. One is an overcorrection in the feedback signals and drive from peripheral chemoreceptors. Thus, instead of the subtle correction to ventilation caused by changes in PCO2, there is an initial overshoot that drives up the tidal volume, causing the visual crescendo to a peak in the tidal volume. The enhanced tidal volume then overcorrects in the opposite direction, causing an interval of apnea (breathing stop). The pattern continues alternating between high and low levels of arterial PCO2.*

Mechanoreceptors TOC

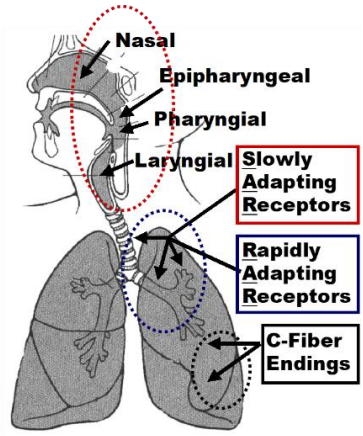
Two main types classified by afferent fiber conduction speed: myelinated (M) = fast; unmyelinated (UM) = slow. For both, main afferent pathway to CNS and respiratory center is via the vagus nerve. M-types are further distinguished as slowly adapting receptors (SARs) and rapidly adapting receptors (RARs). Afferent impulses have respiratory effects and also cardiovascular effects. UM-type receptors include pulmonary and bronchial C-fiber endings.

FIG 16.9 Respiratory Mechanoreceptors

Receptors Located in
- Upper respiratory
- Tracheo-bronchial tree
- Lung parenchyma

Broadly three types
- Slowly Adapting (SAR) Among ASM cells
- Rapidly Adapting (RAR) Among airway epithelial cells
- C-fiber endings (J-receptors) near blood vessels/capillaries

Vagal Afferents
- Connect to respiratory cntr
- Initiate many reflexes



Slowly Adapting Receptors

SAR: *Located near ASM cells are activated by stretch and mechanical distortion. After initial increase in impulse rate, rate slowly decreases (adapts) to a steady-state level as shown in* ***FIG. 16.10.***

Rapidly Adapting Receptors

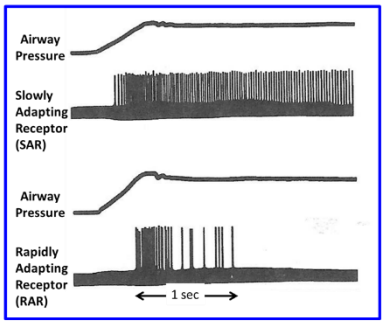
RAR: *Respond to distortion and to irritants, which are also referred to as* ***irritant receptors****. RARs are less numerous than SARS and are anatomically associated with the airway epithelium. RARs are excited if the lung is inflated quickly, but if the lung volume is held fixed, they adapt rapidly and near-completely. Impulse rate increases with increasing translung pressure P_{TL}, but the lung volume at which RAR start firing is greater than for SAR. Details of irritants and J-receptors are summarized below.*

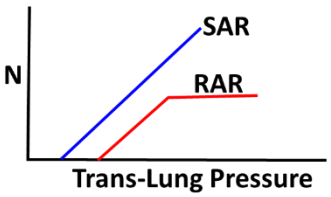
Slowly and Rapidly Adapting Receptors

SAR → Present in Airways – ASM proximity
- Increased activity with increased stretch
- Impulse rate stabilizes if stretch maintained
- Activity increases with lung volume increase
- Involved in the Hering-Breuer inflation reflex (Increased lung volume → curtails inspiration, increases RR, maintains ventilation)

RAR → Present in Airways – Epithelium
- Increases activity with amount & rate of stretch
- Impulse rate recovers if stretch maintained
- Activates at higher stretch than SAR
- Also activated by large lung deflations
- Involved in the Hering-Breuer deflation reflex (Decrease volume → triggers + inspiration & RR

RAR → Activated by chemical/irritant agents
- Dust – noxious fumes – smoke
- Trachea and large airways
- Bronchoconstriction – mucus and cough





Chemical/Irritant Reflexes (RAR)

Receptors in nasal mucosa, upper airways, tracheobronchial tree and possibly alveoli trigger bronchoconstriction and sneeze or cough

Bronchoconstriction:
- *Prevents deeper penetration into airway*
- *Produces higher velocity airstream during sneeze or cough*

Sneeze: Stimulation of nose or nasopharynx receptors
Afferent pathways via trigeminal and olfactory nerves

Cough: Stimulation of tracheobronchial receptors
Afferent pathways via vagus nerves

Cough/Sneeze Process:
- *Deep inspiration is followed by forced expiration with closed glottis*
- *Intrapleural pressure rises precipitously ~ 100 mmHg*
- *Glottis opens and high velocity exhalation air stream results*

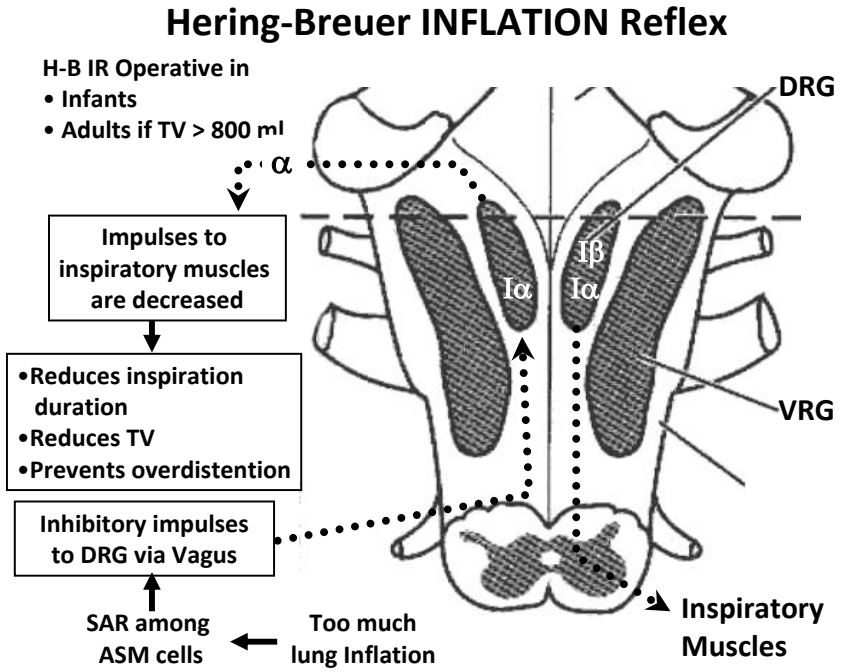
Sneeze: Through nose Cough: Through mouth

C-Fiber Receptors (Juxtacapillary or J Receptors)

- *Network of small unmyelinated axons (C-fibers) innervate receptors in alveoli near or in the walls of pulmonary capillaries*
- *Sensitive to distension and/or distortion caused by increases in capillary or interstitial volume*
- *Increased distention leads to increased ventilation (pulmonary congestion by LV failure)*
- *Decreased distention leads to decreased ventilation (e.g. pulmonary embolism that obstructs flow proximal to capillaries)*

Hering-Breuer Inflation Reflex

This reflex inhibits inspiration and produces slowed breathing in response to large lung inflations. The general stimulus is related to the actions of the SAR located within the airway smooth muscle of both small and large airways. The afferent pathway is via large myelinated fibers in the vagus. The efferent limb shortens the inspiration time and reduces tidal volume and respiratory rate. This reflex is prominent in newborns, but in adults, it is active only at large lung inflations, causing tidal volumes that are in excess of normal eupneic breathing. In adults, a TV of about 800 ml is required to elicit this reflex, which may prevent overdistension of alveoli.

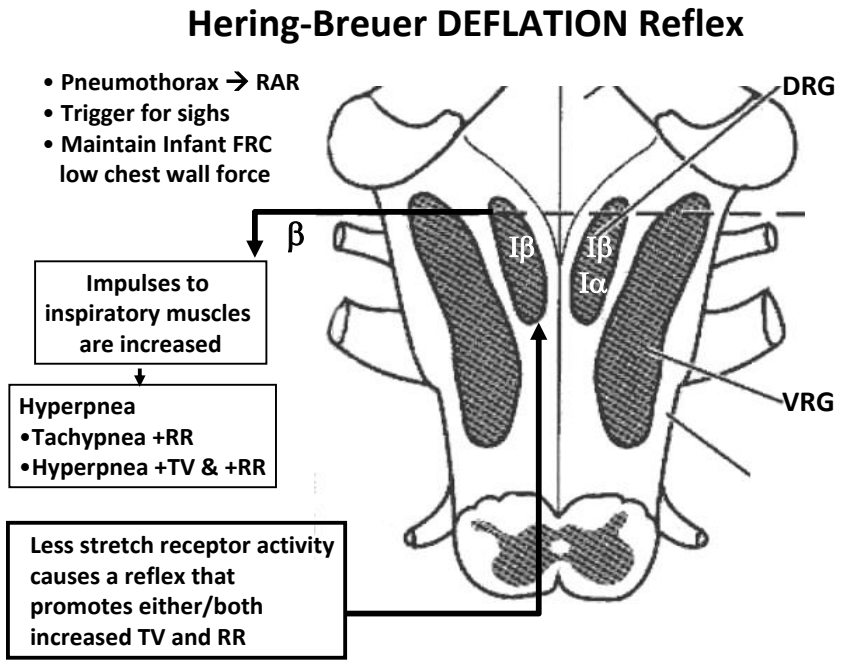


Hering-Breuer Deflation Reflex

The trigger for this reflex is abrupt deflation due to decreased stretch of receptors, including the RAR. The afferent pathway is via the vagus.

This reflex promotes hyperpnea, consisting of an increase in respiratory rate (RR) and inspiratory effort when the lungs are prematurely deflated below FRC.

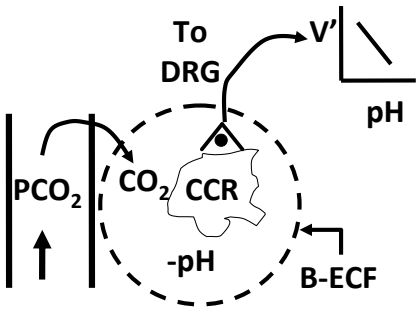
This reflex may be involved with the hyperpnea associated with pneumothorax. It may also be involved with the periodic slow deep breaths of sighing, which serve to expand alveoli to better distribute surfactant to help protect against atelectasis. Finally, it is likely that it plays a role in maintaining the FRC in infants who have a low chest wall force to counteract the inward lung forces.



17.0 CHEMICAL CONTROL OF BREATHING TOC

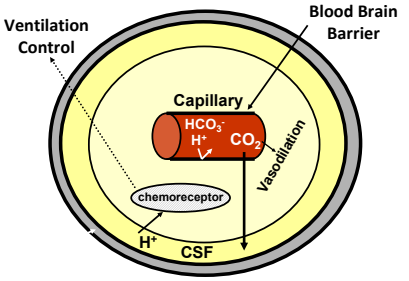
Central Chemoreceptors (CCR)

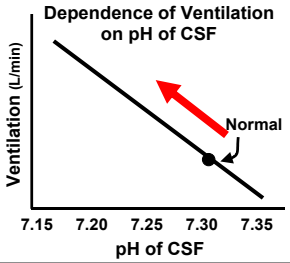
CCR are located near the ventral surface of the medulla near where nerves IX and X exit. The receptors are surrounded by brain extracellular fluid and are mainly sensitive to ***cerebral spinal or extracellular fluid pH.*** *Receptors respond to increased H^+ (directly or due to increased CO_2) causing increased ventilation (TV & RR). A decrease has the opposite effect (ventilation is reduced).*



Central Chemoreceptors (CCR)

- **CCR in brain parenchyma bathed in brain extracellular fluid/CSF**
- **If blood gases and pH near normal CCR are main control of ventilation**
- **CCR are sensitive to arterial hypercapnia (and associated fall in pH)**
- **CCR actually sense pH (H^+) around receptor neurons bathed in CSF**
- **pH changes may occur due to:**
  1) **increased cerebral blood CO_2 diffusing across the blood brain barrier resulting in a rapid (60 sec) decrease in the pH of CSF**
  2) **decreased pH of brain or CSF not due to changes in Pa_{CO2} (delayed)**
- **CCR do not respond to hypoxia**
- **CCR and PCR both affect ventilation response to increased CO_2 levels**

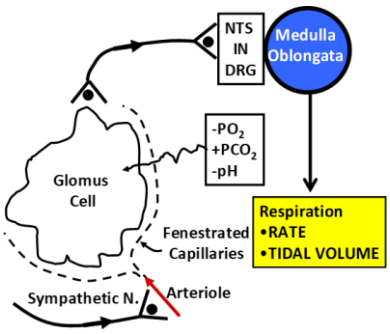




Increased arterial CO_2 causes more CO_2 to diffuse from brain capillaries across the blood brain barrier. CO_2 is then converted to H^+ in CSF and H^+ then acts as the main stimulus for the CCR-induced ventilation reflex. Capillary blood CO_2 excess also causes vasodilation via its direct action on cerebral blood vessels. Blood H^+ and HCO_3^- ions do not easily penetrate the blood-brain barrier. Penetration of these ions, if it occurs at all, needs much time to develop. So, responses to changes in blood pH are handled mainly by peripheral chemoreceptors.

