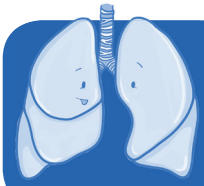


NOTES
GAS TRANSPORT

OXYGEN BINDING CAPACITY & OXYGEN CONTENT

osms.it/oxygen-binding-capacity-oxygen-content

MEASURES OF OXYGEN AVAILABILITY

O_2 binding capacity

- Maximum amount of O_2 bound to hemoglobin when 100% saturated (per blood volume)
  - More hemoglobin → more oxygen (per blood volume)
- Measurement
  - Expose blood to air with high P_{O2} → complete hemoglobin saturation
  - Hemoglobin's oxygen affinity → 1g of hemoglobin A binds 1.34mL of O_2
  - Normal hemoglobin A concentration in blood → 15g/100mL
  - O_2 binding capacity = hemoglobin concentration × hemoglobin's affinity for oxygen
- *Example:* O_2 binding capacity = 15g/100mL × 1.34mL O_2/g hemoglobin = 20.1mL O_2/100mL blood

Oxygen content (CaO_2)

- Oxygen (mL) per 100mL of blood
- CaO_2 = O_2 binding capacity × % saturation + oxygen dissolved in solution
  - Correction for dissolved O_2 → solubility of O_2 in blood → 0.003mL O_2/100mL blood per mmHg
- CaO_2 = hemoglobin concentration (g/100mL blood) × hemoglobin oxygen affinity (mL O_2/g) × SaO_2 (arterial oxygen saturation) + partial pressure of oxygen (mmHg) × solubility of O_2 in blood (mL O_2/blood/mmHg)
- CaO_2 (ml O_2/100mL blood) = ([Hb] × 1.34 × SaO_2) + (PaO_2 × 0.003)

O_2 DELIVERY TO TISSUES

- Dependent on blood flow (determined by cardiac output), blood's oxygen content
- O_2 delivery = cardiac output × oxygen content

OXYGEN TRANSPORT

- Majority of oxygen in blood bound to hemoglobin, remainder dissolved in solution

Dissolved O_2

- Free in solution (1.5% of total blood O_2 content)
- Only free O_2 contributes to partial pressure → drives O_2 diffusion
- O_2 solubility in blood = 0.003mL O_2/100mL blood per mmHg → at normal PaO_2 of 100mmHg → concentration of dissolved O_2 is 0.3mL O_2/100mL blood
- Normal consumption of O_2 = 250mL O_2/minute
- Only dissolved O_2 delivered to tissues (cardiac output 5L/min) × dissolved O_2 concentration → 15mL O_2/min → incompatible with life
- Hemoglobin increases amount of O_2 carried by blood

Hemoglobin bound

- Hemoglobin → greater concentrations of O_2 carried to tissues by blood
- 98.5% of O_2 in blood bound to hemoglobin

- Four subunits of hemoglobin molecule
  - *Each subunit contains heme moiety:* iron-binding porphyrin, polypeptide chain (alpha/beta)
  - *Adult hemoglobin subunits ($\alpha_2\beta_2$):* two alpha chains, two beta chains → each contains one iron molecule (Fe^{2+}) → binds one O_2 molecule → four molecules of O_2 per molecule of hemoglobin → oxyhemoglobin
  - Deoxygenated hemoglobin → deoxyhemoglobin

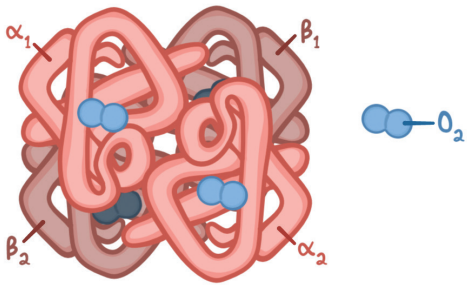


Figure 71.1 Each of the four hemoglobin subunits contains a heme group capable of binding one oxygen molecule.

- Heme binds oxygen in lungs → oxyhemoglobin
  - Oxygen diffuses from alveoli → across single cell thick alveolar walls → diffuses into blood → through red blood cell (RBC) membrane → interacts with heme → oxyhemoglobin (bright red blood)
- Oxygen binding to hemoglobin → conformational shift in heme structure → ↑ oxygen binding affinity → sigmoidal (S-shaped) oxygen-binding affinity/dissociation curve
- *At tissue level:* association process reversed
  - O_2 released → deoxyhemoglobin (dark red blood)
  - 20% of dissolved CO_2 → binds with globin amino acids (not heme group) of deoxyhemoglobin → carbaminohemoglobin

Fetal oxygen transport

- Fetal blood requires higher affinity for oxygen to facilitate movement of O_2 from maternal to fetal blood
- Fetal variant hemoglobin (hemoglobin F)
  - Contains two alpha chains, two gamma chains ($\alpha_2\gamma_2$) → greater affinity for oxygen

OXYGEN-HEMOGLOBIN DISSOCIATION CURVE

osms.it/oxygen-hemoglobin_dissociation_curve

- Proportion of saturated hemoglobin plotted against partial pressure of oxygen
- Illustrates how blood carries, releases oxygen as partial pressures vary
  - *Hemoglobin:* primary oxygen transporter in blood
  - Amount of oxygen bound to hemoglobin at any given time determined by environmental partial pressure of oxygen (high in lungs, lower in tissue capillary beds) → hemoglobin binds to oxygen in lungs, releases at tissue level
  - *Oxyhemoglobin dissociation curve:* determined by hemoglobin affinity for oxygen; rate hemoglobin acquires, releases oxygen into surrounding fluid; plots SO_2 against PO_2

