Tutorial

UNDERSTANDING THE MEANING OF THE SHUNT FRACTION CALCULATION

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ABSTRACT. The pulmonary shunt fraction ($\dot{Q}s/\dot{Q}t$) is frequently calculated in critically ill patients to monitor the effectiveness of pulmonary oxygenation. The breathing of pure oxygen often results in higher calculated $\dot{Q}s/\dot{Q}t$ values that have been attributed to the development of atelectasis, ventilation-perfusion imbalance, or both. To interpret properly the changes in calculated $\dot{Q}s/\dot{Q}t$ that occur when the inspired oxygen fraction is altered, the changes produced in all the variables affecting $\dot{Q}s/\dot{Q}t$ must be known. This tutorial presents an in-depth analysis of the four variables affecting the calculation of $\dot{Q}s/\dot{Q}t$: $\dot{V}O_2$ (oxygen uptake), $\dot{Q}t$ (cardiac output), $Cc'O_2$ (oxygen content in pulmonary end capillaries), and $C\bar{v}O_2$ (oxygen content in mixed venous blood). These variables are related according to the following equation, which is derived by combining the Fick and the classic shunt equations: $\dot{Q}s/\dot{Q}t = 1 - [(\dot{V}O_2/\dot{Q}t)/(Cc'O_2 - C\bar{v}O_2)]$. Three-dimensional surface representations relating these variables are also presented to help the reader understand the effects of these variables on the calculated $\dot{Q}s/\dot{Q}t$.

KEY WORDS. Oxygen content; inspired oxygen fraction. Heart: cardiac output. Lungs: pulmonary oxygenation; oxygen uptake; Fick equation; shunt equation.

Calculations of the pulmonary shunt fraction (Qs/Qt) are performed frequently in critically ill patients to monitor the effectiveness of pulmonary gas exchange. (Symbols used in this article are those approved by the International Union of Physiological Sciences Committee on Nomenclature [1] and are defined in the Glossary of this article.) In pulmonary physiology it is taught that, for the $\dot{Q}s/\dot{Q}t$ to be estimated, the subject must breathe pure oxygen. Under this condition, $\dot{Q}s/\dot{Q}t$ represents mixed venous blood admixed to the oxygenated arterial blood, and it is assumed that impairment of oxygen diffusion at the alveolar-capillary membrane is reduced or abolished and that the influence of ventilation-perfusion ($\dot{V}A/\dot{Q}c$) imbalance is minimized [2]. It is common in clinical practice, however, to calculate the $\dot{Q}s/\dot{Q}t$ at one of several values for the inspired oxygen fraction (FIO_2), i.e., from 0.3 to 0.7. As a consequence, these calculations of $\dot{Q}s/\dot{Q}t$ may include not only the contribution of true pulmonary shunt but the effects of diffusion impairment and uneven $\dot{V}A/\dot{Q}c$ distribution as well. This practice of determining $\dot{Q}s/\dot{Q}t$ at "clinically useful" levels of FIO_2 has arisen because several clinical studies have demonstrated that the calculated $\dot{Q}s/\dot{Q}t$ is higher when patients breathe pure oxygen than when they breathe a lower FIO_2 [3–8]. The increased $\dot{Q}s/\dot{Q}t$ at 100% oxygen is often attributed to the development of atelectasis or $\dot{V}A/\dot{Q}c$ imbalance. However, other reports show no significant change [4,7] or even a decrease

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[4–8] in the calculated Qs/Qt when patients breathe pure oxygen. In the present theoretical article we offer an explanation for how an increase, no change, or a decrease in the calculated $\dot{Q}s/\dot{Q}t$ can occur in the absence of atelectasis or an alteration in $\dot{V}A/\dot{Q}c$ when FIO_2 is increased from 0.3 to 1.0. In addition, we present another way of calculating the $\dot{Q}s/\dot{Q}t$, a way that shows the relationship of cardiac output ($\dot{Q}t$) and oxygen uptake ($\dot{V}O_2$) to the calculated $\dot{Q}s/\dot{Q}t$. Finally, we hope to clarify the importance of determining $\dot{Q}s/\dot{Q}t$ while subjects are breathing pure oxygen if one wishes to interpret the changes in calculated $\dot{Q}s/\dot{Q}t$ as due to changes in anatomic shunt, shunt from nonventilated areas of the lung (atelectasis), or both. This last point is particularly important if $\dot{Q}s/\dot{Q}t$ is being monitored as a goal-directed therapy [9]. A brief review of basic principles in gas exchange is presented first.

PULMONARY GAS EXCHANGE FOR OXYGEN

Oxygen exchange at the pulmonary alveolar–capillary membrane can be evaluated by measuring the difference in partial pressure of oxygen across the membrane ($AaDO_2$) (Fig 1). In clinical practice, the partial pressure of oxygen in arterial blood (PaO_2) is readily measured, whereas the partial pressure of oxygen in the alveoli is calculated according to the alveolar gas equation [10] as

$$PAO_2 = FIO_2(P_B - 47) - PaCO_2\,[FIO_2 + (1 - FIO_2)/R], \quad (1)$$

where PAO_2 is the mean alveolar oxygen partial pressure, FIO_2 is the inspired oxygen fraction, P_B is the barometric pressure, $PaCO_2$ is the arterial carbon dioxide partial pressure, and R is the respiratory quotient, which is the ratio of carbon dioxide elimination ($\dot{V}CO_2$) to oxygen uptake ($\dot{V}O_2$). The $\dot{V}CO_2/\dot{V}O_2$ ratio that is required to calculate PAO_2 is sometimes assumed. The $AaDO_2$ varies with changes in body position, exercise, and changes in FIO_2. At constant alveolar ventilation, the causes of the $AaDO_2$ are as follows: uneven distribution of $\dot{V}A/\dot{Q}c$ ratios throughout the lung; anatomic shunt and shunt from nonventilated areas of the lung; and impairment of oxygen diffusion by the alveolar capillary membrane, the plasma, and the red cell membrane, and by the chemical reaction with hemoglobin. The contribution of diffusion impairment is less than 1 mm Hg in normal, healthy humans.

