The Respiratory System – Ch. 23

*diffusion between blood & air occurs at alveoli of lungs

**Functions of Respiratory System**

*five basic functions:
  * providing extensive area for gas exchange between air & circulating blood
  * moving air to & from exchange surfaces of lungs
  * protecting respiratory surfaces from dehydration, temperature changes, or other environmental variations & defending respiratory system & other tissues from invasion of pathogens
  * producing sounds involved in speaking, singing, & nonverbal communication
  * providing olfactory sensations to CNS from olfactory epithelium in superior portions of nasal cavity
  * in addition, capillaries of lungs indirectly assist in regulation of blood volume & blood pressure, through conversion of angiotensin I to angiotensin II

**Organization of Respiratory System**

*upper respiratory system: consists of nose, nasal cavity, paranasal sinuses, & pharynx
  * these passageways filter, warm, & humidify incoming air – protecting more delicate surfaces of lower respiratory system - & cool & dehumidify outgoing air
*lower respiratory system: includes larynx (voice box), trachea (windpipe), bronchi, bronchioles, & alveoli of lungs
*respiratory tract: consists of airways that carry air to & from exchange surfaces of lungs; divided into:
  * **conducting portion**: begins at entrance to nasal cavity & extends through pharynx & larynx & along trachea, bronchi, & bronchioles to **terminal bronchioles**
  * **respiratory portion**: includes delicate respiratory bronchioles & sites of gas exchange, alveoli

**Respiratory Mucosa**

* lines conducting portion of respiratory system
  * **mucosa is mucosa membrane** – which consists of epithelium & underlying layer of loose connective tissue

**Respiratory Epithelium**

* pseudostratified, ciliated, columnar epithelium with numerous goblet cells lines nasal cavity & superior portion of pharynx
  * structure of epithelium changes as it proceeds along respiratory tract
  * portions of pharynx which conduct air to lower respiratory tract also convey food to esophagus
    * pharyngeal epithelium must therefore provide protection from abrasion & chemical attack

**Lamina Propia**

* underlying layer of loose connective tissue that supports respiratory epithelium
  * in upper respiratory system & in trachea & bronchi, propia contains mucous glands that discharge their secretions onto epithelial surface
  * propia in conducting portions of lower respiratory system contains bundles of smooth muscle cells
*Respiratory Defense System*
*delicate exchange surfaces of respiratory system can be severely damaged if inspired air becomes contaminated with debris or pathogens*
*such contamination is prevented by series of filtration mechanisms that together make up respiratory defense system*
*along much of length of respiratory tract, goblet cells in epithelium & mucous glands in lamina propia produce sticky mucous that bathes exposed surfaces*
*in nasal cavity, cilia sweep that mucous & any trapped debris or microorganisms toward pharynx, where it will be swallowed & exposed to acids & enzymes of stomach*
*filtration here removes most virtually all particles larger than 10µm from inspired air

**The Upper Respiratory Tract**
*consists of nose, nasal cavity, paranasal sinuses, & pharynx

**Nose & Nasal Cavity**
*nose is primary passageway for air entering respiratory system*
*air normally enters system through paired external nares (nostrils), which open into nasal cavity*
*vestibule: space contained within flexible tissues of nose*
*epithelium of vestibule contains coarse hairs that extend across external nares, which trap large airborne particles & prevent them from entering nasal cavity*
*nasal septum divides nasal cavity into left & right portions*
*cartilage plate supports bridge & apex of nose*
*mucous secretions produced in associated paranasal sinuses, aided by tears draining through nasolacrimal ducts, help keep surfaces of nasal cavity moist & clean*
*to pass from vestibule to internal nares, air tends to flow between adjacent conchae, though superior, middle, & inferior meatuses: narrow grooves rather than open passageways, & incoming air bounces off conchal surfaces & churns around like stream flowing over rapids, creating turbulence serves purpose – as air eddies & swirls, small airborne particles are likely to come in contact with mucus that coats lining of nasal cavity*
*also allows extra time for air warming & humidifying*
*bony hard palate, formed by portions of maxillary & palatine bones, forms floor of nasal cavity & separates oral & nasal cavities*
*fleshy soft palate extends posterior to hard palate, marking boundary between superior nasopharynx & rest of pharynx*
*nasal cavity opens into nasopharynx at internal nares*

**Nasal Mucosa**
*prepares air breathed in for arrival at lower respiratory system*
*lamina propia contains extensive network of large & highly expandable veins*
*this extensive vascularization provides mechanism for warming & humidifying incoming air*
*outgoing air, already warm & humidified, warms nasal mucosa, & moisture condenses on epithelial surfaces