Peripheral Chemoreceptors (PCR) TOC

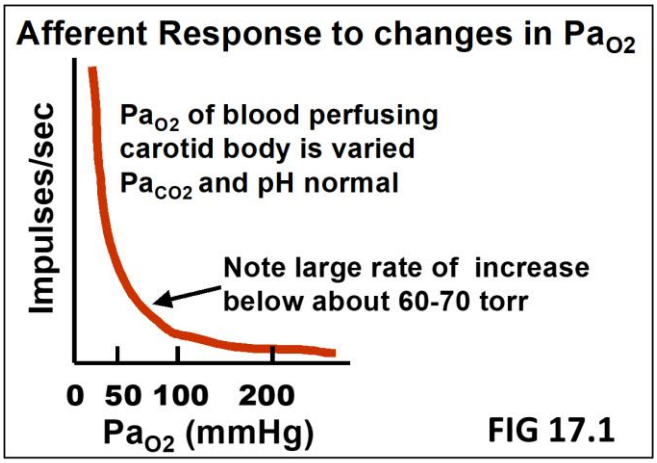
PCR ***are located in carotid and aortic bodies.*** *They have a high capillary density and blood flow/g. In response to blood changes, PCR Glomus cells change their neurotransmitter release, altering the vagus afferent impulse rate to the respiratory center. Responses are similar in aortic and carotid bodies but the carotid reflex is dominant.*



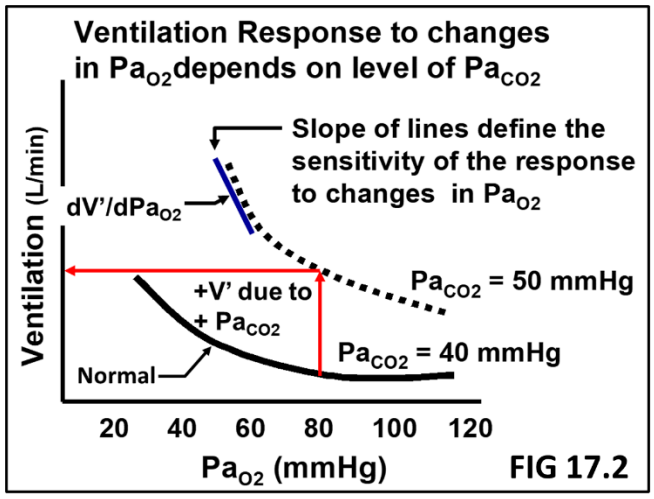
Peripheral Chemoreceptors (PCR)

- **Located bilaterally in carotid and aortic bodies**
- **Respond to Hypoxia, Hypercapnia and Acidosis**
- **Afferent pathways for:**
  Carotid body → Hering's nerve
  Aortic body → vagus nerve
- **Considerable afferent impulse traffic present at normal blood gases**
- **Increased afferent activity caused by (1) decreased arterial Pa_{O2} (2) increased Pa_{CO2} and (3) decreased arterial pH**
- **Feedback to respiratory center causes increased V'**
- **Response to hypoxemia depends on levels of Pa_{CO2} and pH**
  More Pa_{CO2} and/or lower pH → greater $\Delta V'$ for same ΔPa_{O2}

Low Oxygen and Dependence on Carbon Dioxide Tension TOC

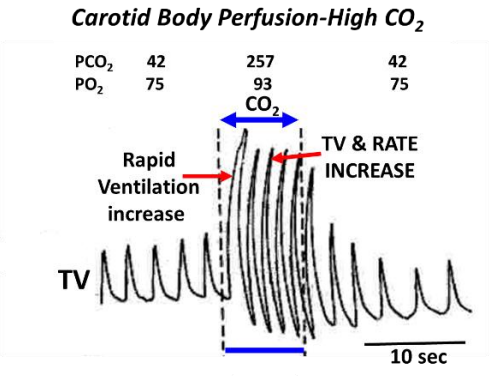


If atrial oxygen tension (PaO2) falls to ~60-70 mmHg, (***FIG. 17.1)*** the afferent impulse rate from peripheral chemoreceptors increases greatly. The increased afferent nerve traffic causes an increase in ventilation (V') via an increase in nerve traffic to the respiratory muscles. Afferent impulse rates also increase if Pa_{CO2} is elevated or pH is lowered. It is noteworthy that the ventilation response to hypoxemia is larger if Pa_{CO2} is elevated or if pH is reduced, as shown in ***FIG. 17.2.***



With no significant arterial hypoxemia present e.g., P_{O2} >~80 mmHg), the receptors are more sensitive to changes in arterial CO_2 and pH (H^+) than to O_2 changes. For example, for a P_{O2} change from 115 to 80 mmHg, there is little change in V' (***FIG. 17.2***). But small changes in either Pa_{CO2} or pH can cause large changes in V'. Also, with hypoxemia (Pa_{O2}<~60-70 mmHg), the sensitivity of V' to changes in PaO2 is increased with hypercapnia or reduced pH. The greater slope of the V'-PaO2 curve shows this. The reflex response initiated by the PCR is in a direction to counteract the arterial blood chemistry change. PCR and CCR respond similarly to changes in CO_2, but CCR causes 2/3 or more of the V' response. Note that pH changes may occur via non-CO2-related processes. If blood pH decreases (e.g., ketone bodies as in diabetes), V' is stimulated via the PCR. If blood pH increases (e.g., H+ loss due to vomiting), V' is depressed by PCR activity.

FIG 17.3 Ventilation Response to CO_2



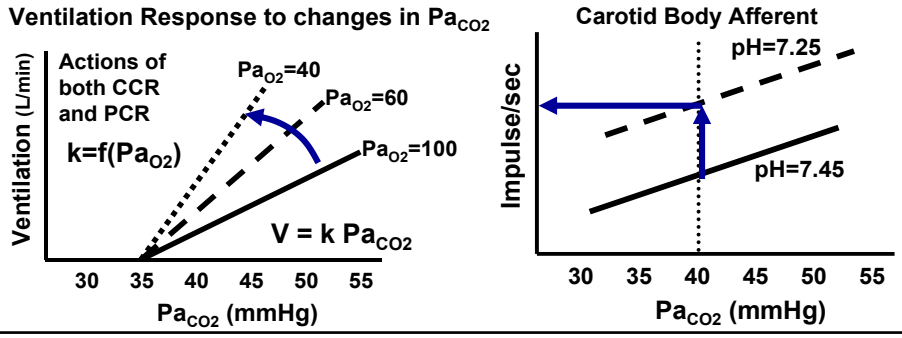
PCR respond to increased Pa_{CO2} and decreased pH with ***increased afferent impulses to the respiratory center.*** The result is increased ventilation via increases in both TV and RR. In ***FIG. 17.3*** the effect of rapidly exchanging the CO2 content of the blood perfusing the carotid body is illustrated. This experiment was done on an animal by cannulating the common carotid and changing the PCO2 of the blood perfusing the carotid body. From a normal level of 42 mmHg, it was increased to 257 mmHg for about 10 seconds. As can be noted the response was large and rapid in onset. There was an increase in both tidal volume (TV) and respiration rate that rapidly returned to prior levels once the PCO2 was normalized. Note the rapid and large response. PCR response to ***hypercapnia*** is less than the CCR response (20% vs. 80%) but is more rapid. Carotid body receptors respond to a fall in arterial pH; aortic receptors don't.

PCR-Induced Ventilation Changes Associated with Changes in CO_2 and pH TOC

In the adjacent **figure, the effect of arterial pH and PO2 (PaO2) on the response to changes in arterial CO2 (PaCO2) is** shown. For the PCR response (carotid body), the afferent impulse rate is greater for all levels of Pa_{CO2} if pH is lowered. The overall ventilation changes that occur due to both PCR and CCR actions are augmented in the presence of reduced levels of arterial oxygen tension.

Ventilatory Responses to CO_2

- **Breath rate & depth regulated to maintain Pa_{CO2} close to 40 mmHg**
- **Ventilation increases nearly linearly with Pa_{CO2}**
- **Change in ventilation for equal changes in Pa_{CO2} depends on Pa_{O2}**
  Lower Pa_{O2} → greater change in ventilation (k is greater)
  So HYPOXEMIA increases sensitivity of the CO_2 ventilatory response
- **At any Pa_{CO2} level → a pH decrease causes greater impulse response**



17.4 High Altitude Effects

High Altitude: Respiratory Adaptation
Decreased Atmospheric Pressure ~ Hypoxemia

Peripheral Chemoreceptors drive increased ventilation

- **Increases Pa_{O2} but Decreases Pa_{CO2}**
- **Decreased CO_2 effects Central Chemoreceptors (+pH)**
- **Initially counter to hypoxia induced hyperpnea**
- **CSF and arterial pH tend to normalize over days**
- **Renal excretion of $HCO3^-$**
- **Early acute Mountain Sickness possible**

Polycythemia - Increases O_2 carrying capacity

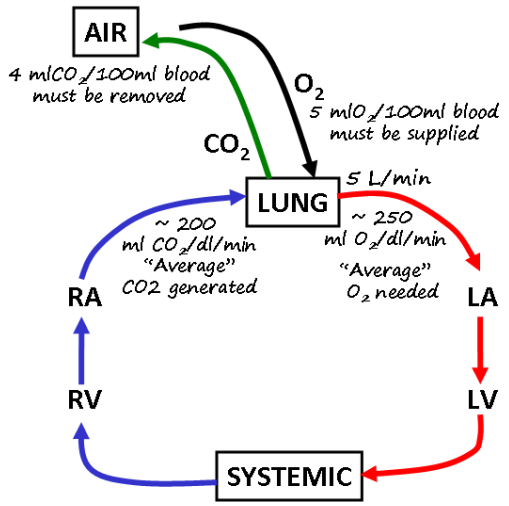
P50 Shift to Right - Better O_2 unloading

