Oxygen Concentration of Blood: $PO_2$, Co-Oximetry, and More

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Objectives

• Define “O$_2$ Content”, listing its 3 major variables

• Define the limitations of pulse oximetry

• Explain why a normal arterial PO$_2$ at sea level on room air is \(~100\) mmHg (13.3 kPa)

• Describe the major features of methemogobin and carboxyhemoglobin
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 Concentration of Blood

- rather, a combination of all three parameters
- a value labs do not report
- a value few medical people even know!

O₂ Content

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

\[
= 0.0225 \times PaO₂ + 1.4 \times [\text{Hgb}] \times [\%O₂\text{Sat}]
\]

- normal value: about 20 mL/dL
Why Is the “Normal” $P_aO_2$ 90-100 mmHg?

- $P_aO_2 = (FiO_2 \times [Patm - PH_2O]) - (PaCO_2 / R)$
  - $P_aO_2$ is alveolar $O_2$ pressure
  - $FiO_2$ is fraction of inspired oxygen (room air ~0.20)
  - $Patm$ is atmospheric pressure (~760 mmHg at sea level)
  - $PH_2O$ is vapor pressure of water (47 mmHg at 37 °C)
  - $PaCO_2$ is partial pressure of $CO_2$
  - $R$ is the respiratory quotient (typically ~0.8)
  - $\Rightarrow 0.21 \times (760-47) - (40/0.8)$
  - ~100 mm Hg

- Alveolar–arterial (A-a) $O_2$ 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 $\text{PAO}_2$ 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” “O₂ Saturation” ~95%?

- sigmoid curve
- hemoglobin can bind ~ 1.4 mL O₂/g when fully saturated
- at PO₂ = 100 mmHg, 100% saturated
- so, at a normal Hgb of ~14 g/dL, it holds 1.4x14 = 19.6 mL/dL

NB: To convert mm Hg to kPa, multiply by 0.133
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:
  
  - $0.003 \times \text{PO}_2 \text{ (mm Hg)}$ [$0.0225 \times \text{PO}_2 \text{ (kPa)}$]  
    i.e., directly proportional to the partial pressure of O₂

  - at typical PO₂’s, it is negligible:
    $0.003 \times 100 \text{ mm Hg} = 0.3 \text{ mL/dL}$
    $0.0225 \times 13.3 \text{ kPa} = 0.3 \text{ mL/dL}$
    (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
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\[
\text{O}_2 \text{ Content} = 0.003 \times \text{PaO}_2 + 1.4 \times [\text{Hgb}] \times [\%\text{O}_2\text{Sat}]
\]

\begin{align*}
\text{dissolved} & : 0.3 \\
\text{Hgb-bound} & : 19.6
\end{align*}

\[\sim 20 \text{ mL O}_2/\text{dL}\]
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>
</tr>
</thead>
<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>
</tr>
<tr>
<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 $\text{PaO}_2 \Rightarrow$ low “$\text{O}_2$ saturation”
  – e.g., lung disease

• low “$\text{O}_2$ saturation” despite normal $\text{PO}_2$
  – 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

Figure 2-2. Transmittance of light through sample and reference cells. Transmittance of sample versus reference = \( I_0/I_R \).

Figure 2-3. Transmittance and absorbance as a function of concentration. A. Per cent T, linear scale. B. Per cent T, logarithmic scale. C. Absorbance, linear scale.

\[
A = -\log I_S/I_R = -\log T = \log \frac{1}{T} = \log \frac{100\%}{\text{per cent } T} = \log 100 - \log \text{per cent } T = 2 - \log \text{per cent } T
\]

With One Measurand, Life is Simple

- \( A = \varepsilon \times b \times C \) (or \( A = abc \))

- Absorbance = (Molar Absorptivity) \times (Pathlength) \times (Concentration)

- Two ways to calculate \( C \) from measured \( A \)
  - Know \( \varepsilon \) and \( b \)
    - co-oximeter
  - Run standard(s) to calculate \( \varepsilon \times b \)
    - 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.

- \( A_{\lambda 1} = (\varepsilon_{M_{\lambda 1}})(b)([M]) + (\varepsilon_{N_{\lambda 1}})(b)([N]) \)

- \( A_{\lambda 2} = (\varepsilon_{M_{\lambda 2}})(b)([M]) + (\varepsilon_{N_{\lambda 2}})(b)([N]) \)

- 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

Adapted from:
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

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

<table>
<thead>
<tr>
<th>Line</th>
<th>O2 saturation (Arterial Venous)</th>
<th>O2 Content (Arterial Venous)</th>
<th>O2 Delivered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>95% 55%</td>
<td>18.9 11.1</td>
<td>7.8</td>
</tr>
<tr>
<td>Black</td>
<td>55%</td>
<td>18.9</td>
<td>11.1</td>
</tr>
<tr>
<td>Red</td>
<td>40%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$$P_{50} = \text{PO}_2 \text{ where O}_2 \text{ saturation is } 50\%$$

Blue: 18 (left-shift)
Black: 25 (normal)
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
Oxyhemoglobin Terminology

- \( SO_2 \) 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
Oxyhemoglobin Terminology

- **FO$_2$Hb**
  - oxyhemoglobin / (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

• $O_2$Sat
  
  - An estimate of what the oxyhemoglobin should be using the measured PO2 and the oxyhemoglobin dissociation curve, assuming that
    
    1) that the patient’s blood sample is absolutely typical (pH, temperature, 2,3-DPG concentration, etc.), and
    
    2) that 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:
  – \( \text{PO}_2 = 120 \) (hyperventilation)
  – hemoglobin fractions:
    oxy=80%, reduced=0%, carboxy=20%, met=0%

• The CLSI values:
  – \( \text{SO}_2 = 100\% \) \[80/(80+0)\]
  – \( \text{FO}_2\text{Hb} = 80\% \) \[80/(80+0+20+0)\]
  – \( \text{O}_2\text{sat} = 100\% \) \[\text{at PO}_2=100 \text{ mmHg, normal hemoglobin is 100\% saturated}\]

• My practice (though it is technically incorrect), is to report the value as 80% and call it \( \text{O}_2\text{Sat} \)

• 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”
  - $\text{FO}_2\text{Hb}$ (co-oximetry) is low despite high $\text{PO}_2$
  - pulse oximetry overestimates oxyhemoglobin
Self-Assessment Question 1

Which is the best indicator of oxygen concentration in blood?

A) \( \text{PO}_2 \)
B) Hematocrit
C) \( \text{O}_2 \text{ content} \)
D) \( \text{O}_2 \text{ saturation} \)
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 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) $O_2$ electrode, followed by interpolation from oxyhemoglobin dissociation curve
Answers

1 (C) $O_2$ content

2 (B) A normal fractional oxyhemoglobin is higher in Denver than Boston because it has less air pollution

3 (C) Beer’s Law