MODELS OF VENOUS ADMIXTURE

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Medical students, residents, and allied health professionals often have difficulty quantitating ventilation-perfusion mismatch in ill patients. This manuscript quantitates ventilation-perfusion mismatch using the underlying physiological concepts and equations that describe mismatch. In addition, clinical problems with diagrams and worked-out solutions are supplied to help students master these equations as well as their practical limitations.


Key words: ventilation

When patients have hypoxemia due to ventilation-perfusion mismatch, clinicians need quantitative methods to measure the severity of illness as a function of time. Medical students, residents, and allied health professionals usually have some familiarity with the virtual shunt equation, shunt nomogram, alveolar-arterial gradient, and arterial/alveolar ratio. These techniques are all commonly used to assess respiratory failure. Nonetheless, students often have difficulty quantitating these measures and do not understand when these methods fail. Standard textbooks may provide the theoretical background for the material above, but they rarely provide clinical examples to solidify these concepts (1, 3, 4). This manuscript presents the derivation of equations describing ventilation-perfusion mismatch. In addition, clinical examples with worked solutions are provided to help students learn to manipulate the formulas necessary to assess respiratory failure. The practical limitations of these formulas are also discussed.

MODEL

The formal method of modeling pulmonary dysfunction in a hypoxemic patient is the patient’s virtual shunt through his lungs. Figures 1 and 2 and Equations 1–3 explain how this is done.

Figure 1A shows a healthy alveolus and pulmonary capillary. In this part of the lung, ventilation and perfusion are matched, and there is no venous admixture. Figure 1B shows a collapsed alveolus and a healthy capillary. Here, all of the mixed venous blood is shunted past the functional part of the lung. This is called venous admixture. Figure 1C shows a healthy alveolus and collapsed pulmonary capillary. This is the definition of dead space. It is included here to avoid confusion, although it is not part of the model.

Figure 2 shows how venous admixture to the systemic arterial blood can occur.

Conservation of blood flow dictates that the pulmonary capillary blood flow and shunted blood flow must equal the total cardiac output through the lungs (Eq. 1)

\[ \dot{Q}_T = \dot{Q}_C + \dot{Q}_S \]  

where \( \dot{Q}_T, \dot{Q}_C, \) and \( \dot{Q}_S \) are cardiac output, pulmonary capillary blood flow, and shunted pulmonary capillary blood flow, respectively.

Conservation of mass dictates that the transport of oxygen through the lung is also conserved (Eq. 2)

\[ \dot{Q}_T C_{O_2} = \dot{Q}_C C_{O_2} + \dot{Q}_S C_{O_2} \]
where $\text{CaO}_2$ is the O$_2$ content in the systemic arterial blood (pulmonary vein), $\text{CcO}_2$ is the O$_2$ content in the pulmonary capillary, and $\text{CvO}_2$ is the O$_2$ content in the shunted or mixed venous blood. Substituting Eq. 1 into Eq. 2 and rearranging yields the familiar virtual shunt equation.

$$\frac{\dot{Q}_s}{\dot{Q}_T} = \frac{\text{CcO}_2 - \text{CvO}_2}{\text{CcO}_2 - \text{CvO}_2}$$

FIG. 1.

FIG. 2.
Virtual shunt model.
To calculate shunt (Eq. 3), one must measure the partial pressure of O\textsubscript{2} in the mixed venous and systemic arterial blood. In addition, one must estimate the partial pressure of O\textsubscript{2} in the pulmonary capillary by calculating the partial pressure of oxygen delivered to the alveolus (P\textsubscript{A}\textsubscript{O}\textsubscript{2}; Eq. 3A)

\[
P\textsubscript{A}\textsubscript{O}\textsubscript{2} = (P\textsubscript{B} - P\textsubscript{H\textsubscript{2}O}) \cdot F\textsubscript{I}\textsubscript{O}\textsubscript{2} - \frac{P\textsubscript{A}\textsubscript{CO\textsubscript{2}}}{R} (3A)
\]

where PB is atmospheric pressure, and PH\textsubscript{2}O is the pressure of water vapor in the lung. P\textsubscript{A}CO\textsubscript{2} is the partial pressure of CO\textsubscript{2} in the systemic arterial blood, and R is the respiratory quotient, which is assumed to be 1 in this model. The use of Eq. 3 is impractical in routine clinical care because the mixed venous blood is rarely sampled.