In pulmonary physiology, shunt is also called venous admixture [11]. In clinical practice, however, venous admixture has been used to represent all three causes of $AaDO_2$ [12]. This has created confusion in the literature, because the standard shunt equation of Berggren [13], which was developed to calculate venous admixture (shunt) from nonventilated parts of the lung (atelectasis) and from the anatomic shunt, is also used in clinical practice [12] to calculate "venous admixture" that is produced by all the mechanisms that contribute to the $AaDO_2$. The confusion is even worse because Philbin et al [12] imply that they use two different equations to calculate shunt and "venous admixture," although they actually use the same equation for both.

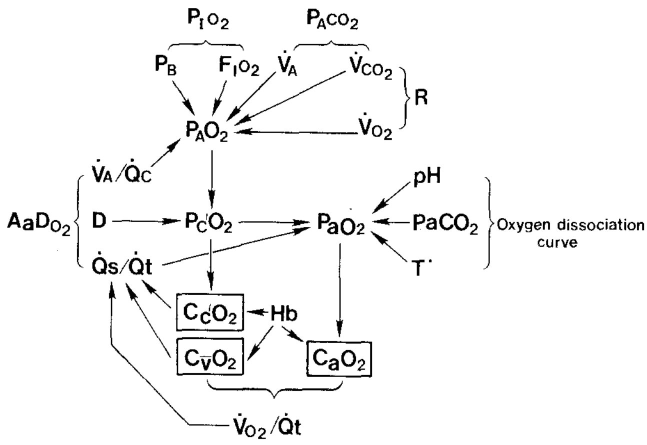

Fig 1. Variables that directly or indirectly affect the arterial oxygen content. The three variables of the standard shunt equation are shown within squares. $\dot{Q}s/\dot{Q}t$ *represents shunt (venous admixture) only. Diffusion* (D) *and ventilation-perfusion ratios* ($\dot{V}A/\dot{Q}c$) *are separate mechanisms affecting oxygenation. Note the influence of* $\dot{V}O_2$ *and* $\dot{Q}t$ *on* $C\bar{v}O_2$ *and* $\dot{Q}s/\dot{Q}t$*. Notice that the calculated mean* PAO_2 *depends on six variables, including* $\dot{V}A/\dot{Q}c$ *imbalance. By taking one single value for* PAO_2*, we are considering the lung as if it were made up of one single compartment. See Glossary for explanation of symbols.*

STANDARD SHUNT EQUATION

The standard equation of Berggren [13] is:

$$\dot{Q}s/\dot{Q}t = (Cc'O_2 - CaO_2)/(Cc'O_2 - C\bar{v}O_2), \quad (2)$$

where $\dot{Q}s/\dot{Q}t$ is the pulmonary shunt ($\dot{Q}s$) expressed as a fraction of total cardiac output ($\dot{Q}t$), and $Cc'O_2$, CaO_2, and $C\bar{v}O_2$ are oxygen content in the blood leaving the pulmonary capillaries, in systemic arterial blood, and in pulmonary arterial blood, respectively (Fig 2). Arterial and mixed venous blood oxygen content are generally not measured directly but are calculated as:

$$CO_2 = SO_2 \times Hb \times 1.34 + \alpha PO_2, \quad (3)$$

where CO_2 is the total blood oxygen content (oxyhemoglobin and oxygen dissolved in plasma), Hb is the

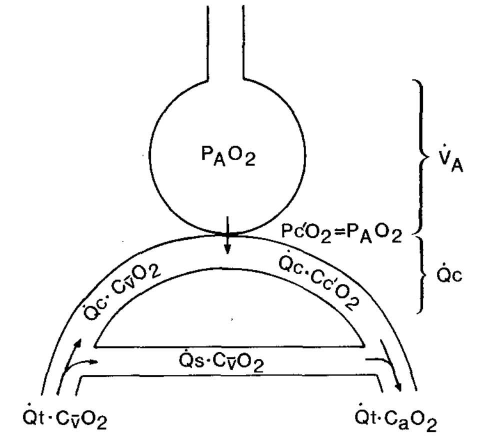

Fig 2. Single-compartment lung model for gas exchange. Alveolar oxygen partial pressure ($P_{A}O_2$) *will drive oxygen through the alveolar-capillary membrane, oxygenating the incoming mixed venous blood* ($\dot{Q}c \cdot C\bar{v}O_2$). *The oxygenated blood* ($\dot{Q}c \cdot Cc'O_2$) *is later admixed with shunted blood* ($\dot{Q}s \cdot C\bar{v}O_2$). *Thus, the amount of oxygen carried out by the arterial blood* ($\dot{Q}t \cdot CaO_2$) *is made up by* $\dot{Q}c \cdot Cc'O_2$ *and* $\dot{Q}s \cdot C\bar{v}O_2$. *Note a single value for alveolar ventilation* ($\dot{V}_A$) *and pulmonary perfusion* ($\dot{Q}c$). *There is no diffusion impairment; thus, the partial pressure of oxygen in the capillaries* ($Pc'O_2$) *is equal to* P_AO_2.

hemoglobin concentration, SO_2 is the Hb oxygen saturation, α is the oxygen solubility coefficient, and PO_2 is the partial pressure of oxygen. SO_2 can be directly measured or can be determined from the measured PO_2 and the standard oxygen dissociation curve (pH = 7.4, PCO_2 = 40 mm Hg, and temperature = 37°C). To calculate $Cc'O_2$, mean P_AO_2 is required. This latter value is calculated by applying equation 1 where the $\dot{V}CO_2/\dot{V}O_2$ ratio is assumed to be 0.85.

