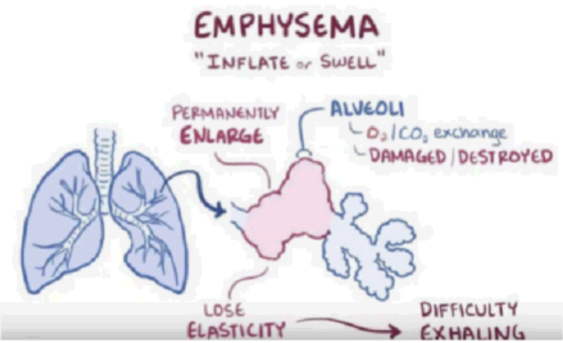
Compliance vs elastance
- High compliance (stretch easily), high elastance (returns quickly)
- A basketball has low compliance and a plastic bag has low reluctance

Lung compliance
- compliance=expansibility=distensibility
- High compliance=stretches easily
- Compliance = ΔV/ΔP → Compliance of the lung and chest wall is measured as the slope of the pressure-volume curve, or as a change in lung volume per unit change in airway pressure
- Pathological conditions in which compliance is reduced are called restrictive lung disease (pulmonary fibrosis)

Obstructive and restrictive lung diseases
- Restrictive- a decrease in lung compliance that affects ventilation because respiratory muscles must work harder to stretch a stiff lung. It is caused by inadequate alveolar production of surfactant that facilitates lung expansion (pulmonary fibrosis) and inelastic scar tissue.
- Obstructive: the airflow is diminished due to increased airway resistance due to airway physical obstruction (muscles, mucus) and bronchoconstriction (asthma, obstructive sleep apnea, emphysema)

Lung elastance
- Elastance (elastic recoil) is the reciprocal of compliance, the ability to resist being deformed or the ability of a body to return to its original shape when deforming force is removed
- Balloon vs, plastic bag: normal healthy lungs vs lungs with emphysema
- Patients with emphysema need to contract their muscles to force out air that is nor leaving from elastic recoil



- The alveoli permanently enlarge and lose elasticity.

- Difficulty with exhaling which depends heavily on the ability of the lungs to recoil like elastic bands

Airway Resistance

- Poiseuille's law: $R \propto L\eta/r^4$

Table 17.2 Factors That Affect Airway Resistance

Factor	Affected by	Mediated by
Length of the system (L)	Constant; not a factor	
Viscosity of air (η)	Usually constant; humidity and altitude may alter slightly	
Diameter of airways	**If radius (r) halves, R increases 16 times**	
Upper airways	Physical obstruction	Mucus and other factors
Bronchioles	Bronchoconstriction due to tightening of smooth muscle	Parasympathetic neurons (muscarinic receptors), histamine, leukotrienes
	Bronchodilation due to relaxation of muscle	Carbon dioxide, epinephrine (β_2-receptors)

When does bronchoconstriction happen?

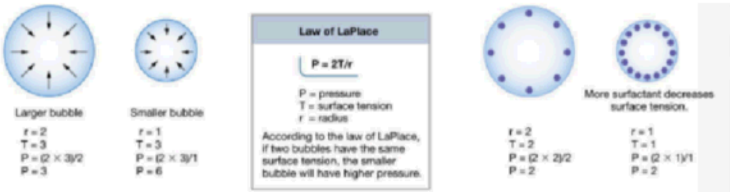
- By histamine: tissue damage, allergic reactions → histamine (released by mast cells) level increased → bronchoconstriction
- By nervous system: inhaling irritants → parasympathetic neurons signal → bronchoconstriction (as a defense mechanism)

When does bronchodilation happen?

- By CO2: during expiration, CO2 level increases → relaxed bronchiolar smooth muscle cells → bronchodilation
- By nervous system: activation of B2 adrenergic receptor by epinephrine that results → sympathetic nervous system signals → bronchodilation by relaxation of the bronchial smooth muscle
- Asthma is caused by the increased airway resistance. treatment is bronchodilator (epinephrine) to relax the muscles or anti-inflammatory drugs

Surfactants prevent alveolar collapse

- Alveolar surface tension is created by a thin film of fluid inside alveoli



- On the left: the two bubbles have the same surface tension. According to the Law of Laplace, pressure is greater in the smaller bubble
- On the right: surfactant reduces surface tension. In the lungs. Smaller alveoli have more surfactant, which equalizes the pressure between large and small alveoli
- Human surfactant is a mixture of proteins and phospholipids that are secreted into the alveolar air space by the type II alveolar cells
- Surfactant is more concentrated in smaller alveoli

