Blood Gases I: Why Oxygen Concentration Can Be Confusing

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Objectives

• Define “O₂ Content”, listing its 3 major variables
• Define the limitations of pulse oximetry
• Explain why a normal arterial PO₂ at sea level on room air is ~100 mmHg (13.3 kPa)
• Describe the major features of methemoglobin and carboxyhemoglobin

22 Year Old Female Comes to ER with “Hyperventilation”

• Healthy female. No known medical problems.
• Fine until a few days ago, when she noticed increasing urinary frequency with no pain; since yesterday, she’s become aware of rapid, deep breathing.
• Physical examination is normal, except for
  – rapid pulse (110, normal 70)
  – deep, rapid breathing (30 /min, normal 12)
O₂ Concentration of Blood

- not simply PaO₂
  - Arterial O₂ Partial Pressure ~100 mm Hg (~13.3 kPa)

- not simply Hct (~40%)
  - or, more precisely, Hgb (14 g/dL, 140 g/L)

- not simply “O₂ saturation”
  - i.e., ~89%

O₂ Content

\[
\text{O₂ Content} = 0.003 \times \text{PaO₂} + 1.4 \times \text{Hgb} \times \%\text{O₂Sat}
\]

= 0.0225 \times \text{PaO₂} + 1.4 \times \text{Hgb} \times \%\text{O₂Sat}

- normal value: about 20 mL/dL

Why Is the “Normal” PaO₂ 90-100 mmHg?

- PAO₂ = (FiO₂ \times [Patm - PH₂O]) - (PaCO₂ / R)
  - PAO₂ is alveolar O₂ pressure
  - FiO₂ is fraction of inspired oxygen (room air ~0.20)
  - Patm is atmospheric pressure (~760 mmHg at sea level)
  - PH₂O is vapor pressure of water (47 mmHg at 37 °C)
  - PaCO₂ is partial pressure of CO₂
  - R is the respiratory quotient (typically ~0.8)
  - \( \rightarrow 0.21 \times (760-47) - (40/0.8) \)
  - ~100 mm Hg

- Alveolar–arterial (A-a) O₂ gradient is normally ~10,
  so PaO₂ (arterial PO₂) should be ~90 mmHg

NB: To convert mm Hg to kPa, multiply by 0.133
Insights from PAO$_2$ Equation (1)

- $\text{PaO}_2 \sim \text{PAO}_2 = (0.21 \times [\text{Patm} - 47]) - (\text{PaCO}_2 / 0.8)$
  - At lower Patm, the PaO$_2$ will be lower
    - ➔ that’s why airplane cabins are pressurized
  - At higher Patm, the PaO$_2$ will be higher
    - ➔ we’ll exploit this later
  - Also:
    - “normal” PaO$_2$ in Boston is higher than in Denver
    - your PaO$_2$ is lower during a storm than on a sunny day

NB: To convert mm Hg to kPa, multiply by 0.133

Insights from PAO$_2$ Equation (2)

- $\text{PaO}_2 \sim \text{PAO}_2 = (0.21 \times [\text{Patm} - 47]) - (\text{PaCO}_2 / 0.8)$
  - On room air ($\text{FiO}_2 = 0.21$), at a given Patm,
    - As PaCO$_2$ decreases, PaO$_2$ increases
      - Patients who hyperventilate should have higher PO$_2$s
      - Don’t be surprised if a patient with a PCO$_2$ of 20 has
        a PO$_2$ of 120 – it’s expected!
    - As PaCO$_2$ increases, PaO$_2$ decreases
      - Patients with lung disease will have not only increased PaCO$_2$
        but lower PaO$_2$
      - Don’t be surprised if a patient with a PaCO$_2$ of 60 has
        a PaO$_2$ of 150-80-10 = 70

NB: To convert mm Hg to kPa, multiply by 0.133

Why is the “Normal” “O$_2$ Saturation” ~95%?

- sigmoid curve
- hemoglobin can bind ~ 1.4 mL O$_2$/g
  - when fully saturated
- at PO$_2 = 100$ mmHg, 100% saturated
- so, at a normal Hgb of ~14 g/dL, it holds
  $1.4 \times 14 = 19.6$ mL/dL

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A Quick Review

• Under typical conditions, for the reasons given, PaO₂ is ~100 mm Hg (~13.3 kPa)

• Based on the oxyhemoglobin dissociation curve, that PaO₂ corresponds to 100% "O₂ saturation", and each gram of Hgb can hold 1.4 mL of O₂

• So, returning to our O₂ content equation, we've explained the right-hand term

\[
= 0.003 \times \text{PaO}_2 + 1.4 \times [\text{Hgb}] \times [\%\text{O}_2\text{Sat}]
\]

So, What's the Other Term?