**The Pharynx**
*chamber shared by digestive & respiratory systems*
*extends between internal nares & entrances to larynx & esophagus*
*divided into three regions:*
*nasopharynx: superior portion of pharynx; lined by same pseudostratified ciliated columnar epithelium as that in nasal cavity*
*oropharynx: extends between soft palate & base of tongue at level of hyoid bone*
*laryngopharynx: narrow; inferior portion of pharynx, includes portion of pharynx that lies between hyoid bone & entrance to larynx & esophagus*
### The Larynx

*inhaled air leaves pharynx by passing through **glottis**, narrow opening
* **larynx**: surrounds & protects glottis

#### Cartilages of Larynx

*three large, unpaired cartilages form body of larynx:
  * **thyroid cartilage**: largest laryngeal cartilage
    *consists of hyaline cartilage, forming most of anterior & lateral walls of larynx
    *is U-shaped in section, incomplete posteriorly
    *prominent anterior surface is **Adam’s apple**
  * **cricoid cartilage**: sits inferior to thyroid cartilage
    *posterior portion is greatly expanded, providing support in absence of thyroid cartilage
    *both cricoid & thyroid cartilage protect glottis & entrance of trachea, & their broad surfaces provide sites for attachment of important laryngeal muscles & ligaments
  * **epiglottis**: shoehorn-shaped; projects superior to glottis
    *composed of elastic cartilage
    *during swallowing, larynx is elevated & epiglottis folds back of glottis, preventing entry of liquids or solid food into respiratory passageways
*contains three pairs of smaller hyaline cartilages:
  * **arytenoid cartilages**: articulate with superior border of enlarged portion of cricoid cartilage
  * **corniculate cartilages**: articulate with arytenoids cartilages; both corniculate & arytenoids cartilages are involved with opening & closing of glottis & production of sound
  * **cuneiform cartilages**: elongated, curving; lie within folds of tissue that extend between lateral aspect of each arytenoid cartilage & epiglottis

#### Laryngeal Ligaments

* **intrinsic ligaments**: bind all nine cartilages together to form larynx
* **extrinsic ligaments**: attach thyroid cartilage to hyoid bone & cricoid cartilage to trachea
* **ventricular ligaments & vocal ligaments**: extend between thyroid cartilage & arytenoid
  *covered by folds of laryngeal epithelium that project into glottis
  *ventricular folds: relatively elastic; known as **false vocal chords**; superior folds within which ventricular ligaments lie
  *help prevent foreign objects from entering glottis & provide protection for more delicate **vocal folds**: guard entrance to glottis; highly elastic; involved with production of sounds → known as true vocal chords

#### Sound Production

*air passing through glottis vibrates vocal folds & produces sound waves
*pitch of sound depends on diameter, length, & tension of vocal folds
  *length & diameter are directly related to size of larynx
  *tension is controlled by contraction of voluntary muscles that change position of arytenoid cartilages relative to that of thyroid cartilage
* **phonation**: sound production at larynx; one component of speech
* **articulation**: required for clear speech; modification of those sounds by other structures

#### Laryngeal Musculature

*larynx is associated with two groups of muscles:
  * **extrinsic laryngeal muscles**: includes muscles of neck & pharynx; positions & stabilizes larynx
  * **intrinsic laryngeal muscles**: regulates tension in vocal folds; opens & closes glottis
The Trachea

*called windpipe; rough flexible tube with diameter of about 2.5cm, & length of about 11cm
*mucosa resembles that of nasal cavity & nasopharynx
*submucosa: thick layer of connective tissue that surrounds mucosa
  *contains mucous glands that communicate with epithelial surface through number of secretory ducts
*contains 15-20 tracheal cartilages, which are bound to each other by elastic annular ligaments
  *tracheal cartilages stiffen tracheal walls & protect airway; also prevent its collapse or overexpansion as pressures change in respiratory system
  *each cartilage is C-shaped – closed portion protects anterior & lateral surfaces of trachea
  *an elastic ligament & trachealis, band of smooth muscle, connect ends of tracheal cartilage
  *contraction of trachealis muscle alters diameter of trachea, changing trachea’s resistance to flow

The Primary Bronchi

*trachea branches within mediastinum, giving rise to right & left bronchi
*carina: ridge that marks line of separation between 2 bronchi
*histological organization is same as that of trachea
*right primary bronchus supplies right lung & is larger in diameter & descends toward lung at steeper angle than left; left bronchi supplies left lung
*before branching further, each primary bronchus travels to hilus of lung, groove along medial surface of its lung
  *hilus provides access for entry to pulmonary vessels & nerves
*entire array is firmly anchored in meshwork of dense connective tissues known as root of lung