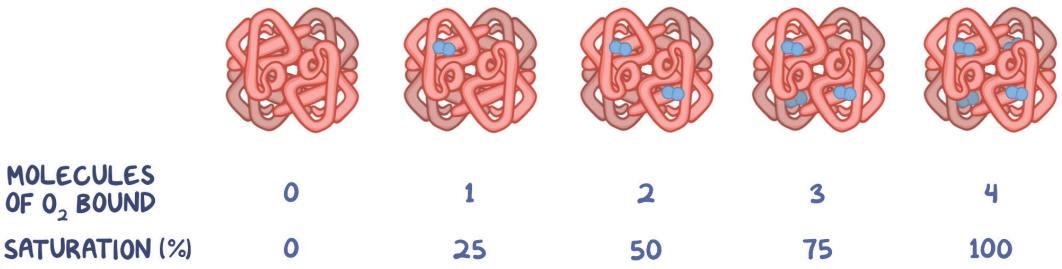


Figure 71.2 Each hemoglobin molecule can bind four O_2 molecules, but each hemoglobin isn't always 100% saturated, or bound, by O_2. A hemoglobin molecule with no O_2 bound (0% saturation) is called deoxyhemoglobin.

SIGMOIDAL SHAPE

- Oxyhemoglobin dissociation curve is sigmoidal
  - Positive cooperativity → each successive oxygen molecule binding to heme group → ↑ affinity
  - Approaches maximum saturation limit → few binding sites remain → little additional binding possible → curve levels off → large ↑ in oxygen partial pressure → no effect on hemoglobin saturation beyond saturation point
  - Partial pressures ↓ at tissue level → oxygen release → with each successive oxygen molecule release, subsequent release eases → rapid oxygen unloading at low partial pressures

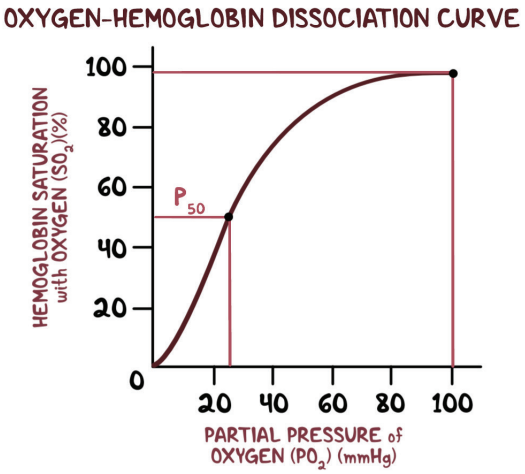


Figure 71.3 The oxygen-hemoglobin dissociation curve. O_2 saturation is influenced by the PO_2 of the blood. P_{50} indicates the partial pressure at which hemoglobin proteins are 50% saturated.

P_{50}

- P_{50}: partial pressure of oxygen in blood when hemoglobin 50% saturated (e.g. 26.6mmHg)
- Conventional measure of hemoglobin affinity for oxygen
- Physiological/disease processes may shift dissociation curve to left/right, alter P_{50}
  - Left shift → lower P_{50} → ↑ oxygen affinity
  - Right shift → raised P_{50} → ↓ oxygen affinity

RIGHT SHIFT

- Right shift → lower oxygen affinity → 50% saturation occurs at higher PO_2 → oxygen unloading

↑ PCO_2, ↓ pH

- ↑ metabolic activity of tissues → ↑ CO_2 → ↑ H^+ concentration → ↓ pH → ↓ hemoglobin oxygen affinity → oxygen unloading in metabolically active tissues
- Effect of PCO_2, pH on oxygen-hemoglobin dissociation curve → Bohr effect

↑ temperature

- Very metabolically active tissue (e.g. active muscle → ↑ heat production → ↓ hemoglobin oxygen affinity)

↑ 2,3-diphosphoglycerate (2,3-DPG) concentration

- 2,3-DPG (glycolysis byproduct) → binds deoxyhemoglobin beta chains → ↓ oxygen affinity → binds to hemoglobin beta chains → oxygen unloading
- 2,3-DPG production ↑ under hypoxic conditions (e.g. living at high altitude) →

hypoxemia → 2,3-DPG production in red blood cells → greater oxygen delivery to tissues

LEFT SHIFT

- Left shift → higher oxygen affinity → 50% saturation occurs at lower PO_2 → impairs oxygen unloading

↓ PCO_2, ↑ pH

- ↓ tissue metabolism → ↓ CO_2 production → ↓ H^+ concentration → ↑ pH → left shift → O_2 tightly bound to hemoglobin

↓ temperature

- ↓ tissue metabolism → ↓ heat production → ↓ O_2 unloading

↓ 2,3-DPG concentration

- ↓ tissue metabolism → ↓ 2,3-DPG concentration → ↓ O_2 unloading

Hemoglobin F

- Alternate molecular structure → ↑ oxygen affinity → left shift
- 2,3-DPG doesn't bind strongly to HbF gamma chains

Carbon monoxide (CO)