Another Way of Writing the Shunt Equation

When equation 2 is applied to calculate $\dot{Q}s/\dot{Q}t$, a tacit assumption is made that $\dot{V}O_2$ and $\dot{Q}t$ remain constant or, alternatively, if $\dot{V}O_2$ and $\dot{Q}t$ vary, that they change proportionally. In other words, it is assumed that the $\dot{V}O_2/\dot{Q}t$ ratio remains constant. In a clinical situation, this assumption may not hold. Thus, it is desirable to derive an equation for calculating $\dot{Q}s/\dot{Q}t$ in which $\dot{V}O_2$ and $\dot{Q}t$ are explicit variables. Inspection of the right-side term of equation 2 reveals that two of the three variables, CaO_2 and $C\bar{v}O_2$, are part of the Fick equation

$$\dot{V}O_2 = \dot{Q}t(CaO_2 - C\bar{v}O_2), \quad (4)$$

where $\dot{V}O_2$ is the uptake of oxygen by the pulmonary capillaries (in steady-state conditions, $\dot{V}O_2$ is equal to total metabolic oxygen consumption) and $\dot{Q}t$ is the cardiac output. Thus, equations 2 and 4 are related to each other, and the common link between the two is the arterial–mixed venous blood oxygen content difference ($a - \bar{v}$). More specifically, they are linked by mixed venous blood oxygen content [14]. By combining equations 2 and 4 (see Appendix) or by rearranging the standard shunt equation (see Appendix), a modified shunt equation is obtained [15,16]:

$$\dot{Q}s/\dot{Q}t = 1 - [(\dot{V}O_2/\dot{Q}t)/(Cc'O_2 - C\bar{v}O_2)]. \quad (5)$$

The assumptions made in equation 5 are the same as those in equation 2 except that $\dot{Q}t$ and $\dot{V}O_2$ are now explicit variables. These assumptions are as follows. First, the lung is considered as a single compartment (see Fig 2) where the incoming mixed venous blood is fully oxygenated at the pulmonary capillaries. Second, there is no diffusion impairment for the transport of oxygen from the alveolar spaces to the pulmonary capillaries. In other words, the partial pressure of oxygen in the alveoli (P_AO_2) is assumed to be equal to the partial pressure of oxygen in the blood leaving the pulmonary capillaries ($Pc'O_2$). Finally, the total amount of oxygen carried by the arterial blood is made up of that coming from the pulmonary veins and that contributed by the shunted blood (bronchial veins, thebesian veins, etc.).

Although equations 2 and 5 will yield the same calculated $\dot{Q}s/\dot{Q}t$ value, the use of equation 5 allows one to examine the effects of changes in $\dot{Q}t$ and $\dot{V}O_2$ on $\dot{Q}s/\dot{Q}t$. This is important because it is recognized on both theoretical [17] and experimental [18,19] grounds that changes in $\dot{Q}t$ may alter arterial oxygenation and thus the calculated $\dot{Q}s/\dot{Q}t$. Although there are no experimental data showing the effect of $\dot{V}O_2$ on the calculated $\dot{Q}s/\dot{Q}t$, this effect has important clinical implications and is postulated here on theoretical grounds. In anesthesia practice, a $\dot{V}O_2$ decrease (hypothermia, anesthetic agents) or increase (shivering, fasciculations) is commonly observed. Under these conditions, and unless $\dot{Q}t$ changes proportionally with $\dot{V}O_2$, there will be a change in the calculated $\dot{Q}s/\dot{Q}t$ (see equation 5). Examples of these changes are given below. Another advantage of using equation 5 to calculate $\dot{Q}s/\dot{Q}t$ is that if $\dot{V}O_2$, $\dot{Q}t$, and CaO_2 are measured, $C\bar{v}O_2$ can be calculated using equation 4. This precludes the necessity of sampling pulmonary arterial blood, which is required to calculate $\dot{Q}s/\dot{Q}t$ using equation 2.

THREE-DIMENSIONAL REPRESENTATIONS OF THE SHUNT EQUATION

There are a total of five variables in equation 5. Analysis of this equation using a conventional x-y plot would require that three variables remain constant. A third variable could be brought into play using isolines that can be applied for each of the variables that are held constant. Because this approach [16] is difficult to follow, we have developed three-dimensional representations [14,20]. These have been generated with a computer program (Johnson and Cruz, unpublished data) in which equation 5 was rearranged five times to solve for each variable. The graphic displacement of the surfaces generated was obtained by changing three variables at a time. These computer-generated surfaces were redrawn to obtain Figures 3 through 6. The three-dimensional representations allow a more comprehensive analysis because one can manipulate up to four variables. First, the simultaneous changes produced in three of the five variables will be presented. Two possible combinations have been selected for relating three variables. The first considers $\dot{V}O_2$, $\dot{Q}s/\dot{Q}t$, and $\dot{Q}t$, and the second considers $C\bar{v}O_2$, $\dot{Q}s/\dot{Q}t$, and $Cc'O_2$. The simultaneous changes in $\dot{V}O_2$, $\dot{Q}s/\dot{Q}t$, and $\dot{Q}t$ generate a surface that resembles a segment of a cone (Fig 3A). The size of the surface is determined by the $Cc'O_2 - C\bar{v}O_2$ difference. When $C\bar{v}O_2$, $\dot{Q}s/\dot{Q}t$, and $Cc'O_2$ change simultaneously, they generate a surface that resembles a segment of an ellipsoid (Fig 3B). The position in space of the surface is determined by the $\dot{V}O_2/\dot{Q}t$ ratio. Notice that Figure 3B may also be obtained by using equation 1. The selection of a given representation depends on what one would like to demonstrate. The ellipsoid figure is best for explaining how an increase in FIO_2 can cause the calculated $\dot{Q}s/\dot{Q}t$ to increase, decrease, or remain the same. The segment of a cone figure demonstrates how changes in $\dot{Q}t$ and $\dot{V}O_2$ affect the calculation of $\dot{Q}s/\dot{Q}t$ at a constant FIO_2. Both figures are presented in detail below.

Ellipsoid Surface

The ellipsoid surface representation is useful for examining the effects of breathing high-oxygen mixtures. To appreciate the changes that occur within the observable clinical values in $Cc'O_2$, $\dot{Q}s/\dot{Q}t$, and $C\bar{v}O_2$, the scale of the axes of Figure 3B has been reduced as shown in Figure 4. When a subject breathes increasing concentrations of oxygen and it is assumed that $\dot{V}O_2$ and $\dot{Q}t$ remain constant, the $Cc'O_2$ and the $C\bar{v}O_2$ will increase [21]. Thus, in the example of Figure 4, $\dot{V}O_2$ and $\dot{Q}t$ are 0.3 and 5 $L \cdot min^{-1}$, respectively. The numerical values of $\dot{Q}s/\dot{Q}t$ for several values of $Cc'O_2$ and $C\bar{v}O_2$ were calculated using equation 5 and are given in the Table. These numerical values have been used to draw Figures 4 and 5. For a subject with 14.9 $g \cdot dl^{-1}$ of Hb and a $PaCO_2$ of 40 mm Hg, breathing 30% oxygen will yield a $Cc'O_2$ of 20.5 $ml \cdot dl^{-1}$ and a $C\bar{v}O_2$ of 14 $ml \cdot dl^{-1}$. The calculated $\dot{Q}s/\dot{Q}t$ will be 0.077. If the subject now