The Lungs

*each lung is blunt cone, with tip, or apex, pointing superiorly, & broad concave inferior portion, or base
*Lobes & Surfaces of Lungs
  *lungs have distinct lobes separated by deep fissures
  *right has 3 lobes: superior, middle, & inferior, separated by horizontal & oblique fissures
  *left has 2 lobes: superior & middle, separated by oblique fissure
  *right lung is broader than left because most of heart & great vessels project into left thoracic cavity
  *left lung is longer than right because diaphragm rises on right side to accommodate mass of liver
*costal surface: curving anterior portion of lung that follows inner contours of rib cage
*mediastinal surface: contains hilus; has more irregular shape; bear grooves that mark passage of great vessels & of cardiac impressions: concavities that conform to shape of pericardium
  *cardiac impression on left lung is deeper than that of right lung
*margin of left lung is indented at cardiac notch
*The Bronchi
  *bronchial tree: formed from primary bronchi & their branches
  *extrapulmonary bronchi: another name for left & right primary bronchi because they are outside lungs
  *as primary bronchi enter lungs they divide to form smaller passageways called intrapulmonary bronchi
*each primary bronchus divides to form secondary bronchi
*right primary bronchus divides into 3 secondary bronchi (right lung has 3 lobes):
  *superior lobar bronchus, middle lobar bronchus, & inferior lobar bronchus
*left primary bronchus divides into 2 secondary bronchi (left lung has 2 lobes):
  *superior lobar bronchus & inferior lobar bronchus
within each lung, secondary bronchi branch to form tertiary bronchi, which supplies air to single bronchopulmonary segment: specific region of one lung
walls of primary, secondary, & tertiary bronchi contain progressively lesser amounts of cartilage

*The Bronchioles*
- each tertiary bronchus branches several times within bronchopulmonary segment, giving rise to multiple bronchioles
- these branch further into finest conducting branches called terminal bronchioles
- walls of bronchioles, which lack cartilaginous supports, are dominated by smooth muscle tissue
- varying diameter of bronchioles provides control over amount of resistance to airflow & distribution of air within lungs
- sympathetic activation leads to enlargement of airway diameter, or bronchodilation
- parasympathetic stimulation leads to bronchoconstriction: reduction in diameter of airways; occurs during allergic reactions
- both bronchodilation & bronchoconstriction alter resistance to airflow toward or away from respiratory exchange surfaces

*Pulmonary Lobules*
- connective tissues of root of each lung extend into lung’s parenchyma
- interlobular septa: finest partitions of trabeculae that divide lung into pulmonary lobules, each supplied by branches of pulmonary arteries, pulmonary veins, & respiratory passageways
- each terminal bronchiole delivers air to single pulmonary lobule
- within lobule, terminal bronchiole branches to form several respiratory bronchioles: thinnest & most delicate branches of bronchial tree; deliver air to exchange surfaces of lungs
- preliminary filtration & humidification of incoming air are completed before air leaves terminal bronchioles

*Alveolar Ducts & Alveoli*
- alveolar ducts: multiple alveoli along regions to which respiratory bronchioles are connected
- alveolar sacs: where alveolar ducts end; common chambers connected to multiple individual alveoli
- each lung contains about 150 million alveoli, & their abundance gives lung an open, spongy appearance
- extensive network of capillaries is associated with each alveoli; capillaries are surrounded by network of elastic fibers
- this elastic tissue helps maintain relative positions of alveoli & respiratory bronchioles
- recoil of these fibers during exhalation reduces size of alveoli & helps push air out of lungs

*The Alveolus & Respiratory Membrane*
- alveolar macrophages: roam & patrol epithelium, phagocytizing any particulate matter that has eluded respiratory defenses & reached alveolar surfaces
- septal cells, also called surfactant cells: scattered among squamous cells; large cells that produce oily secretion, called surfactant, containing mixture of phospholipids & proteins
- surfactant is important because it reduces surface tension in liquid coating alveolar surface
- alveolar walls are very delicate, & without surfactant the surface tension would be so high that alveoli would collapse

*Respiratory Membrane*
- where gas exchange occurs
- composite structure consisting of 3 parts:
  - squamous epithelial cell lining of alveolus
  - endothelial cell lining adjacent capillary
  - fused basement membranes that lie between alveolar & endothelial cells
*diffusion across respiratory membrane proceeds very rapidly because:
  *distance between alveolar air & blood is small
  *both oxygen & carbon dioxide are lipid-soluble

*The Blood Supply to Lungs*
*respiratory exchange surfaces receive blood from arteries of pulmonary circuit
*pulmonary arteries enter lungs at hilus & branch with bronchi as they approach lobules
*each lobule receives an arteriole & a venule, & a network of capillaries surrounds each alveolus
directly beneath respiratory membrane
*blood from alveolar capillaries passes through pulmonary venules & then enters pulmonary veins,
which deliver it to left atrium
*conducting portions of respiratory tract receive blood from external carotid arteries, thyrocervical
arteries, & bronchial arteries
*capillaries supplied by bronchial arteries provide oxygen & nutrients to conducting passageways of
lungs
*venous blood flows into pulmonary veins, bypassing rest of systemic circuit & diluting oxygenated
blood leaving alveoli