Increased Capillary Density

APPENDIX 1 **Major Gas-Related Functions and Processes** TOC

Air in – and –Air out → O_2 delivered and CO_2 removed

For every ml of O_2 used 0.8 ml CO_2 produced



O_2 Dissolved in Blood

$[O_2]_d = KO_2 \times PO_2$

K = solubility = 0.003 mlO_2/ 100ml/mmHg

PO_2 = 100 mmHg

O_2

Dissolved O_2 $[O_2]$ = 0.3ml/dl

blood

If CO = 6 L/min

O_2 delivered = 60x 0.003 = 18 ml O_2/min

Only 18/250 ~ 7% of needed

O_2 Bound to Hemoglobin in RBC

@100% Saturation

(34 g/Hb/100 ml rbc) x Hct

34 x 0.44 = 15 gHb/100 ml blood

Hb O_2 binding capacity ~ 1.34 mlO_2/gHb

PO_2 = 100 mmHg

O_2

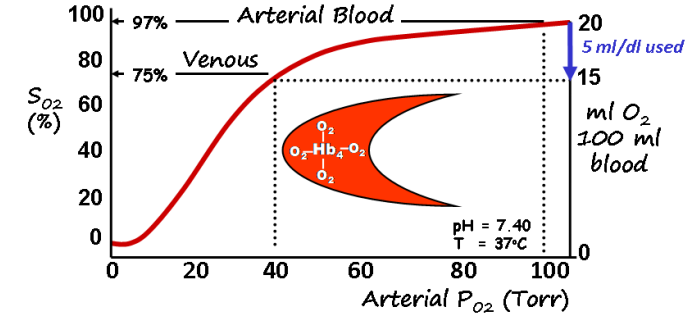
O_2 Bound to Hemoglobin in RBC

15 x 1.34 = 20.1 mlO_2/dl

Normally 97% sat

0.97 x 20.1 = 19.5 mlO_2/dl + 0.3 ml dissolved ~ 20 mlO_2/dl

O_2 Association – and - Disassociation



mlO_2/100ml blood | g/100 ml blood | Amount Dissolved

$[O_2]$ = 1.34 [Hb] (Sat/100) + 0.003PO_2

Carbon Dioxide

$[CO_2]_d = KCO_2 \times PO_2$ = 2.4 ml/dl

K = solubility = 0.06 mlCO_2/ 100ml/mmHg

PCO_2 = 40 mmHg

CO_2

Carbon Dioxide @ PCO_2 of 40 mmHg

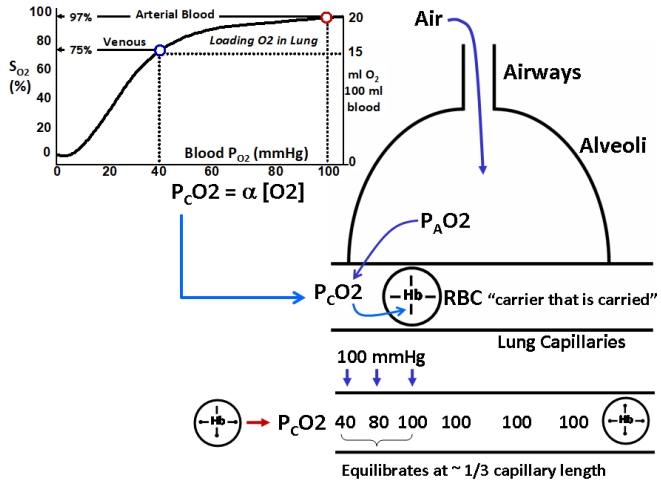
Dissolved CO_2 $[CO_2]$ = 2.4ml/dl

blood 2.4/48 →5%

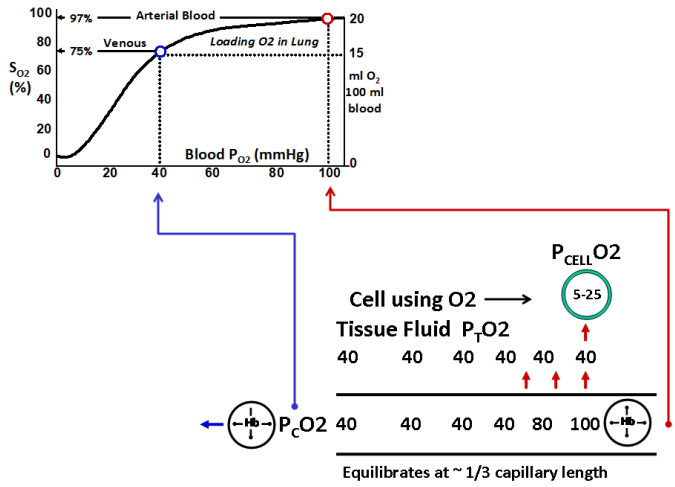
CO_2 in Blood 48 ml/dl

Bicarbonate HCO_3 →90%

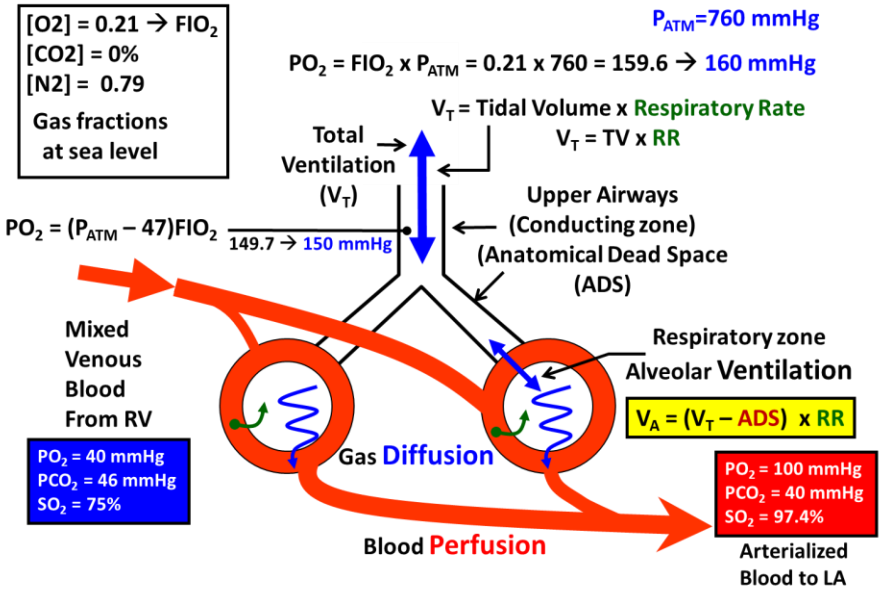
Loading up with O2 in Lung (Descriptive)



Unloading O2 to Tissues (Descriptive)



Respiratory Processes: Ventilation-Perfusion-Diffusion



RESPIRATORY STUDY QUESTIONS TOC

Respiratory STUDY Questions: Courtesy of Dr. HN Mayrovitz: Questions are offered as study aids and should not be viewed as inclusive of material that will be covered or tested. There are three question parts but there are no answers provided. These questions are to stimulate self-directed learning and to identify important concepts to aid in that process.

PART 1= "One-Liners" = 80 questions, PART 2 = short MCQs=45 and PART 3= more in-depth MCQs= 160

PART 1

1. If lung compliance decreases, what is the effect on the work of inspiration?
2. Which alveolar cell types produce lung surfactant?
3. If surfactant production is low or absent, what will be the effect on
Alveolar surface tension? Lung compliance? work of inspiration?
4. Do the effects of lung surfactant depend on lung volume?
5. What is the name given to lung volume at the end of quiet inspiration?
6. By what method can most lung volumes be determined?
7. If your TV was 600 ml, what RR would you need to achieve a total ventilation of 6 liters per minute?
8. Approximately what breathing rate do you need to achieve an alveolar ventilation of 400 ml per minute? (Hint you need to include your personal dead space volume).
9. What would happen to the oxygen tension in your trachea if you were on top of Mt. Everest?
10. Normal PCO_2 of blood entering pulmonary capillaries is about _____ ?
11. Normal PO_2 of blood exiting the pulmonary circulation is about _____?
12. The normal level of water vapor pressure in the lung is about _____?
13. If at atmospheric pressure with alveolar pressure = -5 cm H_2O and intrapleural pressure = -10 cm H_2O What are the translung, transwall and total respiratory system pressure?
14. What is meant by lung compliance? What are its units?
15. Is the compliance of all lung alveoli the same?
16. Do alveoli at the lung apex have a higher or lower compliance than at the apex?
17. If they are different what is the reason?
18. If alveoli have lower compliance, is it easier or harder to inflate them?
19. What would happen to alveolar CO_2 tension if total ventilation were increased?
20. What is meant by the following terms?
Hypocapnia, Hypoxemia, Atelectasis, Hypoventilation, Hyperventilation
21. As you inspire does intrapleural pressure increase or decrease?
22. As you inspire does translung pressure increase or decrease?
23. What main muscles are involved in inspiration during "quiet" breathing?
24. What main muscles are activated during "quiet" expiration?
25. Is total respiratory compliance greater on less than lung compliance?
26. What is a primary defect associated with respiratory distress syndrome?
27. What is meant by restrictive lung disease?
28. What is meant by obstructive lung disease?
29. Which pressures are needed to determine airway resistance

30. What is meant by time constant and how does it affect respiration?
31. Is airway resistance higher in upper or lower airways?
32. Is turbulent air flow normally present anywhere in the airways?
33. In order to minimize work of breathing what pattern may people with obstructive lung adopt?
34. According to the Alveolar Ventilation Equation, if alveolar ventilation decreases in relation to CO2 removal, what happens to alveolar CO2 tension?
35. According to the Alveolar Gas Equation, if alveolar CO2 tension increases, what happens to alveolar PO2
36. If the lung becomes stiffer, what happens to its compliance?
37. If the lung becomes stiffer, what happens to lung recoil pressure? Does this help or hinder inspiration? Does this help or hinder expiration?
38. What are the three main processes associated with respiratory function?
39. What is meant by the term "arterialized" blood?
40. How would you determine the A-a gradient?
41. What airways contribute to anatomical dead space?
42. Which pleura surrounds the lung?
43. Which artery supplies most of the lung tissues?
44. If the tracheal temperature decreases, does the water vapor pressure increase or decrease?
45. If the atmospheric pressure is 600 mmHg what is the partial pressure of oxygen in the trachea?
46. During a normal respiration cycle, when is the air flow zero?
47. What helps prevent collapse of smaller alveoli into larger alveoli?
48. A person with emphysema would have a high or low lung recoil pressure?
49. A person with interstitial fibrosis would have a high or low lung recoil pressure?
50. Which of the above two conditions is usually associated with a reduced lung compliance?
51. What would happen to lung compliance for each of the following?
    - Lung volume increases from FRC to TLC
    - Surfactant concentration decreases
    - Fibrosis develops within interstitial spaces
    - Alveoli walls break as in emphysema
    - Pulmonary capillaries leak fluid (edema)
52. What happens to the energy needed for inspiration if:
    - Lung compliance decreases
    - Lung recoil pressure increases
    - Airway resistance increases
    - Alveolar surface tension decreases
53. If alveolar ventilation falls below normal what happens to the following?
    - Alveolar CO2 tension
    - Alveolar O2 tension
    - PO2 in capillary blood exiting the lung
54. What happens to O2 delivery to tissues if the P50 value is reduced?
55. An increase in which quantities will increase P50?
56. What is the alveolar gas equation?
57. What is the alveolar ventilation equation?
58. What is meant by the term Total Respiratory System Compliance?

59. If lung and chest wall have equal compliances of 0.2 units, what is the total compliance?
60. If a patient breathes 80% oxygen at a pressure of 2 atmospheres, what is the tracheal PO2?
61. What is a shunt?
62. What is the difference between an anatomical and a physiological shunt?
63. What would be the effect of 100% O2 if either of 62 were present?
64. What five major factors can contribute to hypoxemia
65. What is dynamic compression and in what way does it impact respiration?
66. What is meant by the equal pressure point (EPP)?
67. Explain the determinants of the Flow-Volume (F-V) curve in healthy persons
68. In what ways does the F-V curve change in obstructive and restrictive lung disorders?
69. What does the term FEV represent and how is it used clinically?
70. Contrast the pressure effects of the Muller and Valsalva maneuvers.
71. In what forms may oxygen be carried in the blood?
72. In what forms may carbon dioxide be carried in the blood?
73. In what way does carbon monoxide affect oxygen binding and release?
74. What blood changes would cause peripheral chemoreceptors to increase ventilation?
75. What changes would cause central chemoreceptors to increase ventilation?
76. What are the Herrin-Breuer reflexes?
77. What factors can reduce lung diffusion capacity (DL)?
78. Which muscles become activated during eupneic expiration?
79. What is meant by the term "ramping up" with respect to nerve impulses to respiratory muscles?
80. What is the approximate speed of red cells in lung capillaries?