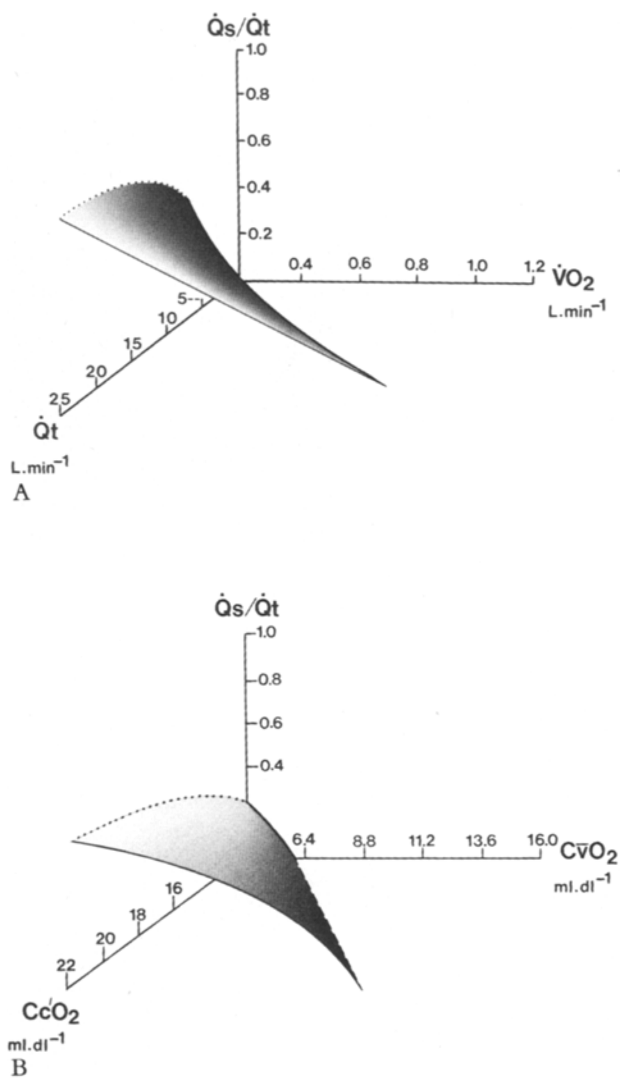

Fig 3. Two ways of relating three of the five variables of the shunt fraction equation. (A) $\dot{V}O_2$ *and* $\dot{Q}t$ *are independent variables,* $C\bar{v}O_2$ *and* $Cc'O_2$ *are held constant at 14 and 20 ml* $\cdot$ *dl*$^{-1}$*, respectively. The origin of the three axes is given by* $\dot{V}O_2$ = *0.2 L* $\cdot$ *min*$^{-1}$*,* $\dot{Q}s/\dot{Q}t$ = *0, and* $\dot{Q}t$ = *0 L* $\cdot$ *min*$^{-1}$*. The simultaneous changes in* $\dot{V}O_2$*,* $\dot{Q}t$*, and the calculated* $\dot{Q}s/\dot{Q}t$ *generates a surface that looks like a segment of a cone. The base of the cone is on the* $\dot{Q}s/\dot{Q}t$*,* $\dot{Q}t$ *plane (dotted line). (B)* $C\bar{v}O_2$ *and* $Cc'O_2$ *are independent variables.* $\dot{V}O_2$ *and* $\dot{Q}t$ *are held constant at 0.3 and 5 L* $\cdot$ *min*$^{-1}$*, respectively. The origin of the three axes is given by* $C\bar{v}O_2$ = *4 ml* $\cdot$ *dl*$^{-1}$*,* $\dot{Q}s/\dot{Q}t$ = *0, and* $Cc'O_2$ = *12 ml* $\cdot$ *dl*$^{-1}$*. The simultaneous changes in* $C\bar{v}O_2$*,* $Cc'O_2$*, and the calculated* $\dot{Q}s/\dot{Q}t$ *generate a surface that looks like a segment of an ellipsoid. The dotted line is on the* $\dot{Q}s/\dot{Q}t$*,* $Cc'O_2$ *wall. The distal continuous line is on the* $\dot{Q}s/\dot{Q}t$*,* $C\bar{v}O_2$ *plane, and the interrupted line is on the* $Cc'O_2$*,* $C\bar{v}O_2$ *floor plane. See Glossary for explanation of symbols.*

