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Detection & Correction of Hypoxia During Anesthesia

Hypoxia is a life-threatening condition in which oxygen delivery (DO_2) is inadequate to meet metabolic demands.



Photo by Elizabeth Harbin

D O_2 is the product of blood flow and oxygen content; thus, hypoxia may result from alterations in tissue perfusion, decreased oxygen partial pressure in the blood, or decreased oxygen-carrying capacity. Hypoxia may also result from restricted oxygen transport from the microvasculature to cells or impaired utilization within the cells.

An inadequate supply of oxygen ultimately causes cessation of aerobic metabolism and oxidative phosphorylation, depletion of high-energy compounds, cellular dysfunction, and death. A systematic approach to diagnosis and treatment will save valuable time when dealing with this imminently life-threatening problem.

Detection of Hypoxia

An arterial blood gas sample suggests tissue hypoxia if:

- The partial pressure of oxygen is < 90 mm Hg (hypoxemia)
- The bicarbonate level is < 20 mEq/L
- The base deficit is > -4

- The serum lactate level is > 5 mmol/L.

If the latter 2 variables are increasing, this is highly suggestive of ongoing tissue hypoxia. Tissue hypoxia can also be inferred when the pulse oximetry reading is less than 97%. False hypoxemic readings are common with pulse oximeters, so any value less than 97% should prompt an immediate assessment of the patient's clinical signs before deciding whether a reading is spurious.

Clinical Signs of Hypoxia

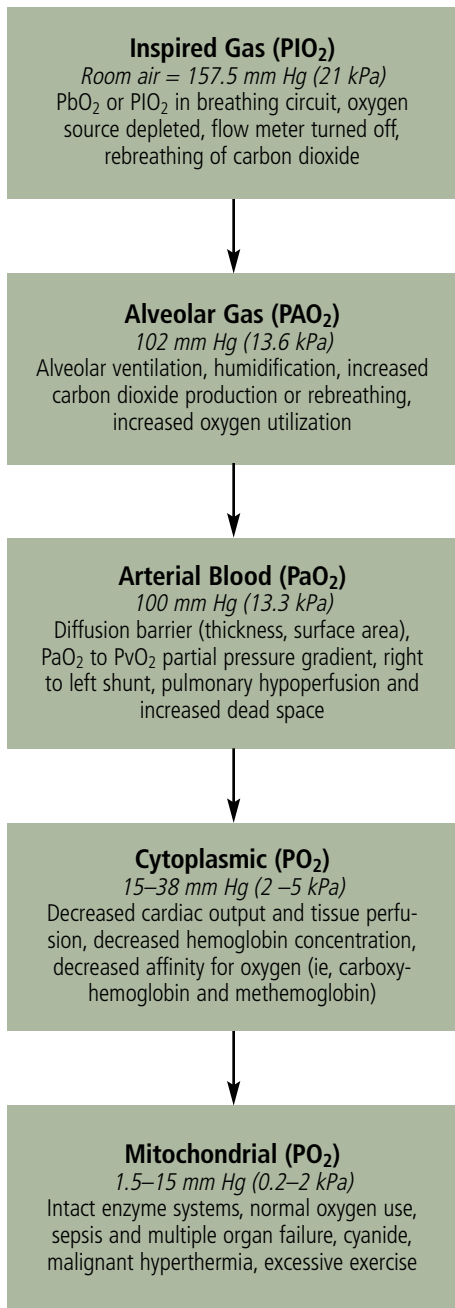
- **Mild arterial hypoxemia** (SaO_2 , 94%–96%; PaO_2 , 70–90 mm Hg) causes increased heart rate, cardiac output, and systemic vascular resistance. Mild hypertension may occur.
- **Moderate arterial hypoxemia** (SaO_2 , 91%–94%; PaO_2 , 60–70 mm Hg) results in local vasodilation and decreases in blood pressure. Heart rate may continue to increase if the baroreceptor reflex response is intact.