*The Pleural Cavities & Pleural Membranes*
*pleural cavity: each one holds one lung; separated by mediastinum; lined by serous membrane called
pleura
*each cavity actually represents potential space rather than open chamber
*parietal pleura: covers inner surface of thoracic wall & extends over diaphragm & mediastinum
*visceral pleura: covers outer surfaces of lungs, extending into fissures between lobes
*pleural fluid: small amount secreted by both pleurae
  *gives moist, slippery coating that provides lubrication, thereby reducing friction between parietal &
visceral surfaces during breathes
*pleuridy: condition where normal coating of pleural fluid is unable to prevent friction causing pain &
pleural inflammation

*Respiratory Physiology*
*external respiration: includes all processes involved in exchange of oxygen & carbon dioxide between
interstitial fluids of body & external environment
*goal & primary function: meet respiratory demands of living cells
*internal respiration: absorption of oxygen & release of carbon dioxide by those cells
*4 integrated steps of external respiration:
*Pulmonary Ventilation
*breathing; which involves physical movement of air into & out of lungs
*primary function is to maintain adequate alveolar ventilation, air movement into & out of alveoli
  *prevents buildup of carbon dioxide in alveoli & ensures continuous supply of oxygen that keeps
pace with absorption by bloodstream
*Boyle’s Law: Gas Pressure & Volume
*primary differences between liquid & gas reflects interactions between individual molecules
*gas molecules are in constant motion; whereas liquid molecules are held tightly together
*gas pressure changes indirectly with volume of closed container
*Pressure & Airflow to Lungs
*air moves from area of higher pressure to area to lower pressure
*inhalation & exhalation involve changes in volume of lungs → which create pressure gradients
that move air into & out of respiratory tracts
*Fluid bond exists between parietal & visceral pleura covering lungs
*as result surface of each lung sticks to inner wall of chest & superior surface of diaphragm
*Volume of thoracic cavity changes when diaphragm changes position or rib cage moves:
*When diaphragm contracts, it tenses & moves inferiorly, increasing volume of thoracic cavity & exerting pressure on contents of abdominopelvic cavity
*Superior movement of cage increases volume of thoracic cavity
*At start of breath, pressure inside & outside thoracic cavity are identical; when thoracic cavity enlarges, pleural cavities expand to fill space, lowering pressure inside lungs, & pulling air into lungs (from high pressure to low)
*Compliance: indication of lungs expandability
*Lower compliance, the greater force required to fill & empty lungs
*Factors affecting:
*Connective tissue structure of lungs – loss will increase compliance
*Level of surfactant production – collapse of alveoli on expiration, due to inadequate surfactant, reduces compliance
*Mobility of thoracic cavity – arthritis reduce compliance

*Pressure Changes during Inhalation & Exhalation

*Intrapulmonary Pressure
*Direction of airflow is determined by relationship between atmospheric pressure & intrapulmonary pressure
*Intrapulmonary pressure: intra-alveolar pressure; pressure measured inside respiratory tract, at alveoli
*Size of pressure gradient increases greatly when breathing is heavy as opposed to when it is quiet
*When abdominal & intrapleural pressures rise, venae cavae collapse & venous return decreases
*Resulting fall of cardiac output & blood pressure stimulates aortic & carotid baroreceptors → whose stimulation causes reflexive increase in heart rate & peripheral vasoconstrictions

*Intrapleural Pressure
*Pressure measures in space between parietal & visceral pleurae
*Pressure is below atmospheric pressure due to relationship between lungs & body wall
*Elastic fibers are continuously fighting bond between parietal & visceral pleurae & pulling lungs away from chest wall & diaphragm → this pull lowers intrapleural pressure

*Respiratory Cycle
*Respiratory cycle: single cycle of inhalation & exhalation
*Tidal volume: amount of air moved into & out of lungs during single respiratory cycle
*At start of cycle, intrapulmonary & atmospheric pressures are equal & there is no air movement occurring
*Inhalation begins with fall of intrapleural pressure that accompanies expansion of thoracic cavity
*Intrapulmonary pressure begins to drop; then begins to rise as air flows into lungs
*When exhalation begins, intrapleural & intrapulmonary pressures rise rapidly, forcing air out of lungs
*At end of expiration, air movement again ceases when pressure difference between intrapulmonary & atmospheric pressure has been eliminated

*Respiratory Muscles
*Diaphragm & external intercostals – important muscles involved in normal breathing at rest
*Accessory muscles: become active when depth & frequency of respiration must be increasingly marked
*Muscles used in Inhalation (active process)  
*contraction of diaphragm increases volume of thoracic cavity by tensing & flattening its floor; responsible for roughly 75% of air movement in normal quiet breathing  
*external intercostals assist by elevating ribs \( \rightarrow \) contributes for roughly 25% to volume of air in lungs  
*accessory muscles, like sternocleidomastoid & scalenes can assist external intercostals in elevating ribs; these muscles increase speed & amount of rib movement

