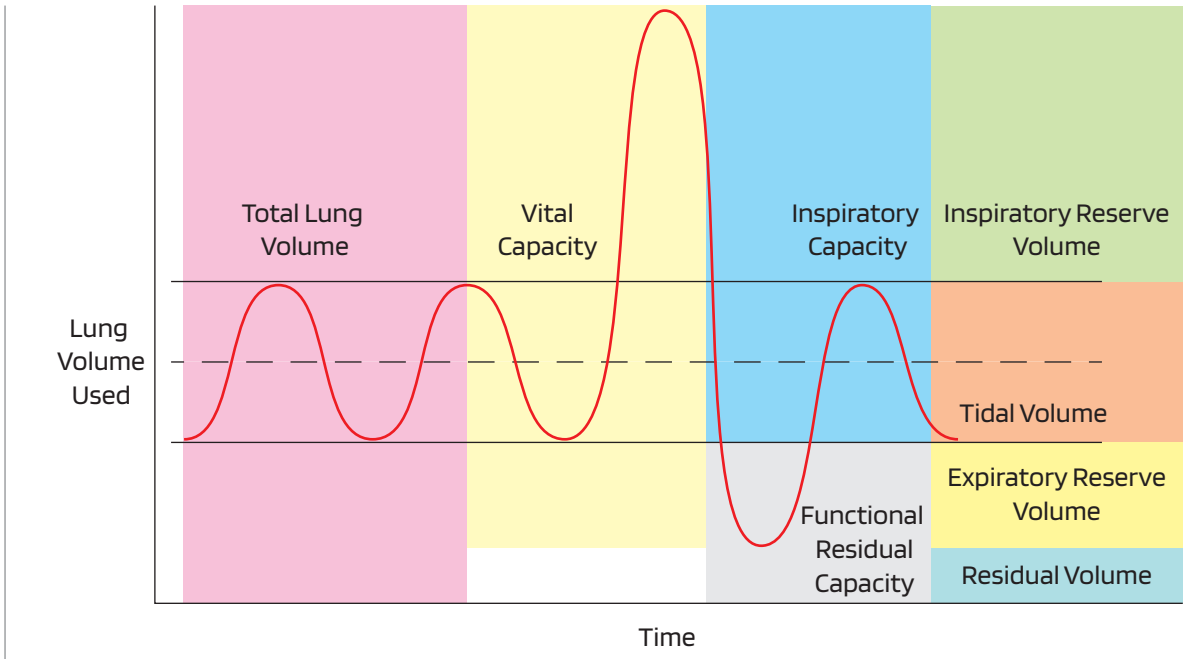
Physiology

Lung volumes and spirometry



Spirometry

Tidal volume	The volume of air inspired or expired during each ordinary breath
Inspiratory reserve volume	Maximum amount of air inspired after tidal volume
Expiratory reserve volume	Maximum amount of air expired after tidal volume
Residual volume	Amount of air left in the lungs after maximum expiration
Vital capacity	The sum of tidal volume, inspiratory and expiratory reserve volumes
Functional residual capacity	Residual volume plus expiratory reserve volume
Total lung capacity	Vital capacity plus residual volume
Inspiratory capacity	Tidal volume plus inspiratory reserve volume
FEV1	Forced expiratory volume in the first second after a deep breath
FVC	Total amount of air possible to exhale after a deep breath
FEV1/FVC	Differentiates obstructive from restrictive disorders

Respiratory volumes

Alveolar ventilation & dead space

Anatomical dead space	- Volume of air inside conducting airway (airways without alveoli) - 150 mL of tidal volume
Physiologic (total) dead space	- Volume of the lungs that does not perform gas exchange - In healthy subjects it is about anatomical dead space $V_D = V_T$ (alveolar PCO_2 – expired PCO_2) / alveolar PCO_2
Minute ventilation	Tidal volume × RR
Alveolar ventilation	(tidal volume – dead space) × RR

Dead space and alveolar ventilation

V_D, physiologic dead space;
V_T, tidal volume;
RR, respiratory rate

Mechanics of Respiration

Quiet expiration is a passive process that only requires relaxation of the inspiratory muscles.
The lungs and chest wall form an elastic system that has a tendency to go back to its desired volume (elastic recoil). However, it would never collapse because of negative pressure in the pleural space.