- Causes left shift, ↓ maximum saturation possible (curve levels off at lower PO_2)
- CO binds to hemoglobin with 250x affinity of O_2 (at partial pressure; 1/250 O_2, = O_2; CO bound to hemoglobin) → forms carboxyhemoglobin (longer-living molecule than oxyhemoglobin)
- CO binding to heme → confirmation shift → ↑ remaining heme molecules' affinity for oxygen (reducing oxygen release efficiency) → CO poisoning reduces blood's absolute oxygen-carrying capacity, impairs oxygen release → hypoxic injury

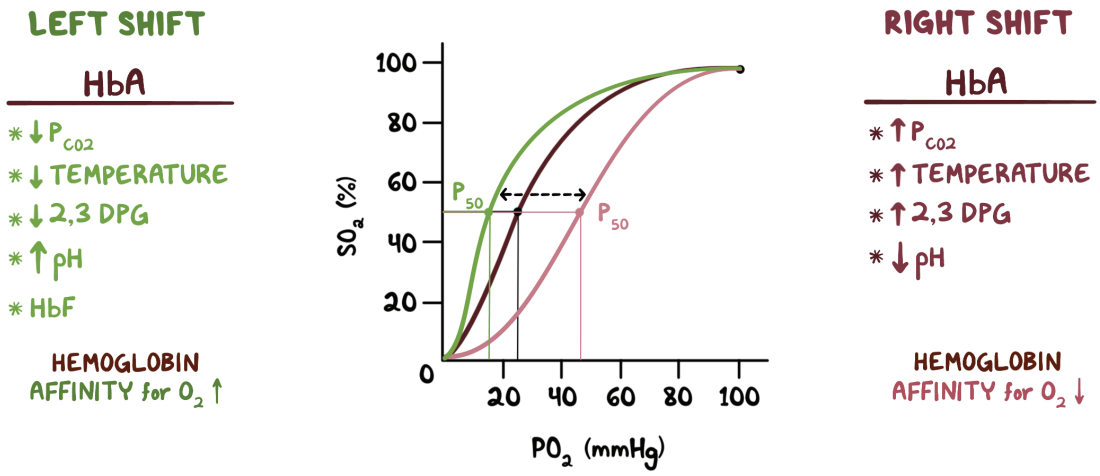


Figure 71.4 Summary of factors that can shift the oxygen-hemoglobin dissociation curve to the left (↑ hemoglobin's affinity for O_2) and to the right (↓ hemoglobin's affinity for O_2).

ERYTHROPOIETIN (EPO)

osms.it/erythropoietin

- Glycoprotein cytokine secreted by kidney (cellular hypoxia response) → stimulates erythropoiesis → RBCs

RENAL INDUCTION OF EPO SYNTHESIS

- ↓ O_2 delivery to kidneys (↓ hemoglobin concentration/PaO_2) → increased production of alpha subunit of hypoxia-inducible factor 1 (HIF1)
- Hypoxia-inducible factor 1-alpha (HIF1A) → acts on fibroblasts in renal cortex, medulla → upregulation of EPO messenger RNA (mRNA) → increased EPO synthesis
- EPO → promotes proerythroblast differentiation → mature to form erythrocytes (maturation not EPO-dependent)

RENAL SENSING OF HYPOXIA

- To effectively regulate EPO secretion, kidneys must distinguish between following:

Decreased blood flow

- → ↓ O_2 availability
  - ↓ renal blood flow → ↓ glomerular filtration → ↓ sodium (Na^+) filtration/reabsorption → ↓ O_2 consumption (Na^+ resorption closely linked to O_2 consumption in kidney)
  - O_2 delivery, consumption remain matched → EPO production not triggered

Decreased arterial blood O_2 content

- → ↓ O_2 availability
  - Renal blood flow remains normal → normal glomerular filtration → normal Na^+ filtration/reabsorption → reduced oxygen availability for given metabolic demand → stimulus for EPO secretion

CARBON DIOXIDE TRANSPORT IN BLOOD

osms.it/carbon-dioxide-transport-in-blood

- Carried as dissolved carbon dioxide (CO_2), carbaminohemoglobin (bound to hemoglobin), bicarbonate (HCO_3^-)

DISSOLVED CO_2

- Small fraction of CO_2 dissolved in blood (similar to oxygen)
- *Henry's law:* CO_2 concentration in blood = partial pressure x solubility of CO_2
- *Solubility:* 0.07mL CO_2/100mL blood per mmHg
- *Partial pressure:* 40mmHg
- Concentration = 2.8mL CO_2/100mL blood (5% of total CO_2 content of blood)

CARBAMINOHEMOGLOBIN

- CO_2 binds to terminal amino groups on proteins (e.g. albumin, hemoglobin)
- CO_2 bound to hemoglobin → carbaminohemoglobin (3% of total blood CO_2)
  - CO_2 binding to hemoglobin at different site than oxygen → conformational shift of protein structure → ↓ oxygen affinity

→ right shift in dissociation curve

- *Haldane effect*: less O_2 bound to hemoglobin → ↑ CO_2 affinity

BICARBONATE

- 90% of CO_2 in blood
- *Tissue level*: CO_2 produced by aerobic metabolism → driven by partial pressure gradient → CO_2 diffuses across cell membrane, capillary wall → enters RBCs