*Muscles used in Exhalation (may be active or passive process)  
*when active: internal intercostals & transverses thoracis depress ribs & reduce width & depth of thoracic cavity  
*when active: abdominal muscles, including external & internal obliques & others, can assist internal intercostals in expiration by compressing abdomen & forcing diaphragm upwards

*Modes of Breathing  
*respiratory muscles are usually classified as quiet breathing, or forced breathing, depending on pattern of muscle activity in course of single respiratory cycle

*Quiet Breathing  
*eupnea; inhalation involves muscular contractions, but exhalation is passive process  
*during diaphragmatic breathing, or deep breathing, contraction of diaphragm provides necessary change in thoracic volume; air is drawn into lungs as diaphragm contracts, & exhalation occurs passively when diaphragm relaxes  
in costal breathing, or shallow breathing, thoracic volume changes because rib cage changes shape; inhalation occurs when contractions of external intercostals elevate ribs & enlarge thoracic cavity; exhalation occurs passively when these muscles relax  
*expansion of lungs stretches their elastic fibers; when inspiratory muscles relax, these elastic components recoil, returning diaphragm, rib cage, or both to their original positions \( \rightarrow \) phenomenon is known as elastic rebound  
*at minimal levels of activity, eupnea involves primarily diaphragmatic movement with little costal motion; as increased volumes of air are required, inspiratory movements become larger & contribution of costal movement increases

*Forced breathing  
*hyperpnea; involves active inspiratory & expiratory movements  
calls on accessory muscles to assist with inspiration, & expiration involves contraction of internal intercostals

*Respiratory Rates  
*respiratory rate: number of breathes taken per minute; normal rate in adult is 12-18 breathes per minute; children breathe more rapidly

*Respiratory Minute Volume \( (V_T) \)  
*used to calculate amount of air moved each minute; multiply respiratory rate by tidal volume \( (V_T) \)  
*measures pulmonary ventilation

*Alveolar Ventilation \( (V_A) \)  
anatomic dead space: volume of air in conducting passage  
alveolar ventilation: amount of air reaching alveoli each minute; less than respiratory minute volume, because some air never reaches alveoli but remains in dead space of lungs  
calculated by subtracting dead space from tidal volume  
at rest, alveolar ventilation rates are about 4.2 liters per minute  
air in alveoli contains less oxygen & more carbon dioxide than atmospheric air

*Relationships among \( V_T, V_E, \) & \( V_A \)  
*respiratory minute volume can be increased by (1) increasing tidal volume, or (2) increasing respiratory rate
*in functional terms, alveolar ventilation rate is more important than respiratory minute rate, because it determines rate of oxygen delivery to alveoli:
  *for given respiratory rate, increasing tidal volume will increase alveolar ventilation rate
  *for given tidal volume, increasing respiratory rate will increase alveolar ventilation rate
  *alveolar rate can change independently of respiratory minute volume
  *whenever demand for oxygen increases, both tidal volume & respiratory rate must be regulated closely
*Respiratory Performance & Volume Relationships
*only small proportion of air in lungs is exchanged during single quiet respiratory cycle; tidal volume can be increased by inhaling more vigorously & exhaling more completely
*pulmonary volumes include:
  *residual tidal volume: amount of air moved into & out of lungs during single quiet respiratory cycle; averages about 500ml in both men & women
  *expiratory reserve volume (ERV): amount of air that is voluntarily expelled after normal quiet respiratory cycle is completed
  *residual volume: amount of air that remains in lungs even after maximal exhalation – typically about 1200ml in males & 1100 ml in females; minimal volume: amount of air that would remain in lungs if they were allowed to collapse – component of residual volume
  *inspiratory reserve volume (IRV): amount of air that can be taken in over tidal volume; average in males is 3300ml & is 1900ml in females
  *inspiratory capacity: amount of air that can be drawn into lungs after quiet respiratory cycle is completed; sum of tidal volume & inspiratory reserve volume
  *functional residual capacity (FRC): amount of air remaining in lungs after quiet respiratory cycle is completed; sum of expiratory reserve volume & residual volume
  *vital capacity: maximum amount of air that can move into & out of lungs in single respiratory cycle; sum of expiratory reserve, tidal volume, & inspiratory reserve
  *total lung capacity: total volume of lungs; sum of vital capacity & residual volume; averages about 6L in males & 4.2 L in females
*Gas Diffusion across Respiratory Membrane
*between alveolar air spaces & alveolar capillaries
*Dalton’s Law & Partial Pressures
*air breathed in is not single gas but mixture – nitrogen being most abundant, oxygen being second, & rest being water molecules & carbon dioxide
*Dalton’s Law: each gas contributes to total pressure in proportion to its relative abundance
*partial pressure: of gas is pressure contributed by single gas within mixture of gases
*Henry’s Law: Diffusion between Liquids & Gases
*Henry’s Law: amount of particular gas in solution is directly proportional to partial pressure of that gas
*when gas under pressure contacts liquid, pressure tends to force gas molecules into solution; at given pressure, number of dissolved gas molecules will rise until equilibrium becomes established
*actual amount of gas in solution at given partial pressure & temperature depends on solubility of gas in that particular liquid
*carbon dioxide is very soluble; oxygen is somewhat less soluble; & nitrogen has very limited solubility in body fluids
*Composition of Alveolar Air
*as soon as air enters respiratory tract, its characteristics being to change
*in passing through nasal cavity, air becomes warmer & amount of water vapor increases
*on reaching alveoli, incoming air mixes with air that had remained in alveoli from previous respiratory cycle
during subsequent expiration, departing alveoli air mixes with air in dead space of lungs to produce yet another mixture that differs from both atmospheric & alveolar samples