PART II: Please note that Part II MCQs have only a-b-c-d choices your exam will have 5 choices **TOC**

1) Alveolar oxygen gets to the pulmonary capillaries by
a) convection
b) osmosis
c) active transport
d) diffusion

2) Which is part of the anatomical dead space?
a) alveolar ducts
b) alveoli
c) respiratory bronchioles
d) trachea

3) Which of the following occurs during inspiration?
a) Alveolar wall tension decreases
b) Lung recoil pressure decreases
c) Intrapleural pressure becomes more negative
d)Translung pressure decreases

4) Lung compliance decreases if
a) Airway resistance decreases
b) Temperature decreases
c) Alveoli become stiffer
d) Alveolar surfactant increases

(5) Airway resistance is
a) Decreased in the presence of turbulent air flow
b) Least in the upper airways
c) Least in the smaller airways
d) Decreased by stretching & thinning of term bronchioles

6) Which of the following is not associated with a decreased compliance?
a) Alveolar edema
b) Interstitial fibrosis
c) Decreased work of breathing
d) Decreased pulmonary surfactant

7) During quiet breathing the volume in the lung at the end of a normal expiration is
a) residual volume
b) inspiratory reserve capacity
c) functional reserve capacity
d) expiratory reserve capacity

8) If breathing rate is 10/min & TV is 400 ml then
a) total ventilation is 400 ml/min
b) alveolar ventilation is 400 ml/min
c) alveolar ventilation is 4000 ml/min
d) total ventilation is 4000 ml/min

9) Normal venous blood carbon dioxide tension is about
a) 40 torr
b) 46 torr
c) 75 torr
d) 104 torr

10) Which of the following will decrease oxygen transport from alveoli to capillary?
a) Increased interstitial fluid volume
b) increased alveoli surface area
c) increased alveoli O2 tension
d) decreased alveoli CO2 tension

11) If alveolar surfactant were reduced
a) the lung would be easier to inflate
b) the lung compliance would tend to increase
c) alveolar ventilation would tend to decrease
d) small airway resistance would tend to increase

12) If alveolar ventilation increases above normal the
a) alveolar PO2 decreases
b) alveolar PCO2 decreases
c) arterial PO2 decreases
d) arterial PCO2 increases

13) If barometric pressure is 1000 torr, PO2 is closest to
a) 40 torr
b) 100 torr
c) 150 torr
d) 200 torr

14) Hypoventilation will tend to
a) increase arterial PCO2
b) decrease alveolar PCO2
c) increase arteriolar PO2
d) increase alveolar PO2

15) If alveolar ventilation is constant,
a large increase in pulmonary blood flow will tend to
a) increase the oxygen saturation of arterial blood
b) increase the oxygen tension in arterial blood
c) increase the arterial CO2 tension
d) have no effect on arterial CO2 tension

16) With no change in blood flow, a large decrease in alveolar ventilation will tend to
a) cause alveolar oxygen to rise
b) cause alveolar carbon dioxide to fall
c) produce respiratory acidosis
d) produce respiratory alkalosis

17) Which tends to cause arterial hypoxemia?
a) increased ventilation/perfusion ratio
b) decreased barometric pressure
c) increased arterial PCO2
d) increased lung diffusion capacity

18) Quiet breathing is normally regulated to maintain
a) Alveolar PO2
b) Arterial PO2
c) Arterial PCO2
d) Blood pressure

19) Which is mainly responsible for rhythmic breathing
a) Pneumotaxic center
b) Apneustic center
c) Medullary inspiratory area
d) Medullary expiratory area

20) Increased stretch of the pulmonary receptors
a) Decreases afferent nerve impulses to respiratory center
b) Causes a reflex inhibition of expiration
c) Causes a reflex inhibition of inspiration
d) Causes none of the above

21) Pulmonary irritant receptors
a) do not respond to gaseous irritants
b) if activated may produce bronchoconstriction
c) if activated send afferent nerve impulses to the apneustic center
d) recover slowly once activated

22) The central chemoreceptors cause an increase in ventilation in response to
a) an increase in cerebral blood PCO2
b) an increase in cerebral blood HCO3-
c) an increase in alveolar PO2
d) an increase in cerebral spinal fluid PO2

23) Pulmonary surfactant
a) acts like standard detergents at body temperature
b) is produced by type I alveolar epithelial cells
c) reduces pulmonary airway resistance
d) reduces alveolar surface tension

24) Compared to systemic, the pulmonary circulation has
a) low pressure and low resistance
b) low pressure and high resistance
c) high pressure and high resistance
d) high pressure and low resistance

25) A shift to the left of the oxygen dissociation curve
a) will facilitate oxygen delivery to tissue
b) will hinder oxygen delivery to tissue
c) will cause a decrease in hemoglobin saturation
d) is caused by a decrease in blood pH

26) Which statement is NOT correct?
a) During inspiration, the diaphragm descends causing the thoracic cavity to enlarge
b) Quiet breathing requires contraction of the diaphragm during inspiration & expiration
c) With forced expiration, abdominal muscles decrease lung volume by lowering the ribs
d) During inspiration, intrapleural pressure becomes more negative

27) Which statement regarding pulmonary blood circulation is correct
a) Flow to alveolar capillaries is mainly from the pulmonary artery
b) Flow to a large fraction of alveoli is from the bronchial artery
c) Flow in pulmonary veins is much less than in the bronchial artery
d) Pulmonary blood vessel structure makes them insensitive to gravity

28) During inspiration, intrapleural pressure becomes
a) more positive
b) more negative
c) equal to the pressure in the alveoli
d) greater than atmospheric pressure

29) Lung gas volume at the end of a normal inspiration is
a) equilibrium volume
b) inspiratory capacity
c) greater than functional residual capacity
d) inspiratory reserve volume

30) A patient has an ERV=1000 ml, IRV=2500ml TV= 400 ml and RV =1500 ml. What is the vital capacity?
a) 2900 ml
b) 3900 ml
c) 3500 ml
d) 4400 ml

31) A pt gets hyperbaric 50% O2 in a chamber at an atm. pressure of 1447 Torr. Tracheal PO2 is closest to
a) 104 torr
b) 160 torr
c) 725 torr
d) 700 torr

32) A pt. has a dead space of 100 ml, a TV= 300 ml and a rate of 20/minute. The pt's alveolar ventilation is
a) 2000 ml/min
b) 3000 ml/min
c) 4000 ml/min
d) 5000 ml/min

33) A student increases breathing rate from 10 to 20/min. What happens to alveolar gas tensions?
a) -PCO2 & +PO2
b) -PCO2 & -PO2
c) no change in PCO2 & +PO2 increases
d) +PCO2 & -PO2

34) Reduced or absent pulmonary surfactant plays an important role in
a) Emphysema
b) Alveolar interstitial fibrosis
c) Respiratory distress syndrome
d) Alveolar interstitial edema

35) Changes in ventilation normally affect arterial CO2 content more than O2 content because
a) O2 is more soluble in blood than CO2
b) O2 is more soluble in alveolar epithelial cells than CO2
c) CO2 dissociation curve is more linear than O2 curve
d) Hemoglobin has a higher affinity for CO2 than for O2

36) Breathing characterized as tachypnea and hypopnea is
a) deep and slow
b) shallow and slow
c) shallow and rapid
d) deep and rapid

37) A patient who has normal total ventilation but a reduced PaO2 likely has
a) an elevated alveolar PO2
b) a decreased alveolar PCO2
c) an increased total lung diffusion capacity
d) a decreased ventilation/perfusion ratio

38) All the following statements about changes in pulmonary circulation are true EXCEPT
a) Resistance of alveolar capillaries increases during normal inspiration
b) At large lung volumes vascular resistance is decreased
c) Resistance of extra-alveolar blood vessels decreases during normal inspiration
d) A decrease in venous transmural pressure will increase venous resistance

39. End-capillary PO2 in a normal lung is lower than the PO2 in the alveoli mainly because
a) the transit time for red cells through alveolar capillaries is too short to fully saturate
b) oxygen transfer from alveoli to blood requires a higher arterial oxygen tension
c) a small fraction of the O2 that would go to the blood is used by the lung itself
d) there is a mismatch between ventilation and blood perfusion

40) During normal inspiration, more air goes to lung base alveoli than to apex alveoli because
a) alveoli at base have more surfactant
b) alveoli at base are more compliant
c) alveoli at base have a higher ventilation/perfusion ratio
d) there is more blood flow to the base of the lung

41) The oxygen need of respiratory muscles would be increased by all of the following EXCEPT
a) a decrease in lung compliance
b) a decrease in the production of pulmonary surfactant
c) an increase in the tidal volume
e) a decrease in the airway resistance

42) Which of the following is higher at the lung apex than the base when a person is standing?
a) ventilation/perfusion ratio
b) blood flow
c) alveolar ventilation
d) compliance

43) Which of the following is LEAST likely to be associated with an increase in arterial CO2?
a) decreased ventilation/perfusion ratio
b) increased alveolar CO2
c) increased ventilation
d) increased blood flow

44) Normal O2 saturation of blood entering lung is about
a) 97%
b) 75%
c) 46%
d) 40%

45) If blood temperature is decreased to about 20oC
a) Oxygen delivery to tissues is facilitated
b) Oxygen uptake by the blood in the lung is impeded
c) Oxygen delivery to tissues is impeded
d) Blood O2 saturation is less for the same PO2

PART III **TOC**

1. The basic respiratory rhythm is generated by the

A) apneustic center

B) nucleus parabrachialis

C) dorsal medulla

D) pneumotaxic center

E) cerebrum

2. At the end of a quiet inspiration, intra-alveolar pressure is normally

A) -40 cmH_2O

B) -4 cmH_2O

C) 0 cmH_2O

D) +4 cmH_2O

E) +40 cmH_2O

3. Immediately after performing a forced vital capacity (VC) test, Mary starts to breathe into a 12 L spirometer containing 10% helium (He). At equilibrium the spirometer He concentration is 8.5%. If her VC is 5 L, her total lung capacity (TLC) is closest to which of the following volumes?

A) 3 L

B) 5 L

C) 7 L

D) 9 L

E) 11 L

4. Rose has a respiratory rate (RR) of 18, a tidal volume (TV) of 350 ml and an anatomic dead space of 100 m. She also has a normal alveolar CO2 tension (PACO2) of 40 mmHg. What is her alveolar ventilation?

A) 4.0 L

B) 4.5 L

C) 5.0 L

D) 5.5 L

E) 6.0 L

5. If Rose now increases her tidal volume by 75 ml (with CO2 production unchanged), her PACO2 is now closest to

A) 15 mmHg

B) 10 mmHg

C) 25 mmHg

D) 30 mmHg

E) 35 mmHg

6. In emphysema, which of the following would be expected to occur?

A) reduced airway resistance

B) reduced lung compliance

C) more negative intrapleural pressure

D) reduced FEV_1

E) both C and D

7. Which of the following would increase in obstructive but not in restrictive lung disease?
A) Vital capacity
B) Maximum breathing capacity
C) FEV_1
D) Functional residual capacity
E) Breathing frequency

8. Providing O2 to a patient with long standing chronic obstructive pulmonary disease (COPD) may cause a decrease in ventilation. Which one of the following statements best explains this observation?
A) Mucous secretion increases
B) Airway resistance increases
C) Physiologic dead space increases
D) Peripheral chemoreceptor activity decreases
E) Diffusing capacity for oxygen decreases

9. At which of the following sites is the partial pressure of carbon dioxide highest?
A) exhaled gas
B) alveolar gas
C) systemic arterial blood
D) systemic venous blood
E) about the same in all of the above (40 mmHg)

10. At which of the following is the partial pressure of oxygen (PO2) highest?
A) exhaled gas
B) anatomical dead space at the end of expiration
C) anatomical dead space at the end of inspiration
D) alveolar gas
E) about the same in all of the above (100 mmHg)

11. At the top of a 3000 m high mountain, which alveolar partial pressures is expected to be lower than normal?
A) Alveolar oxygen
B) Alveolar carbon dioxide
C) Alveolar water vapor
D) all of the above
E) only A and B above

12. Low arterial O2 tension and content is most likely to be observed in association with which of the following?

A) hypertension

B) fever

C) anemia

D) carbon monoxide poisoning

E) respiratory acidosis

13. Which one of the following is higher at the apex of the lung than at the base when a person is standing?

A) V/Q ratio

B) Blood flow

C) Ventilation

D) PA_{CO2}

E) Lung compliance

14. The bulk of CO_2 is transported in arterial blood as

A) dissolved CO_2

B) carbonic acid

C) carbaminohemoglobin

D) bicarbonate

E) carboxyhemoglobin

15. At 100 feet below sea level (4 atmospheres) what would be the O2 partial pressure of inspired air?

A) 160 mmHg

B) 320 mmHg

C) 640 mmHg

D) 1280 mmHg

E) none of the above

16. A patient is on a ventilatory adjusted for a tidal volume of 1 L at a frequency of 10/min. If the patient's anatomic dead space is 200 mL and the machine's dead space 50 mL, the alveolar ventilation is

A) 10 L/min

B) 8.5 L/min

C) 7.5 L/min

D) 5 L/min

E) not determinable from the information given

17. Subjects A and B have identical TV and RR and are subjected to spirometry and blood gas measurements. Subject A doubles her TV and decreases her RR to one-half of baseline. Subject B decreases her TV to one-half of baseline and doubles her RR. Which statement about the resulting alveolar ventilation in correct?

