Teaching ventilation/perfusion relationships in the lung

Robb W. Glenny

Departments of Medicine and of Physiology and Biophysics, University of Washington, Seattle, Washington

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Glenny RW. Teaching ventilation/perfusion relationships in the lung. Adv Physiol Educ 32: 192–195, 2008; doi:10.1152/advan.90147.2008.—This brief review is meant to serve as a refresher for faculty teaching respiratory physiology to medical students. The concepts of ventilation and perfusion matching are some of the most challenging ideas to learn and teach. Some strategies to consider in teaching these concepts are, first, to build from simple to more complex by starting with a single lung unit and then adding additional units representing shunting, mismatch, and deadspace. Second, use simplified analogies, such as a bathtub, to help students conceptualize new ideas. Third, introduce the concept of alveolar to arterial O2 differences as the models become more complex, 4) use the various mechanisms of hypoxemia through the lecture to maintain continuity and provide clinical relevance. Finally, use clinically relevant examples at each step and solidify new concepts by discussing differential diagnoses at the end of the lecture(s).

Beginning Simple

At an introductory level, the lung can be thought of as one large unit in which fresh air and deoxygenated blood are delivered to a single unit with exhaled gases and oxygenated blood leaving the unit. A simple schematic of this single unit is shown in Fig. 1 and can be used to introduce nomenclature and abbreviations to the students. A simple analogy, such as a bathtub, may help students visualize how the relationship between ventilation and perfusion determines the level of O2 or CO2 in the alveolar space. When used to explore determinants of alveolar PO2 (PAO2), the level of water in the bathtub represents the level of O2 in the alveolus (PAO2), ventilation (VA) bringing air with O2 into the alveolus is analogous to the spigot pouring water into the tub, and the O2 leaving the alveolus by way of blood flow (Q) is represented by the water leaving the tub via the drain (Fig. 2). If the amount of water coming in the spigot is greater than that leaving the drain, the water level (PAO2) will rise. If the water leaving the drain is greater than the water coming in the spigot, the water level (PAO2) will fall.

It must be acknowledged that this is a simplified model because, in reality, the level in the bathtub influences the flows in and out of the spigots and drains. However, as an initial simple model, it is readily understood by students. In addition, students should be shown that the level of CO2 in the alveolus is related to the spigot and drain flows but in an inverse relationship with O2 because CO2 delivery to the alveolus is via the blood and CO2 excretion is via ventilation (Fig. 3). As O2 consumption and CO2 delivery are tightly tied to local blood flow (Q), a high ventilation-to-perfusion ratio (V/Q ratio) will produce an increased PAO2 and a decreased alveolar PCO2 (PACO2), whereas a low V/Q ratio will result in a decreased PAO2 and an increased PACO2. The take-home message from this introduction is that PAO2 and PACO2 are determined by the ratio between VA and Q. Students can easily see that the levels of O2 and CO2 are related inversely through shared ventilation and blood flow (Fig. 4). This is an especially important concept because it sets the stage for understanding why hypoxemia occurs due to hypoventilation.

Mathematical equations can be intimidating to students, but if they comprehend the concepts the equations embody, the students are more likely to understand and remember the equations. With the bathtub analogy as a foundation, the concept and equation for determining PAO2 in a lung unit can be introduced. Under steady-state conditions, the amount of O2 consumed must be equal to the amount of O2 removed from inhaled air, as follows:

\[ V_{O2} = V_A (F_{O2} - F_{A02}) \]  \hspace{1cm} (1)

where \( V_{O2} \) is O2 consumption, \( F_{O2} \) is the fraction of inspired O2, and \( F_{A02} \) is the fraction of alveolar O2. For those students who have had cardiovascular physiology, it is nice to show the similarities between Eq. 1 and the Fick principle for measuring VO2. By rearranging Eq. 1 as follows:

\[ F_{A02} = \frac{V_{O2}}{V_A} - F_{O2} \]  \hspace{1cm} (2)

and changing the fractions of gases to partial pressures, one can arrive at the following equation (1):
where \( \text{PIO}_2 \) is the inspired PO2 and PB is barometric pressure. This equation represents the concept that the level of O2 in the alveolus (\( \text{PAO}_2 \)) is determined by the difference between what comes in (\( \text{PIO}_2 \)) and the amount taken out [(\( \text{V}_\text{O}_2/\text{V}_\text{A} \)) \( \times \) PB] 47 mmHg].

