Teaching pulmonary gas exchange physiology using computer modeling

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Kapitan KS. Teaching pulmonary gas exchange physiology using computer modeling. Adv Physiol Educ 32: 61–64, 2008; doi:10.1152/advan.00099.2007.—Students often have difficulty understanding the relationship of O₂ consumption, CO₂ production, cardiac output, and distribution of ventilation-perfusion ratios in the lung to the final arterial blood gas composition. To overcome this difficulty, I have developed an interactive computer simulation of pulmonary gas exchange that is web based and allows the student to vary multiple factors simultaneously and observe the final effect on the arterial blood gas composition (available at www.siumed.edu/medicine/pulm/vqmodeling.htm). In this article, the underlying mathematics of the computer model is presented, as is the teaching strategy. The simulation is applied to a typical clinical case drawn from the intensive care unit to demonstrate the interdependence of the above factors as well as the less-appreciated importance of the Bohr and Haldane effects in clinical pulmonary medicine. The use of a computer to vary the many interacting factors involved in the arterial blood gas composition appeals to today’s students and demonstrates the importance of basic physiology to the actual practice of medicine.

Understanding the physiology of pulmonary gas exchange is difficult for most students. Despite clear presentations in classic textbooks (9), many students leave medical training with only a qualitative grasp of the determinants of hypoxemia and hypercarbia. Although they may understand the relationship of shunt to hypoxemia and ventilation to PCO₂, the more complicated dependence of the arterial blood composition on O₂ consumption, CO₂ production, cardiac output, and distribution ventilation-perfusion ratios in the lung is far more difficult. One reason for this difficulty is the fairly complex interrelationship of these factors to the final arterial blood gas, which makes it hard to guess the relative effects when several factors change simultaneously.

To overcome this difficulty, I have developed an interactive computer simulation of pulmonary gas exchange that is web based and allows the student to vary multiple factors simultaneously and observe the final effect on the arterial blood gas composition (available at www.siumed.edu/medicine/pulm/vqmodeling.htm). This gives the student an opportunity to literally play with the ventilation-perfusion distribution, O₂ consumption, cardiac output, etc. until s/he is comfortable with the various interactions. I usually introduce my students to the simulation with a lecture covering the basic quantitative physiology of gas exchange in a single compartment and in a multicompartment model of the lung. I then have them use this simulation to work through several clinical cases taken from the pulmonary clinic and intensive care unit. Although interested senior medical students can take on this subject, it is more advanced than the introductory respiratory physiology to which they are usually exposed. The simulation therefore is intended more for senior medical residents and pulmonary fellows who have had some clinical experience to draw upon.

In the introductory lecture, I begin by focusing on a single gas exchange unit in the lung. This is the volume of lung within which gas composition is uniform due to diffusive mixing. In humans, the respiratory unit appears to be the distal alveolar duct (1, 2), which subtends ~1,000 alveoli. I then describe gas exchange across this unit by simply pointing out that in a steady state, the rate at which O₂ enters the unit from the atmosphere is the same as the rate at which O₂ leaves the unit in the capillary blood (Fig. 1). I write this down as an equation:

\[
\text{Rate of O}_2 \text{ entering unit} = \text{Rate of O}_2 \text{ leaving unit}
\]

\[
V_I \times FIO_2 - VA \times FAO_2 = Q \times CCO_2 - Q \times CVO_2
\]

(1)

where \(V_I\) and \(VA\) are the inspired and alveolar ventilations, \(FIO_2\) and \(FAO_2\) are the inspired and alveolar fractional O₂ concentrations; \(Q\) is the blood flow to and from the unit; and \(CCO_2\) and \(CVO_2\) are the mixed venous and capillary O₂ contents in the blood flowing into and out of the unit. It is important to pause and ensure that everyone understands that this equation is a satisfactory description of O₂ flow across the unit.

I then point out that identical statements can be written down for the other gases present in the unit, namely, CO₂ and \(N_2\). It is helpful to put all three equations side by side so that the students can see the similarities, as follows:

for O₂:

\[
V_I \times FIO_2 - VA \times FAO_2 = Q \times CCO_2 - Q \times CVO_2
\]

(2)

for CO₂:

\[
-VA \times FACO_2 = Q \times CACO_2 - Q \times CCVO_2
\]

(3)

for \(N_2\):

\[
V_I \times FN2 - VA \times FAN2 = Q \times CCN2 - Q \times CVN2
\]