RBC blood pH regulation

- RBCs regulate blood pH via interaction with CO_2 in blood
- RBCs contain enzyme, carbonic anhydrase → catalyzes conversion of CO_2, water → carbonic acid (also catalyzes reverse reaction)
- Carbonic acid dissociates into bicarbonate, hydrogen ion in blood
  - $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$
  - Mass action drives reaction to right as tissues continuously supply CO_2
- H_2CO_3 dissociates → H^+, HCO_3^-
- H^+ remains in RBCs → buffered by deoxyhemoglobin
  - If H^+ remains free in solution → acidifies RBCs, venous blood → H^+ must be buffered
  - H^+ buffered by deoxyhemoglobin, carried in venous blood (deoxyhemoglobin more efficient buffer than oxyhemoglobin)
  - H^+ production favors oxyhemoglobin conversion → deoxyhemoglobin (Bohr effect)
- HCO_3^- transported into plasma (exchanged for chloride)
  - Band 3 protein facilitates anion exchange of Cl^- for HCO_3^- (chloride shift)
  - HCO_3^- carried in plasma to lungs

Respiratory system blood pH regulation

- Respiratory system further regulates blood pH
  - Controls CO_2 elimination rate → CO_2 elimination ↑ pH by shifting equation to left
  - RBCs, carbonic anhydrase allow rapid reaction in lungs → reverse processes in blood at tissue level

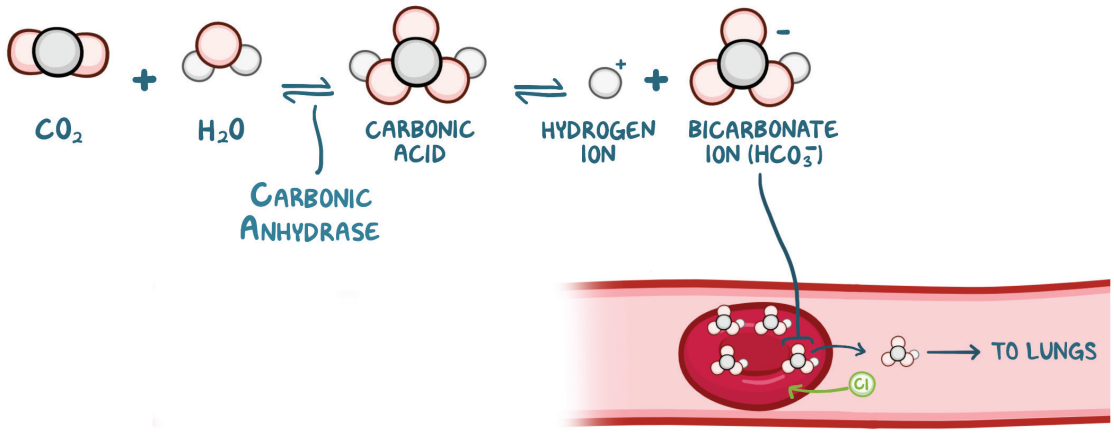


Figure 71.5 CO_2 transport in the form of bicarbonate. CO_2 undergoes a chemical reaction with H_2O to form carbonic acid, which then dissociates into hydrogen ions and bicarbonate ions. This reaction can occur in the plasma, but is sped up in red blood cells by the presence of carbonic anhydrase enzymes. Ionic exchange of bicarbonate ions and chloride occurs via facilitated diffusion to ensure charges stay balanced. Bicarbonate then travels to the lungs in the plasma.

REGULATION OF PULMONARY BLOOD FLOW

osms.it/pulmonary-blood-flow-regulation

- Regulated by altering arteriole resistance → controlled by arteriolar smooth muscle tone
- Regulatory changes mediated by local vasoactive substance concentrations

PULMONARY VASOACTIVE SUBSTANCES & STATES

Nitric oxide (NO)

- Retains similar function on pulmonary vascular beds (compared to systemic) → vasodilation
- Nitric oxide (NO) synthase inhibition → hypoxic vasoconstriction enhancement
- Inhaled NO → reduction in/prevention of hypoxic vasoconstriction

Thromboxane A_2

- Product of arachidonic acid metabolism via cyclooxygenase pathway (macrocytes, leukocytes, endothelial cells)
- Lung injury → potent vasoconstrictor of pulmonary arterioles, veins

Prostaglandin I_2 (prostacyclin)

- Product of arachidonic acid metabolism via cyclooxygenase pathway (endothelium)
- Potent local vasodilator

Leukotrienes

- Product of arachidonic acid metabolism via lipoxygenase pathway
- Potent airway constrictor

LUNG VOLUME

- Pulmonary blood vessels → alveolar capillaries that surround alveoli, extra-alveolar vessels which do not (arteries, veins)

Increased lung volume

- Crushes alveolar capillaries → ↑ resistance to blood flow
- Intrapleural pressure becomes more negative (↓ resistance) → pulls open extra alveolar vessels
- *Total pulmonary vascular resistance:* sum of alveolar, extra-alveolar resistance → increased lung volume effect dependent on larger effect
  - Low lung volumes (extra-alveolar vessels dominate) → ↑ volume → extra-alveolar vessels pulled open → ↓ resistance
  - High lung volume (alveolar capillaries dominate) → ↑ lung volume → alveolar vessels crushed, sharp ↑ resistance