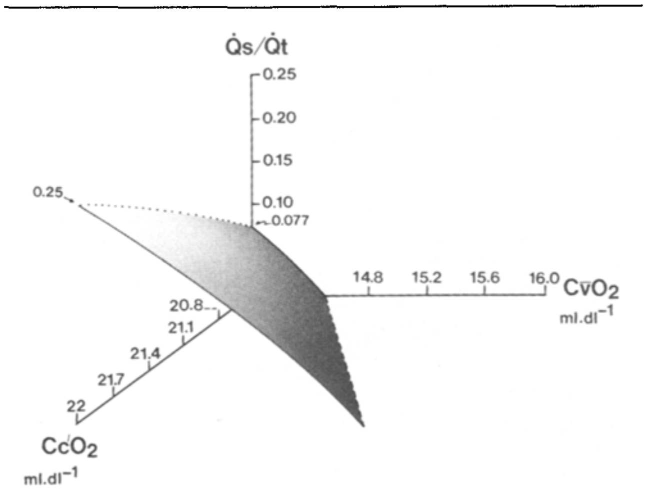

Fig 4. A portion of Figure 3B in which the scales for the axes have been reduced to within the physiological range. The origin of the three axes is given by $C\bar{v}O_2 = 14\ ml \cdot dl^{-1}$, $Cc'O_2 = 20.5\ ml \cdot dl^{-1}$, and $\dot{Q}s/\dot{Q}t = 0$. $\dot{V}O_2$ and $\dot{Q}t$ are held constant at 0.3 and 5 $L \cdot min^{-1}$, respectively. The dotted line on the $\dot{Q}s/\dot{Q}t$, $Cc'O_2$ plane shows the increase in the calculated $\dot{Q}s/\dot{Q}t$ from 0.077 to 0.25 when $Cc'O_2$ increases from 20.5 to 22 ml dl^{-1}, at a constant $C\bar{v}O_2$ of 14 $ml \cdot dl^{-1}$, simulating the changes that occur when FIO_2 is increased from 0.3 to 1. This effect is modified by an increase in $C\bar{v}O_2$. If $C\bar{v}O_2$ does not increase (1.5 $ml \cdot dl^{-1}$) to the same extent as $Cc'O_2$, there may be a true increase in $\dot{Q}s/\dot{Q}t$, an increase in $\dot{V}O_2$, a decrease in $\dot{Q}t$, or a combination of them. If $C\bar{v}O_2$ increases to the same extent as $Cc'O_2$, i.e., to 15.5 $ml \cdot dl^{-1}$, the calculated $\dot{Q}s/\dot{Q}t$ will remain at 0.077. (This point is not shown. However, it is on the continuous proximal line.) If $C\bar{v}O_2$ increases to a greater extent than $Cc'O_2$, i.e., from 14 to 16 $ml \cdot dl^{-1}$, the calculated $\dot{Q}s/\dot{Q}t$ will decrease from 0.25 to 0. The continuous proximal line shows the decrease in $\dot{Q}s/\dot{Q}t$ from 0.25 to 0 when $C\bar{v}O_2$ increases from 14 to 16 $ml \cdot dl^{-1}$. Thus, if FIO_2 is increased, the calculated $\dot{Q}s/\dot{Q}t$ may increase, remain the same, or decrease. See Glossary for explanation of symbols.

breathes pure oxygen, the $Cc'O_2$ will rise from 20.5 $ml \cdot dl^{-1}$ to 22 $ml \cdot dl^{-1}$ (FIO_2 from 0.3 to 1), assuming that ventilation, $\dot{Q}t$, and $\dot{V}O_2$ do not change. If $C\bar{v}O_2$ is held constant at 14 $ml \cdot dl^{-1}$, as demonstrated on the left border of Figure 4 (dotted line), the calculated $\dot{Q}s/\dot{Q}t$ increases from 0.077 to 0.25. Because $C\bar{v}O_2$ is also expected to rise when FIO_2 is increased, the true change in the calculated $\dot{Q}s/\dot{Q}t$ will depend on the final level of $C\bar{v}O_2$. If $C\bar{v}O_2$ increases from 14 to 16 $ml \cdot dl^{-1}$ at a constant $Cc'O_2$ of 22 $ml \cdot dl^{-1}$, the calculated $\dot{Q}s/\dot{Q}t$ will decrease from 0.25 to 0, as shown in the proximal border of the figure. If $C\bar{v}O_2$ increases to the same extent as $Cc'O_2$, i.e., from 14 to 15.5 $ml \cdot dl^{-1}$, the calculated $\dot{Q}s/\dot{Q}t$ will remain at 0.077. Finally, if $C\bar{v}O_2$ increases more than $Cc'O_2$ does, the calculated $\dot{Q}s/\dot{Q}t$ will be less than 0.077. Thus, the calculated value of $\dot{Q}s/\dot{Q}t$ will be higher, remain the same, or decrease depending on the final value of $C\bar{v}O_2$.

In Figure 4, the effects of $Cc'O_2$ and $C\bar{v}O_2$ on $\dot{Q}s/\dot{Q}t$ are examined at constant values of $\dot{Q}t$ and $\dot{V}O_2$. Because the $C\bar{v}O_2$ is affected by changes in $\dot{Q}t$ or $\dot{V}O_2$ (Fick), it is also important to examine how changes in $\dot{Q}t$ and $\dot{V}O_2$ influence the calculated $\dot{Q}s/\dot{Q}t$. Examples of these are given in the Table and in Figure 5. In Figure 5, three different surfaces (from inferior to superior) are drawn corresponding to three levels of $\dot{V}O_2/\dot{Q}t$ ratios: 0.07, 0.06, and 0.05. Notice that as the $\dot{V}O_2/\dot{Q}t$ ratio decreases (i.e., $\dot{Q}t$ increases or $\dot{V}O_2$ decreases) the surface becomes larger and its position in space is elevated. In other words, the calculated $\dot{Q}s/\dot{Q}t$ will be larger the greater the $\dot{Q}t$ or the smaller the $\dot{V}O_2$, provided the other variables remain the same. When the subject is breathing pure oxygen at atmospheric pressure, $\dot{Q}t$ may decrease by 10% to 20% [22]. If all other variables remain con-

Calculated $\dot{Q}s/\dot{Q}t$ at Several Values of $C\bar{v}O_2$ and $Cc'O_2$ for Three Levels of $\dot{V}O_2$ and a Constant $\dot{Q}t$ (5 $L \cdot min^{-1}$)[a]

	$\dot{Q}s/\dot{Q}t$																
	$\dot{V}O_2 = 0.25\ L \cdot min^{-1}$						$\dot{V}O_2 = 0.30\ L \cdot min^{-1}$						$\dot{V}O_2 = 0.35\ L \cdot min^{-1}$			
	$Cc'O_2\ (ml \cdot dl^{-1})$						$Cc'O_2\ (ml \cdot dl^{-1})$						$Cc'O_2\ (ml \cdot dl^{-1})$			
$C\bar{v}O_2$ $(ml \cdot dl^{-1})$	20.5	20.8	21.1	21.4	21.7	22.0	20.5	20.8	21.1	21.4	21.7	22.0	21.1	21.4	21.7	22.0
14.0	0.23	0.27	0.30	0.32	0.35	0.38	0.077	0.12	0.16	0.19	0.22	0.25	0.01	0.05	0.09	0.13
14.4	0.18	0.22	0.25	0.29	0.32	0.34	0.02	0.06	0.11	0.14	0.18	0.21		0.00	0.04	0.08
14.8	0.12	0.17	0.21	0.24	0.28	0.31		0.00	0.05	0.09	0.13	0.17				0.03
15.2	0.06	0.11	0.15	0.19	0.23	0.27				0.03	0.08	0.12				
15.6		0.04	0.09	0.14	0.18	0.22					0.02	0.06				
16.0			0.02	0.07	0.12	0.17						0.00				

[a]Calculated by applying equation 5 (see text). The same calculated $\dot{Q}s/\dot{Q}t$ values are obtained by holding $\dot{V}O_2$ constant at 0.3 $L \cdot min^{-1}$ and taking $\dot{Q}t$ values 6, 5, and 4.3 $L \cdot min^{-1}$, respectively. These values were used to draw Figures 4 and 5.