(4)

where \(FACO_2\) is the alveolar fractional CO₂ concentration, \(CCVO_2\) and \(CCCO_2\) are the mixed venous and capillary CO₂ contents, \(FAN2\) and \(FAN2\) are the inspired and alveolar fractional \(N_2\) concentrations, and \(CCN2\) and \(CCN2\) are the mixed venous and capillary \(N_2\) contents. These equations are nonlinear, coupled, and simultaneous. Their complete solution requires a computer. However, for the purposes of discussion only, we can make the simplifying assumption that \(V_I\) and \(VA\) are approximately the same (\(V\)) and then rearrange these equations algebraically to show O₂ and CO₂ contents in the blood flowing from the unit, as follows:

\[
CCO_2 = CVCO_2 + V/Q \times (FIO_2 - FAO_2)
\]

(5)

\[
CCCO_2 = CVCO_2 - V/Q \times FACO_2
\]

(6)

I point out that, consequently, the gas contents in the blood coming from the unit depend on only three things: the mixed
venous composition entering the unit, the inspired O₂ fraction, and the ratio of ventilation to perfusion of the unit. Of course, to then calculate the corresponding PO₂ and PCO₂, we must also know several additional details, namely, the blood hemoglobin concentration, the oxyhemoglobin dissociation curve, and the relationship between CO₂ content and PCO₂, which were discussed in a previous lecture. This mathematical approach explicitly reveals the fundamental importance of the mixed venous composition and the V-to-Q (V/Q) ratio to the final arterial blood gas.

To transfer these conclusions to the real lung, I note that there are about half a million respiratory units in the lung (8), each with its own V/Q ratio, but fortunately each receiving the same mixed venous blood and the same FIO₂. Thus, all of the respiratory units in the lung share two of the three determinants of gas exchange. The blood from each unit drains ultimately into the left atrium, where the contributions from all of the units mix in proportion to their perfusion to form the final mixed arterial blood. So, the determinants of arterial blood gas composition in the lung are identical to those of the single unit, with the V/Q distribution taking the place of the V/Q ratio.

At this point I introduce the parallel multicompartment model of the lung (Fig. 2) and emphasize that it is just a number of single compartments each receiving the same mixed venous blood and inspiring the same FIO₂, and each contributing to the final arterial mixture in proportion to its perfusion, just like the real lung. If we specify a different V/Q ratio for each compartment and know the distribution of perfusion to each compartment (the V/Q distribution), then we can calculate the mixed arterial contents by solving Eqs. 2–4 above exactly using a computer (10). The computer solution does not require the simplifying assumption we made in the algebraic solution. We can then use the hemoglobin dissociation curve and the CO₂ solubility curve to transform the O₂ and CO₂ contents into the PO₂ and PCO₂ of the mixed arterial blood.

To demonstrate that this actually works, I use the computer program to calculate the arterial blood gas composition for a normal resting adult using a normal ventilation-perfusion distribution (Fig. 3) and mixed venous composition (9). The output is shown in Table 1. Perfusion is distributed among 10 compartments of varying V/Q ratio, and the PO₂, PCO₂, and contents of the capillary blood from each compartment are calculated and displayed. The compartment gas contents are added together in proportion to the fractional perfusion of each compartment to form the mixed arterial blood contents, and the corresponding final PO₂ and PCO₂ are obtained from the hemoglobin dissociation and CO₂ solubility curves. Additionally, overall O₂ consumption and CO₂ production are calculated by adding together the individual compartment O₂ consumptions and CO₂ productions, again in proportion to each compartment’s fractional perfusion.

I then repeat the process with an abnormal V/Q distribution, such as may be seen in a patient with pneumonia, and comment on the differences. I also point out the interesting “paradox” that the PCO₂ of the blood coming from the low V/Q ratio compartments is actually higher than the PCO₂ of mixed venous blood. This is a consequence of the Haldane effect, shifting the CO₂ solubility curve rightward, as can be seen by comparing the CO₂ content of a low V/Q compartment with that of the mixed venous blood.

To make the final jump to the bedside, I point out that although we have seen that the mixed venous composition is one of the fundamental determinants of arterial composition, in reality, the mixed venous composition is itself determined by the total O₂ consumption and CO₂ production of the body and by the mean and dispersion of the V/Q distribution. Consequently, the basic determinants of arterial composition are...
now pH 7.25, PCO2 evidence of any other complication. His arterial blood gas is X-ray is unchanged, he remains sedated, and there is no (39°C), rigors, and hypoxemia. Reevaluation reveals his chest is deeply sedated. He is found to have pneumonia and is heart failure is admitted to the intensive care unit in respiratory lying obstructive pulmonary disease and advanced congestive failure. He is intubated, placed on mechanical ventilation, and is monitored consistently on the final blood gas values.