• Actually, it's quite simple: dissolved O₂

• And the equation for it is equally simple:

  – 0.003 x PO₂ (mm Hg) [0.0225 x PO₂ (kPa)]
    i.e., directly proportional to the partial pressure of O₂

  – at typical PO₂'s, it is negligible:
    0.003 x 100 mm Hg = 0.3 mL/dL
    0.0225 x 13.3 kPa = 0.3 mL/dL
    (vs Hgb-bound O₂ of 19.6 mL/dL, which we just calculated)

O₂ Concentration of Blood

• rather, a combination of all three parameters

• a value labs do not report

• a value few medical people even know!

\[
\text{O}_2\text{ Content} = 0.003 \times \text{PaO}_2 + \frac{1.4 \times [\text{Hgb}] \times [\%\text{O}_2\text{Sat}]}{0.3} \approx 20\text{ mL O}_2/\text{dL}
\]
Different Scenarios Illustrating Oxygen Content Concepts

<table>
<thead>
<tr>
<th>comments</th>
<th>PaO2</th>
<th>%O2Sat</th>
<th>Hgb</th>
<th>Hct</th>
<th>Dissolved Oxygen</th>
<th>Hgb-Bound O2</th>
<th>O2 Content</th>
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<tbody>
<tr>
<td>Normal</td>
<td>100</td>
<td>100</td>
<td>14</td>
<td>42</td>
<td>0.3</td>
<td>19.6</td>
<td>19.9</td>
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<td>Low Hct</td>
<td>100</td>
<td>100</td>
<td>7</td>
<td>21</td>
<td>0.3</td>
<td>9.8</td>
<td>10.1</td>
</tr>
<tr>
<td>Low PaO2 (lung disease)</td>
<td>25</td>
<td>50</td>
<td>14</td>
<td>42</td>
<td>0.1</td>
<td>9.8</td>
<td>9.9</td>
</tr>
<tr>
<td>50% Methemoglobin</td>
<td>100</td>
<td>50</td>
<td>14</td>
<td>42</td>
<td>0.3</td>
<td>9.8</td>
<td>10.1</td>
</tr>
<tr>
<td>Very Low Hct No Transfusion</td>
<td>100</td>
<td>100</td>
<td>2</td>
<td>6</td>
<td>0.3</td>
<td>2.8</td>
<td>3.1</td>
</tr>
<tr>
<td>Hyperbaric Chamber</td>
<td>2200</td>
<td>100</td>
<td>2</td>
<td>6</td>
<td>6.6</td>
<td>2.8</td>
<td>9.4</td>
</tr>
</tbody>
</table>

Causes of Low Oxygen Concentration

- anemia (low hemoglobin/hematocrit)
  - what most physicians focus on
  - probably the most frequent cause
- low PaO2 $\rightarrow$ low “O2 saturation”
  - e.g., lung disease
- low “O2 saturation” despite normal PO2
  - i.e., carboxyhemoglobin or methemoglobin

Hemoglobin Species

- Oxyhemoglobin
  - *oxygenated*
- Reduced (Non-Oxygenated) Hemoglobin
  - *capable of becoming oxygenated*
- Carboxyhemoglobin (carbon monoxide)
  - *cannot be oxygenated*
- Methemoglobin (oxidized Fe moiety)
  - *cannot be oxygenated*

How do we measure/distinguish them?
**Spectrophotometry**

With One Measurand, Life is Simple

- **\( A = \epsilon \times b \times C \)** (or **A=abc**)
  - Absorbance = (Molar Absorptivity)*(Pathlength)*(Concentration)

- Two ways to calculate **C** from measured **A**
  - Know **\( \epsilon \) and **b**
    - co-oximeter
  - Run standard(s) to calculate **\( \epsilon \times b \)**
    - most assays

Absorbances Are Additive

- If two species (M and N) are present, and each has absorbances at two wavelengths, you can solve two simultaneous equations to determine their concentrations
  
  - \( A_{\lambda 1} = (\epsilon_{M1})(b)([M]) + (\epsilon_{N1})(b)([N]) \)
  - \( A_{\lambda 2} = (\epsilon_{M2})(b)([M]) + (\epsilon_{N2})(b)([N]) \)

- \( 0.845 = 0.0265[M] + 0.0543[N] \)
- \( 0.675 = 0.0453[M] + 0.0277[N] \)

  \( \Rightarrow [M] = 7.9, [N] = 11.7 \)
Absorbances Are Additive: General Principle

- To measure n species, you need measurements at n wavelengths
- Pulse oximeters: 2 wavelengths → 2 species
- Co-Oximeters: >4 wavelengths → >4 species


Pulse Oximeters & Abnormal Hemoglobins

- “simplifying” assumption: only oxyhemoglobin and reduced hemoglobin are present
- works most of the time, but not all of the time
- tends to overestimate oxyhemoglobin, just what you don’t want


Oxygen Delivered to Tissues

\[ \text{oxygen delivered} = \text{arterial O}_2 \text{ content} - \text{venous O}_2 \text{ content} \]

\[ P_{50} = \text{PO}_2 \text{ where } O_2 \text{ saturation is 50%} \]