*Diffusion at Respiratory Membrane
*gas exchange is efficient at respiratory membrane because:
  * differences in partial pressure across respiratory membrane are substantial – greater the difference in partial pressure, faster rate of gas diffusion
  * distances involved in gas exchange are small – fusion on capillary & alveolar basement membranes reduces distance to avg. .5um; inflammation of lung tissue or fluid buildup inside alveoli will increase diffusion & impair alveolar gas exchange
  * gases are lipid-soluble – both oxygen & carbon dioxide diffuse readily through surfactant layer & alveolar & endothelial cell membranes
  * total surface area is large – combined alveolar surface area at peak inspiration may approach 140m²
  * blood flow & air flow are coordinated – this arrangement improves efficiency of both pulmonary ventilation & pulmonary circulation

*Partial Pressures in Alveolar Air & Alveolar Capillaries
*diffusion between blood in pulmonary capillaries & alveolar air occurs very rapidly – equilibrium must be reached between alveolar air & blood

*Partial Pressures in Systemic Circuit
*oxygenated blood now leaves alveolar capillaries & returns to heart, to be discharged into systemic circuit
*as it enters pulmonary veins, oxygenated blood from alveolar capillaries mixes with blood that flowed through capillaries around conducting passageways
*partial pressure of oxygen in pulmonary veins drops to about 95 mm Hg, & won’t change until blood reaches peripheral capillaries

*Storage & Transport of Oxygen & Carbon Dioxide (Gas Pickup & Delivery)
*between alveolar capillaries & capillary beds in other tissues
*oxygen & carbon dioxide have limited solubilities in blood plasma
*limited solubilities of these gases are problem because peripheral tissues need more oxygen & generate more carbon dioxide than plasma can absorb & transport
*problem is solved by RBCs which remove dissolved oxygen & carbon dioxide molecules & either bind them (in the case of oxygen) or use them to manufacture soluble compounds (in the case of CO₂)
*important things are these reactions is that they are temporary & completely reversible

*Oxygen Transport
*blood leaving alveolar capillaries carries away roughly 20ml of oxygen per 100ml – some consists of oxygen molecules in solution but most are bound to hemoglobin molecules

*Hemoglobin Saturation
*percentage of heme units containing bound oxygen
*at most, each Hb molecule can carry four oxygen molecules

*Hb & P₀₂
  *oxygen-hemoglobin saturation curve; oxygen-hemoglobin dissociation curve; graph that relates saturation of Hb to partial pressure of oxygen
  *binding & dissociation of oxygen to Hb is typical reversible reaction
  *at equilibrium, oxygen molecules are binding to heme at same rate as other oxygen molecules are being released
  *each arriving oxygen molecule increases affinity of Hb for next oxygen molecule
  *if partial pressure of oxygen increases percent saturation goes up & Hb stores oxygen
  *if partial pressure of oxygen decreases, Hb releases oxygen into its environment
*relationship between partial pressure of oxygen & Hb saturation provides mechanism for automatic regulation of oxygen delivery

*Hb & pH
*in addition to consuming oxygen, active tissues generate acids that lower pH of interstitial fluid
*when pH drops, there is change in shape of Hb molecules \( \rightarrow \) as result slope of Hb saturation curve changes & Hb molecules release their oxygen reserves more readily – saturation percentage declines
*Bohr effect: increased oxygen released by Hb in presence of elevated carbon dioxide levels

*Hb & Temperature
*as temperature rises, Hb releases more oxygen
*temperature effects are significant only in active tissues where large amounts of heat are being generated \( \rightarrow \) as blood warms, Hb molecules release more oxygen that can be used by active muscle fibers