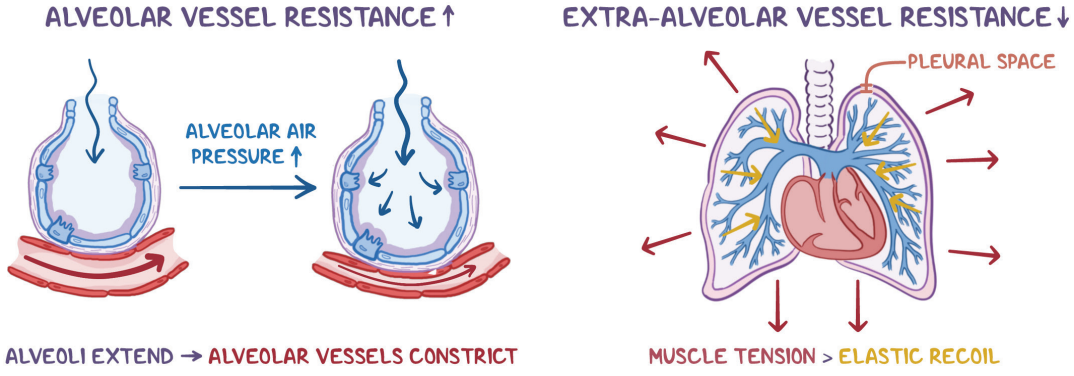


Figure 71.6 Blood vessel resistance associated with increased lung volume.

ZONES OF PULMONARY BLOOD FLOW

osms.it/zones-of-pulmonary-blood-flow

POSITIONAL EFFECT

- Supine gravitational effect largely uniform
- Upright distribution of blood flow (perfusion), ventilation throughout lungs not uniform
- Blood flow favors gravity-dependent lung regions → ↑ pulmonary arterial hydrostatic pressure moving inferiorly → blood flow in inferior (basal) regions > superior (apical) regions
- Ventilation favors apices → ventilation ↓ with move towards bases of lungs

LUNG ZONES

- Lungs divided into three vertical sections (based on pressure differences between compartments)

Zone I

- *Unobserved in healthy lung:* pulmonary arterial pressure (P_a) > alveolar pressure (P_A) in all parts of lung
- P_A generally = atmospheric pressure; can be overcome by low-pressure lung circulation
- Positive pressure ventilation → $P_A > P_a$ in apices of lung → blood vessels collapse → physiological dead space (ventilated, not perfused)

Zone II

- $P_a > P_A >$ pulmonary venous pressure (P_V)
- Capillary compression not problematic
- Perfusion driven by difference between P_a, P_A (not P_a, P_V; as in systemic vascular beds)

Zone III

- Majority of healthy lung volume
- No external resistance to blood flow
- Flow determined by P_a - P_V (both exceed P_A)

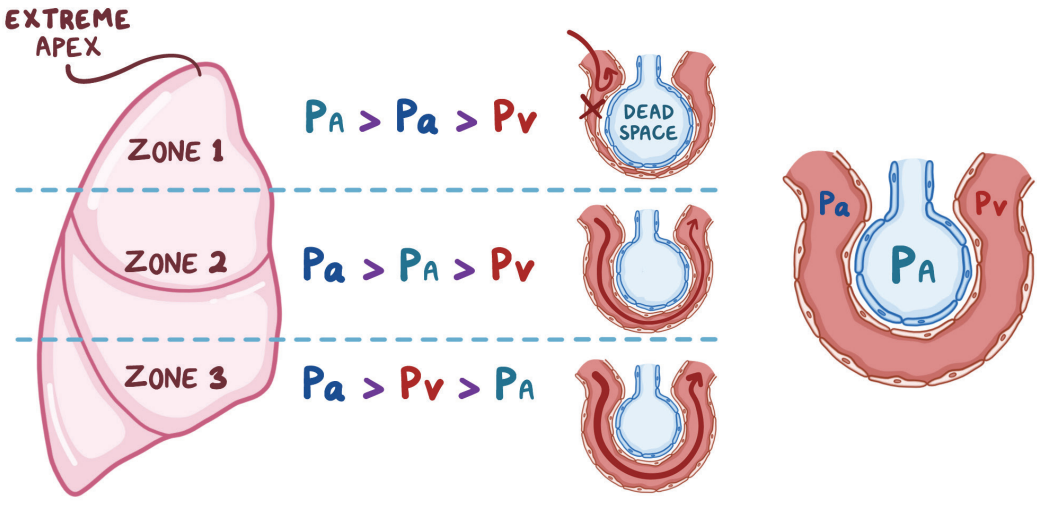


Figure 71.7 Relationships between P_A, P_a, and P_v in the three lung zones.

PULMONARY SHUNTS

osms.it/pulmonary-shunts

- Shunts occur when blood flow redirected from expected route, bypassing circulatory conduit

PHYSIOLOGICAL SHUNTS (ANATOMICALLY NORMAL)

- *Bronchial blood flow:* fraction of pulmonary blood which bypasses alveoli to supply bronchi
- *Coronary blood flow:* thebesian venous network allows for alternative myocardium drainage directly into left ventricle (not reoxygenated)

LEFT-TO-RIGHT SHUNTS

- More common
- Blood shunted from left to right heart
  - Due to septal defects (e.g. trauma, patent ductus arteriosus)
- Blood intended for systemic circulation directly circulated back to lungs → pulmonary blood flow exceeds systemic blood flow → fraction of blood does reach systemic circulation fully oxygenated → no hypoxia