Inspiration	Details
Diaphragm	Used in quiet breathing
External intercostal	Used in quiet breathing
Levator costae	On the posterior side attaches to vertebrae and ribs
Scalene (pump handle)	Only in heavy breathing
Sternocleidomastoid	Only in heavy breathing
Shoulder girdle and neck muscles	Trapezius, latissimus dorsi, pectoralis major and minor, serratus anterior, platysma & teres major

Expiration	Details
Internal intercostal	Used in labored breathing
Pectoralis major	Only the clavicular head and is used in labored breathing
Abdominal muscles	External & internal oblique, transversus & rectus abdominis (only in labored breathing)

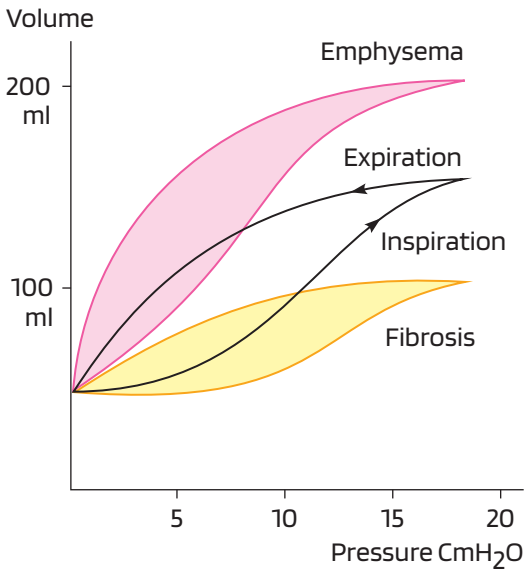
Muscles of respiration

Compliance

Compliance or the degree of distensibility is inversely related to stiffness or elastic recoil. It is the slope of the pressure-volume graph.

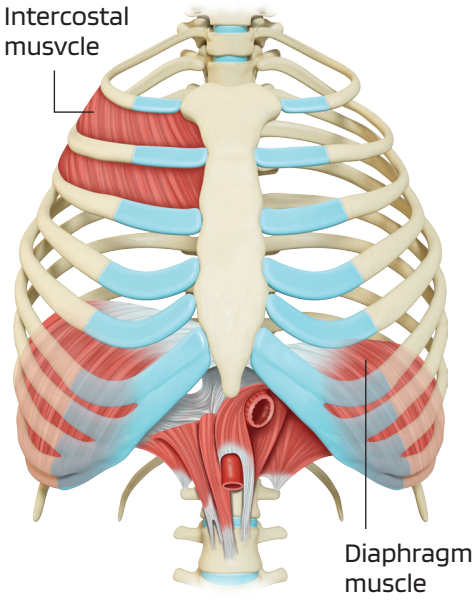
C=V/P

Compliance is increased in emphysema, and decreased in pulmonary fibrosis.



Compliance & hysteresis

Note the difference between the inspiration and expiration graphs



Respiratory muscles

Diaphragm and the intercostal muscles

Hysteresis is the difference between the expiration and inspiration graphs. It is due to surface tension, which is higher when inspiration starts and is lower when the expiration starts.

Compliance of chest wall and lungs

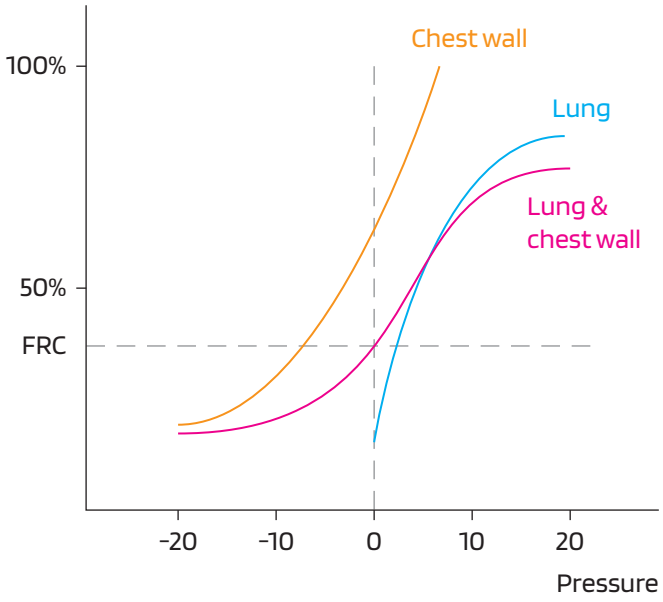
The compliance of the lung-chest wall system is less than the lungs' compliance alone; it is also less than the compliance of the chest wall.

At functional residual capacity, there is equilibrium in the system, and the airway pressure is zero. The two forces are equal; however, if the volume is less than FRC, the elastic recoil of the lungs is less, and it is easier to expand the lungs; if the volume is more than FRC, the elastic recoil is more than it is easier to deflate the lungs.

The more vertical the graph, the higher the compliance; therefore, the lung fibrosis compliance graph becomes more horizontal.

In patients with emphysema, compliance is increased, and the graph becomes more vertical.

The **relaxation pressure-volume curve** explains the elastic properties of the lung-chest wall system. At FRC volume, there is equilibrium in the system, and the opposing forces of the chest wall and the lung is the same. During quiet inspiration, the diaphragm contracts, and the negative intrapleural pressure increases the lung volume. The increase in lung volume increases the whole system's recoil pressure, which increases the elastic recoil and decreases the lung volumes. Relaxation of the inspiratory muscles of quiet inspiration is enough to perform a quiet expiration. The expiratory muscles are needed to create lung volumes below FRC.



Relaxation pressure-volume curve

FRC, functional residual capacity.