*Hb & BPG
*RBC can produce ATP only through glycolysis, which involves formation of lactic acid
*metabolic pathways involved in glycolysis in RBC also generate compound called 2,3-biphosphoglycerate which has direct effect on oxygen binding & release
*higher concentration of BPG, more oxygen will be released by Hb molecules
*BPG synthesis & Bohr effect improve oxygen delivery when pH changes: BPG levels rise when pH increases, & Bohr effect appears when pH decreases

*Fetal Hb
*fetal hemoglobin’s structure in fetus gives it much higher affinity for oxygen that that of adult

*Carbon Dioxide Transport
*CO\(_2\) is generated by aerobic metabolism in peripheral tissues
*after leaving bloodstream, CO\(_2\) molecule may be (1) converted to molecule of carbonic acid, (2) bound to protein portion of Hb molecules within RBCs, or (3) dissolved in plasma

*Carbonic Acid Formation
*most of carbon dioxide absorbed by blood will be transported as molecules of carbonic acid
*CO\(_2\) converted to carbonic acid through activity of enzyme carbonic anhydrase within RBCs
*carbonic acid molecules immediately dissociate into hydrogen ion & bicarbonate ion
*most of hydrogen ions bind to Hb molecules – Hb molecules thus function as buffers
*bicarbonate ions move into surrounding plasma with aid of countertransport mechanism that exchanges intercellular bicarbonate ions for extracellular chloride ions \( \rightarrow \) results in mass movement of chloride ions into RBC, an event known as chloride shift

*Hb Binding
*roughly 23% of CO\(_2\) carried by blood will be bound to globular protein portions of Hb molecules inside RBCs
*these CO\(_2\) molecules are attached to exposed amino acids groups of Hb molecules \( \rightarrow \) result is called carbaminohemoglobin

*Plasma Transport
*plasma becomes saturated with carbon dioxide quite rapidly, & only about 7% of CO\(_2\) absorbed by peripheral capillaries is transported in form of dissolved gas molecules; rest is absorbed by RBCs for conversion by carbonic anhydrase or storage as carbaminohemoglobin

**Control of Respiration**

*peripheral cells are continuously absorbing oxygen from interstitial fluids & generating CO\(_2\)
*under normal conditions cellular rates of absorption & generation are matched by capillary rates of delivery & removal
*these rates are identical to those of oxygen absorption & CO₂ excretion at lungs

**Local Regulation of Gas Transport & Alveolar Function**
*rate of oxygen delivery in each tissue & efficiency of oxygen pickup at lungs are largely regulated at local level
*local factors regulate blood flow, *perfusion*, & airflow, *ventilation*, over wide range of conditions & activity levels

**Changes in Lung Perfusion**
as blood flows toward alveolar capillaries, it is directed toward lobules in which partial pressure of oxygen is relatively high
*this movement occurs because alveolar capillaries constrict when partial pressure of oxygen is low
*such a shift tends to eliminate temporary differences in oxygen & CO₂

**Changes in Alveolar Ventilation**
*smooth muscles in wall of bronchioles are sensitive to partial pressure of CO₂ of air they contain
*when partial pressure goes up, bronchioles increase in diameter (bronchodilation)
*by directing blood flow to alveoli with low levels of CO₂ & improving airflow to alveoli with high levels of CO₂, local adjustments improve efficiency of gas transport
*when activity levels increase & demand for oxygen rises, cardiac output & respiratory rates increase under neural control, but adjustments in alveolar blood flow & bronchiolar diameter occur automatically

**Respiratory Centers of Brain**
*respiratory control has both involuntary & voluntary components
*brain’s involuntary centers regulate activities of respiratory muscles & control respiratory minute volume by adjusting frequency & depth of pulmonary ventilation
*voluntary control of respiration reflects activity in cerebral cortex that affects either output of respiratory centers in medulla oblongata & pons or motor neurons in spinal cord that control respiratory muscles
*respiratory centers: three pairs of nuclei in reticular formation of medulla & pons

**Respiratory Centers in Medulla Oblongata**
*respiratory *rhythmicity centers* are paired centers that set pace for respiration
*each center can be subdivided into dorsal respiratory group (DRG) (functions in either quiet or forced respiration) & ventral respiratory group (VRG) (functions in only forced respiration)
during quiet respiration:
*activity in DRG increases over period of about 2 seconds, providing stimulation to inspiratory muscles; over this period inspiration occurs
*after 2 seconds, DRG neurons become inactive; they remain quiet for next 3 seconds & allow inspiratory muscles to relax; over this period, passive expiration occurs
during forced respiration:
*as level of activity of DRG increases, it in some way stimulates neurons of VRG that activate accessory muscles involved in inspiration
*at end of each inspiration, active expiration occurs as neurons of expiratory center stimulate appropriate accessory muscles