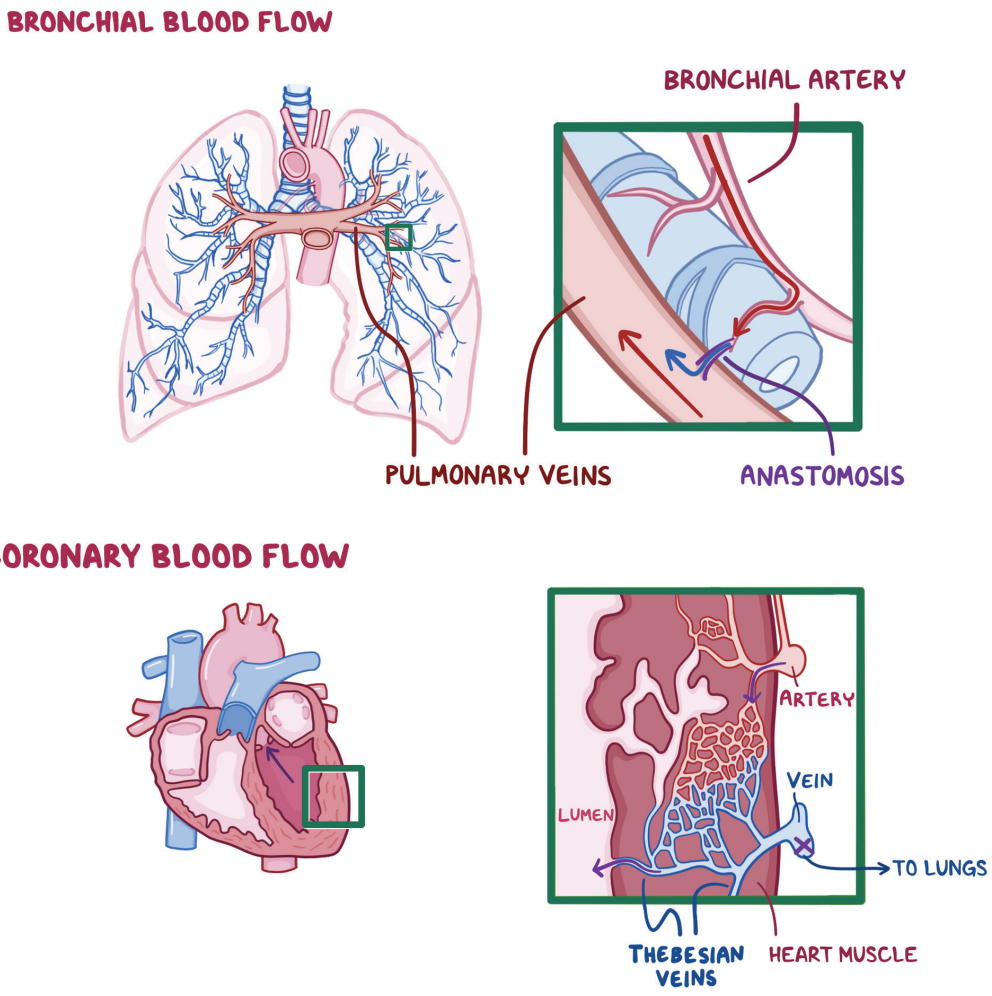


Figure 71.8 Physiologic shunts.

RIGHT-TO-LEFT SHUNTS

- Defect in wall between right, left sides of heart → blood shunted from right to left side of heart
- Allows for large cardiac output fraction to be shunted (approx. 50%) → bypasses lungs → oxygenated blood diluted with shunted deoxygenated blood → hypoxemia
- Not responsive to high P_{O2} gas treatment → complete pulmonary blood saturation doesn't improve shunted blood oxygenation
- Causes minimal Pa_{CO2} change → central chemoreceptors responsive to small Pa_{CO2} increases (shunted blood not available for gas exchange) → ↑ ventilation rate → extra CO_2 expired
- Central O_2 receptors significantly less sensitive than CO_2 receptors → only ↑ ventilation once Pa_{O2} < 60mmHg

Shunt fraction equation

- Oxygenation bypass of venous blood in lung capillaries
- $Q_S/Q_T = (C_{CO2} - C_{AO2})/(C_{CO2} - C_{VO2})$
- Q_S: blood flow through right-to-left shunt (L/min)
- Q_T: cardiac output (L/min)
- C_{CO2}: oxygen content of nonshunted pulmonary capillary blood
- C_{aO2}: oxygen content of systemic arterial blood
- C_{VO2}: oxygen content of venous blood