Here is a typical clinical case. An elderly man with underlying obstructive pulmonary disease and advanced congestive heart failure is admitted to the intensive care unit in respiratory failure. He is intubated, placed on mechanical ventilation, and is deeply sedated. He is found to have pneumonia and is wheezing diffusely. Based on these findings, one can assume his V/Q distribution is abnormal and is composed of a combination of shunt, low V/Q and high V/Q ratios (3). His arterial blood gas is pH 7.44, PCO2 = 36 mmHg, and Po2 = 65 mmHg on 30% inspired O2. Later that evening, he develops a fever (39°C), rigors, and hypoxemia. Reevaluation reveals his chest X-ray is unchanged, he remains sedated, and there is no evidence of any other complication. His arterial blood gas is now pH 7.25, PCO2 = 74 mmHg, and Po2 = 56 mmHg. What has happened? [Clue: what do fever and shivering do to the patient’s O2 consumption and CO2 production (4, 11)?]

Here is the solution: using the program, the student creates an abnormal V/Q distribution containing perfusion of shunt, low V/Q and high V/Q ratios and sets the FIO2 at 0.30. Since the patient is sedated, default values of O2 consumption, CO2 production, and cardiac output are used, and the arterial blood gas is computed. Paradoxically, the Po2 rises by ~6 mmHg. Why? This is the Bohr effect, which is confirmed by noting that the total arterial O2 content has not increased, despite the higher Po2, implying a shift to the right of the hemoglobin dissociation curve. Next, O2 consumption and CO2 production are doubled to 500 ml/min and 400 ml/min, respectively. The arterial blood gas is recalculated and reveals the development of hypoxemia and hypercarbia. Why?

The output of the calculation (Table 2) shows that because of the higher O2 consumption, the mixed venous O2 content declines significantly. Since areas of shunt and low V/Q ratios are present, the lower mixed venous content, in turn, drives the mixed arterial O2 content lower, resulting in hypoxemia. The converse applies to CO2.

A few other teaching points can be made. First, since our patient has become hypercarbic, evidently he is too sedated to increase his minute ventilation and return his PCO2 to normal. How does increased total minute ventilation affect the V/Q distribution? If the distribution of ventilation remains unchanged, increasing total ventilation will raise the V/Q ratio of each compartment and increase the total V/Q ratio of the lung. This will decrease the arterial PCO2. Second, because of heart failure, he cannot increase his cardiac output adequately in

Table 1. Program output for a normal V/Q distribution

<table>
<thead>
<tr>
<th>V/Q</th>
<th>Percent Cardiac Output</th>
<th>pH</th>
<th>PO2, mmHg</th>
<th>PCO2, mmHg</th>
<th>CCO2, vol%</th>
<th>CCCO2, vol%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.0</td>
<td>7.38</td>
<td>40.0</td>
<td>45.0</td>
<td>15.3</td>
<td>51.8</td>
</tr>
<tr>
<td>0.05</td>
<td>0.0</td>
<td>7.37</td>
<td>49.9</td>
<td>46.1</td>
<td>17.6</td>
<td>51.6</td>
</tr>
<tr>
<td>0.1</td>
<td>0.0</td>
<td>7.37</td>
<td>52.9</td>
<td>45.9</td>
<td>18.1</td>
<td>51.3</td>
</tr>
<tr>
<td>0.3</td>
<td>2.7</td>
<td>7.37</td>
<td>67.0</td>
<td>44.7</td>
<td>19.5</td>
<td>50.3</td>
</tr>
<tr>
<td>0.5</td>
<td>18.7</td>
<td>7.38</td>
<td>81.2</td>
<td>43.1</td>
<td>20.2</td>
<td>49.3</td>
</tr>
<tr>
<td>1.0</td>
<td>69.0</td>
<td>7.41</td>
<td>103.8</td>
<td>39.2</td>
<td>20.7</td>
<td>47.3</td>
</tr>
<tr>
<td>2.0</td>
<td>8.4</td>
<td>7.45</td>
<td>121.6</td>
<td>33.2</td>
<td>20.9</td>
<td>44.1</td>
</tr>
<tr>
<td>3.0</td>
<td>1.3</td>
<td>7.49</td>
<td>129.1</td>
<td>29.1</td>
<td>21.0</td>
<td>41.7</td>
</tr>
<tr>
<td>6.0</td>
<td>0.0</td>
<td>7.57</td>
<td>137.8</td>
<td>21.5</td>
<td>21.1</td>
<td>36.8</td>
</tr>
<tr>
<td>10</td>
<td>0.0</td>
<td>7.65</td>
<td>141.8</td>
<td>16.3</td>
<td>21.1</td>
<td>32.9</td>
</tr>
</tbody>
</table>