To get around this, Eq. 3 was recast in nomogram form. Nunn assumed that the C\textsubscript{v}O\textsubscript{2} had a constant value and that the hemoglobin and P\textsubscript{A}CO\textsubscript{2} were within common ranges (2). Using these assumptions, he created the isoshunt lines shown in Fig. 3.

This nomogram allows one to estimate the patient’s virtual shunt and follow his pulmonary dysfunction as his F\textsubscript{I}\textsubscript{O}\textsubscript{2} and ventilatory therapy are adjusted by measuring his Pa\textsubscript{O}\textsubscript{2}. Despite their simplicity, the isoshunt lines did not achieve popularity because pulmonary critical care involves treating more than a single parameter and because it was impractical to carry the nomogram around.

A number of years later, interest was renewed in Eq. 3 with the advent of pulse oximeters and oxymetric pulmonary artery catheters. Manipulation of Eq. 3 shows why. The oxygen content of blood is given by

\[
C\textsubscript{O}\textsubscript{2} = 1.34 \cdot Hgb \cdot \text{saturation} + 0.003 P\textsubscript{O}\textsubscript{2} (4)
\]

where P\textsubscript{O}\textsubscript{2} is the partial pressure of oxygen in the blood. The term (0.003 P\textsubscript{O}\textsubscript{2}) represents dissolved O\textsubscript{2} in the plasma and will be ignored here. If we assume that the amount of dissolved oxygen is negligible, then we can substitute Eq. 4 into Eq. 3 to yield.
\[
\frac{Q_s}{Q_T} = \frac{1.34 \cdot \text{Hgb (end-capillary sat - arterial sat)}}{1.34 \cdot \text{Hgb (end-capillary sat - mixed venous sat)}}
\]

(5)

With oximetry, both the arterial saturation and mixed venous saturation could be measured continuously to give a good estimate of shunt. Unfortunately, Eq. 5 still involved a cumbersome calculation and the cost and morbidity of an oxymetric pulmonary artery catheter. For these reasons, Eq. 5 never achieved common usage either. Eq. 5, however, can be simplified to make it useful for clinicians.

In patients with stable cardiac outputs who are administered a high concentration of O\(_2\) (F\(_{\text{IO}_2}\)), the difference between end-capillary saturation and mixed venous saturation is \(\sim 0.25\). Thus Eq. 5 becomes

\[
\frac{Q_s}{Q_T} = \frac{\text{end-capillary sat - arterial sat}}{0.25}
\]

(6)

Equation 6 is made usable by relating \(\text{O}_2\) saturation to \(\text{Pa}_{\text{O}_2}\). Reference to the oxyhemoglobin dissociation curve shows how this is done (Fig. 4).

At a \(\text{Pa}_{\text{O}_2} > 100\) Torr, the graph is nearly a flat line. Thus \(\text{O}_2\) saturation and \(\text{Pa}_{\text{O}_2}\) are related by the formula for a straight line (Eq. 7)

\[
\text{O}_2\text{ saturation} = m \cdot \text{Pa}_{\text{O}_2} + b
\]

(7)

where \(m\) is the slope of the line, and \(b\) is the intercept on the saturation axis. Substituting Eq. 7 into Eq. 6 yields

\[
\frac{Q_s}{Q_T} = \frac{m(\text{Pa}_{\text{O}_2} - \text{Pa}_{\text{O}_2})}{0.25}
\]

(8)

where we have assumed that the \(\text{Pa}_{\text{O}_2}\) is the same as \(\text{P}_{\text{O}_2}\) in the pulmonary capillary. Using the slope \((m = 1.4 \times 10^{-3} \text{ saturation/Torr})\) on the flattest part of Fig. 4 allows Eq. 8 to be recast as

\[
\frac{Q_s}{Q_T} = \frac{1.4 \cdot 10^{-4}(\text{Pa}_{\text{O}_2} - \text{Pa}_{\text{O}_2})}{0.25}
\]

(9)

Equation 10 shows that the commonly used alveolar-arterial gradient divided by a constant yields an easy estimate of shunt when the patient’s cardiac output and hemoglobin are stable and when the \(\text{Pa}_{\text{O}_2}\) and \(\text{P}_{\text{O}_2}\) lie along the flat part of the oxyhemoglobin dissociation curve. Using a similar approach, the shunt fraction can be estimated when the \(\text{P}_{\text{A}\text{O}_2}\) < 100 Torr and the \(\text{Pa}_{\text{O}_2}\) lies between 50 and 100 Torr. In this case, Eq. 10 becomes

\[
\text{Shunt fraction} = \frac{\text{P}_{\text{A}\text{O}_2} - \text{P}_{\text{O}_2}}{2}
\]