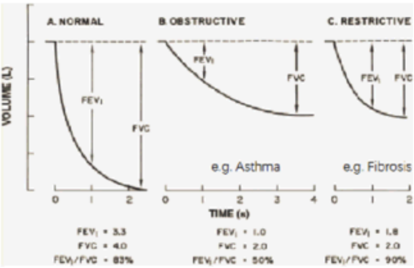
Surfactants increase lung compliance

- With surfactants, the surface tension of the alveolar fluid decreases, work needed to expand the alveoli decreases, the resistance of the lung to stretch decreases, and lung compliance increases the (ability of the lung to stretch)

Newborn respiratory distress syndrome (NRDS)

- Disease for babies who are born prematurely without adequate concentration of surfactant in their alveoli
- Alveoli that collapse each time they expand. Having “stiff” (low-compliance lungs. These infants must use a tremendous amount of energy to expand their collapsed lungs with each breath
- Unless treatment is initiated rapidly, about 50% of these infants die
- Treatment: they can be treated with aerosol administration of artificial surfactant. The current treatment also includes artificial ventilation that forces air into the lungs and keeps the alveoli open.

Pathological Measurements during Ventilation



FEV1: Forced expiratory volume in the first second
FVC: Forced vital capacity

Pulmonary vs. Alveolar Ventilation

- The total pulmonary ventilation= ventilation rate X tidal volume
- Normal ventilation rate for an adult is 12-30 breaths per minute
- Some air that enters the respiratory system remains in the conducting airways (the trachea and bronchi)- anatomic dead space. Approximately 150mL

- The alveolar ventilation- the amount of fresh air that reaches the alveoli per each minute. Alveolar ventilation=ventilation rate X (tidal volume-dead space volume)

What is the alveolar ventilation (=total volume per min) during quiet breathing with an alveolar ventilation rate of 12 breaths/min?

- Alveolar ventilation=ventilation rate X(tidal volume-dead space volume)
- 12 breath/min X (500-1500 mL)/breath=4.2 L/min
- Although 6L of fresh air is inhaled (total pulmonary ventilation), only 4.2 L reaches the alveoli per minute.

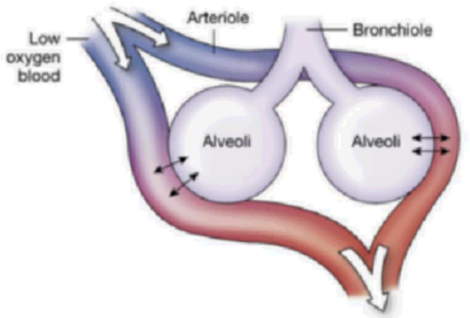
Effects of Ventilation on alveolar partial pressure

- The Po2 and Pco2 in the alveoli change a little during normal quiet breathing. Why?
    - The amount of O2 enters the alveoli is roughly equal to the amount of O2 that enters the blood
    - The amount of fresh air that enters the lungs in each breath is only 10% of the total lung volume
    - Changes in alveolar ventilation rates can significantly affect the amount of fresh air and oxygen that reaches the alveoli

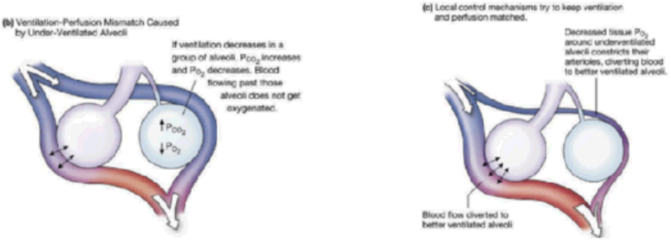
Ventilation and alveolar blood flow are matched

- Capillaries and bronchioles in the lungs are collapsible as their function of blood pressure, so capillaries and bronchioles can open and close back and forth

(a) Normally, perfusion of blood past alveoli is matched to alveolar ventilation to maximize gas exchange.