The second term of Eq. 3 can be estimated from a surrogate for the ratio between \( \text{V}_\text{O}_2 \) and \( \text{V}_\text{A} \) that is more easily obtained. Using the PCO2 in arterial blood (\( \text{PaCO}_2 \)) as an estimate of alveolar CO2 and the respiratory quotient (R), the second term of Eq. 3 can be estimated by \( \text{PaCO}_2/R \). The following all-important alveolar gas equation falls out of these relatively simple mathematical gymnastics:

\[
\text{PAO}_2 = \text{FI}_\text{O}_2 \times (\text{PB} - 47 \text{ mmHg}) - \frac{\text{PA}_\text{CO}_2}{R} \quad (4)
\]

It is very important to solidify the concept that the alveolar equation represents the balance between O2 delivery to the alveolus and O2 removal through the blood and is dependent on the ratio between regional V and Q. Some students and instructors falsely interpret the alveolar gas equation to mean that as the level of CO2 rises, the level of O2 must decrease because partial pressures of all gases must sum to PB. The concept that needs to be highlighted is that \( \text{PA}_\text{CO}_2 \) drops with hyperventilation due to a decrease in the V/Q ratio and that \( \text{PA}_\text{CO}_2 \) rises because of the same change in V/Q (Fig. 4). Conversely, \( \text{PAO}_2 \) increases and \( \text{PA}_\text{CO}_2 \) decreases with hyperventilation due to an increase in the V/Q ratio. One can think of \( \text{PA}_\text{CO}_2 \) as a marker of hypoventilation (low V/Q = low \( \text{PA}_\text{CO}_2 \)) or hyperventilation (high V/Q = high \( \text{PA}_\text{CO}_2 \)).

The definition of hypoxemia (\( \text{PaO}_2 \) less than normal for the subject’s age) and the first two of the five causes of hypoxemia can be introduced at this point. A decrease in \( \text{P}_\text{O}_2 \), as encountered at high altitude, will lead to hypoxemia if there is not a compensatory increase in minute ventilation. Students should be reminded that \( \text{P}_\text{O}_2 \) does not change with altitude and the decreasing PB results in a lower \( \text{P}_\text{IO}_2 \). A decrease in \( \text{V}_\text{A} \) (hypoventilation) will lead to hypoxemia. Hence, the first two causes of hypoxemia are low \( \text{P}_\text{O}_2 \) and hypoventilation.

Due to asymmetries in the airway and vascular geometry and due to differences in ventilation and perfusion between the top and bottom of the lung, the lung is much more complicated than a single gas exchanging unit. As a next step in building a more complex model of gas exchange in the lung, students can be introduced to regions of shunt (V/Q = 0) and dead space (V/Q = \( \infty \)). The bathtub concept holds for each of these regions, with \( \text{PAO}_2 \) and \( \text{PA}_\text{CO}_2 \) being determined solely by the local V/Q of each region. These V/Q relationships and their expected partial pressures of gases are shown in Fig. 5. In fact, there is a spectrum of V/Q relationships throughout the lung, with shunt and dead space representing the two ends of the distribution (Fig. 6).

To comprehend the effect of V/Q heterogeneity within the lung on arterial gas pressures, students need to understand the concepts of gas partial pressures and contents in blood and be introduced to the shape of the hemoglobin dissociation curve. With this information in mind, students should be introduced to the concepts of how a distribution of V/Q regions can contribute to hypoxemia. Low V/Q regions will contribute blood with low contents of O2 and produce hypoxemia. However, the content...
of blood coming from high V/Q regions is not significantly greater than that from normal V/Q regions, and high V/Q regions will not be able to compensate for the low V/Q regions. Hence, V/Q mismatch contributes to gas exchange inefficiencies, but only low V/Q regions cause hypoxemia.

One measure of the heterogeneity of V/Q distributions in a lung is the alveolar to arterial O2 difference \((A-aO_2)\). Because end-capillary blood gases are usually completely equilibrated with alveolar gases, there should not be any difference between \(P_{O_2}\) in postalveolar capillaries (\(P_{C_{O_2}}\)) and the \(P_{aO_2}\) within a given lung unit. However, with a distribution of V/Q ratios, there will be a distribution of \(P_{aO_2}\) (see Fig. 6). The low V/Q regions will cause the \(P_{O_2}\) to be lower in the capillary (and eventually) arterial blood than the mean alveolar value and hence a widened \(A-aO_2\) (Fig. 7). The word “difference” should be stressed over “gradient” because the gap between \(P_{aO_2}\) and \(P_{O_2}\) is due to a difference in V/Q ratios and not a gradient in \(P_{O_2}\) from the alveolar space into the blood. A third cause of hypoxemia is now apparent to the students: V/Q mismatching. The difference between V/Q mismatch and the first two causes of hypoxemia is that V/Q mismatch has a widened \(A-aO_2\), whereas hypoventilation and low \(P_{O_2}\) have normal \(A-aO_2\).