- **Severe hypoxemia** ($SaO_2 < 91\%$; $PaO_2 < 60$ mm Hg) allows local depressant effects to dominate; blood pressure falls rapidly, the heart rate slows, shock develops, and ventricular fibrillation or asystole follows.
- Hypoxemia promotes cardiac arrhythmias, stimulates respiration, and increases minute ventilation, although inadequate supply of oxygen to the brain stem eventually causes depressed respiration and apnea.
- In sedated or anesthetized patients, the early sympathetic nervous system reactivity to hypoxemia may be reduced, and bradycardia, severe hypotension, cardiovascular collapse, and apnea may occur before a problem is detected, particularly if monitoring is inadequate.
- Tissue hypoxia can be inferred if prolonged hypotension has occurred (mean arterial pressure < 60 mm Hg, systolic arterial pressure < 80 mm Hg for > 10 minutes).

continues

DO_2 = oxygen delivery; PaO_2 = arterial oxygen partial pressure; SaO_2 = saturation of hemoglobin

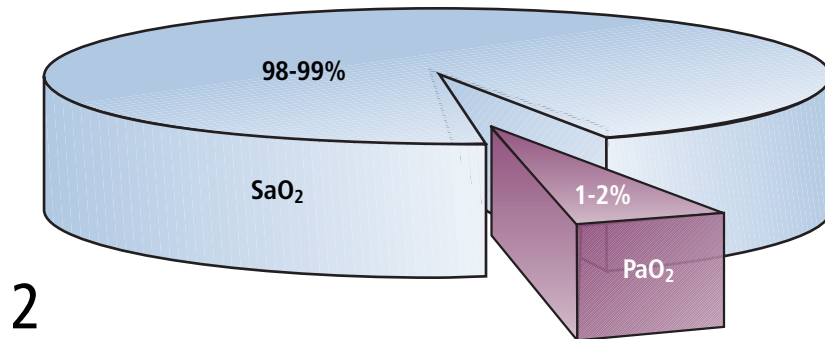
Physiological Oxygen Cascade



1 The oxygen cascade demonstrating the pathway of oxygen from the atmosphere to the mitochondria including the normal partial pressure of oxygen and the factors that can affect partial pressure of oxygen at each level.

kPa = kilopascal; PAO₂ = partial pressure of oxygen in alveolar gas; PaO₂ = arterial oxygen partial pressure; PbO₂ = atmospheric partial pressure of oxygen; PIO₂ = partial pressure of inspired oxygen; PO₂ = partial pressure of oxygen; PvO₂ = venous partial pressure of oxygen

Oxygen Content of Blood



2 Oxygen content of blood, including oxygen bound to hemoglobin (98%–99% of total oxygen content) and oxygen dissolved in plasma (1%–2% of total oxygen content)

Review of Oxygen Transport

- Oxygen passes from the atmosphere into the lungs, arterial circulation, extracellular fluid, interstitium, cytoplasm, and finally into the mitochondria, where it acts as the final electron acceptor in oxidative phosphorylation and production of adenosine triphosphate.
- As oxygen moves from the atmosphere to the tissues, it moves down a series of pressure gradients from the atmosphere (Figure 1).
- 1% to 2% of total oxygen in the blood is dissolved in plasma and is measured by PaO₂, the rest is bound to hemoglobin (Figure 2).
- SaO₂ in arterial blood under normal conditions is 97% to 100%; saturation of hemoglobin in venous blood is about 75%.
- If metabolic tissue requirements are met, oxygen extraction is constant at around 25% in most tissues regardless of delivery (flow-independent); 75% is returned to the heart and lungs.
- As DO₂ decreases, oxygen extraction increases up to 75% and sympathetic nervous system stimulation results in vasoconstriction, increased venous return, myocardial contractility, heart rate, and cardiac output in an attempt to maintain DO₂.
- In many tissues, once 75% extraction has been reached, the DO₂ becomes flow-dependent and there is a linear relationship between oxygen delivery and uptake.
- The heart normally extracts about 70% of the oxygen in coronary arterial blood and can-

not increase extraction much beyond that. Thus, it must rely on increased coronary blood flow via sympathetic nervous system stimulation, simultaneously resulting in increased myocardial oxygen consumption, which makes the heart particularly susceptible to hypoxia.

- The brain is another organ that is particularly susceptible to hypoxia—it has a very limited ability for anaerobic metabolism and neurons have very high metabolic activity.
- Hypoxia can result from problems located anywhere along the oxygen pathway, and systematically considering the main categories of hypoxia can help to determine the cause and facilitate appropriate treatment.

Main Categories of Hypoxia

See Table for summary of etiology and treatment.