Surface tension

Hydrogen bonding of water molecules generates a force that tries to hold water molecules together. At the surface, water molecules that are exposed to air try to go back inside water. This force tries to collapse the lungs. Surface tension can collapse the smaller alveoli easily. This is explained by Laplace's law (the collapsing pressure is inversely proportional to the radius).

The **surfactant**, a form of **phosphatidylcholine** made by pneumocyte type 2, decreases the surface tension. Its synthesis starts around 26 weeks of gestation and is nearly completed around 33rd to 35th week of gestation.

Respiratory distress syndrome in premature babies is due to insufficient surfactant. It presents with hypoxemia and atelectasis throughout the lungs.

Airflow and resistance

Flow is inversely proportional to resistance (R). R is inversely proportional to the fourth power of the radius.

$R \propto 1/r^4$

The lung volumes, bronchial smooth muscle contraction, and air density affect airflow.

The medium-sized bronchi have higher airway resistance than small-sized bronchi. The small-sized bronchi are parallel, and there are many of them; therefore, compared with medium-sized bronchi, the overall **resistance decreases in the small-sized bronchi**.

Bronchial smooth muscle contraction, as seen in asthma, increases airway resistance significantly.

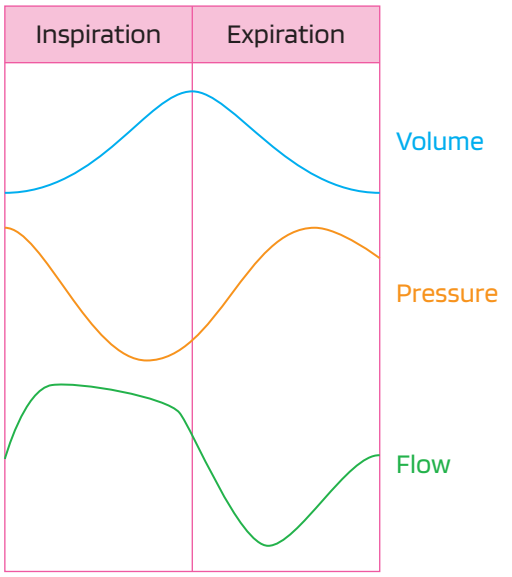
The sympathetic system causes bronchodilation (β-2) & the parasympathetic system causes bronchoconstriction.

Breathing cycle

Transmural pressure (transpulmonary pressure) = interalveolar pressure – intrapleural pressure

As long as intra-pleural pressure is negative, the lungs will not collapse, and the chest wall will not expand too much. When a sharp object cuts the pleural space open, the lung collapses, and the chest wall expands to its maximum.
At functional residual capacity (FRC), the lungs collapsing force, and the chest wall expanding force are equal.

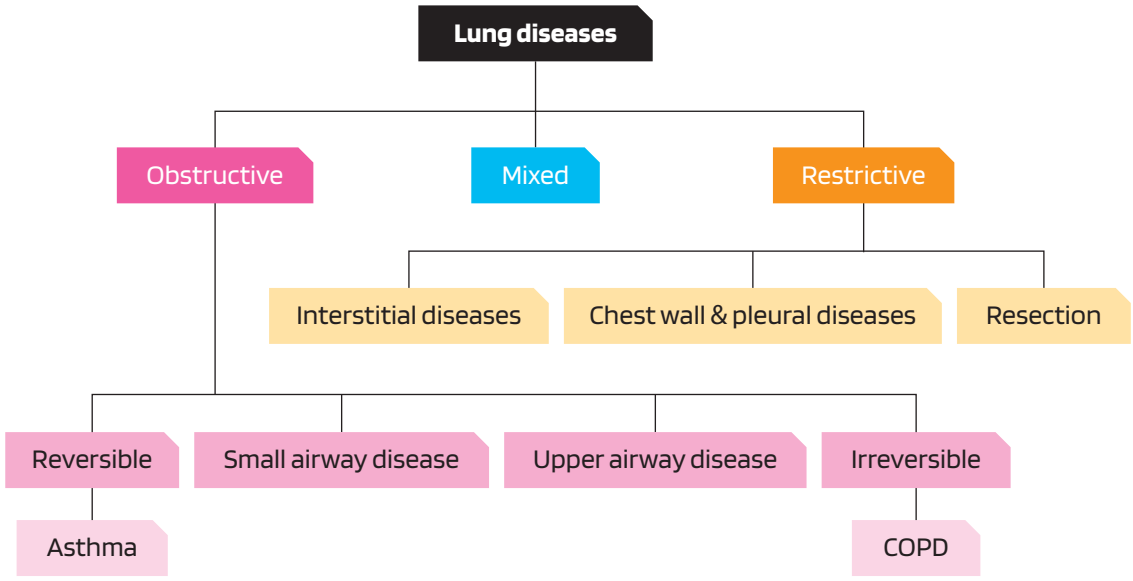
At functional residual capacity, alveolar pressure is zero, and intrapleural pressure is -3. As inspiration begins, intrapleural pressure goes to -6, and the lung volumes increase. When expiration starts, the increase in intrapleural pressure decreases the lung volumes.