A) Alveolar ventilation is unchanged in both subjects

B) Alveolar ventilation increases in both subjects

C) Alveolar ventilation decreases in both subjects

D) Alveolar ventilation increases in subject A and decreases in subject B

E) Alveolar ventilation decreases in subject A and increases in subject B

18. The concentration of CO_2 is lowest in
A) the anatomic dead space at end inspiration
B) the anatomic dead space at end expiration
C) the alveoli at end inspiration
D) the alveoli at end expiration
E) the blood in the pulmonary veins

19. Complete transection of the brainstem above the pons would
A) result in cessation of all breathing movements
B) prevent any voluntary holding of breath
C) prevent the central chemoreceptors from exerting any control over ventilation
D) prevent the peripheral chemoreceptors from exerting any control over ventilation
E) abolish the Hering-Breuer reflex

20. Peripheral & central chemoreceptors may both help increase ventilation that occurs as a result of
A) decreased arterial oxygen content
B) decreased arterial blood pressure
C) increased arterial CO2 tension
D) decreased arterial O2 tension
E) increased arterial pH

21. The water vapor pressure of alveolar gas at a barometric pressure of 380 mmHg is
A) 23.5 mmHg
B) 47.0 mmHg
C) 76.0 mmHg
D) 94.0 mmHg
E) 105.0 mmHg

22. A deficiency of pulmonary surfactant would
A) decrease surface tension in the alveoli
B) decrease the change in intrapleural pressure required to achieve a given tidal volume
C) decrease lung compliance
D) decrease the work of breathing
E) increase functional residual capacity (FRC)

23. Bill breathes room air at sea level has an alveolar ventilation of 2 L/min. Blood gases show a Pa_{CO2} of 48 mmHg and a Pa_{O2} of 70 mmHg. Bill's alveolar O2 tension is equal to which of the following?
A) 150 mmHg
B) 110 mmHg
C) 100 mmHg
D) 90 mmHg
E) 60 mmHg

24. When the respiratory muscles are relaxed, the lungs are at
A) residual volume (RV)
B) expiratory reserve volume (ERV)
C) functional residual capacity (FRC)
D) inspiratory reserve volume (IRV)
E) total lung capacity (TLC)

25. Which one of the following is the most likely to cause a high arterial P_{CO2}?
A) Increased metabolic activity
B) Increased alveolar dead space
C) Depressed medullary respiratory centers
D) Alveolar capillary block
E) Increased alveolar ventilation

26. Which of the following best represents a "right-to-left shunt"?
A) pulmonary blood flow through a region of lung atelectasis
B) blood flow from the left ventricle to the right ventricle through a hole in the interventricular septum
C) blood flow from skin arteries to skin veins which does not pass through skin capillaries
D) blood flow from the aorta into the pulmonary artery through the ductus arteriosis
E) Both A and B

27. Normal resistance of large and medium-sized airways as a percentage of the total airway resistance is approximately
A) 10 percent
B) 20 percent
C) 40 percent
D) 60 percent
E) 80 percent

28. Tom's alveolar PO2 is 60 mmHg and his systemic arterial PO2 is 56 mmHg. Which is the most likely explanation?
A. hypoventilation
B. diffusion limitation
C. right-to-left shunt
D. V/Q non-uniformity
E. V/Q is abnormally large

29. Pulmonary vascular resistance increases
A) as the lung volume approaches TLC
B) as the lung volume approaches FRC
C) as the cardiac output increases
D) as the pulmonary artery pressure increases
E) as left atrial pressure increases

30. Reduced functional Hb due to anemia or CO poisoning doesn't produce increased ventilation because the
A) blood flow to the carotid body is decreased
B) total arterial O2 content is maintained within the normal range
C) carotid body chemoreceptors are stimulated
D) central chemoreceptors are stimulated
E) P_{O2} of arterial blood does not change

31. Sam's systemic arterial O2 content is normal but her systemic venous O2 content is low. This is characteristic of
A) diffusion limitation
B) right-to-left shunt
C) pulmonary V/Q increase
D) low Hb concentration
E) low cardiac output

32. Alice has a normal O2 tension and O2 content in pulmonary venous blood but her systemic arterial blood shows a significantly lower than normal O2 tension and O2 content. This is most likely due to a
A) diffusion limitation
B) right-to-left shunt
C) pulmonary V/Q increase
D) low cardiac output
E) high cardiac output

33. As blood passes through systemic capillaries, what happens to the affinity of hemoglobin for oxygen and what happens to the Hb-O_2 dissociation curve?
A) Hb affinity for O2 increases and the dissociation curves shifts to the left
B) Hb affinity for O2 increases and the dissociation curves shifts to the right
C) Hb affinity for O2 decreases and the dissociation curves shifts to the left
D) Hb affinity for O2 decreases and the dissociation curves shifts to the right
E) neither Hb affinity for O2 nor the Hb-O2 dissociation curve change

34. Pulmonary compliance is characterized by which of the following statements?
A) It is independent of lung volume
B) It is inversely related to the elastic recoil properties of the lung
C) It increases in patients with pulmonary edema
D) It is equivalent to □P□□V
E) It increases when there is a deficiency of surfactant

35. The percentage of hemoglobin saturated with O2 will increase if
A) arterial P_{CO2} is increased
B) hemoglobin concentration is increased
C) temperature is increased
D) arterial P_{O2} is increased
E) arterial pH is decreased

36. Activity of central chemoreceptors is stimulated by
A) an increase in the P_{CO2} of blood flowing through the brain
B) a decrease of the P_{CO2} of blood flowing through the brain
C) a decrease in the oxygen content of blood flowing through the brain
D) a decrease in the metabolic rate of the surrounding brain tissue
E) an increase in the pH of the CSF

37. In an acclimatized person at high altitudes, O2 delivery to tissues may be adequate at rest because of
A) an increase in hematocrit and thereby Hb concentration
B) the presence of an acidosis
C) a decrease in the number of tissue capillaries
D) the presence of a normal arterial P_{O2}
E) the presence of a lower-than-normal arterial P_{CO2}

38. During quiet resting inspiration, more air normally goes to lung base alveoli than to alveoli at lung apex because
A) the alveoli at the base of the lung have more surfactant
B) the alveoli at the base of the lung are more compliant
C) the alveoli at the base of the lung have higher V/Q ratios
D) there is a more negative intrapleural pressure at the base of the lung
E) there is more blood flow to the base of the lung

39. Which of the following increases due to stimulating parasympathetic nerves to smooth muscle in bronchioles?
A) Lung compliance
B) Airway diameter
C) Elastic work of breathing
D) Resistive work of breathing
E) Anatomic dead space

40. A spirometer can be used to measure directly
A) functional residual capacity
B) inspiratory capacity
C) residual volume
D) total lung capacity
E) none of the above

41. The oxygen required by the respiratory muscles would be increased by all the following **EXCEPT**
A) a decrease in lung compliance
B) a decrease in airway resistance
C) an increase in the rate of respiration
D) a decrease in the production of pulmonary surfactant
E) an increase in tidal volume

42) What is the expected systemic arterial O2 content if a normal person inhales 100% oxygen for an hour?
A) 100 ml O_2 / dl blood
B) 40 ml O_2 / dl blood
C) 22 ml O_2 / dl blood
D) 11 ml O_2 / dl blood
E) none of the above, since pure O2 is toxic and would cause death within the hour

43. Functions of alveolar macrophages include all the following EXCEPT
A) phagocytosis of bacteria
B) secretion of surfactant
C) release of lysosomal enzymes into the alveolar space
D) transport of inhaled particles out of the alveoli
E) release of leukocyte chemotactic factors

44. In a standing person, all contribute significantly to the presence of an A-a gradient for O_2 EXCEPT
A) variations in the V/Q ratios throughout the lungs
B) a small right-to-left absolute shunt
C) the nonlinearity of the oxyhemoglobin dissociation curve
D) the disequilibrium of end-pulmonary P_{O2} and alveolar P_{O2}
E) blood flow from the bronchial circulation

45. When is the resistance to blood flow of the pulmonary vascular bed <u>lowest</u>?
A) When a person is at rest sitting up
B) When a person is at rest lying down
C) When a person is breathing air at high altitude
D) When a person is exercising maximally
E) None of the above because pulmonary vascular resistance is approximately constant

46. Surfactant is accurately described by all the following statements EXCEPT
A) it is a lipoprotein containing lecithin
B) it is in part responsible for hysteresis in the pressure-volume curve of the human lung
C) it reduces surface tension in the alveoli
D) it is made in type II cells
E) it is present in increased amounts in hyaline membrane disease

47. While standing which lung region has the highest ventilation and which region has the highest blood perfusion?
A) highest ventilation: Apex; highest perfusion: Apex
B) highest ventilation: Apex; highest perfusion: Base
C) highest ventilation: Base; highest perfusion: Apex
D) highest ventilation: Base; highest perfusion: Base
E) there is no "highest" region as the apex and base have equal ventilation and perfusion rates

48. Metabolic functions of the lung include all the following EXCEPT
A) inactivation of angiotensin II
B) inactivation of bradykinin
C) inactivation of prostaglandins
D) synthesis of prostaglandins
E) synthesis of surfactant

49. Normally, end-pulmonary capillary blood reaches diffusion equilibrium with alveolar partial pressure of all EXCEPT
A) oxygen
B) nitrogen
C) carbon dioxide
D) carbon monoxide
E) nitrous oxide (N_2O)

50. A stroke that destroyed the respiratory center of the medulla would be expected to lead to
A) quick cessation of breathing
B) apneustic breathing
C) ataxic breathing
D) very rapid breathing
E) very slow and deep breathing

For the following, questions marked with a # have more than one answer that is a correct choice!!!
51. Hypoxemia at a PO2 of 55 mmHg has all the following effects EXCEPT
A) it stimulates carotid body chemoreceptors
B) it stimulates central chemoreceptors
C) it stimulates aortic body chemoreceptors
D) it causes a reflex increase in ventilation
E) it causes a reflex increase in arterial blood pressure

52. Increased ventilation may be produced by stimulation of all the following receptors EXCEPT
A) peripheral chemoreceptors
B) irritant receptors
C) peripheral pain receptors
D) pulmonary stretch receptors
E) J receptors

#53. The functional residual capacity (FRC) in the lungs of a young healthy adult of average size:
A) is about 500 ml
B) becomes smaller if airflow resistance increases
C) can be estimated using a helium dilution method
D) has the effect of damping fluctuations of alveolar gas concentrations during the breathing cycle
E) is the volume at which some airways normally begin to close during expiration

#54. Sam is healthy and sitting upright at rest. For Sam, which one of the following is true?

A) His tidal volume is 10% or less of total lung volume

B) His lungs inflate and deflate around a mean volume that is about 25% of their full capacity

C) During a forced exhalation his small airways start to close in lower parts of the lungs sooner than in upper parts

D) During a forced exhalation to RV the first air subsequently inhaled enters the apical regions of the lungs

E) If a resistance is added to the airways, the tidal exchange will shift to a higher lung volume

#55. While breathing room air petite Sally is found to have the following lung volumes:

Vital capacity	3.5 liters
Forced expiratory volume in 1 sec (FEV_1)	2.8 liters
Functional residual capacity (FRC)	1.8 liters
Residual volume (RV)	0.8 liters

For Sally:

A) airflow resistance is normal

B) the subject must be abnormal

C) the expiratory reserve volume is 1 liter

D) all of these measurements could have been made using only a spirometer

#56. Compliance of the lungs:

A) is defined as the change in volume per unit change in expanding (inflating) pressure

B) is greatest, for the whole lung, between residual volume and functional residual capacity

C) is decreased if surfactant is depleted

D) within the tidal range, is greater at the apex than at the base of the lungs in the upright position

#57. Concerning mechanical factors in breathing:

A) in the tidal range, there is more muscular work involved in breathing in than in breathing out

B) forced expiration is more difficult than forced inspiration

C) recoil of the chest wall assists inspiration

D) the pressure holding the lungs inflated is less effective at the base than at the apex

E) respiratory muscles use about 10% of the whole body oxygen consumption in normal people at rest

#58. The muscular work done during inspiration:

A) is made less by the effect of surfactant

B) is greater if the elastic recoil of the lungs is greater

C) is greater if inspiration starts at a high lung volume than if it is in the normal tidal range

D) could be lessened by bronchiole dilatation

E) is partly spent in overcoming surface tension forces

59. Respiration of a paralyzed man, who has a dead space of 200 ml, is maintained with a respirator. When the Tidal volume (TV) is set to 600 ml at a RR of 10, his alveolar PCO2 is 60 mmHg. To obtain a normal PACO2 (40 mmHg), what changes should be made to the respirator?