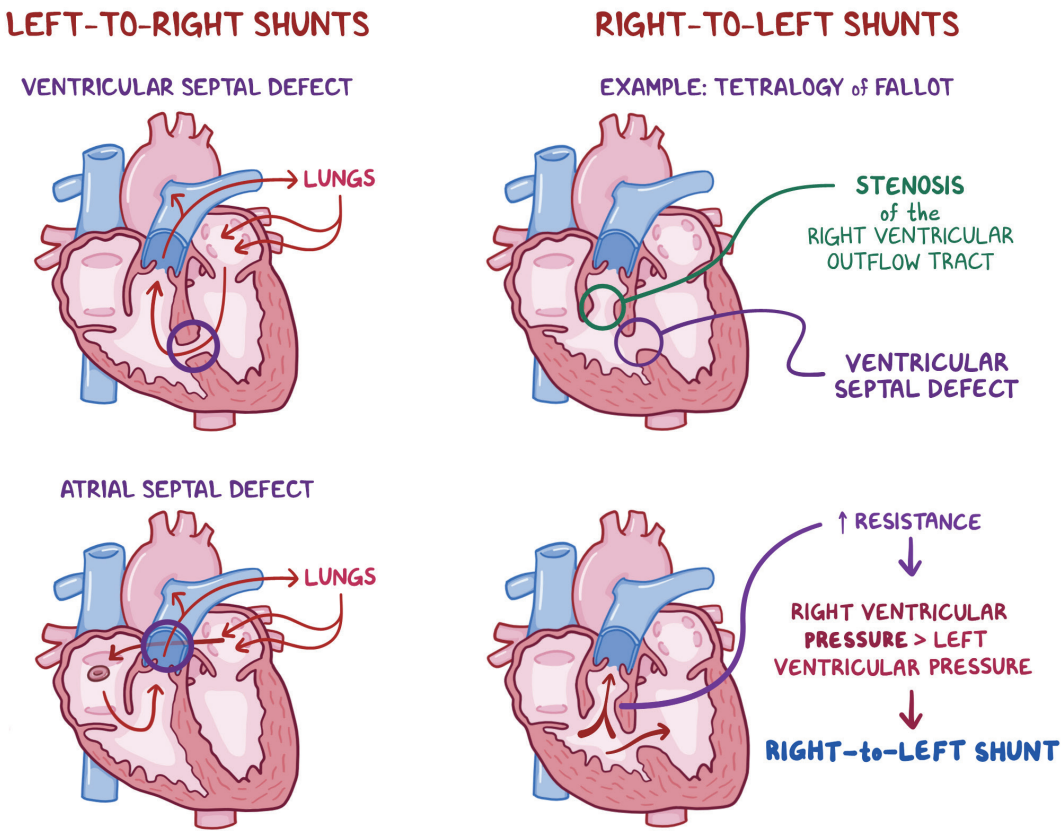


Figure 71.9 Pathologic shunts occurring in the left-to-right (more common) and right-to-left directions.

VENTILATION PERFUSION RATIOS & V Q MISMATCH

osms.it/ventilation-perfusion-ratios-V-Q-mismatch

- Ratio of amount of air to amount of blood reaching alveoli per minute ($\dot{V}/\dot{Q}$ ratio)

IDEAL SCENARIO

- Oxygen provided saturates blood fully → ratio of 1

NORMAL SCENARIO

- Average across entire lung → ratio of 0.8 (apex higher, bases lower)
- Normal breathing rate, tidal volume, cardiac output

DEFECTS

- Mismatching between ventilation, perfusion → abnormal gas exchange

Dead space

- Ventilation of lung regions not perfused
- No gas exchange (no blood to facilitate gas exchange)
- Alveolar gas same composition as humidified inspired air (PA_{O2} = 150mmHg, PA_{CO2} = 0)
- Pulmonary embolism

High $\dot{V}/\dot{Q}$

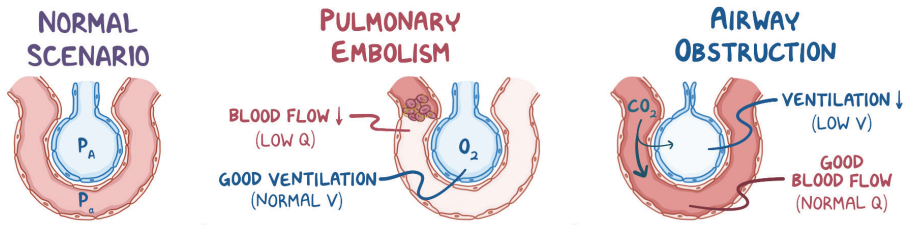
- High ventilation relative to perfusion (ventilation wasted)
- Usually due to ↓ blood flow (limited blood flow → limited gas exchange)
- Relatively high ventilation → pulmonary capillary blood with high P_{O2}, low P_{CO2}
- Emphysema

Low $\dot{V}/\dot{Q}$

- Low ventilation relative to perfusion (perfusion wasted)
- Usually due to ↓ ventilation → pulmonary capillary blood with low P_{O2}, high P_{CO2}
- Asthma, chronic bronchitis, pulmonary edema, etc.

Right-to-left shunt

- Perfusion of lung regions not ventilated
- No gas exchange occurs (no gas available to exchange)
- Same blood composition as mixed venous blood (Pa_{O2} = 40mmHg, Pa_{CO2} = 46mmHg)
- Airway obstruction, right-to-left cardiac shunts, etc.



V/Q	NORMAL (0.8)	HIGH (can equal ∞)	LOW (can equal zero)
Pa_{O_2}	95 mmHg	N/A	↓ to 40 mmHg
Pa_{CO_2}	40 mmHg	N/A	↑ to 40 mmHg
PA_{O_2}	100 mmHg	150 mmHg	N/A
PA_{CO_2}	40 mmHg	0 mmHg	N/A

Figure 71.10 Normal $\dot{V}/\dot{Q}$, P_a, and P_A compared to pulmonary embolism and airway obstruction.

HYPOXEMIA & HYPOXIA

osms.it/hypoxemia-and-hypoxia

HYPOXEMIA

- Decrease in arterial Pa_{O2}

High altitude

- Barometric pressure is decreased → decrease in P_{O2} of inspired air → decreased PA_{O2}
- Equilibration of alveolar air, pulmonary capillary blood (normal)
- Systemic arterial blood achieves same (lower) P_{O2} of alveolar air
- Normal alveolar–arterial (A–a) gradient
- High altitude breathing supplemental O_2 → raised inspired P_{O2} → raised PA_{O2} → raised Pa_{O2}

Hypoventilation

- Less inspired fresh air → decrease in PA_{O2}
- Normal equilibration → pulmonary capillary blood achieves same (lower) PA_{O2} as A–a gradient
- *Hyperventilation:* breathing supplemental O_2 → raised PA_{O2} → raised Pa_{O2}