(10A)

Equations 10 and 10A are only estimates of shunt fraction and are insensitive to larger gradients in the denominator of Eq. 5. Larger gradients in the denominator of Eq. 5 may occur in some patients with decreased cardiac output or significant shunt. Nonetheless, as long as cardiac output is stable, Eqs. 10 and 10A will track changes in shunt fraction as the patient’s pulmonary function improves or declines. If one wishes to account for larger gradients in \(\text{Pa}_{\text{A}_2}\) on June 22, 2017 http://advan.physiology.org/ Downloaded from eq. 5, then the slope in Eq. 7 must be adjusted to fit Eqs. 10 and 10A to clinical data.

The following clinical cases below are illustrative:

An 18-yr-old male with a history of asthma presents to the emergency department in respiratory distress. A nasal cannula supplies oxygen at 28%. His blood gas shows the following values: 7.32/31/74/23, \(\text{O}_2\) saturation 95%. In this case, his alveolar \(\text{O}_2\) is given
by Eq. 3A. Thus \( PAO_2 = (760 - 47) \cdot 0.28 - 31 = 168 \) Torr. The patients’ alveolar-arterial gradient is given by \( PAO_2 - [PaO_2] = 168 - 74 = 94 \) Torr. Reference to Fig. 3 shows the patient has a virtual shunt of 15–20%. His estimated shunt using the \( PAO_2 - PaO_2 \) gradient (Eq. 10) is \( \sim 6\% \).

Now consider a very different patient. A 74-yr-old male with a 50-pack/yr history of cigarettes undergoes a Whipple procedure. At the end of the surgery, the patient is intubated and ventilated with an FIO\(_2\) of 50%. His blood gas shows the following values: 7.32/34/115/27, O\(_2\) saturation 98%. Using the same analysis as above, we find that this patient has \( PAO_2 - PaO_2 \) gradient of 207 Torr, a virtual shunt of 10–15%, and estimated shunt using the \( PAO_2 - PaO_2 \) gradient (Eq. 10) of 12%. This is summarized in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>( FIO_2 )</th>
<th>( PAO_2 )</th>
<th>( PaO_2 )</th>
<th>A-a Gradient</th>
<th>Virtual Shunt</th>
<th>Estimated Shunt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1 (asthma)</td>
<td>0.28</td>
<td>168</td>
<td>74</td>
<td>94</td>
<td>15%–20%</td>
<td>6%</td>
</tr>
<tr>
<td>Patient 2 (surgery)</td>
<td>0.5</td>
<td>322</td>
<td>115</td>
<td>207</td>
<td>10%–15%</td>
<td>12%</td>
</tr>
</tbody>
</table>

Notice that patient 1 (asthma) is sicker (virtual shunt \( \sim 15–20\% \)) even though his \( PAO_2 - PaO_2 \) gradient is smaller than patient 2. This shows the value of the virtual shunt method, i.e., virtual shunt remains constant regardless of the FIO\(_2\) administered. The \( PAO_2 - PaO_2 \) gradient, however, widens as the FIO\(_2\) is increased, even in the absence of increased pulmonary dysfunction. The estimated shunt of patient 1 (Eq. 10) is 6%, which compares poorly with his virtual shunt (Eq. 3). This is because his Pa\(_O_2\) lies along the steep part of the oxyhemoglobin dissociation curve. In this situation, Eq. 10 is not a good measure of venous admixture. Conversely, the estimated shunt of patient 2 (12%) is similar to his virtual shunt. This is because both his Pa\(_O_2\) and Pa\(_O_2\) lie along the flat part of the oxyhemoglobin dissociation curve (Fig. 4).

Figure 5 shows the relationship between virtual shunt and estimated shunt. Notice that when the Pa\(_O_2\) is greater than 100 Torr, the virtual shunt lines and estimated shunt lines have slopes and absolute values that are similar. Below 100 Torr, the estimated shunt (Pa\(_O_2\) - Pa\(_O_2\)) reproduces the virtual shunt poorly.

Now let’s look at the problem in a different way. Suppose we consider the right heart and lungs to be an engine whose job is to convert mixed venous blood into oxygenated blood. If the engine is ideal (Fig. 6A), then the blood will be fully saturated with oxygen when it leaves the engine.