Effects of Under-Ventilated Alveoli

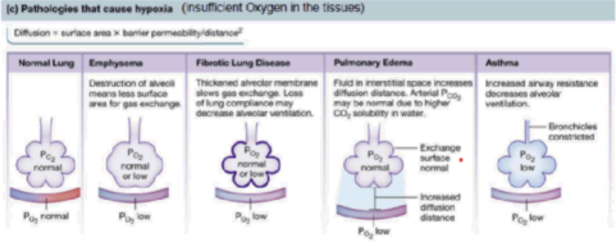


- On the left: bronchiolar diameter is primarily mediated by CO2 contents
- Pulmonary arteriole diameter is regulated primarily by the O2 content of the interstitial fluid around the arterioles

Cause of low alveolar Po2
- Inspired air has low O2 content (high altitude)
- Alveolar ventilation is inadequate (hypoventilation) and it could be caused by
    - Decreased lung compliance
    - Increased airway resistance
    - Central nervous system depression due to alcohol poisoning and drug overdoses

Oxygen diffusion at the alveoli
- The exchange of gases between compartments, which requires diffusion
- Plasma gas concentration in partial pressure (Po2 high → P02 low; Pco2 high → Pc02 low)

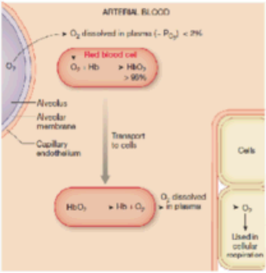
Diffusion rate affects the membrane
- Fick's law of diffusion says: rate of diffusion=(available surface area * concentration gradient)/(membrane resistance * thickness of membrane)
- Assuming that membrane resistance is constant, the diffusion rate in the lung influenced by
    - Concentration gradient, surface area, membrane thickness, and diffusion distance
    - The most important factor for gas exchange in normal physiology is the concentration gradient

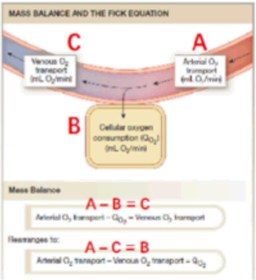


Transport of oxygen by hemoglobin

- Dissolved in plasma (<2%), increase at low temperature, more than 98% of the oxygen is transported inside red blood cells bound to hemoglobin
- Only dissolved O2 can be utilized in the body, bound to hemoglobin (Hb): HD +O2 ←> HbO2 (oxyhemoglobin)

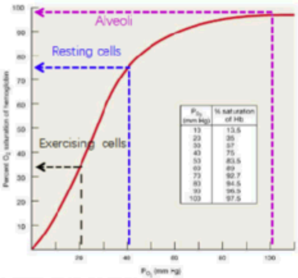
Oxygen Transport in the Blood





Po2 determines O2-Hb binding: the saturation curve

- Saturated = 100% oxygenated blood → If half of binding sites are open, 50% saturated
- At alveoli, P_{O_2} **≈ 100 mm Hg**
- In resting cells, Hb is 75% saturated.
- At the partial pressure for exercising muscle (**P_{O_2}= 20 mm Hg**), Hb is ~35% saturated.



P_{O_2} (mm Hg)	% saturation of Hb
10	13.5
20	35
30	57
40	75
50	83.5
60	89
70	92.7
80	94.5
90	96.5
100	97.5

Factors affecting O_2-Hb binding

- Any factors that change the conformation of hemoglobin protein may affect its ability to bind O_2
- Plasma pH, P_{co2}, temperature
- Changes are more pronounced in the steep part of the curve → O_2 delivery at the tissue (20-40 mmHg range) is significantly altered by this shift.

- Hemoglobin has a stronger affinity for oxygen at lower temperatures so levels of oxygen bound to hemoglobin will increase
- The solubility of gases increases at lower temperatures so levels of oxygen dissolved in plasma increase
- Low temptation: because oxygen is bound to hemoglobin more tightly, less O_2 will be released and tissues will not get enough oxygen and be damaged

Decrease of pH change hemoglobin saturation

- Hemoglobin's oxygen binding affinity is inversely related to acidity and the concentration of CO_2. the lower pH changes the protein structure

An increase in temperature changes hemoglobin saturation

- When the exercising muscle cell warms up..,
    - % HBO_2 saturation decreases, Hb releases more O_2, accumulated lactic acid in the muscle may contribute to the reduction in pH, also releasing more O_2

Fetal hemoglobin has different O_2 binding properties

- Fetal hemoglobin (Hbf) has 2 gamma protein chains, which enhance the ability of fetal hemoglobin to bind to O_2 even in the low O_2 environment of the placenta.
- On the chart- fetal hemoglobin is an r-shaped curve first, then maternal hemoglobin is another r-shaped curve, and there's a gap in the middle