Hypoxic Hypoxia

- Results from the inhalation of inadequate oxygen due to low partial pressure of inspired oxygen (PIO₂) or low fraction of inspired oxygen (FIO₂).
- Atmospheric oxygen partial pressure is determined by altitude, temperature, and other weather conditions. This pressure determines the PIO₂ in patient's breathing room air (21% FIO₂). At higher altitudes with lower barometric pressures, FIO₂ is 21%, but it is 21% of 620 mm Hg (PIO₂ = 130 mm Hg) instead of the sea level value of 21% of 760 mm Hg (PIO₂ = 160 mm Hg);

DO₂ = oxygen delivery; FIO₂ = fraction of inspired oxygen; PaO₂ = arterial oxygen partial pressure; PIO₂ = partial pressure of inspired oxygen; SaO₂ = saturation of hemoglobin

Table. Classifications, Etiology, & Treatment of Hypoxia

Type of Hypoxia	Etiology	Treatment
Hypoxic hypoxia	<ul style="list-style-type: none"> - Low PIO_2 or low FIO_2 - Oxygen flowmeter turned off - Oxygen source depleted - Patient is rebreathing carbon dioxide - Hypoxic mixture of nitrous oxide or carbon dioxide with oxygen, high altitude 	<ul style="list-style-type: none"> - Deliver supplemental oxygen via face mask, nasal cannula, oxygen cage, or tracheal intubation - Check flowmeter and oxygen source - Confirm fresh gas flow is adequate for nonbreathing circuit - Confirm carbon dioxide absorber not exhausted; rebreathing circuit 1-way valves not stuck - Discontinue nitrous oxide or carbon dioxide and administer 100% oxygen
Ventilatory hypoxia	<p>Hypoventilation (decreased respiratory rate and/or tidal volume) due to deep anesthesia, hypotension, increased intraabdominal pressure, upper or lower airway obstruction, hypothermia, thoracic or cranial abdominal pain, diaphragmatic hernia, opioid overdose, central or peripheral nervous system disease, paralysis, exhaustion or weakness</p>	<ul style="list-style-type: none"> - Deliver supplemental oxygen via face mask, nasal cannula, or tracheal intubation - Provide positive pressure ventilation - Lighten anesthesia - Reverse opioids (naloxone, 0.04 mg/kg, IV or IM) - Treat hypotension: Administer IV fluids, dobutamine or dopamine (5–10 μg/kg per min) - Avoid head-down positioning - Correct hypothermia - Treat thoracic or cranial abdominal pain (local or regional analgesia, opioids, IV lidocaine) - Reduce intraabdominal pressure
Diffusional hypoxia	<p>Pneumonia, pulmonary edema, pulmonary aspiration, pulmonary thromboembolism</p>	<ul style="list-style-type: none"> - Deliver supplemental oxygen via face mask, nasal cannula, tracheal intubation, or positive-pressure ventilation - Suction airway - Administer diuretics, antibiotics, antithrombotics
V/Q mismatch	<ul style="list-style-type: none"> - Increased physiologic dead space* due to low cardiac output, pulmonary hypoperfusion, cardiac arrest, pulmonary thromboembolism - Increased right-to-left shunt due to atelectasis (pleural effusion, pneumothorax, recumbency, general anesthesia), anatomic shunts (ventricular septal defect, patent ductus arteriosus) with decreased systemic vascular resistance and/or increased peripheral vascular resistance 	<ul style="list-style-type: none"> - Improve cardiac output and pulmonary perfusion with cardiopulmonary resuscitation, IV fluids, dopamine or dobutamine - Administer antithrombotics - Perform thoracocentesis, positive-pressure ventilation, alveolar recruitment maneuver to reinflate collapsed alveoli - Apply positive end-expiratory pressure (2.5–10 cm H_2O) - Correct hypoxia, hypercarbia, and hypotension
Perfusional hypoxia	<ul style="list-style-type: none"> - Decreased cardiac output resulting in pulmonary hypoperfusion and increased physiologic dead space, decreased DO_2 due to hypotension and poor tissue perfusion, low hemoglobin concentration, carbon monoxide poisoning, methemoglobinemia 	<ul style="list-style-type: none"> - Improve cardiac output with IV fluids, dopamine, or dobutamine - Transfuse packed red blood cells, whole blood, or Oxyglobin (www.biopure.com) - Deliver supplemental oxygen via face mask, nasal cannula, or tracheal intubation - Administer methylene blue (1 mg/kg)
Excessive utilization or inability to utilize oxygen	<ul style="list-style-type: none"> - Increased metabolism (ie, fever, malignant hyperthermia), sepsis and multiple organ failure, cyanide poisoning 	<ul style="list-style-type: none"> - Discontinue anesthetic - Provide IV fluids - Perform positive-pressure ventilation - Deliver supplemental oxygen via face mask, nasal cannula, or intubation - Correct acid-base and electrolyte abnormalities - Cool body (apply alcohol to pads, use fans, infuse room-temperature IV fluids) - For malignant hyperthermia, administer dantrolene (2–6 mg/kg IV) - Treat sepsis