A) Don't change TV but increase RR to 15

B) Don't change TV but increase RR to 20

C) Increase RR to 15 and increase TV to 800 ml

D) Don't change RR but increase TV to 700 ml

E) Don't change RR but increase TV to 900 ml

60. In a measurement of FRC via the helium dilution method, the initial and final concentration of He are 6% and 5% respectively. The initial volume of the helium gas mixture in the spirometer is 10 liters. What is his FRC in liters?

A) 10

B) 7

C) 4

D) 3

E) 2

#61. Decreased arterial O2 tension is a consequence of:

A) hypoventilation

B) low hemoglobin concentration

C) carbon monoxide poisoning

D) living at high altitude

E) ventilation-perfusion mismatch in the lungs

#62. In a healthy person, the following values were found for end-tidal (end expired) gas, and can be taken to represent alveolar partial pressures: PO_2: 115 mmHg PCO_2: 25 mmHg

A) the subject was overbreathing (hyperventilating)

B) the O2 percentage in the inspired gas must have been higher than in room air

C) the arterial PCO_2 would be close to 25 mmHg

D) the arterial PO_2 would be 90-100 mmHg

E) there must be a respiratory alkalosis

#63. With reference to the control of breathing:

A) the increase in ventilation in exercise is proportional to a rise in arterial PCO_2

B) peripheral (arterial) chemoreceptors are stimulated by any form of diminished O2 content in arterial blood

C) afferent fibers in the vagus nerves carry information on the state of inflation of the lungs

D) breathing can continue when the brain stem is the only functioning part of the brain

#64. A healthy person (Bill) at rest breathes 100% O2 for 5 minutes. Which of the following is true?

A) During the 1st minute, ventilation will be considerably depressed

B) During the 5th minute, ventilation will be virtually the same as it was breathing air

C) Over the O2 breathing interval the arterial PCO_2 will decrease considerably

D) Over the O2 breathing interval the arterial PO_2 will rise to over 600 mmHg

E) Bill can hold his breath at the end of the 5 min for significantly longer than if he was breathing room air

#65. Concerning breathing, in a healthy person:
A) speech involves modified expiration
B) inhalation of 100% oxygen results in apnea (cessation of breathing)
C) inhalation of a gas mixture containing 5% CO_2 stimulates breathing
D) the respiratory centers lie in the diencephalon
E) after hyperventilating, the breath can be held for longer than after normal breathing

#66. The neurons whose activity causes inspiratory muscle activity:
A) are situated in the medulla
B) are stimulated by their own extracellular acidity
C) show increase AP frequency during inspiration when chemoreceptor stimulation is increased
D) cease firing at the end of inspiration
E) project directly on to spinal motorneurons

#67. The central (medullary) chemoreceptors:
A) are stimulated by a rise in the acidity of the cerebral interstitial fluid
B) are stimulated when arterial CO2 tension increases
C) are stimulated when arterial O2 tension decreases
D) are stimulated when arteria pH decreases because of metabolic acidemia (e.g. lactic acid)
E) are entirely responsible for the increase in ventilation in response to rebreathing expired air

#68. Stimulation of the carotid bodies
A) occurs when there is a low arterial O2 tension
B) occurs when there is a raised arterial CO2 tension
C) causes an increase in ventilation
D) causes an increase in arterial blood pressure
E) is attenuated by breathing a high percentage of O2

#69. Concerning the carriage of gases by the blood:
A) a rise in PCO_2 increases the oxygen carrying capacity of the blood
B) at a fixed PO_2 of 40 mmHg, a rise in PCO_2 would increase the O2 content of the blood
C) a rise in PCO_2 assists in off-loading of oxygen in the tissues
D) for blood with a given content of CO_2 a rise in PO_2 increases the PCO_2 of the blood
E) a rise in PO_2 assists in off-loading of CO_2 in the pulmonary capillaries

#70. 2,3-DPG (diphosphoglycerate):
A) decreases the affinity of hemoglobin for oxygen
B) increases in concentration in the erythrocytes in chronic hypoxia
C) increases in concentration in stored blood
D) binds to deoxygenated hemoglobin

#71. As blood passes through the lungs, the CO_2 that is released into the alveolar gas:
A) has been carried in the blood mainly as bicarbonate
B) has been carried in the blood partly in physical solution
C) has been carried in the blood partly by attachment to hemoglobin
D) is released with the assistance of carbonic anhydrase
E) is actively transported across the capillary-alveolar barrier

#72. As blood passes through the lungs, the CO_2 that is released into the alveolar gas:
A) matches, in a steady state, the rate of metabolic production of CO2 by the tissues
B) is greater than the amount of O2 taken into the blood, at a respiratory quotient (RQ) if 0.8
C) diffuses down a partial pressure gradient of about 45 mmHg at rest
D) causes the alveolar CO2 partial pressure to rise even during expiration

#73. With reference to carbon dioxide:
A) more is taken up at any given PCO_2 by desaturated than by fully oxygenated blood
B) most of the blood 'CO_2 content' is in the form of bicarbonate in the plasma
C) it readily diffuses in and out of red blood cells
D) it forms carbonic acid more readily in plasma than in red blood cells
E) its uptake by blood passing through the tissues is enhanced by carbonic anhydrase inhibitors

#74. In the pulmonary circulation:
A) the vascular resistance decreases at birth
B) hypoxia is a vasodilator
C) the arterioles are thinner walled than systemic arterioles of similar diameter
D) the vascular resistance is about 18 times lower than the total peripheral (systemic) resistance
E) if cardiac output doubles, e.g. in exercise, pulmonary artery pressure also doubles

#75. Concerning the pulmonary circulation, in the upright position:
A) the pulmonary artery pressure at the apex is close to zero
B) vessels are more distended at the base of the lungs than at the apex
C) pulmonary artery and vein pressures increase by about the same amount from heart level to lung base
D) the blood flow per unit lung volume is greater at the base than at the apex
E) there is a greater tendency for fluid to escape from pulmonary capillaries at the apex than at the base

#76. Movement of fluid out of pulmonary capillaries:
A) is increased if surfactant is deficient
B) normally occurs to some extent all the time
C) implies movement of fluid into the alveoli
D) is increased in rate by any increase in pulmonary capillary pressure
E) is increased in rate by any increase in pulmonary blood flow

#77. Consider blood leaving a lobe of the lung for which the ventilation-perfusion (V'/Q) ratio is initially 1.0. If the V'/Q ratio then increases to 2.0, in the blood leaving this lobe:
A) the O2 content will rise
B) the PO_2 will rise
C) the PCO_2 will will be reduced
D) the CO_2 content will be reduced
E) both CO2 and O2 content will increase

#78. Concerning ventilation-perfusion (V'/Q) matching/mismatching:
A) in the upright posture, alveolar ventilation per unit lung volume is greater at the apex than at the base
B) in the upright posture, the V'/Q ratio is greater at the apex than at the base
C) in the supine posture, the V'Q ratio is lowest in the back of the lungs
D) blockage of pulmonary capillaries by scattered emboli causes an increase in alveolar dead space
E) collapse of alveoli causes an increase in venous admixture

#79. Concerning alveolar V'/Q ratios in different regions of the lungs:
A) an 'infinite' ratio implies alveolar dead space
B) a ratio of zero implies venous admixture
C) a high ratio causes a higher than average PO_2 in the blood leaving that region
D) a low ratio causes pulmonary capillary blood to leave without reaching the PO_2 in the alveoli of that region
E) an excess of areas with low ratios would necessarily cause a rise in arterial PCO_2

#80. Mary has 13.5 g Hb/100 ml blood with 100% saturated Hb at a PO_2 of 100 mmHg. When she breathes room air, her cardiac output (CO) is 6 L/min, and her O2 use is 300 ml/min. Assuming that Hb carries 1.34 mlO_2/g, and that 0.3 ml of O_2 dissolve per 100 ml of blood at a PO_2 of 100 mmHg, which of the following is true for Mary?
A) her whole-body arteriovenous difference for oxygen is 5 ml per 100 ml
B) her mixed venous oxygen content is 1.5 ml per 100 ml
C) if O2 use increases to 1.2 L/min & CO doubles, tissues are extracting 2X O2 from each liter of blood
D) if she breathes 100% O2 sand alveolar PO_2 becomes 600 mmHg, arterial O2 content increases by 15 ml/L
E) when the alveolar PO_2 becomes 600 mmHg, the arterial PO_2 will rise above 120 mmHg

#81. A 150 lb healthy normal weight man is under anesthesia and is mechanically ventilated at 8 L/min. Respirator TV is 0.8 liters. Inspired gas has 50% O2, CO_2 production is 195 ml/min, O2 use is 240 ml/min:
A) the alveolar ventilation is 6.5 liters per min
B) the patient is being hyperventilated
C) the respiratory quotient (RQ) is greater than 1.2
D) his alveolar CO2 tension is near 327 mmHg

82 All of the following statements concerning lung dead space and airways are correct EXCEPT which one?
A) Physiological dead space = (anatomic dead space) + (alveolar dead space)
B) Anatomic dead space is the volume of the conducting airways
C) Physiological dead space (PDS) increases as a result of pulmonary embolism
D) If ventilation is fixed, increased PDS leads to an increase in arterial CO2 tension
E) The ventilation/perfusion ratio is zero in the alveolar dead space

83) All of the following statements concerning intrapleural pressure (IPP) are correct EXCEPT which one?
A) During quiet breathing IPP is always less than atmospheric
B) When standing, IPP at lung apex is more negative than at the lung base
C) During inspiration, IPP becomes more negative
D) At FRC the IPP equals the alveolar pressure

84. Which one of the following lung volumes or capacities can be measured by spirometry?
A) Functional residual capacity (FRC)
B) Physiologic dead space
C) Residual volume (RV)
D) Total lung capacity (TLC)
E) Vital capacity (VL)

85. An infant born prematurely in gestational week 25 has neonatal respiratory distress syndrome. Which one of the following would be expected in this infant?
A) arterial PO_2 of 100 mmHg
B) collapse of the small alveoli
C) increased lung compliance
D) normal breathing rate

86. Which one of the following is true during inspiration?
A) intrapleural pressure is positive
B) the volume in the lungs is less than the functional residual capacity (FRC)
C) alveolar pressure equals atmospheric pressure
D) alveolar pressure is higher than atmospheric pressure
E) intrapleural pressure is more negative than it is during expiration

87. Which one of the following remains in the lungs after tidal volume (TV) is expired?
A) Vital capacity (VC)
B) Expiratory reserve volume (ERV)
C) Residual volume (RV)
D Functional residual capacity (FRC)
E) Inspiratory capacity

88. Bob has a severe asthmatic attack with wheezing: He has rapid breathing and becomes cyanotic. His arterial PO_2 is 60 mmHg and his PCO_2 is 30 mmHg. For Bob, which one of the following statements is most likely true?
A) forced expiratory volume/forced vital capacity (FEV_1/FVC) is increased
B) ventilation/perfusion (V/Q) ratio is increased in the affected areas of his lungs
C) his arterial PCO_2 is higher than normal because of inadequate gas exchange
D) his arterial PCO_2 is lower than normal because hypoxemia is causing him to hyperventilate
E) his residual volume (RV) is decreased

89. A person has a vital capacity (VC) of 5 L, a tidal volume (TV) of 0.5 L, an inspiratory capacity of 3.5 L, and a functional residual capacity (FRC) of 2.5 L. What is his expiratory reserve volume (ERV)?
A) 4.5 L
B) 3.9 L
C) 3.6 L
D) 3.0 L
E) 1.5 L

90. During quiet breathing at rest, elastic recoil of the lung and chest wall balance each other at which lung volume?
A) TLC
B) RV
C) End of a normal expiration
D) End of a normal inspiration
E) VC

91. Mary is anemic but has normal pulmonary function. All values of the following will be lower than normal EXCEPT:
A) arterial O2 tension
B) arterial O2 content
C) venous O2 tension
D) venous O2 content
E) O2 carrying capacity

92. If blood flow to the left lung is completely blocked by a pulmonary artery embolism, what occurs?
A) Ventilation/perfusion (V/Q) ratio in the left lung will be zero
B) Systemic arterial PO_2 will be elevated
C) V/Q ratio in the left lung will be lower than in the right lung
D) Alveolar PO_2 in the left lung will be approximately equal to the PO_2 in inspired air
E) Alveolar PO_2 in the right lung will be approximately equal to the PO_2 in venous blood

