Changes in Blood P50

Effects on Oxygen Delivery When Arterial Hypoxemia is due to Shunting

Leonard Rosoff, M.D.; Robert Zeldin, M.D.; Ernest Hew, M.B.;
and Arnold Aberman, M.D.

The theoretic effect of increased values for the oxygen pressure at an oxygen saturation of 50 percent on oxygen delivery in arterial hypoxemia due to right-to-left shunting was analyzed using a mathematical model of the oxygen-hemoglobin equilibrium curve. We found that, regardless of the size of the shunt, a rightward shift of the curve resulted in increased mixed venous oxygen tension, increased arterial oxygen pressure, and, hence, a decreased alveolar-arterial oxygen pressure difference compared to the standard curve (hemoglobin level, cardiac output, and oxygen consumption remaining constant).

A rightward shift in the position of the oxygen-hemoglobin equilibrium curve, reflecting decreased affinity of hemoglobin for oxygen, has been documented in diverse diseases characterized by impaired oxygen transport and hence threatened oxygen consumption (VO2). This shift to the right or increased oxygen pressure at an oxygen saturation of 50 percent (P50) is considered beneficial because, without changing VO2, cardiac output, or hemoglobin, an increase in mixed venous oxygen tension (PvO2) results, when compared to the standard oxygen-hemoglobin equilibrium curve (P50 = 26.6 mm Hg). The increase in PvO2 is assumed to be advantageous, since it represents "driving pressure" of oxygen to the tissues.

It is recognized that the arterial oxygen pressure (PAO2) is important in determining whether a rightward shift in the curve is beneficial. When the PAO2 is more than 60 mm Hg, an increase is advantageous. Although the rightward-shifted curve, under these conditions, has both a lower arterial oxygen saturation (SaO2) and mixed venous oxygen saturation (SvO2), compared to the standard curve, the decrease in SaO2 is negligible compared to the decrease in SvO2 (assuming PaO2 and PvO2 remain constant for both curves), hence increasing the arteriovenous oxygen saturation difference. Thus, in diseases in which cardiac output or hemoglobin or both are decreased but PaO2 remains greater than 60 mm Hg, increases in P50 have been documented. This change is considered adaptive in that PvO2 is increased at the same VO2.

When PaO2 is decreased, the beneficial effect of a rightward shift is less clear. It has been shown that when the low PaO2 is consequent to alveolar hypoxemia (eg, ascent to altitude), a shift to the right may result in a fall of PvO2. This is because when PaO2 is decreased, the decrease in SaO2 in the rightward-shifted curve, as compared to the standard curve, may be greater than the corresponding fall in SvO2 (again assuming constant PaO2 and PvO2 for both curves). Most animals who reside at high altitude have been shown to have a leftward-shifted curve, which is considered adaptive.

In contrast to situations in which the decreased PaO2 is caused by alveolar hypoxemia, the effect of a rightward shift in the curve when arterial hypoxemia is caused by right-to-left shunt (eg, cyanotic congenital heart disease) has not been clarified. It is well documented that, in fact, in children with cyanotic congenital heart diseases, the P50 is increased; however, using the model of altitude-induced hypoxemia, a number of investigators have questioned the adaptive benefits of the observed increase in P50 in cyanotic congenital heart disease. In fact, we will show that the model for altitude is inappropriate and that in patients with a right-to-left shunt, an increase in P50 will always increase PvO2. This is true even if the shunt is large enough to result in severe arterial hypoxemia. We emphasize that if such a low PaO2 were caused by alveolar hypoxia, a rightward shift would be clearly disadvantageous.

Method

Mathematical Analysis

Objectives. For any specified level of hemoglobin,
fractional concentration of oxygen in the inspired gas (FI02), arteriovenous oxygen content difference (C(a-v)O2), and shunt fraction (S), calculate the PaO2, SaO2, PvO2 and SvO2 for the standard curve (P50 = 26.8 mm Hg) and for any rightward-shifted curve (P50 > 34.6 mm Hg).