$\dot{Q}s/\dot{Q}t$ = pulmonary shunt fraction; $C\bar{v}O_2$ = mixed venous oxygen content; $Cc'O_2$ = pulmonary end-capillary oxygen content; $\dot{V}O_2$ = oxygen uptake; $\dot{Q}t$ = cardiac output.

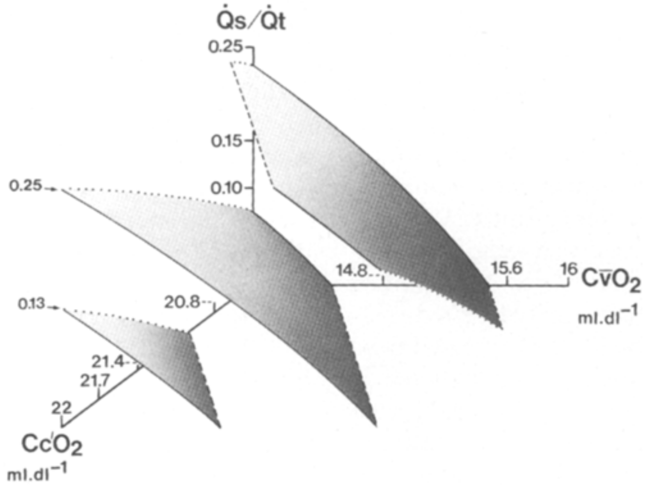

Fig 5. The effects of changing $\dot{V}O_2$, $\dot{Q}t$, or both on the relationship of $C\bar{v}O_2$, $\dot{Q}s/\dot{Q}t$, and $Cc'O_2$. Three surfaces are drawn at $\dot{V}O_2/\dot{Q}t$ ratios of 0.07, 0.06, and 0.05 (lower to upper surfaces, respectively). The axes and the middle surface are exactly as in Figure 4. As shown numerically in the Table, the decrease or increase in $\dot{V}O_2/\dot{Q}t$ ratio was obtained by altering $\dot{V}O_2$ and keeping the $\dot{Q}t$ constant, or vice versa. The dotted lines (iso $\dot{V}O_2/\dot{Q}t$ lines) are on the $\dot{Q}s/\dot{Q}t$, $Cc'O_2$ plane. They show an increase in $\dot{Q}s/\dot{Q}t$ with increasing $Cc'O_2$. If the $\dot{V}O_2/\dot{Q}t$ ratio decreases (increasing $\dot{Q}t$ or decreasing $\dot{V}O_2$), the calculated $\dot{Q}s/\dot{Q}t$ will be higher at a constant $Cc'O_2$. For example, at a $\dot{V}O_2$ of 0.35 L · min^{-1} (lower surface) the calculated $\dot{Q}s/\dot{Q}t$ is 0.13 (left). When $\dot{V}O_2$ decreases to 0.30 L · min^{-1} (middle surface), the calculated $\dot{Q}s/\dot{Q}t$ increases to 0.25 (left). The right border of each surface is shown by interrupted lines on the floor plane where $\dot{Q}s/\dot{Q}t$ = 0. They represent the increases in arterial oxygenation ($Cc'O_2$ = CaO_2) and $C\bar{v}O_2$ as FIO_2 increases at a constant $\dot{V}O_2/\dot{Q}t$ ratio. See Glossary for explanation of symbols.

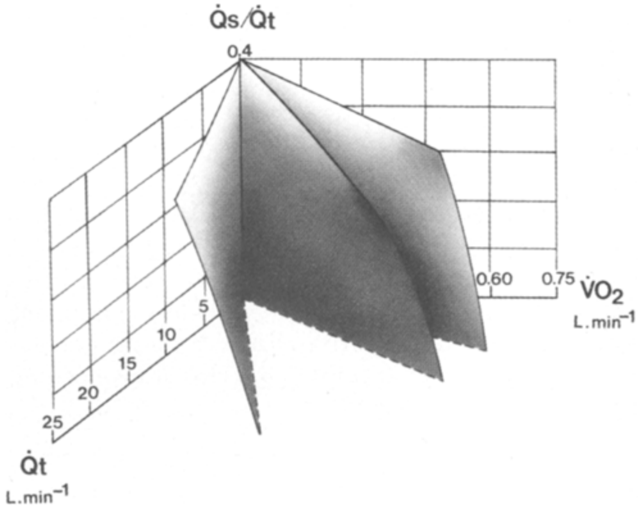

Fig 6. The open-book model for the $\dot{V}O_2$, $\dot{Q}s/\dot{Q}t$, and $\dot{Q}t$ relationships. A grid has been built in the two vertical planes, simulating the covers of a book. The axes are the same as those in Figure 3A, but with reduced scales in the $\dot{V}O_2$ and $\dot{Q}s/\dot{Q}t$ axes. The simultaneous variation of $\dot{V}O_2$, $\dot{Q}t$, and the calculated $\dot{Q}s/\dot{Q}t$ generates the pages whose positions are determined by the $Cc'O_2 - C\bar{v}O_2$ difference. With FIO_2 held at 1.0 ($Cc'O_2$ = 22 ml · dl^{-1}), each page represents, from proximal to distal position to the viewer, $C\bar{v}O_2$ values of 20, 17, and 14 ml · dl^{-1}, respectively. Another way of looking at this figure is to observe the changes in the four variables simultaneously by turning the page. Notice that the lower border of each page (interrupted lines) is on the floor plane $\dot{V}O_2$, $\dot{Q}t$. Thus, they represent the increase in $\dot{Q}t$ due to an increase in $\dot{V}O_2$ at a constant arterial-mixed venous oxygen content difference of 2.0, 5.0, and 8.0 ml · dl^{-1}, respectively (proximal to distal page). See Glossary for explanation of symbols.

stant, this would cause a decrease in the calculated $\dot{Q}s/\dot{Q}t$. These changes are easily seen by analyzing the anterior border of each plane at a given $C\bar{v}O_2$. For example, if there is a decrease in $\dot{Q}t$ from 5 L · min^{-1} (middle plane) to 4.3 L · min^{-1} (inferior plane), the calculated $\dot{Q}s/\dot{Q}t$ decreases from 0.25 to 0.13 at a $C\bar{v}O_2$ of 14 ml · dl^{-1} (data also in the Table).