Shunt is the extreme example of V/Q mismatch and a fourth cause of hypoxemia. With local shunt, a fraction of the total blood returning to the lung does not exchange gases, and this blood has a content of \(O_2\) equal to that of mixed venous blood. The \(O_2\) content of the arterial blood is simply a weighted average of the \(O_2\) content of the shunted blood flow [fraction of shunted blood flow compared with total blood \((Q_s/Q_t)\) times the \(O_2\) content of venous blood] and the remaining fraction \((1 - Q_s/Q_t)\) times the \(O_2\) content of blood that undergoes gas exchange \(C_{CO_2}\), as follows:

\[
Ca_{O_2} = \frac{Q_s}{Q_t} \times C_{V_{O_2}} + \left(1 - \frac{Q_s}{Q_t}\right) \times C_{CO_2}
\]

(5)

where \(Q_s\) and \(Q_t\) are the blood flow through the shunt and entire lung, respectively. This equation can be easily manipulated to produce the following formula for calculating the shunt fraction in an individual:

\[
\frac{Q_s}{Q_t} = \frac{CC_{O_2} - Ca_{O_2}}{CC_{O_2} - CV_{O_2}}
\]

(6)

By measuring the arterial \((Ca_{O_2})\) and venous \((CV_{O_2})\) \(O_2\) content of blood that undergoes gas exchange and by estimating \(CC_{O_2}\) from the alveolar gas equation, the fraction of shunted blood \((Q_s/Q_t)\) can be calculated. Due to deoxygenated blood returning to the left atrium from the thebesian veins and from the bronchial circulation of the airways, there is a normal (anatomic) shunt of \(\sim 5\%\) in normal individuals. It is this anatomic shunt that contributes to the normal \(A-aO_2\) of
As we grow older, there is increasing V/Q mismatch that contributes further to the widening \( (A-a)O_2 \) with age.

Hypoxemia due to shunt can be differentiated from that due to low V/Q in that hypoxemia from shunt does not improve with increasing PIO2. This is due to the fact that the shunted blood does not come in contact with alveoli that have a much increased PO2 and the blood that does exchange gas is not able to increase its content significantly as the hemoglobin is nearly completely saturated in the normal V/Q region before adding supplemental O2. In contrast, the PAO2 in low V/Q regions increases with a higher PIO2, and the blood to these regions will have an increased capillary content of O2 that will produce a higher PaO2.

A fifth cause of hypoxemia is diffusion limitation, which is rarely seen even in pathological conditions such as pulmonary edema. The hypoxemia of pulmonary edema is due to low V/Q regions rather than an inability of O2 to diffuse across thickened alveolar membranes. Hypoxemia due to diffusion limitation can be seen in elite athletes, such as thoroughbred race horses and some humans, where a huge cardiac output causes such short transit times through the alveolar capillaries that the blood is not able to fully oxygenate. This will result in a decreased PCO2 and a widened \( (A-a)O_2 \).

The above foundation of information can be strengthened through an algorithm for identifying causes of hypoxemia in patients (Fig. 8). This approach also provides an opportunity to present case scenarios and a clinically relevant application for medical students. A typical case includes a young man found unresponsive who is hypoxemic and has a normal \( (A-a)O_2 \). The normal \( (A-a)O_2 \) provides evidence for hypoventilation and normal lung function and is consistent with a narcotic overdose. A complementary case involves a young woman who is very anxious, hypoxic, and has a widened \( (A-a)O_2 \). The widened \( (A-a)O_2 \) is consistent with asthma, and there is a high likelihood of V/Q mismatch as the cause of hypoxemia.

In summary, teaching ventilation and perfusion relationships in the lung introduces new concepts that are challenging for medical students but very relevant to clinical care. As with all complex concepts, it is best to begin simple with a single lung unit and build toward greater complexity. An intuitive model such as a bathtub can be used to provide insights as to how gas partial pressures are determined by the ratio between regional ventilation and perfusion. One of the most important concepts is that the levels of O2 and CO2 are linked but inversely related through V/Q ratios. All of this new information can be woven around a story of the five causes of hypoxemia. \( (A-a)O_2 \) can be used as a measure of the V/Q distribution in the lung and is helpful in narrowing differential diagnoses in clinical cases.

**REFERENCE**