Development of Mathematical Model. From the shunt equation,\textsuperscript{12}

\[
\frac{CcO2 - CaO2}{CcO2 - SvO2} = S
\]  
(1)

where CcO2 is the end pulmonary capillary oxygen content, CaO2 is the arterial oxygen content, and CvO2 is the mixed venous oxygen content. Substituting \(CvO2 = CaO2 - C(a-v)O2\) in equation 1 and rearranging,

\[
CaO2 = \frac{S \times CcO2 + S \times C(a-v)O2 - CcO2}{S - 1}
\]  
(2)

Now, CcO2 = 0.0031 × PaCO2 + 1.38 × Hb × ScO2, where ScO2 is the end pulmonary capillary oxygen saturation, PaCO2 is the end pulmonary capillary oxygen tension, and Hb is the concentration of hemoglobin; but PaCO2 = PAO2 = FI02 × (Pb − 47) − 1.25 × PaCO2 (where Pb is barometric pressure, and PaCO2 is the arterial carbon dioxide tension), and ScO2 = f(PaO2, P50) and can be calculated using a model for the oxygen-hemoglobin equilibrium curve.\textsuperscript{13} Thus, CcO2 can be determined. Therefore CaO2 can be calculated from equation 2.

From CaO2, the PaO2 and SaO2 can be calculated by solving the following two simultaneous equations:

\[
0.0031 \times PaO2 + 1.38 \times Hb \times SaO2 = CaO2
\]  
(3)

\[
SaO2 = f(PaO2, P50)
\]  
(4)

Substituting equation 4 into equation 3,

\[
0.0031 \times PaO2 + 1.38 \times Hb \times f(PaO2, P50) = CaO2
\]  
(5)

We have written a routine for the computer which, when the concentration of hemoglobin and CcO2 are known, determines the unique values for PaO2 and SaO2 of equation 5 using an iterative technique. The PvO2 and SvO2 can be determined in a similar manner from CvO2.

Using the previously described process, the PaO2, SaO2, PvO2 and SvO2 can be determined for a curve with any P50.

**Example.** Figure 1 shows the effect on PvO2 of changing P50 when the concentration of hemoglobin equals 14 gm/100 ml, the shunt fraction equals 50 percent, C(a-v)O2 equals 5 volume percent, and FI02 equals 0.21, and assuming that PaCO2 equals 40 mm Hg and Pb equals 760 mm Hg.

Note that as P50 increases, the PvO2 increases. The PvO2 will increase with increased P50 as long as the alveolar oxygen pressure (PAO2) is greater than the "crossover" oxygen pressure.\textsuperscript{7} Thus, as long as the FI02 is at least 0.21, a shift to the right in the curve increases the PvO2, regardless of the size of the shunt and the resulting hypoxemia.

**Graphic Analysis**

To illustrate, graphically, the effect of P50 on PvO2, we will use the classic two-compartmental model of shunt (Fig 2). The blood leaving the so-called "perfect" compartment has an oxygen pressure (PpO2) equal to PAO2. The "perfect" oxygen saturation (SpO2) is a function of PpO2 and P50. The "perfect" oxygen content (CpO2) then reflects the PpO2, SpO2, and the concentration of hemoglobin. In contrast, the oxygen pressure, oxygen saturation, and oxygen content of the shunted blood is equal to PvO2, SvO2, and CvO2, respectively. The arterial values (PaO2, SaO2, and CaO2) simply reflect the relative proportion of shunted blood and nonshunted blood and their respective oxygen contents. Figure 3 illustrates that the cardiac output (CO) can be divided into two separate streams, shunted (Qs/Qt) and nonshunted (Qns/Qt).

\[
V_o = CO \times \frac{Qs}{Qt} \times (CvO2 - CVO2) + CO \times \frac{Qns}{Qt} \times (CpO2 - CvO2)
\]

\[
= CO \times \frac{Qns}{Qt} \times (CpO2 - CvO2)
\]

\[
= 13.8 \times CO \times \frac{Qns}{Qt} \times Hb \times (SpO2 - SvO2)
\]

Note that since PpO2 is equal to PAO2, the SpO2

**Changes in Blood P50**

---

*CHEST, 77: 2, FEBRUARY, 1980*
Figure 2. Classic two-compartmental model of shunt.

Figure 3. Graphic analysis of two-compartmental model of shunt.

Figure 4. Oxygen-hemoglobin curves of values of P50 of 28.6 mm Hg and 34.4 mm Hg (see text).