93. Which one of the following remains in the lungs after a maximal expiration?
A) Tidal volume (TV)
B) Vital capacity (VC)
C) Expiratory reserve volume (ERV)
D) Residual volume (RV)
E) Functional residual capacity (FRC)

94. The lung diffusion capacity decreases in all of the following EXCEPT:
A) Interstitial edema
B) Interstitial fibrosis
C) Alveolar edema
D) Emphysema
E) Exercise

95. Compared with the apex of the lung, the base of the lung has
A) a higher pulmonary capillary PO_2
B) a higher pulmonary capillary PCO_2
C) a higher ventilation/perfusion (V/Q) ratio
D) the same V/Q ratio

96. Hypoxemia produces hyperventilation by a direct effect on the
A) phrenic nerve
B) J receptors
C) lung stretch receptors
D) medullary chemoreceptors
E) carotid and aortic body chemoreceptors

97. All of the following cause tissue hypoxia and all reduce O2 content of systemic venous blood EXCEPT
A) Hypoxic hypoxia (e.g. diffusion impairment)
B) Histotoxic hypoxia (e.g. cyanide poisoning)
C) Anemic hypoxia (e.g. low Hb concentration ~ 10g/100 ml of blood)
D) Carbon Monoxide poisoning (e.g. 50% Hb bound with CO)
E) Hypoperfusion hypoxia (e.g. low CO)

98. A lung area is not ventilated due to bronchial obstruction. Pulmonary capillary blood serving that area will have a PO_2 that is
A) equal to atmospheric PO_2
B) equal to mixed venous PO_2
C) equal to normal systemic arterial PO_2
D) higher than inspired PO_2
E) lower than mixed venous PO_2

99. Which causes of hypoxia is characterized by a decreased arterial PO_2 and an increased A-a gradient?
A) Hypoventilation
B) Right-to-left cardiac shunt
C) Anemia
D) Carbon monoxide poisoning
E) Ascent to high altitude

100. A patient with severe pulmonary fibrosis is evaluated and has the following arterial blood gases: pH = 7.48, Pao_2 = 55 mmHg, and $Paco_2$ = 32 mmHg. Which statement best explains the observed value of $Paco_2$?
A) The increased pH stimulates breathing via peripheral chemoreceptors
B) The increased pH stimulates breathing via central chemoreceptors
C) The decreased Pao_2 inhibits breathing via peripheral chemoreceptors
D) The decreased Pao_2 stimulates breathing via peripheral chemoreceptors
E) The decreased Pao_2 stimulates breathing via central chemoreceptors

101. At rest the O2 tension is lowest in the venous blood coming from which one of the following?

A) Brain

B) Kidney

C) Skeletal Muscle

D) Heart

E) Skin

102. Which of the following will occur as a result of residing at high altitude?

A) Hypoventilation

B) Arterial PO_2 greater than 100 mmHg

C) Decreased 2,3-diphosphoglycerate (DPG) concentration

D) Shift to the right of the hemoglobin-O_2 dissociation curve

E) Respiratory acidosis

103. The pH of venous blood is only slightly more acid than the pH of arterial blood because

A) CO_2 is a weak base

B) there is no carbonic anhydrase in venous blood

C) the H^+ generated from CO_2 and H_2O is buffered by HCO_3^- in venous blood

D) the H^+ generated from CO_2 and H_2O is buffered by deoxyhemoglobin in venous blood

E) oxyhemoglobin is a better buffer for H^+ than is deoxyhemoglobin

104. In a maximal expiration, the total volume expired is

A) tidal volume (TV)

B) vital capacity (VC)

C) expiratory reserve volume (ERV)

D) residual volume (RV)

E) functional residual capacity (FRC)

105. Which person would be expected to have the largest A-a O2 gradient?

A) Person with pulmonary fibrosis

B) Person who is hypoventilating

C) Person at 12,000 feet above sea level

D) Person with normal lungs breathing 50% O_2

E) Person with normal lungs breathing 100% O_2

106. If ventilation demand becomes greater than normal, normally quiet neurons of which structure become active?

A) Apneustic center

B) Dorsal respiratory group

C) Nucleus tractus solitarius

D) Pneumotaxic center

E) Ventral respiratory group

107. A 43-year-old woman is biking in the mountains, where the atmospheric pressure is 700 mmHg and the relative humidity is close to zero. What is the partial pressure (mmHg) of oxygen in the mountain air?

A) 100
B) 110
C) 133
D) 147
E) 92

108. The basic rhythm of respiration is generated by neurons located in the medulla. Which of the following limits the duration of inspiration and increases respiratory rate?

A) Apneustic center
B) Dorsal respiratory group
C) Nucleus of the tractus solitarius
D) Pneumotaxic center
E) Ventral respiratory group

109. The forces governing the diffusion of a gas through a biological membrane include the pressure difference across the membrane ΔP, the cross-sectional area of the membrane (A), the solubility of the gas (S), the distance of diffusion (d), and the molecular weight of the gas (MW). Which of the following changes decreases gas diffusion?

	ΔP	A	S	d	MW
A)	Decrease	Decrease	Decrease	Decrease	Decrease
B)	Decrease	Decrease	Decrease	Increase	Increase
C)	Decrease	Decrease	Increase	Decrease	Decrease
D)	Decrease	Increase	Increase	Decrease	Decrease
E)	Increase	Increase	Increase	Increase	Increase

110. At FRC, Doris' intrapleural pressure is -5cm H_2O. What is her intrapleural pressure during inspiration?

A) +1 cm H_2O
B) +4 cm H_2O
C) 0 cm H_2O
D) -3 cm H_2O
E) -7 cm H_2O

111. Tom is at the top of Pike's Peak, where the barometric pressure is 462 mmHg. Partial pressures of the various gases in his alveolar air are as follows:

Nitrogen 328 mmHg
Carbon dioxide 20 mmHg
Water vapor pressure 47 mmHg

What is the oxygen partial pressure (PO_2) in his alveoli?

A) 52 mmHg
B) 67 mmHg
C) 75 mmHg
D) 96 mmHg
E) 104 mmHg

112. Dan has a static pulmonary compliance of 0.25 L/cm H_2O. His intrapleural pressure changes from -4 cm H_2O to -8 cm H_2O when he inhales. How much air did he inhale?

A) 0.5 liter
B) 0.75 liter
C) 1.0 liter
D) 1.5 liter
E) 2.0 liter

113. Jon breathes in as much air as he can and then exhales as much air as possible. His lung volume at maximum inspiration is 6.0 L, and the lung volume after maximum expiration is 1 L. His TV at rest is 0.5 liter, and his FRC is 3.5 liters. What is his VC?

A) 3.0 liters
B) 3.5 liters
C) 4.0 liters
D) 5.0 liters
E) 5.5 liters

114. Normal inspiration results from

A) decreased intrapleural pressure
B) increased alveolar pressure
C) decreased intrapleural pressure and an increased alveolar pressure
D) depression of the thorax
E) relaxation of the diaphragm

115. During the initial phase of inspiration in a healthy subject at rest,

A) intrapulmonary pressure rises
B) intra-abdominal pressure rises
C) intrapulmonary and intra-abdominal pressures rise
D) there is less muscular effort than during the initial phase of expiration
E) the larynx is elevated

116. In young, healthy men the compliance for both the pulmonary system and the thoracic cage are each 0.2 L/cm of H_2O. What is the compliance of the respiratory system?

A) 0.01
B) 0.1
C) 1.0
D) 10
E) 100

117. Which of the following statements is correct about surfactant?

A) It is distributed homogeneously throughout the liquid that covers the alveolar epithelium
B) It s usually at a high concentration in the lung of the premature infant
C) It causes surface tension of small alveoli to be less than that of large alveoli
D) It increases surface tension
E) It is not formed by alveolar cells

118. In a standing person, which best describes the pattern of ventilation in the lungs during quiet breathing?

A) surfactant keeps each region of the lung equally distended and ventilated

B) gravity keeps the lung base more poorly expanded and ventilated than the apex

C) gravity keeps the lung base more poorly expanded and better ventilated than the apex

D) gravity keeps the lung base more expanded and ventilated than the apex

E) gravity keeps the lung base more expanded and less ventilated than the apex

119. Which one of the following best describes factors that increase the work of breathing?

A) airway constriction

B) increased tidal volume

C) airway constriction and increased tidal volume

D) increased compliance of the lungs

E) decreased density of the inspired gas

120. What is the most efficient method for an asthmatic to use during respiration?

A) hyperventilation

B) higher RR and lower TV than a healthy subject

C) lower RR and higher TV than the healthy subject

D) a RR and TV comparable to that of a healthy person

E) a RR and TV comparable to that for a person with a reduced lung compliance

121. The only factor below that is not a determinant of the quantity of gas that diffuses through a barrier is:

A) surface area available for diffusion

B) thickness of barrier

C) molecular weight of diffusing particle

D) viscosity of the medium

E) driving pressure

122. When inhaled, which of the following gases would diffuse most slowly from the lungs into the blood:

A) CO_2 at a PCO_2 of 60 mmHg

B) CO at a PCO of 0.5 mmHg

C) O_2 at a PO_2 of 130 mmHg

D) O_2 at a PO_2 of 150 mmHg

E) nitrous oxide at a PN_2O of 0.3 mmHg

123. Which of the following procedures will cause an immediate cessation of respiration?

A) transection of the cord at C6

B) transection of the cord at C2

C) transection between the medulla and pons

D) transection of the cord at T3

E) transection of the cord at L1

124. Which of the following statements can be said about the pneumotaxic center?
A) it is in the midbrain
B) it inhibits inspiratory activity
C) it contains the major central chemoreceptor area
D) it causes long inspiratory gasps when separated from the more superior parts of the brain
E) it causes long expiratory gasps when separated from the more superior parts of the brain

125. Which is most important in increasing ventilation in response to small increases in body fluid PCO_2?
A) pulmonary chemoreceptors
B) venous chemoreceptors
C) lung receptors
D) peripheral chemoreceptors
E) medullary chemoreceptors

126. A major importance the peripheral chemoreceptors is that they respond to
A) decreases in PO_2 in the venous blood
B) decreases in PO_2 in the arterial blood
C) decreases in PO_2 in the cerebrospinal fluid
D) increases in PO_2 in the venous blood
E) increases in PO_2 in the arterial blood

127. Chemoreceptors in the carotid and aortic bodies send impulses via the 9^{th} and 10^{th} cranial nerves to the respiratory centers. Which of the following best characterizes their function?
A) send increasing frequencies of impulses up their nerves as the PO_2 of arterial blood increases
B) breath holding causes a more rapid increase in ventilation in response to PCO_2 than do central chemoreceptors
C) are less sensitive to hypoxia than the central chemoreceptors
D) are least important to the control of respiration during sleep and barbiturate depression
E) affect only respiratory rate

128. The peripheral chemoreceptors produce a more pronounced increase in ventilation in response to
A) a decrease in arterial PO_2 from 150 to 90 mmHg than from 70 to 40 mmHg under usual resting conditions
B) a change in arterial PO_2 from 100 to 80 mmHg at a PCO_2 of 48 mmHg than at a PCO_2 of 40 mmHg
C) both of the above statements
D) a 30% reduction in the O_2 content of arterial blood, as in anemia, than to a 30% reduction in arterial PO_2
E) a change in pH from 7.4 to 7.3 than cyanide poisoning

129. If the 9^{th} and 10^{th} cranial nerves are blocked in the neck, the subject will no longer respond to
A) hypercapnia by causing an increased respiratory minute volume
B) alkalosis by causing an increased respiratory minute volume
C) hypoxia by causing an increased respiratory minute volume
D) hypercapnia or acidity by causing an increased respiratory minute volume
E) acidity or hypoxia by causing an increased respiratory minute volume

130. Which of the following usually causes an increased impulse frequency in afferent neurons from carotid bodies?

A) CO poisoning
B) anemia
C) hyperoxemia
D) hypoxic hypoxia
E) a 20% reduction in carotid body blood flow

131. A patient is brought to the ER suffering from an overdose of a barbiturate. He exhibits hypoventilation caused by respiratory center depression. He is given 100% O_2 and his ventilation decreases markedly, but his mixed venous plasma PO_2 rises to 130 mmHg. The patient probably