*May also be classified as perfusional hypoxia

FIO_2 = fraction of inspired oxygen; PIO_2 = partial pressure of inspired oxygen; V/Q = ventilation-perfusion

the result is a lower PIO_2 .

- The pressure of oxygen in the breathing circuit determines PIO_2 in patients receiving supplemental oxygen, either via mask or tracheal intubation.
- Low FIO_2 and PIO_2 can occur when the oxygen flowmeter is turned down or off, the oxygen source is depleted, the patient is rebreathing carbon dioxide, or a hypoxic mixture of nitrous oxide or carbon dioxide and oxygen is administered.

Ventilatory Hypoxia

- Occurs with inadequate delivery of oxygen to the alveolus due to hypoventilation
- The PAO_2 can be calculated from the alveolar gas equation:

$$PaO_2 = FIO_2 (P_B - 47) - 1.2 (PaCO_2)$$

- P_B = atmospheric pressure
- 47 = saturated vapor pressure of water (mm Hg)
- 1.2 = constant (based on respiratory quotient of 0.8)
- $PaCO_2$ = partial pressure of carbon dioxide in arterial blood (assumed to equal the partial pressure of carbon dioxide in alveolar gas [$PACO_2$])
- As indicated by the equation, PAO_2 is determined by the following:
 - FIO_2 and PIO_2 in the atmosphere or breathing circuit
 - *Humidification*: The addition of water vapor reduces the PAO_2 slightly compared with PIO_2 ; humidification does not occur in a tracheally intubated patient attached to a nonhumidified breathing circuit.

- Minute ventilation

(*respiratory rate* × *tidal volume*):

Hypoventilation reduces delivery of oxygen to the alveolus and can be caused by upper or lower airway obstruction, increased intraabdominal pressure (obesity, pregnancy, gastric distention), thoracic or upper abdominal pain, hypothermia, central or peripheral nervous system disease, paralysis, exhaustion, weakness, high doses of opioids, and brain stem depression due to severe hypotension or high doses of

volatile and injectable anesthetics.

- *Carbon dioxide production and elimination*: Hypoventilation and increased production of carbon dioxide (ie, fever, malignant hyperthermia) result in increased $PACO_2$, thereby displacing oxygen and decreasing PAO_2 .

Diffusional Hypoxia

- PaO_2 is determined by the following:
 - **The partial pressure gradient of oxygen from the alveolus to the arterial blood, called the PAO_2 - PaO_2 gradient:**
 - Carbon dioxide is 20 times as diffusible as oxygen, so the partial pressure gradient for carbon dioxide is much lower than for oxygen.
 - Because oxygen is less diffusible, its uptake is greatly affected by alterations in the gradient (ie, low PAO_2).
 - **The diffusion barrier:**
 - Oxygen and carbon dioxide move across type I alveolar cells by simple diffusion, dependent on Fick's law of diffusion, which states that the volume of gas that moves across a sheet of tissue is directly proportional to its surface area and inversely proportional to its thickness.
 - Pulmonary thromboembolism dramatically reduces surface area for gas exchange and negatively affects oxygen uptake and carbon dioxide elimination.
 - Barrier thickness increases with pulmonary aspiration, pneumonia, pulmonary edema, and fibrosis and negatively affects oxygen diffusion.