Blue: 18 (left-shift)  \quad 10.9
Black: 25 (normal) \quad 8.0
Red: 37 (right shift)
Oxyhemoglobin Terminology

- Currently, there are 3 terms used for “oxygen saturation” (CLSI C-46, 2009)
  - hemoglobin oxygen saturation (SO₂)
  - fractional oxyhemoglobin (FO₂Hb)
  - estimated oxygen saturation (O₂Sat)

- in normal individuals, these values match closely
- but, in patients, they can be significantly different

- In general, physicians and other health care professionals
  - use the term O₂sat (#3) to mean hemoglobin oxygen saturation (#1)
  - have never heard of the term fractional oxyhemoglobin (#2),
    though that is what co-oximeters “should” report

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Oxyhemoglobin Terminology

- SO₂ is calculated as:
  - \( \frac{\text{oxyhemoglobin}}{\text{oxyhemoglobin} + \text{reduced hemoglobin}} \)
  - represents the percentage of hemoglobin capable of being oxygenated
    that is oxygenated
  - in other words, the denominator explicitly omits from consideration
    methemoglobin or carboxyhemoglobin

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Oxyhemoglobin Terminology

- FO₂Hb
  - \( \frac{\text{oxyhemoglobin}}{\text{total hemoglobin}} \)
  - represents the percentage of all hemoglobin present that is oxygenated
  - when methemoglobin or carboxyhemoglobin is present, they are included in the denominator
Oxyhemoglobin Terminology

- **O₂Sat**
  - An estimate of what the oxyhemoglobin should be using the measured PO₂ and the oxyhemoglobin dissociation curve, assuming that:
    1) The patient’s blood sample is absolutely typical (pH, temperature, 2,3-DPG concentration, etc.), and
    2) No methemoglobin or carboxyhemoglobin is present
  - This calculation, common on ABG analyzers, should not be reported

Example: Fireman Brought Into Emergency Room With Smoke Inhalation

- The facts:
  - PO₂ = 120 (hyperventilation)
  - Hemoglobin fractions: oxy=80%, reduced=0%, carboxy=20%, met=0%
- The CLSI values:
  - SO₂ = 100% \[80/(80+0)\]
  - FO₂Hb = 80% \[80/(80+0+20+0)\]
  - O₂sat = 100% \[at PO₂= 100 mmHg, normal hemoglobin is 100% saturated\]
- My practice (though it is technically incorrect), is to report the value as 80% and call it O₂Sat
- At a minimum, make sure your clinicians know how your lab is handling these values

Methemoglobin

- We all make methemoglobin continuously
- Normal values are roughly 1%
- Represents oxidation of heme Fe atom from ferrous (+2) to the ferric (+3) state
- Normally, our bodies reduce methemoglobin back to hemoglobin
- With increased oxidative stress (e.g., drugs) or with defective enzymes, methemoglobin can increase to pathologic levels
- Patients present with shortness of breath (low O₂ content) and cyanosis (blue color)
- Arterial blood looks brown, despite high PO₂
Carboxyhemoglobin
• represents hemoglobin complexed with carbon monoxide (CO)
• causes:
  • fires (smoke inhalation)
  • using gas or charcoal grills indoors
  • smoking
  • air pollution (living in urban areas)
• every home should have a CO (as well as a smoke) detector!
• patients present with shortness of breath (low O2 content)
• in contrast to methemoglobin,
  • blood is “cherry red”
  • FO2Hb (co-oximetry) is low despite high PO2
  • pulse oximetry overestimates oxyhemoglobin

Let’s Return to Our Patient with “Hyperventilation”
• Pulse oximetry reveals “O2 sat” of 100%
• Concerned about an abnormal hemoglobin,
  ER physicians order co-oximetry, which shows:
  – 98% oxyhemoglobin (O2 saturation)
  – 1% methemoglobin (normal value)
  – 3% carboxyhemoglobin (normal for Philadelphia)
  – Total Hemoglobin 12 grams/dL (120 g/L)
• ➔ oxygen content is fine (>1.4*98%*12.0= 16.5)
• Something else must be going on . . .
Self-Assessment Question 1
Which is the best indicator of oxygen concentration in blood?
A) $\text{PO}_2$
B) Hematocrit
C) $\text{O}_2$ content
D) $\text{O}_2$ saturation

Self-Assessment Question 2
Which of the following is true?
A) A normal alveolar $\text{PO}_2$ is higher in Denver than in Boston because the air is cleaner
B) A normal fractional oxyhemoglobin is higher in Denver than Boston because it has less air pollution
C) Typical pulse oximeters provide reliable measurements of “oxygen saturation” for use in patients with smoke inhalation
D) One must use arterial blood to get an accurate assessment of methemoglobin concentrations

Self-Assessment Question 3
What method principle is involved in measuring oxyhemoglobin percentages?
A) Gas chromatography
B) Ion selective electrodes
C) Beer’s Law
D) $\text{O}_2$ electrode, followed by interpolation from oxyhemoglobin dissociation curve