Volume, pressure & flow changes during breathing cycle

Obstructive versus restrictive diseases

In COPD and asthma, the airflow obstruction is mainly during expiration.

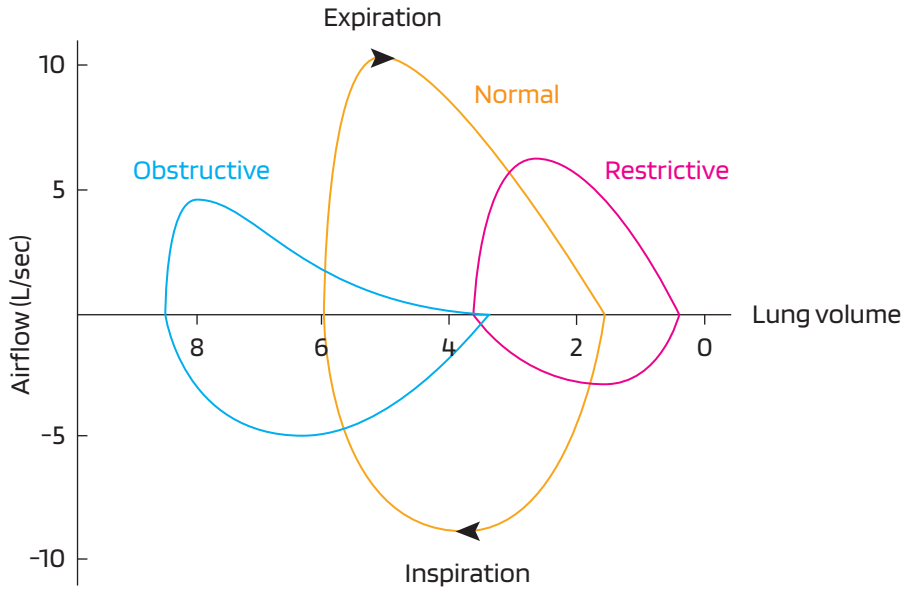


Obstructive versus restrictive diseases

Disease pattern	FEV1/FVC%	Lung volumes	DICO
Obstructive emphysema dominant	↓	↑	↓
Obstructive chronic bronchitis dominant	↓	↑	N
Obstructive reversible (asthma)*	↓	↑	N
Restrictive - interstitial	N or ↑	↓	↓
Restrictive - chest wall & pleural diseases	N	↓	N
Restrictive - resection	N	↓	↓
Mixed restrictive and obstructive	↓	↓	↓

*Improves with bronchodilators; appears with methacholine

Obstructive versus restrictive spirometry patterns

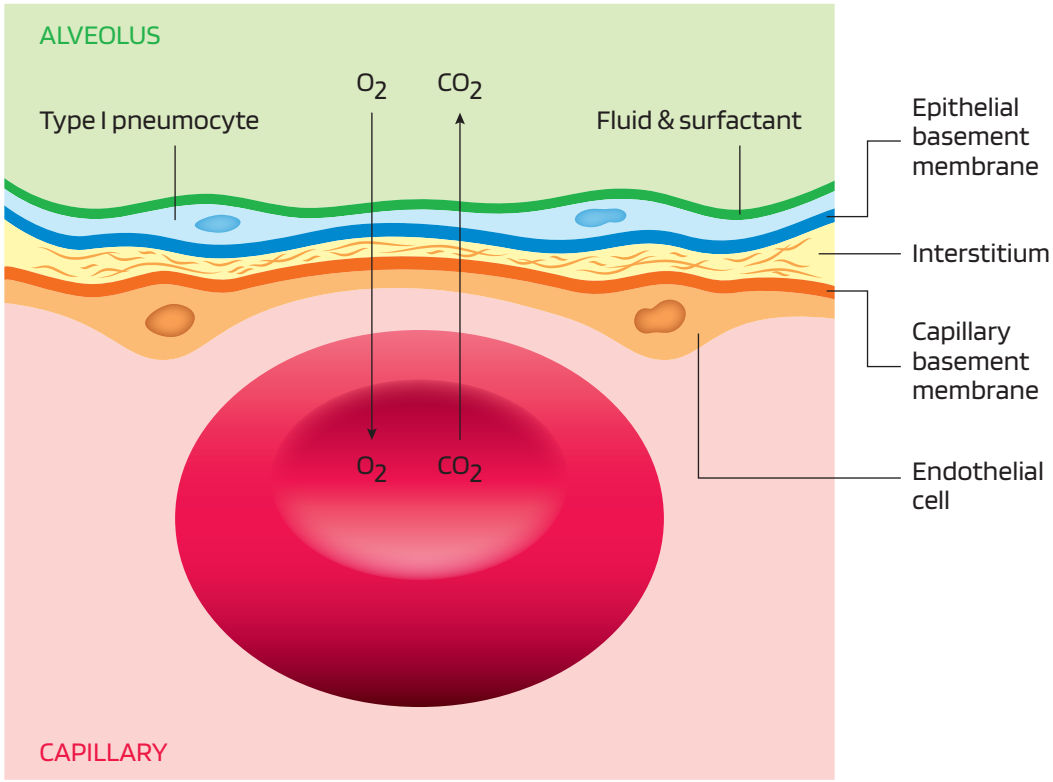


Flow volume loop

Gas exchange

The blood-air barrier is made of the endothelial cell and its basement membrane, interstitium, the type I pneumocyte, and its basement membrane.