Ventilation-Perfusion (V/Q) Mismatch Hypoxia

- Ideally, ventilation is perfectly matched with perfusion ($V/Q = 1$) at the alveolus, but there is always some mismatch.
- General anesthesia tends to increase mismatch in 2 possible ways:
 - **High V/Q (> 1 to ∞)** occurs when perfusion is low compared with ventilation because of increased dead space. Dead space in an anesthetized patient includes

the following:

- *Anatomic dead space*, or airways not involved in gas exchange
- *Mechanical dead space*, or portions of the breathing circuit in which there is no separation of inspired and expired gas streams (excessively long endotracheal tubes or extensions of the Y-connector)
- *Physiologic dead space*, or alveoli that are being ventilated but not perfused due to low cardiac output, pulmonary arterial hypotension, cardiopulmonary arrest, or pulmonary thromboembolism; increased physiologic dead space can also be classified as a type of perfusional hypoxia (see category below).
- **Low V/Q (< 1 to 0)** occurs when ventilation is low compared with perfusion, and effectively causes a right-to-left shunt. Shunt occurs whenever blood passes from the right to left side of the circulation without exposure to oxygen.
 - *Normal shunt fraction* is about 5% because venous blood from the myocardial and bronchial circulations empties into the left ventricle.
 - *A congenital shunt*—such as a ventricular septal defect, patent foramen ovale, or patent ductus arteriosus—shunts blood from the left side of the heart to the right side, as long as pulmonary vascular resistance, or right-heart afterload, is lower than systemic vascular resistance, or left-heart afterload. If pulmonary vascular resistance exceeds systemic vascular resistance, blood is shunted from the right side of the heart to the left side, resulting in reduced pulmonary blood flow and increased mixing of deoxygenated and oxygenated blood in the arterial circulation. Increases in pulmonary vascular resistance can result from hypoxemia, hypercarbia, and significant atelectasis during anesthesia. A significant decrease in systemic vascular resistance due to systemic arterial hypotension can also increase right-to-left shunting with congenital shunts.

DO_2 = oxygen delivery; FIO_2 = fraction of inspired oxygen; $PACO_2$ = partial pressure of carbon dioxide in alveolar gas; $PaCO_2$ = partial pressure of carbon dioxide in arterial blood; PAO_2 = partial pressure of oxygen in alveolar gas; PaO_2 = arterial oxygen partial pressure; PIO_2 = partial pressure of inspired oxygen; SaO_2 = saturation of hemoglobin; V/Q = ventilation-perfusion

- *Recumbency, general anesthesia, and positive intrathoracic pressure* (pneumothorax, pleural effusion) predispose to the development of atelectasis, which effectively causes shunting of blood from the right to the left side of the circulation without exposure to oxygen (these alveoli are perfused but not well ventilated).
- Oxygen uptake is greatly compromised by shunt, resulting in low PaO₂, even with supplemental oxygen.
- Carbon dioxide elimination is not compromised until the shunt is very severe (> 50%) because of its high diffusibility.

Perfusional Hypoxia

- Perfusional causes of hypoxia include the following:
 - Pulmonary hypoperfusion: Increased physiologic dead space and V/Q mismatch
 - Stagnant hypoxia: Tissue hypoperfusion and inadequate DO₂ to cells due to low cardiac output and systemic arterial hypotension

- Anemic hypoxia:
 - Oxygen content is determined by the amount dissolved in plasma (PaO₂) and the amount bound to hemoglobin.
 - The amount of oxygen bound to hemoglobin depends on the hemoglobin concentration, the affinity of the hemoglobin for oxygen, and the PaO₂, which provides the “driving pressure” for oxygen binding to hemoglobin.
 - SaO₂ indicates how much of the hemoglobin is saturated with oxygen, but doesn’t indicate whether hemoglobin concentration is adequate.
 - Anemia and reduced oxygen-carrying capacity of hemoglobin (carboxy-hemoglobin or methemoglobin) result in anemic hypoxia.

Excessive Utilization or Inability to Use Oxygen

- The final stage of oxygen delivery to tissues is diffusion from capillary blood into tissue

cells and uptake by the mitochondria, which requires an intact mitochondrial enzyme system.

- Histotoxic hypoxia can occur with cyanide poisoning and sepsis with multiple organ failure because both result in uncoupling of oxidative phosphorylation and inability of the cells to use oxygen.
- Examples of excessive utilization of oxygen are malignant hyperthermia, fever, and excessive exercise.

Conclusion

Timely detection and correction of hypoxia in sedated and anesthetized patients is imperative to avoid serious complications, including cardiac dysfunction, blindness, acute renal failure, and death. ■

See Aids & Resources, back page, for references, contacts, and appendices.

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