Segment of a Cone Surface

The cone surface representation is useful for examining the effects of changes in $\dot{Q}t$ and $\dot{V}O_2$ on the calculated $\dot{Q}s/\dot{Q}t$ at a constant FIO_2. At a given $\dot{V}O_2$, the calculated $\dot{Q}s/\dot{Q}t$ increases as $\dot{Q}t$ increases, following a curvilinear function. For instance, at a $\dot{V}O_2$ of 0.2 L · min^{-1}, as $\dot{Q}t$ increases from 5 to 25 L · min^{-1}, the calculated $\dot{Q}s/\dot{Q}t$ increases from 0.33 to 0.87 (base of the cone of Figure 3A). Undoubtedly, these are extreme values that are not seen in patients. The scale for $\dot{Q}s/\dot{Q}t$ (0 to 1) was drawn in Figure 3A to demonstrate the whole spectrum of the changes as a function of $\dot{Q}t$ and $\dot{V}O_2$. By reducing the $\dot{Q}s/\dot{Q}t$ scale to values usually calculated in clinical practice (0 to 0.4), a portion of the cone surface is now obtained that resembles a page in an open book [20]. The position of the page within the open book depends on the changes in the $Cc'O_2 - C\bar{v}O_2$ difference. Figure 6 shows an example of the simultaneous changes in $\dot{V}O_2$, $\dot{Q}s/\dot{Q}t$, and $\dot{Q}t$ at three different levels of $C\bar{v}O_2$. In this example, $Cc'O_2$ remains constant at 22 ml · dl^{-1}, corresponding to an FIO_2 equal to 1.0. As $C\bar{v}O_2$ increases from 14 to 20 ml · dl^{-1}, the page moves from the distal to the proximal cover of the book, i.e., from right to left. The increase in $C\bar{v}O_2$ simulates what occurs in a patient who receives a continuous infusion of sodium nitroprusside (toxic effect). Another way of looking at the relationship among the four variables is to consider three different pages, each corresponding to a given $Cc'O_2 - C\bar{v}O_2$ difference. The superior and inferior borders of the pages are determined by the linear relationship between $\dot{V}O_2$ and $\dot{Q}t$ at the calculated $\dot{Q}s/\dot{Q}t$ of 0.4 and 0, respectively. Notice that each page is bent. This inclination is due to the effect of $\dot{Q}t$ on the calculated $\dot{Q}s/\dot{Q}t$ (curvilinear relationship) and is similar for each page. However, the inclination appears more pronounced in the proximal page because of the effect of perspective. As shown in Figures 3A, 5, and 6, larger variations in the calculated $\dot{Q}s/\dot{Q}t$ are produced by altering $\dot{V}O_2$ and $\dot{Q}t$. Thus, although $\dot{V}O_2$ and $\dot{Q}t$ are not required to calculate $\dot{Q}s/\dot{Q}t$, the interpretation of changes in $\dot{Q}s/\dot{Q}t$ would be meaningless unless one knows how $\dot{V}O_2$ and $\dot{Q}t$ have changed. This is particularly important when therapy is directed at maintaining certain values of $\dot{Q}s/\dot{Q}t$ [9].

THE $\dot{V}A/\dot{Q}c$ PROBLEM

In equations 2 and 5 and the three-dimensional surface models generated from them, a single-compartment model of the lung has been used without considering changes in $\dot{V}A/\dot{Q}c$ and diffusion impairment. However, the human lung is more complicated. There is no doubt that, even in normal lungs, there is uneven distribution of $\dot{V}A/\dot{Q}c$ ratios. A more representative three-compartment model of the human lung is given in Figure 7. Compartments 1 and 3 in this model simulate the base and apex of the West lung model [23]. During the breathing of room air the regional difference in $\dot{V}A/\dot{Q}c$ from the base to the apex of the lung results in regional differences in PAO_2 values from 89 to 132 mm Hg, respectively. When pure oxygen is breathed, the PAO_2 in compartment 1 would increase to 671 mm Hg and that in compartment 3 would increase to 685 mm Hg, provided that ventilation and perfusion do not change. In other words, the difference in PAO_2 between compartments would be reduced from 43 to 14 mm Hg when the FIO_2 is increased from 0.21 to 1.0. This 14 mm Hg difference is exactly the difference between the apex and base for $PACO_2$ [23]. The effect of this small difference may not be detected experimentally. Furthermore, even if a 43 mm Hg difference existed between the apex and the base while the patient breathed pure oxygen, the effect on $Cc'O_2$ would be only 0.13 ml · dl^{-1} of dissolved oxygen, an amount that could go undetected even if $Cc'O_2$ could be measured. It is important to understand that $Cc'O_2$, calculated from the mean PAO_2, is a weighted average of hundreds of compartments within the lung; in spite of true uneven $\dot{V}A/\dot{Q}c$ ratios, by considering a single value for $Cc'O_2$ (see Figure 1) while the patient is breathing pure oxygen, one observes