Carbon dioxide transport in blood

- High P_{co2} can depress CNS function, causing confusion, coma or even death
- It is more soluble in body fluids than O_2 is (7% dissolves in the blood), but cells produce far more CO_2 than can dissolve in the plasma
- The remaining 93% diffuse into red blood cells (RBCs), where 70% is converted to bicarbonate ion and 23% binds to hemoglobin

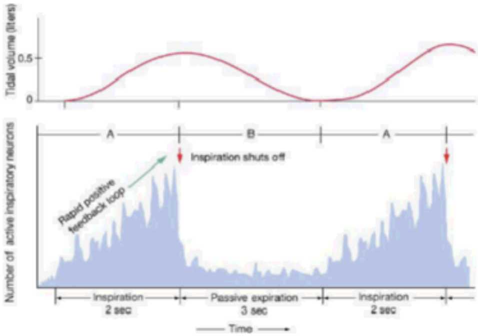
Control of ventilation

- Respiratory neurons in the medulla oblongata control inspiration and expiration
- Neurons in the ons modulate ventilation
- The rhythmic pattern of breathing arises from a network of spontaneously discharging neurons
- Ventilation is modulated by $C0_2$, O_2, and H^+

Respiratory neurons: two nuclei in the medulla oblongata

- Poutine respiratory groups (PRG) in pons: provide tonic input to the medullary network
- Two nuclei in the medulla oblongata
    - The Dorsal respiratory group- inspiratory neurons control muscles of the thorax and the diaphragm
    - The ventral respiratory group- neurons that control the muscles used for active expiration and dor greater-than-normal inspiration
    - Nucleus tractus solitarius receives sensory info from peripheral chemo-receptor and central chemoreceptor

Inspiratory Neuron Activity during Rhythmic Breathing

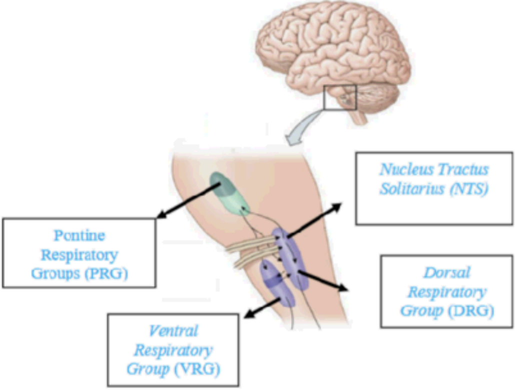


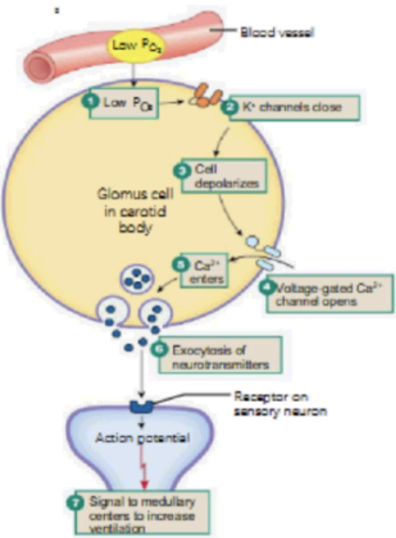
During inspiration, the acitvity of inspiratory neurons increases

Chemoreceptors in ventilation

- Central chemoreceptors
    - Located in the medulla, close to neurons involved in respiratory control
    - Monitor cerebrospinal fluid (CSF) composition and respond to changes in Co2

- Peripheral chemoreceptors
    - Located in the aortic wall and carotid artery
    - Sense changes in the O2, pH, and Pco2





Peripheral chemoreceptors

Protective reflexes and voluntary control

- Bronchoconstriction, coughing, and sneezing
    - In response to inhaled particles or noxious gases

- Regulation of respiratory rate in dependent upon
    - Conscious and unconscious thought, emotional state, anticipation

Technology

1. Mattress with vibrotactile stimulation for infants with breaching problems
    - For infants with immature patterns of breathing: apnea and/or oxygen desaturation events
    - Mattress with actuators for vibrotactile stimulation to stabilize breathing, stimulation below the threshold for causing arousal during sleep
    - Result in stabilization and reduction in apnea/hypoxia
    - Going through clinical trials
2. Hypoglossal nerve stimulation for treating sleep apnea
    - Activation of genioglossus muscle via stimulation of the hypoglossal nerve for treatment of obstructive sleep apnea (OSA)
    - When the breathing sensing lead placed between the external and intercostal muscles detects inspiration is occurring, the impulse generator stimulates the hypoglossal nerve, which results in slight forward displacement of the stiffened tongue