Diffusion defects (fibrosis, pulmonary edema)

- Increased diffusion distance/decreased surface area → impaired equilibration
- Normal PA_{O2}, decreased Pa_{O2} → ↑ A–a gradient
- Breathing supplemental O_2 → raised PA_{O2} → increased driving force for diffusion → raised Pa_{O2}

Ventilation/perfusion mismatches

- Regions of well-ventilated (high PA_{O2}), poorly-ventilated (low PA_{O2}), well-perfused, poorly-perfused lung
- Poor perfusion to well-ventilated areas, adequate perfusion to areas poorly ventilated → low Pa_{O2}
- Supplemental oxygen → raised PA_{O2} in poorly-ventilated areas with adequate perfusion → increase in Pa_{O2}
- ↑ A–a gradient

COMMON HYPOXEMIA CAUSES/THEIR EFFECT ON GAS EXCHANGE

CAUSE	PaO2	A–a GRADIENT	SUPPLEMENTAL O2 BENEFICIAL?
HIGH ALTITUDE	↓	Normal	Yes
HYPOVENTILATION	↓	Normal	Yes
DIFFUSION DEFECT	↓	↑	Yes
VENTILATION/PERFUSION MISMATCH	↓	↑	Yes
RIGHT-TO-LEFT-SHUNT	↓	↑	↑ shunt severity → ↓ effect

Right-to-left shunts (right-to-left cardiac shunts, intrapulmonary shunts)

- Shunted blood completely bypasses alveoli, cannot equilibrate
- Shunted blood mixes with, "dilutes" blood that did pass through alveoli → ↓ Pa_{O2} (even if PA_{O2} normal)
- ↑ A–a gradient
- Limited supplemental O_2 effect → raises PA_{O2}, Pa_{O2} of nonshunted blood, does not address underlying shunted blood/oxygenated blood mixing → larger shunt, less effective supplemental O_2

HYPOXIA

- ↓ O_2 delivery to/utilization by tissues
- O_2 delivery → determined by cardiac output, O_2 content of blood
- ↓ cardiac output/localized blood flow → hypoxia
- Hypoxemia (any cause) → ↓ Pa_{O2} → ↓ hemoglobin saturation → ↓ oxyhemoglobin concentration in blood → ↓ oxygen delivery to tissues → hypoxia
- Anemia (↓ hemoglobin concentration) → ↓ oxyhemoglobin concentration in blood → decreased oxygen delivery to tissues → hypoxia
- Carbon monoxide poisoning → irreversible binding with hemoglobin → ↓ oxyhemoglobin concentration in blood → ↓ oxygen delivery to tissues → hypoxia
- Cyanide poisoning → interferes with O_2 utilization on cellular level

HYPOXIC VASOCONSTRICTION

- Alveolar partial pressure of oxygen (PA_{O2}) major factor controlling pulmonary blood flow
- ↓ PA_{O2} → vasoconstriction (opposite to systemic vasculature where ↓ in Pa_{O2} → vasodilation)
  - Vasoconstriction in response to poor oxygenation ensures blood flow coupled to areas of good ventilation → optimal gas exchange
  - In localized lung disease, areas of poorly-ventilated, diseased lung circumvented → blood directed towards healthy lung

COMMON HYPOXIA CAUSES/ARTERIAL OXYGENATION STATUS

CAUSE	MECHANISM	PaO2
↓ CARDIAC OUTPUT	↓ blood flow	Equilibrated
HYPOXEMIA	↓ PaO2 ↓ O2 saturation of hemoglobin ↓ O2 content of blood	↓
ANEMIA	↓ hemoglobin concentration ↓ O2 concentration of blood	Equilibrated
CARBON MONOXIDE POISONING	↓ O2 concentration of blood Left shift of O2-hemoglobin curve	Equilibrated
CYANIDE POISONING	↓ O2 utilization of blood	Equilibrated

Alveolar P_{O2} direct action on vascular smooth muscle → hypoxic vasoconstriction

- Pulmonary microcirculation surrounds alveoli
- O_2 highly lipid soluble → permeable across cell membranes
- Normal PA_{O2} (100mmHg), O_2 diffuses from alveoli → arteriolar smooth muscle → maintains relaxation, dilation of arterioles
- PA_{O2} decreases (70–100mmHg) → vascular smooth muscle sense change (hypoxia) → vasoconstriction → ↓ pulmonary blood flow to region
  - Vasoconstriction mechanism likely due to hypoxia → vascular smooth muscle depolarization → voltage-gated calcium channels open → calcium enters smooth muscle → contraction

HIGH ALTITUDE & HYPOXIC VASOCONSTRICTION

- Entire lung exposed to ↓ PA_{O2} (e.g. high altitudes) → global ↑ in pulmonary arteriolar resistance → ↑ pulmonary vascular resistance
- Chronic ↑ pulmonary vascular resistance → ↑ right heart afterload → right heart hypertrophy

FETAL HYPOXIC VASOCONSTRICTION

- Fetal circulation must acquire oxygen from maternal circulation via placenta → significantly lower Pa_{O2} → fetal lung vasoconstriction → reduction of blood flow to lungs (15% of cardiac output)
- At birth low pressure placenta circuit removed → ↑ systemic blood pressure → first breath after birth → ↑ PA_{O2} → 100mmHg → ↓ hypoxic vasoconstriction → ↓ pulmonary vascular resistance → pulmonary blood flow begins to normalize