The fractional gas concentration of any gas determines its partial pressure. The partial pressure of oxygen at atmospheric pressure is 160 mmHg; however, as it travels down toward the alveoli, humidification reduces that to 150 mmHg. In the alveoli, gas exchange decreases it to 100 mmHg.



Blood-air barrier

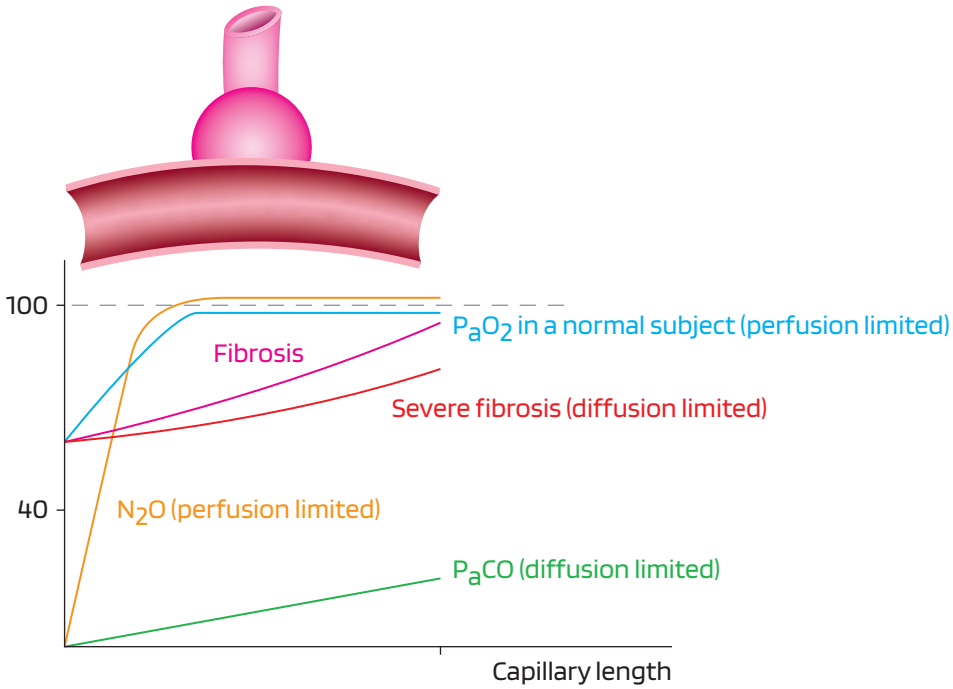
	Partial pressure of O_2	Partial pressure of CO_2
Atmosphere	160 (150 after humidification)	Zero
Alveoli	104	40
Arterial	100	40
Venous	40	46

Partial pressure of O_2 and CO_2

The partial pressure of any gas represents the dissolved amount of gas in blood, and depends on the solubility of the gas in the blood.

Diffusion-limited versus perfusion-limited gases

Gas diffusion depends on partial pressure differences across the membrane. If the gas equilibrates early and it depends on only blood flow, it is **perfusion-limited**. Under normal conditions, this is the case for CO2 and O2. If the gas does not equilibrate by the time blood reaches the end of the capillary, it is **diffusion-limited**. This is the case for CO and O2 under strenuous exercise. In the case of fibrosis or emphysema, the gas exchange becomes diffusion-limited.



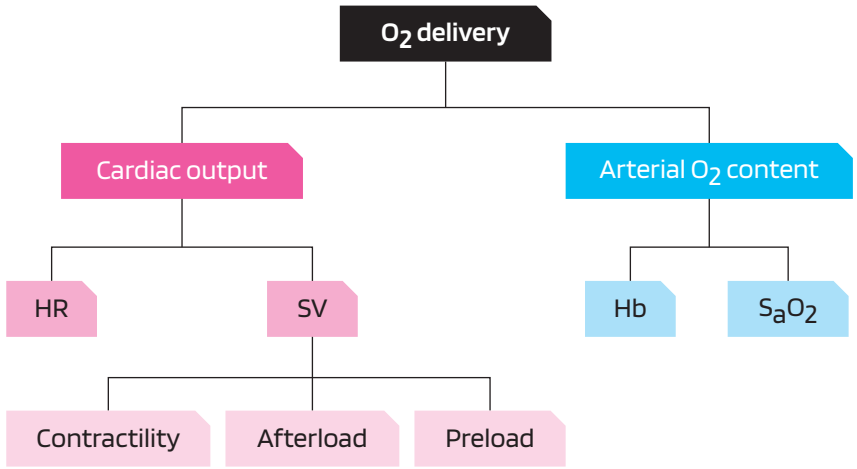
Diffusion limited vs. perfusion limited

Oxygen transport

O_2 transport depends on the arterial O_2 content and cardiac output. The arterial O_2 content depends on hemoglobin level or oxygen saturation.