**Apneustic & Pneumotaxic Centers**
*apneustic & pneumotaxic centers: of pons are paired nuclei that adjust output of respiratory rhythmicity centers
*their activities adjust respiratory rates & depth of respiration in response to sensory stimuli or input from other centers in brain
*each apneustic center provides continuous stimulation to DRG on that side of brain stem
*interactions between DRG & VRG establish basic pace & depth of respiration
*pneumotaxic centers modify that pace; an increase in pneumotaxic output quickens pace of respiration by shortening duration of each inhalation
Respiratory Reflexes
*activities from respiratory centers are modified by sensory info from:
*chemoreceptors sensitive to $P_{CO_2}$, pH, &/or $P_{O_2}$ of blood or CSF
*changes in blood pressure in aorta or carotid sinuses
*stretch receptors that respond to changes in volume of lungs
*irritating physical or chemical stimuli in nasal cavity, larynx, or bronchial tree
*other sensations, including pain, changes in body temperature
*information from these receptors alters pattern of respiration

Chemoreceptor Reflexes
*respiratory centers are strongly influenced by chemoreceptor inputs & from receptors that monitor CSF composition:
*glossopharyngeal nerve carries chemoreceptive info from carotid bodies, adjacent to carotid sinuses; carotid bodies are stimulated by decrease in pH or partial pressure of oxygen of blood
*vagus nerve monitors chemoreceptors in aortic bodies, near aortic arch; these receptors are sensitive to same stimuli as carotid bodies
*chemoreceptors are located on ventrolateral surface of medulla oblongata in region known as chemosensitive area
*stimulation of these chemoreceptors leads to increase in depth & rate of respiration
*although receptors monitoring $CO_2$ levels are more sensitive, oxygen & carbon dioxide receptors work together in crisis
*chemoreceptors are subject to adaptation if partial pressure of $O_2$ or $CO_2$ remains abnormal for an extended period
*because chemoreceptors monitoring carbon dioxide levels are also sensitive to pH, any condition altering pH of blood or CSF will affect respiratory performance

Hypercapnia & Hypocapnia
*hypercapnia: increase in partial pressure of $CO_2$ of arterial blood
*triggered by stimulation of chemoreceptors in carotid & aortic bodies & reinforced by stimulation of CNS chemoreceptors
*$CO_2$ crosses blood-brain barrier quite rapidly, so rise in arterial partial pressure of $CO_2$ almost immediately elevates CSF $CO_2$ levels, lowering pH of CSF & stimulating chemoreceptive neurons of medulla oblongata
*these receptors stimulate respiratory centers to increase rate & depth of respiration
*hyperventilation: condition existing when rate & depth of respiration exceed demands for oxygen delivery & $CO_2$ removal; gradually leads to hypocapnia
*hypocapnia: abnormally low partial pressure of $CO_2$
*hypoventilation: condition where respiratory rate remains abnormally low & is insufficient to meet demands for normal oxygen delivery & $CO_2$ removal $\rightarrow$ $CO_2$ will then accumulate in blood; most common cause of hypocapnia

Baroreceptor Reflexes
*output from baroreceptors affects respiratory centers $\rightarrow$ when blood pressure falls, respiratory rate increases, & vice versa
*this adjustment results from stimulation or inhibition of respiratory centers by sensory fibers in glossopharyngeal & vagus nerve

Hering-Breuer Reflexes
*sensory information from these reflexes is distributed to apneustic centers & VRG
*not involved in normal quiet breathing or tidal volumes under 1000ml
*inflation reflex: prevents overexpansion of lungs during forced breathing
*stretch receptors are located in smooth muscle tissue around bronchioles & are stimulated by lung expansion
*deflation reflex*: inhibits expiratory centers & stimulates inspiratory centers when lungs are deflating
*this reflex normally functions only during forced expiration when both inspiratory & expiratory centers are active

*Protective Reflexes*
*operate when body is exposed to toxic vapors, chemical irritants, or mechanical stimulation of respiratory tract
*receptors involved are located within epithelium of respiratory tract
*apnea*: temporary period in which respiration is suspended; ex: sneezing, coughing
*usually followed by forceful expulsion of air intended to remove offending stimulus
*laryngeal spasms*: result from entry of chemical irritants, foreign objects, or fluids into area around glottis
*reflex generally closes airway temporarily

*Voluntary Control of Respiration*
*activity of cerebral cortex has indirect effect on respiratory centers
*conscious thought
*emotional states
*anticipation of strenuous exercise
*also have conscious control over respiratory activities ➔ which may bypass respiratory centers completely
*this control mechanism is essential part of speaking, singing, or swimming, when respiratory activities must be precisely timed
*chemoreceptor reflexes are extremely powerful respiratory stimulators, & cannot be consciously suppressed