Foundations Frameworks

Approach to Hypoxemia

Author: Andrew Ketterer, MD, MA
Editors: Thomas Corbridge, MD; James Walter, MD; Kristen Grabow Moore, MD, MEd

Is your patient hypoxic, hypoxemic, or both?

Hypoxia is insufficient delivery of oxygen to the tissues

- Due low cardiac output, low Hb concentration, or low SaO_2

Hypoxemia is an abnormally low arterial oxygen tension in the blood

- Defined as $PaO_2 \leq 60$ mmHg (with the patient on room air)

Can occur independently:

- Patient with polycythemia can have low PaO_2 (hypoxemia) but no hypoxia due to increased O2 delivery
- Patient that is severely anemic can have normal PaO_2 but are hypoxia due to decreased O2 delivery

Hypoxemia can be caused by four major categories of disease:

1. Hypoventilation
2. V/Q mismatch (shunt physiology)
3. Delivery/uptake mismatch
4. Diffusion impairment

The alveolar-arterial O_2 gradient[1] is the best tool to differentiate these, so an ABG may be helpful in an otherwise undifferentiated hypoxemic patient. However, this is only obtainable in intubated patients whose FiO_2 can be definitively determined, and additionally these categories can significantly overlap, so this analysis is more applicable to the ICU than to the ED.

Hypoventilation

This is mainly from the following three categories:

- Brainstem respiratory depression (e.g. drug-induced, obesity-hypoventilation syndrome)
- Peripheral neuropathy (e.g. Guillain-Barre syndrome)
- Muscle weakness (e.g. myasthenia gravis, myopathy)

Note that hypoventilation is the ONLY cause of hypoxemia that does not alter the A-a gradient (under normal atmospheric partial pressures of oxygen, which can be decreased by e.g. fires or altitude).

V/Q Mismatch

Pretty much any lung disease can be included in this category, but the big four include:

- Blood (e.g. alveolar hemorrhage)
- Water (e.g. pulmonary edema, ARDS, CHF)
- Pus (e.g. pneumonia, empyema)
- Atelectasis (including COPD/asthma due to blood flow to ineffectively ventilated lung)

Note that cardiac abnormalities (e.g. PFO, VSD) can create shunt physiology as well (i.e. ventilation of the lungs without perfusion, with V/Q close to zero). Conversely, V/Q can approach infinity, creating perfusion without ventilation, or dead space (e.g. PE, pneumothorax).

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[1] A-a gradient = $PAO_2 - PaO_2$. PAO_2 (ideal alveolar O_2) is $PiO_2 - PaCO_2/0.8$. Because the A-a gradient increases with age, a "normal" gradient can be estimated as < (age in years/4) + 4.

Delivery/uptake Mismatch
The mismatch here only really matters when the lungs are impaired from extracting O_2 from the air, because during normal gas exchange a low mixed venous O_2 will be compensated by increased alveolar uptake. The mismatch can be from the following two categories:

- Decreased O_2 delivery (e.g. anemia, low-output shock, impaired O_2 binding)
- Increased tissue O_2 utilization (e.g. sepsis, thyrotoxicosis, hyperthermia, etc.)

Diffusion Impairment
This is a rare cause of acute hypoxemia, as it is frequently due to chronic structural lung problems (e.g. emphysema and pulmonary fibrosis). Still, acute pathology producing hypoventilation, V/Q mismatch, or delivery/uptake mismatch may complicate an underlying diffusion impairment.

Approach to Supplemental Oxygen
This only works reliably for hypoventilation, diffusion impairment, and delivery/uptake mismatch (not VQ mismatch)

- Hypoventilation: supplemental O_2 increases amount of alveolar O_2, which increases uptake by alveolar capillary blood
- Delivery/uptake mismatch: supplemental O_2 saturates available hemoglobin and increases the plasma saturation, increasing the amount of O_2 deliverable to tissues
- Diffusion impairment: supplemental O_2 helps overcome the lung's underlying difficulty in transporting oxygen into the alveolar capillary blood
- V/Q mismatch can *sometimes* be alleviated by supplemental O_2 if $V/Q < 1$, but it can also act as a shunt ($V/Q = 0$). In shunt physiology, blood circulates to alveoli unavailable for gas exchange, so supplemental O_2 won't help you here. Instead, you need to modify your respiratory support to treat the structural problem (e.g. PEEP/BiPAP, thrombolysis, etc.).

General Treatment for Hypoxia
1. Administer supplemental O_2:
    - This will improve most etiologies of hypoxemia except for severe V/Q mismatch leading to shunt physiology
2. Simultaneously address underlying pathophysiology:
    - Hypoventilation: give naloxone or other targeted drug antidote, provide NIPPV or intubate for impending (or actual) ventilatory failure
    - V/Q Mismatch: thrombolysis (or catheter-directed therapy) for PE, NIPPV for obstructive lung disease or CHF pulmonary edema, intubate as necessary
    - Delivery/Uptake Mismatch: blood transfusion for anemia, pressors for shock, 100% O_2 or hyperbaric therapy for CO poisoning, methylene blue for methemoglobinemia, propranolol for thyroid storm, etc.
    - Diffusion Impairment: be aware of underlying pathology that may be worsened by other causes of hypoxemia (e.g. prostaglandin-dependent pulmonary hypertension)

References:
Marino, Paul. *The ICU Book*. Chapter 20: Hypoxemia and Hypercapnia.