Overall V/Q = 1.0; FIO2 = 0.21; CAO2 = 20.6 vol%; VO2 = 265 ml O2/min; CACO2 = 47.4 vol%; VCO2 = 220 ml O2/min; pH = 7.41; Po2 = 98 mmHg; PCO2 = 39 mmHg. CCO2 and CCCO2, capillary O2 and CO2 contents; CAO2 and CACO2, arterial O2 and CO2 content; FIO2, fraction of inspired O2; VO2 and VCO2, O2 and CO2 consumption.

Table 2. Program output for a patient in respiratory failure

<table>
<thead>
<tr>
<th>V/Q</th>
<th>Percent Cardiac Output</th>
<th>pH</th>
<th>PO2, mmHg</th>
<th>PCO2, mmHg</th>
<th>CCO2, vol%</th>
<th>CCCO2, vol%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>20.0</td>
<td>7.21</td>
<td>25.7</td>
<td>89.3</td>
<td>6.3</td>
<td>71.9</td>
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<tr>
<td>0.05</td>
<td>6.7</td>
<td>7.19</td>
<td>38.2</td>
<td>93.2</td>
<td>10.5</td>
<td>71.4</td>
</tr>
<tr>
<td>0.1</td>
<td>2.6</td>
<td>7.19</td>
<td>41.4</td>
<td>92.8</td>
<td>11.5</td>
<td>70.8</td>
</tr>
<tr>
<td>0.3</td>
<td>1.3</td>
<td>7.19</td>
<td>54.2</td>
<td>90.8</td>
<td>15.0</td>
<td>68.7</td>
</tr>
<tr>
<td>0.5</td>
<td>9.7</td>
<td>7.19</td>
<td>68.1</td>
<td>88.0</td>
<td>17.6</td>
<td>66.8</td>
</tr>
<tr>
<td>1.0</td>
<td>35.3</td>
<td>7.22</td>
<td>104.4</td>
<td>78.9</td>
<td>20.2</td>
<td>62.8</td>
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<tr>
<td>2.0</td>
<td>9.2</td>
<td>7.27</td>
<td>144.4</td>
<td>63.7</td>
<td>20.9</td>
<td>57.1</td>
</tr>
<tr>
<td>3.0</td>
<td>14.6</td>
<td>7.32</td>
<td>162.3</td>
<td>53.9</td>
<td>21.0</td>
<td>53.2</td>
</tr>
<tr>
<td>6.0</td>
<td>0.0</td>
<td>7.42</td>
<td>183.6</td>
<td>37.6</td>
<td>21.2</td>
<td>45.7</td>
</tr>
<tr>
<td>10</td>
<td>0.0</td>
<td>7.50</td>
<td>193.6</td>
<td>27.4</td>
<td>21.3</td>
<td>40.1</td>
</tr>
</tbody>
</table>

Overall V/Q = 1.0; FIO2 = 0.30; CAO2 = 16.3 vol%; VO2 = 500 ml O2/min; CACO2 = 63.9 vol%; VCO2 = 400 ml O2/min; pH = 7.25; Po2 = 56 mmHg; PCO2 = 74 mmHg.
response to an increased metabolic demand. If he could, what would the effect be on his blood gases? Increasing his cardiac output from 5 to 7 L/min increases his PO2 back to 64 mmHg and decreases his PCO2 to 53 mmHg. Examination of the mixed venous composition again reveals the mechanism.

Hands-on, interactive computer simulations appeal to today’s students, many of whom don’t recall a time when computer games didn’t exist. The ability to step through a clinically relevant gas exchange problem taken from the intensive care unit and see how varying the many interacting factors involved affects the final arterial blood gas composition provides the opportunity to really understand the physiology of each piece. This observation is certainly not new. Computer simulations have a long history in the teaching of respiratory physiology, beginning with the many contributions of Dr. Harold Modell (5, 7). The present simulation is offered as an addition to the collection of software currently available (6). The differences between previous simulations and the present simulation are mainly in terms of presentation and format. The present simulation has the convenience of being web based and allows somewhat more interactive variation of parameters than past programs. It also explicitly includes N2 exchange in the output. The goal remains the same, however: namely, to promote an active learning experience for the individual student that demonstrates the essential importance of basic physiology to the actual practice of medicine.

REFERENCES