O_2 content = O_2 attached to hemoglobin + dissolved O_2

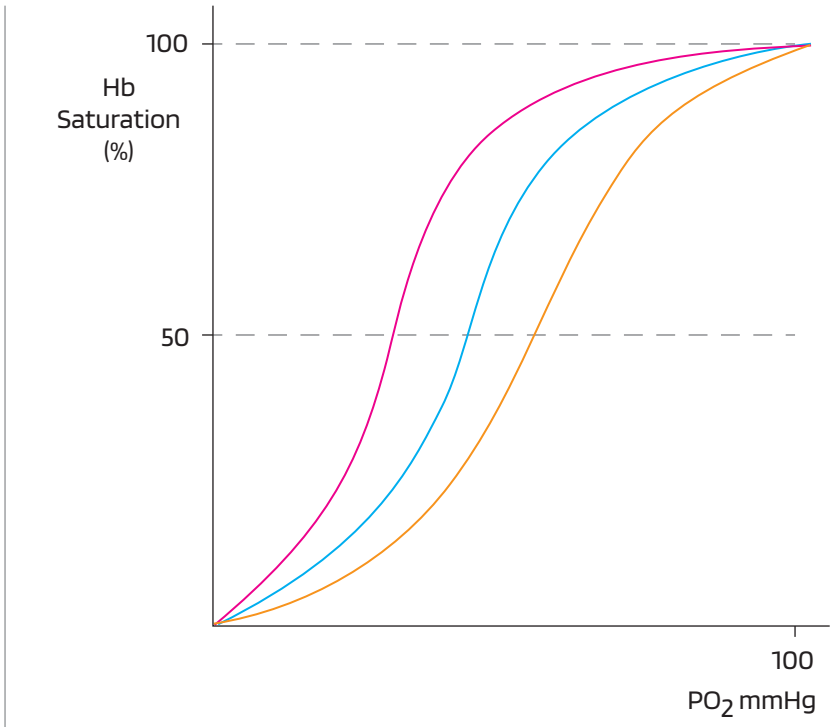
Oxygen carried by hemoglobin= O_2 binding capacity x saturation (percentage of heme groups attached to O_2)



O_2 delivery

Hb, hemoglobin; HR, heart rate; S_aO_2, oxygen saturation; SV, stroke volume.

Hemoglobin oxygen dissociation graph



Shift to the left
↓ PCO_2, ↓ H^+, ↑ pH
CO, methemoglobin
↓ T°
↓ 2,3 DPG
HB F

Shift to the right
↑ PCO_2, ↑ H^+, ↓ pH
↑ 2,3 DPG
↑ T°
Exercise

Hemoglobin oxygen dissociation graph

P50 is a partial pressure of oxygen at which 50% of hemoglobin is oxygenated, which is normally around 25 mmHg.
Even in venous blood, about 70% of hemoglobin is saturated. At partial pressures of oxygen above 60 mmHg, the graph becomes almost horizontal.
The sigmoid shape of the graph is a sign of positive cooperativity. This means by adding each molecule of oxygen, it becomes easier to add the next molecule of oxygen; therefore, the 4th oxygen molecule has the highest affinity.
A low O_2 affinity shifts the graph to the right. Increased H^+ ion unloads oxygen (**Bohr effect**).

Hypoxia versus hypoxemia

Decreased O_2 availability to the cells is called **hypoxia**.
Hypoxemia (decreased partial pressure of oxygen in the blood) is a cause of hypoxia. A-a gradient is alveolar O_2 minus the arterial O_2.

A-a gradient depends on the age of the patient and is normally around 10-15 mmHg. Hypoxemia increases the A-a gradient.

Causes of hypoxia	Causes of hypoxemia
Oxidative phosphorylation defects	Hypoventilation
Hypoxemia	Diffusion defect
Hb disorders	V/Q mismatch
Ischemia	Right to left shunt
Low cardiac output	Low inspired O2

Causes of hypoxia and hypoxemia

Pulmonary circulation

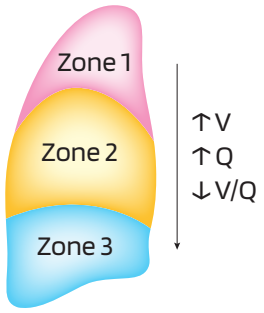
Pulmonary circulation is a low-resistance and low-pressure system. Pulmonary circulation is unique since it shows **hypoxic vasoconstriction**. In this way, the blood is shifted to the areas which are ventilated more.

From top to bottom, both ventilation (V) and perfusion (Q) increases; however, the V/Q ratio decreases because the ventilation does not increase as much as the perfusion.