If the engine is less than ideal (Fig. 6B), then the blood will be only partially oxygenated when it leaves the heart-lung engine. We can calculate an efficiency for this real engine by comparing it with the ideal engine (Eq. 11).

\[
\text{Efficiency} = \frac{\text{O}_2 \text{ content of partially oxygenated blood}}{\text{O}_2 \text{ content of fully oxygenated blood}} \tag{11}
\]

Substituting Eq. 4 into Eq. 11 yields

\[
\text{Efficiency} = \frac{1.34 \cdot \text{Hgb} \cdot \text{arterial sat}}{1.34 \cdot \text{Hgb} \cdot \text{end-capillary sat}} \tag{12}
\]

Now, recall that on the flat part of the oxyhemoglobin dissociation curve (Fig. 4), the O\(_2\) saturation \( = m \times \frac{P_{O_2}}{b} \) (Eq. 7). Substituting Eq. 7 into Eq. 11 yields

\[
\text{Efficiency} = \frac{\text{P}_{O_2}}{\text{PAO}_2} \tag{13}
\]

This is commonly called the a/A ratio. Our derivation shows that the a/A ratio is only a good measure of pulmonary dysfunction (venous admixture) when the Pa\(_O_2\) and Pa\(_O_2\) both lie along the flat part of the oxyhemoglobin dissociation curve.

Figure 7 shows the graphical relationship of Pa\(_O_2\)/PA\(_O_2\) to the isoshunt lines. When the Pa\(_O_2\)/PA\(_O_2\) ratio is near 1, isoshunt and Pa\(_O_2\)/PA\(_O_2\) correlate well. As the ratio...
falls, the correlation becomes poorer because the $\text{Pa}_A$, no longer lies along the flat part of the oxyhemoglobin dissociation curve.

As an example, consider patients 1 and 2 again. The efficiency of patient 1 ($\text{Pa}_A/\text{PA}_A$) is 0.44, whereas that of patient 2 is 0.36. By comparing $a/A$ ratios, patient 1 appears healthier than patient 2, although his virtual shunt is greater. This is because his $\text{Pa}_A$ lies along the steep part of the oxyhemoglobin dissociation curve, and the $a/A$ ratio is less accurate in this case. This is summarized in Table 2.
SUMMARY
Virtual shunt remains the best way of quantitating venous admixture in patients with pulmonary pathology. It is a cumbersome technique that requires pulmonary artery catheterization and data from the oxyhemoglobin dissociation curve. The isoshunt lines approximate virtual shunt when the mixed venous saturation, hemoglobin, and \( \text{PaCO}_2 \) are within common ranges and are stable. Most clinicians do not carry this nomogram with them. The A-a gradient and a/A ratio both give a good estimate of venous admixture when the conditions for the isoshunt lines are met and when both \( \text{PaO}_2 \) and \( \text{P}_{\text{A}}\text{O}_2 \) lie along the flat part of the oxyhemoglobin dissociation curve. \( \text{PaO}_2 \) is easily measured, and \( \text{P}_{\text{A}}\text{O}_2 \) is easily calculated. For these reasons, they have become the standards in clinical care.

PRACTICE PROBLEM
An 18-mo-old child presents to the emergency department with respiratory distress and a chest X-ray consistent with pneumonia. A facemask supplies oxygen at 35%. His arterial blood gas shows the following values: 7.31/29/67/23, \( \text{O}_2 \) saturation 93%.

TABLE 2

<table>
<thead>
<tr>
<th>Patient 1 (asthma)</th>
<th>( \text{PaO}_2 )</th>
<th>( \text{P}_{\text{A}}\text{O}_2 )</th>
<th>( \text{PaCO}_2 )</th>
<th>A-a Gradient</th>
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<td>207</td>
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<td>0.36</td>
</tr>
</tbody>
</table>
1) Use Eq. 3A to calculate the patient’s alveolar O₂ (PAO₂). Answer, 220 Torr.

2) Calculate the patient’s alveolar arterial gradient, i.e., PAO₂ − PaO₂. Answer, 153 Torr.

3) Use Fig. 3 to estimate the patient’s virtual shunt. Answer, 25%.

4) Now use Eq. 10 to estimate the patient’s shunt. Answer, 9%. Can you explain why Eq. 10 gives such a poor estimate of virtual shunt? Hint, see the discussion of patient 1.

5) Now use Eq. 19 to calculate the patient’s arterial-alveolar ratio. Answer, 0.3. Does Eq. 13 overestimate or underestimate the patient’s illness and why? Hint, see the discussion of patient 1.

REFERENCES