A) is well oxygenated and needs no additional treatment
B) should be switched to 95% O_2 + 5% CO_2
C) should receive a vasoconstrictor agent
D) should be treated for systemic acidosis
E) should be treated for systemic alkalosis

132. Which of the following would not be a useful change with acclimatization to high altitude?

A) hyperventilation
B) polycythemia
C) increased number of systemic capillaries
D) shift to the right of the O_2 dissociation curve
E) a decrease in plasma 2,3-diphosphoglycerate concentration

133. A decrease in plasma pH

A) causes a decrease in ventilation through the stimulation of the carotid bodies
B) is frequently associated with a decrease in arterial PCO_2
C) is frequently associated with an increase in ventilation in metabolic acidosis
D) may not cause as great a decrease in the pH of the cerebrospinal fluid because the blood-brain barrier and blood-cerebrospinal fluid barrier are not freely permeable to H^+
E) is caused by a decrease in hydrogen ion concentration

134. The trachea, bronchi, and bronchioles do all of the following EXCEPT

A) warm the air
B) filter the air to remove impurities
C) distribute air to exchange surfaces
D) remove O_2 from the air
E) humidify the air

135. Which one of the following conditions does **NOT** occur on a large inspiration?

A) inspiratory muscles contract
B) size of the thoracic cavity increases
C) pleural pressure becomes more positive
D) transpulmonary pressure becomes more positive
E) lung becomes more inflated

136. During expiration, which of the following does **NOT** occur?

A) respiratory muscles relax

B) pleural pressure becomes less negative

C) transpulmonary pressure decreases

D) lung deflates

E) alveolar pressure decreases below atmospheric pressure

137. Transpulmonary pressure is greatest at the

A) end of expiration

B) middle of inspiration

C) end of inspiration

D) middle of expiration

E) beginning of inspiration

138. All of the following can be determined from a spirogram **EXCEPT**

A) expiratory reserve volume

B) inspiratory reserve volume

C) FEV1

D) functional residual capacity

E) inspiratory capacity

139. Blood circulation to the lung is greatest in the parts

A) furthest from the heart

B) closest to the ground

C) closest to the midline

D) furthest from the ground

E) closest to the heart

140. The greatest partial pressure gradient across the alveolar membrane is found for

A) H_2O

B) CO_2

C) N_2

D) O_2

141. The carbon dioxide transport route that is most used is:

A) carbamino hemoglobin

B) bicarbonate

C) dissolved in plasma

D) carbonic acid

E) dissolved in RBC intracellular fluid

142. Carbonic anhydrase is:

A) a carrier of CO2 in the blood

B) a storage site for CO2

C) an enzyme that accelerates the combination of CO2 and water

D) an enzyme that splits the bicarbonate ion

E) an enzyme that splits carbonic acid into hydrogen and bicarbonate ions

143. For small changes in the following, which is the most powerful stimulant to alveolar ventilation?

A) increased P_{O2}

B) decreased P_{O2}

C) increased H^+

D) decreased arterial pH

E) increased P_{CO2}

144. Which causes a substantial increase in total O2 carrying capacity of arterial blood (ml of O_2/100 ml)?

A) Breathing pure oxygen

B) Increasing blood temperature

C) Increasing hydrogen-ion concentration

D) Increasing alveolar ventilation

E) Increasing the hematocrit

145. Which one of the following statements regarding intrapleural pressure is true?

A) It is defined as the pressure inside the lungs

B) It is defined as the difference between alveolar and atmospheric pressures

C) It becomes more negative when the residual volume increases

D) It prevents the lungs from collapsing at the end of expiration

E) It is generally more positive than alveolar pressure

146. A healthy person is flying in an airplane that has been pressurized to 10,000 feet above sea level (atmospheric pressure = 500 mmHg). Which of the following statements is true in this person while flying?

A) Alveolar PO_2 remains normal since the fractional composition of the air O2 remains unchanged (O_2 = 21%)

B) Alveolar PO_2 will be increased because water vapor pressure will be decreased

C) Alveolar PO_2 decreases but not enough to significantly affect Hb saturation in the passenger's arterial blood

D) Hemoglobin saturation in the passenger's arterial blood will be less than 80%

147. A 27-year-old man is breathing quietly. He then inhales as much air as possible and exhales as much air as he can, producing the spirogram shown. What is his expiratory reserve volume?

A) 2.0 liters

B) 2.5 liters

C) 3.0 liters

D) 3.5 liters

E) 4.0 liters

148. For the spirogram shown, what is his vital capacity?

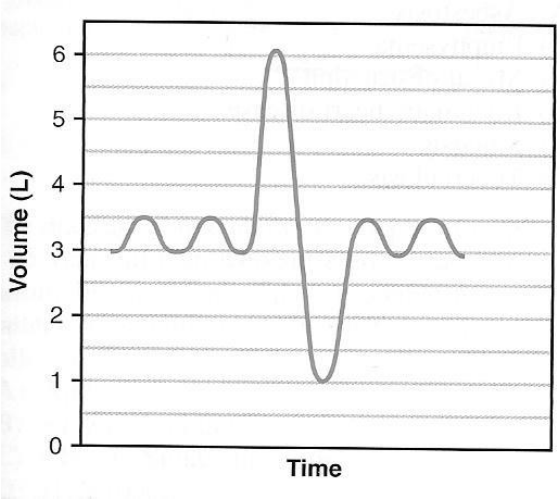
A) 2.0 liters

B) 2.5 liters

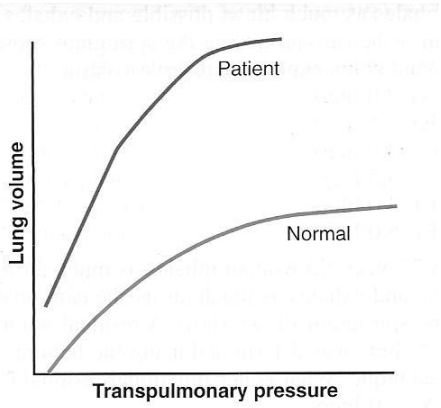
C) 3.0 liters

D) 3.5 liters

E) 5.0 liters

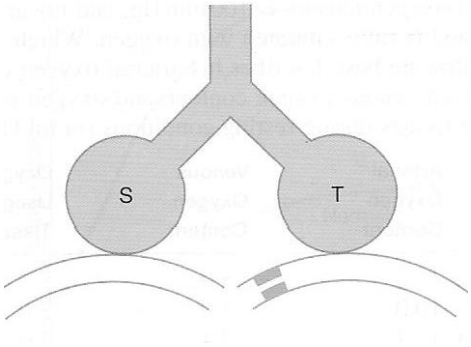


149. The volume-pressure curves shown were obtained from a normal subject and a patient suffering from a pulmonary disease.
Which of the following abnormalities is more likely present in the patient?



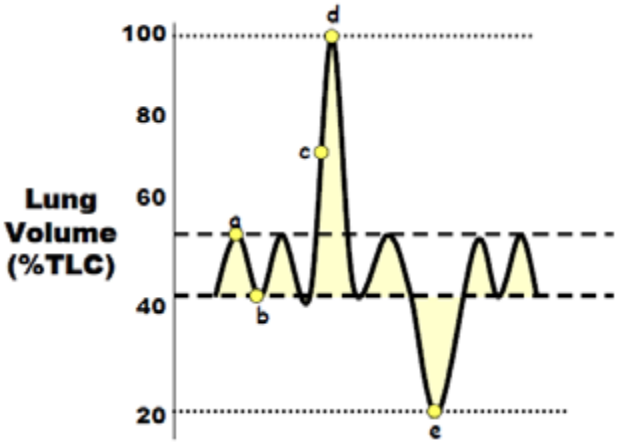
A) Asbestosis
B) Emphysema
C) Mitral obstruction
D) Rheumatic heart disease
E) Silicosis

150. The diagram shows two lung units (S and T) with their blood supplies. Lung unit S has an ideal relationship between blood flow and ventilation. Lung unit T has a compromised blood flow. What is the relationship between alveolar dead space (D_{ALV}), physiologic dead space (D_{PHY}), and anatomic dead space D_{ANAT} for these lung units?



	Lung Unit S	Lung Unit T
A)	$D_{PHY} < D_{ANAT}$	$D_{PHY} = D_{ANAT}$
B)	$D_{PHY} = D_{ALV}$	$D_{PHY} > D_{ALV}$
C)	$D_{PHY} = D_{ANAT}$	$D_{PHY} < D_{ANAT}$
D)	$D_{PHY} = D_{ANAT}$	$D_{PHY} > D_{ANAT}$
E)	$D_{PHY} > D_{ANAT}$	$D_{PHY} < D_{ANAT}$

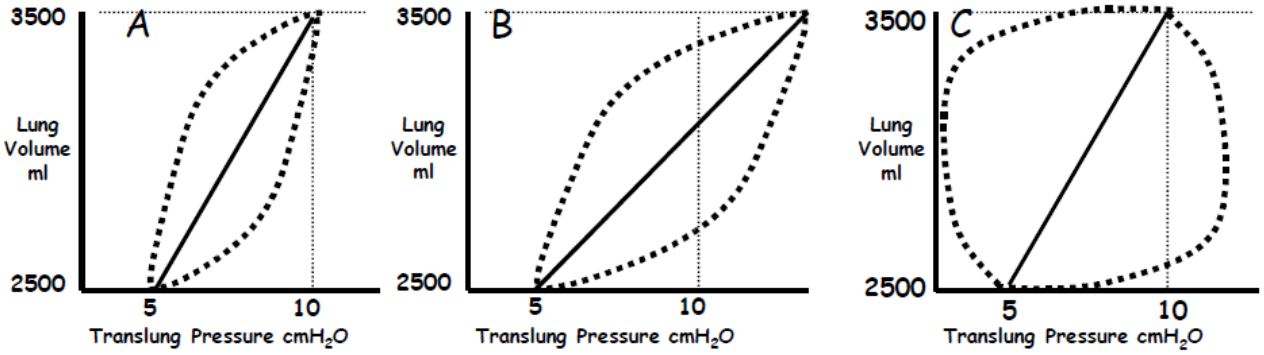
<u>For the next two questions use the adjacent figure</u>



151. Which point most closely corresponds to zero chest wall pressure?
a)
b)
c)
d)
e)

152. At which point is the chest and lung recoil force equal but oppositely directed?
a)
b)
c)
d)
e)

For the next two questions refer to the tidal volume pressure-volume loops that were obtained from three different patients, A, B & C as shown below



153. Which statement best describes the relative elastic energy required for inspiration?

a) B is greater than A

b) B is greater than C

c) A is greater than C

d) B is greater than both A and C

e) C is greater than B

154. The lung compliance of Patient C is closest to which of the following expressed in ml/cmH20?

a) 50

b) 100

c) 200

d) 250

e) 500

155. Respiratory tests of a patient indicate the following: expiratory reserve volume=1200 ml, inspiratory reserve volume=3200 ml, tidal volume=500 ml and residual volume= 1000 ml.

What is the patient's vital capacity?

a) 2200 ml

b) 2800 ml

c) 4900 ml

d) 5800 ml

156. A patient is placed in a chamber that has a pressure of 1047 Torr. He receives hyperbaric 02 therapy of 100%

02. The 02 tension in his trachea is closest to which of the following?

a) 700 torr

b) 725 torr

c) 1000 torr

d) 1047 torr

e) 1050 torr

157. A patient with a normal body weight has a TV of 800 ml, an anatomical dead space of 300 ml and a respiratory rate of 10 breaths per minute. His alveolar ventilation is closest to which of the following?

a) 3500 ml/min

b) 4000 ml/min

c) 5000 ml/min

d) 5500 ml/min

158. Which of the following would hinder the release of O2 from blood to tissues?

a) An increase in P50

b) A shift in the SO2 curve to the right

c) A decrease in the affinity of Hb for O2

d) An increase in blood CO content

e) All of the above

159. Which statement best describes the features of the pulmonary vascular resistance?

a) It depends on lung volume

b) It depends on whether blood vessels are intra or extra- alveolar

c) It depends on pulmonary intravascular blood pressure

d) It depends on the location of the blood vessels within the lung

e) It depends on all of the above

160. What is the effect of regional airway obstructions in the lung?

a) Increases blood shunting

b) Increases O2 tension of inspired air

c) Decreases total ventilation

d) Decreases pulmonary artery pressure

e) Increases the ventilation/perfusion ratio