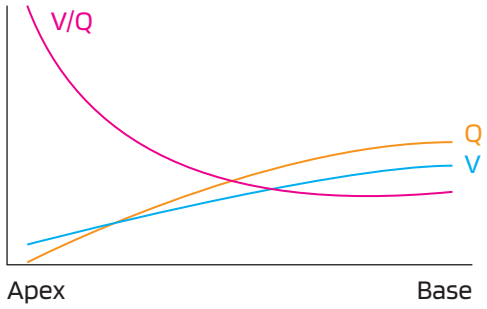
Zone 1 is the most superior one with the lowest perfusion. **Zone 3** is the lowest and has the highest perfusion due to gravitational force.

Ventilation-perfusion mismatch

Normally the V/Q ratio is 0.8. Ventilation-perfusion mismatch is the most common cause of lung-related hypoxemia. In pulmonary embolism, there is no perfusion, and the V/Q ratio approaches infinity; therefore, dead space is increased. In ARDS, perfusion is not affected, and ventilation is decreased, which is similar to a right to left shunt. V/Q ratio approaches zero.



Changes in ventilation and perfusion



Ventilation (V), perfusion (Q) & (V/Q) ratio

Shunts

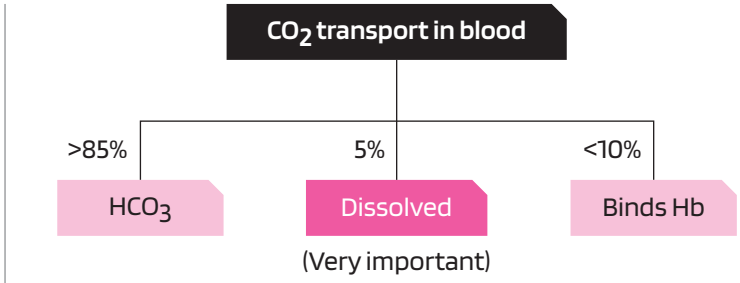
A shunt is mixing oxygenated blood with deoxygenated blood. Left-to-right shunts are more common and will not cause hypoxemia.

Right-to-left shunts are seen under physiologic conditions when the bronchial veins enter the systemic circulation.

Other causes of the right-to-left shunt are cyanotic heart diseases such as tetralogy of Fallot.

CO_2 transport

CO_2 generated in the peripheral tissue enters the RBCs and combines with H_2O (carbonic anhydrase) to form H_2CO_3, which dissociates into H^+ and HCO_3^-.
Bicarbonate is exchanged with chloride and hydrogen ion binds hemoglobin. This is about 85% of CO_2.
About 5% is dissolved in the blood, and the rest is bound to hemoglobin.



CO_2 transport in blood

Control of Respiration

Central & peripheral receptors are involved in the control of respiration. The peripheral receptors include chemoreceptors, **J receptors** and lung stretch receptors, muscle spindles, and irritant receptors.
The central control of respiration is both voluntary (cortex) and involuntary (by medulla).
The medullary centers include the **dorsal (inspiratory)** and the **ventral (expiratory)** group of cells.
The pons centers include a **pneumotaxic center (upper pons)** and an **apneustic center (lower pons)**.
The central chemoreceptors in the medulla are sensitive to PCO2 changes. This area is without a blood-brain barrier.
The peripheral chemoreceptors in the carotid and aortic bodies are sensitive to hypoxemia and H^+ ion concentration.