144 ROSSOFF ET AL

CHEST, 77: 2, FEBRUARY, 1980
will be on the flat part of the oxygen-hemoglobin equilibrium curve when the patient is breathing room air. Thus, in contradistinction to the model of alveolar hypoxemia (in which oxygen loading takes place at the decreased PaO₂), in shunt hypoxemia, loading of oxygen takes place at a normal PaO₂, regardless of the PaO₂. Thus, analogous to anemia or decreased cardiac output, a shift in P50 has virtually no effect on SpO₂ but has, of course, a major effect on SvO₂. Figure 4 illustrates this point. In the patient with the leftward-shifted curve (P50-26.6 mm Hg) who is breathing room air with a shunt of 50 percent, a cardiac output of 5 L/min, and a hemoglobin concentration of 15 g/100 ml, the SpO₂ is 97 percent, and PaO₂ is 100 mm Hg (Fig 4, X). The SvO₂ is 52 percent at a PVO₂ of 28 mm Hg (Fig 4, Z). The resulting PaO₂ is 40 mm Hg, and SvO₂ is 76 percent (Fig 4, Y). If the oxygen-hemoglobin equilibrium curve shifts to the right (P50-34 mm Hg), with the shunt, cardiac output and hemoglobin concentration remaining the same, then with a PpO₂ of 100 mm Hg, the SpO₂ will be 95 percent (Fig 4, X'). The new SvO₂ will be 50 percent at a PVO₂ of 37 mm Hg (Fig 4, Z'). The new PaO₂ will be 49 mm Hg, and SaO₂ will be 74 percent (Fig 4, Y').

Note that an increase in P50 increases the PVO₂ by 9 mm Hg. Therefore, by increasing the PVO₂, the decrease in oxygen-hemoglobin affinity which has been documented in cyanotic congenital heart disease is adaptive in the very same way as it is in anemia and decreased cardiac output. The confusion in the literature has resulted from a failure to distinguish between alveolar hypoxemia (model of altitude) and shunt hypoxemia (model of cyanotic congenital heart disease).

In our analysis, we noted that as the P50 increases, the PaO₂ increases (Fig 5), and thus the arterial oxygen pressure gradient (P[A-a]O₂) decreases (Fig 6). This decrease in P(A-a)O₂ occurs even though the FiO₂ and shunt do not change. Moreover, although it is well known that an increase in SvO₂ will decrease the P(A-a)O₂ without a change in shunt, as the P50 goes up and the P(A-a)O₂ falls, the SvO₂ actually decreases (Fig 7).

**Discussion**

Our theoretic finding that in the hypoxemia of a right-to-left shunt, a rightward shift is always beneficial has several implications. In the disease which most resembles our mathematical model (namely, intracardiac shunt), it is clear that an increase in P50 would increase the PVO₂. Indeed, studies of patients with cyanotic congenital heart disease have documented an increase in P50. The hypoxemia associated with pulmonary disease is, unfortunately, not subject to such simple analysis. To the extent that the hypoxemia is due to simple shunting, a rightward shift would be advantageous, regardless of the severity of the resulting hypoxemia; how-

**Figure 5.** Effect on PaO₂ of changes in P50 of blood.

**Figure 6.** Effect on P(A-a)O₂ of changes in P50 of blood.

**Figure 7.** Effect on SvO₂ of changes in P50 of blood.
ever, to the extent that the hypoxemia is due to alveolar hypoxia, thus resembling conditions at altitude, the rightward shift may not only not be beneficial, but actually be deleterious. The appreciation of these facts makes it possible to reconcile apparently conflicting observations, namely, the wide range of P50 found in various pulmonary diseases.15-19 Assuming that physiologic adjustments occur adaptively, one can only speculate that in those diseases in which shunting predominates as a major cause of hypoxemia, an increase in P50 will be found. In contrast, in those diseases in which alveolar hypoxia is a major cause of arterial hypoxemia, the P50 will be normal or even low.

REFERENCES
8 Turek Z, Kreuzer F, Hoof LJC: Advantage or disadvantage of decrease of blood oxygen affinity for tissue oxygen supply at hypoxia: A theoretical study comparing man and rat. Pluegers Arch 342:185-197, 1973

Postgraduate Course:

SLEEP AND BREATHING:
SLEEP APNEA AND RELATED TOPICS
March 6-8, 1980
Hotel Royal Plaza
Lake Buena Vista, Florida
Course Director: A. Jay Block, M.D., FCCP
For further information, please write Department of Education, AMERICAN COLLEGE OF CHEST PHYSICIANS, 911 Busse Highway, Park Ridge, IL 60068 (312) 698-2200