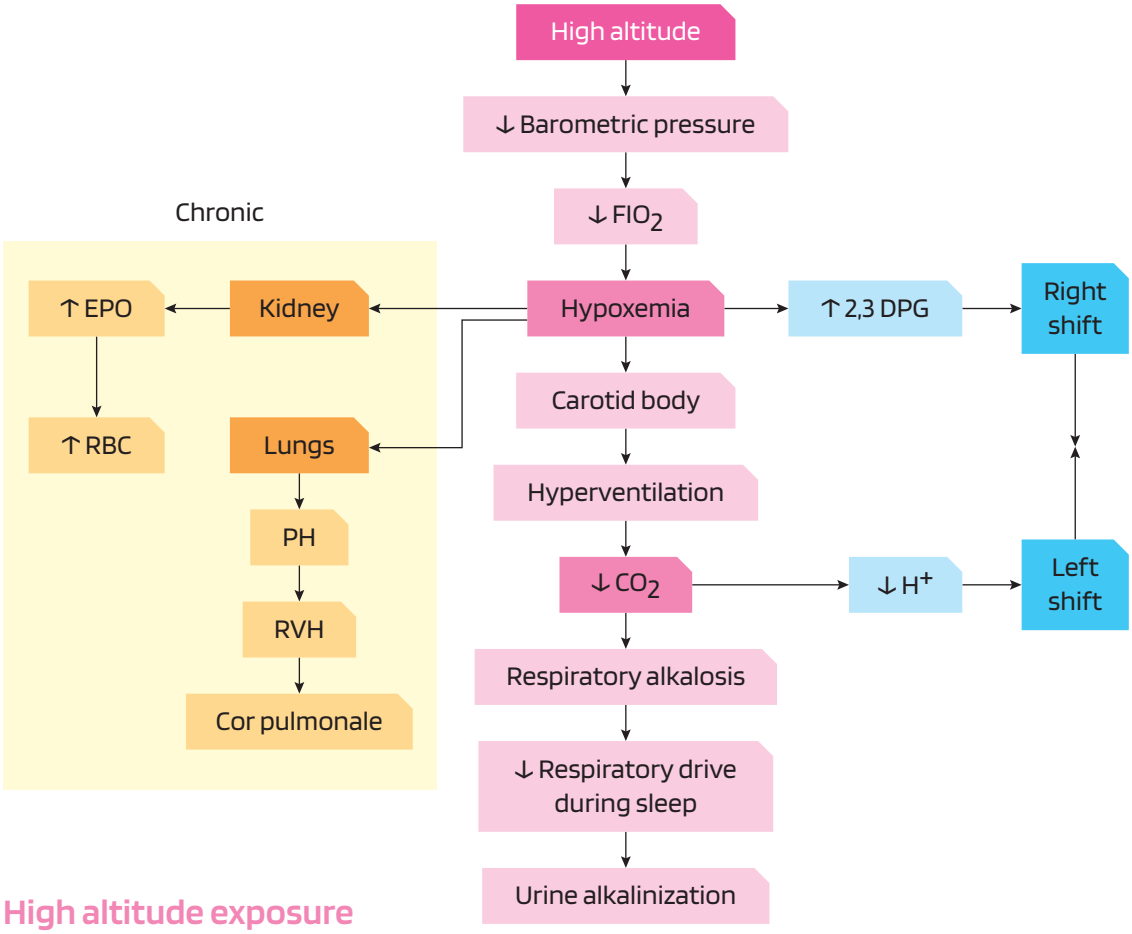
Respiratory changes during exercise

Increased	Constant
O_2 consumption	PaO_2
CO_2 production	$PaCO_2$
Tidal volume & respiratory rate	V/Q is more uniform throughout the lungs
Pulmonary blood flow	
Lactate & H^+ (right shift)	
Venous CO_2 content (O_2 is decreased)	
Anatomic dead space (distention of airways)	

Respiratory changes during exercise

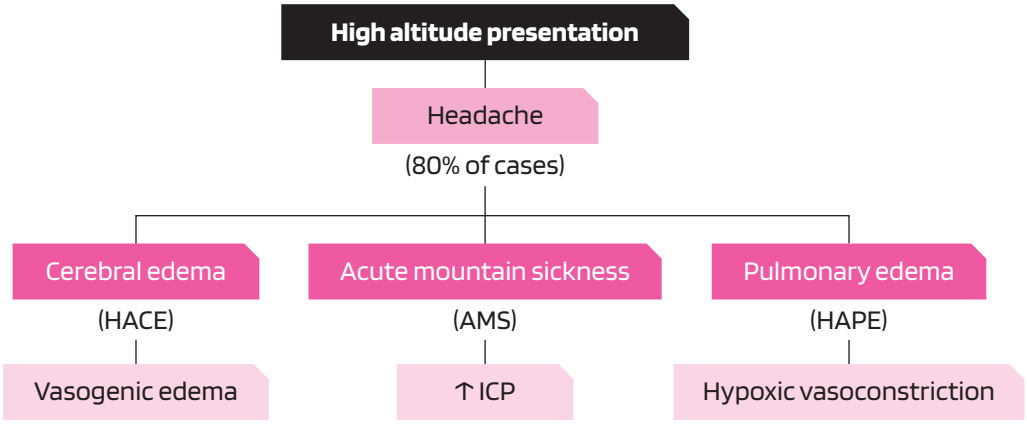
High-altitude

Acute exposure to high-altitude conditions causes respiratory alkalosis; however, chronic exposure causes erythrocytosis and pulmonary hypertension (vasoconstriction due to hypoxemia).



High altitude exposure

High altitude presentation



High altitude presentation

Aging and respiratory system

Aging of the respiratory system
↓ respiratory muscles power
↓ vital capacity
↓ response to hypercapnia & hypoxemia
↓ physiologic reserve
↑ chest wall rigidity
↑ residual volume (TLC stays the same since vital capacity decreases)
↑ terminal air space
↑ V/Q mismatch
↑ pulmonary artery pressure

Aging of the respiratory system

Respiratory formulas

A-a gradient	$< 2.5 + (\text{Age} \times 0.21)$
Alveolar PO_2	$PIO_2 - O_2$ used $(150 - 50) = 100$
Total dead space	$\text{Tidal volume} \times \frac{(PaCO_2 - PECO_2)}{PaCO_2}$
Minute ventilation	Tidal volume × RR
Alveolar ventilation	(Tidal volume − dead space) × RR

Respiratory formulas

A-a gradient is the difference between the alveolar and arterial O2;
PaCO2, arterial PCO2;
PECO2, PCO2 in the expired air;
RR, respiratory rate