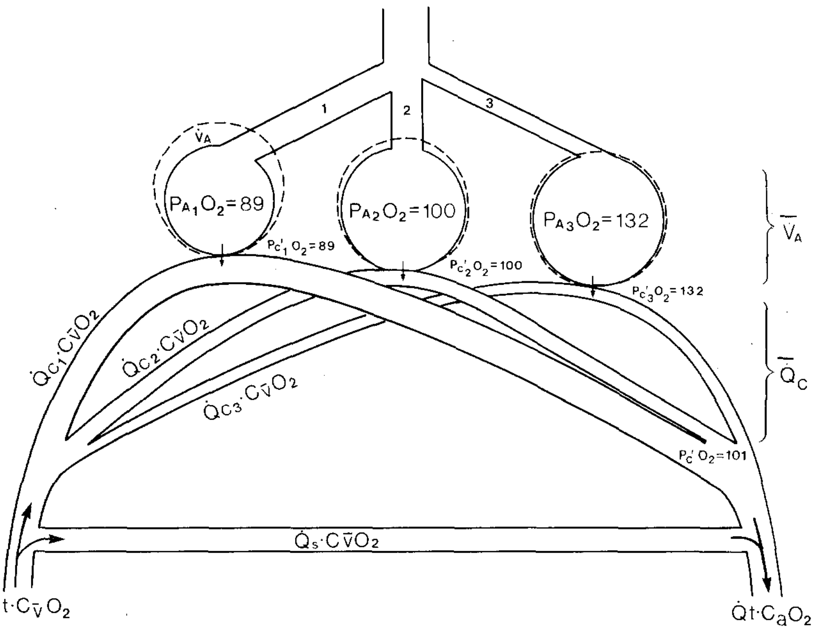

Fig 7. A three-compartment lung model with a (1) *low,* (2) *ideal, and* (3) *high ventilation-perfusion relationship. Compartments 1 and 3 simulate the base and apex of the West lung model [23]. When the shunt equation is applied to this model, the uneven* $\dot{V}A/\dot{Q}c$ *ratio is minimized by having the subject breathe pure oxygen. A weighted average* $\dot{V}A$ *and* $\dot{Q}c$ *will give one single value for* $Cc'O_2$ *that is calculated from mean* $Pc'O_2$*, similar to the approach shown in Figure 1. In other words, the true multicompartment model of the lung breathing room air is transformed to a single-compartment model by having the patient breathe pure oxygen. See Glossary for explanation of symbols.*

that the multicompartment model of Figure 7 behaves as a single-compartment model. Despite the multicompartment nature of the lung, the changes that occur in $Cc'O_2$ due to changes in F_IO_2 are predictable [21]. The unpredictable values are $C\bar{v}O_2$ and CaO_2 [21]. The former value is probably due to changes in $\dot{Q}t$ or $\dot{V}O_2$, and the latter probably has several causes (see Figure 1).

DOES $\dot{Q}s/\dot{Q}t$ CHANGE WITH INCREASING F_IO_2?

In 1976, Douglas et al [3] reported significant changes in the calculated $\dot{Q}s/\dot{Q}t$ when F_IO_2 was increased from 0.21 to 1. At an F_IO_2 of 0.21, $\dot{Q}s/\dot{Q}t$ was approximately 24% and fell to between 12 and 15% when the F_IO_2 was between 0.3 and 0.7. Thereafter, $\dot{Q}s/\dot{Q}t$ progressively increased to approximately 19% at an F_IO_2 of 1. From these data, it was recommended that "respiratory function be evaluated during inhalation of a clinically useful concentration of oxygen rather than at an F_IO_2 of 1." [3]. A more recent publication reached the same conclusion [8]. Undoubtedly, these recommendations are against the classic view [2] of giving the patient pure oxygen in order to estimate the $\dot{Q}s/\dot{Q}t$. Several mechanisms have been suggested to explain the changes in $\dot{Q}s/\dot{Q}t$ produced by an F_IO_2 of 1: absorption atelectasis, alteration in $\dot{V}A/\dot{Q}c$, and release of hypoxic pulmonary vasoconstriction. As explained above, because we are dealing with a single compartment when the patient is breathing pure oxygen, none of these mechanisms can account for the changes in $\dot{Q}s/\dot{Q}t$. However, changes in $Cc'O_2$, $C\bar{v}O_2$, $\dot{V}O_2$, or $\dot{Q}t$ can account for the changes in the calculated $\dot{Q}s/\dot{Q}t$, a circumstance that is self-evident from consideration of equation 5.

We have come to the following conclusions: (1) The calculated $\dot{Q}s/\dot{Q}t$ depends on the changes produced in $Cc'O_2$, $C\bar{v}O_2$, $\dot{V}O_2$, and $\dot{Q}t$, with changes in $C\bar{v}O_2$ probably resulting from the combined effect of the changes in the other three variables; (2) all these variables must be considered when examining changes in calculated $\dot{Q}s/\dot{Q}t$ that occur at various F_IO_2 values; and (3) in clinical practice, it is important to calculate $\dot{Q}s/\dot{Q}t$ while patients are breathing pure oxygen.

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APPENDIX

Derivation of the Shunt Fraction Equation

Applying the Fick principle to the lung capillaries, represented by the single-compartment lung model in Figure 2, we have

$$\dot{V}O_2 = \dot{Q}cCc'O_2 - \dot{Q}cC\bar{v}O_2, \quad (6)$$

where $\dot{Q}cCc'O_2$ is the amount of oxygen carried by the pulmonary capillaries after the oxygen uptake ($\dot{V}O_2$) and $\dot{Q}cC\bar{v}O_2$ is the amount of oxygen reaching the pulmonary capillaries for oxygenation.

If the pulmonary shunt blood flow is taken into account, we have

$$\dot{V}O_2 = \dot{Q}tCaO_2 - \dot{Q}tC\bar{v}O_2, \quad (7)$$

where $\dot{Q}tCaO_2$ is the amount of oxygen carried by the arterial blood and $\dot{Q}tC\bar{v}O_2$ is the amount of oxygen returned to the lung (mixed venous blood of the pulmonary artery).

Thus, from the model in Figure 2 (or by equating equations 6 and 7) we have

$$\dot{Q}tCaO_2 = \dot{Q}cCc'O_2 + \dot{Q}sC\bar{v}O_2. \quad (8)$$

In words, the oxygen carried by arterial blood ($\dot{Q}tCaO_2$) is the result of the oxygen carried by the pulmonary capillaries ($\dot{Q}cCc'O_2$), to which is added the amount of oxygen carried by the shunted mixed venous blood ($\dot{Q}sC\bar{v}O_2$). From the same model,

$$\dot{Q}c = \dot{Q}t - \dot{Q}s, \quad (9)$$

where pulmonary capillary blood flow ($\dot{Q}c$) is equal to cardiac output ($\dot{Q}t$) minus the shunt blood flow ($\dot{Q}s$).

Substituting equation 9 in equation 8,

$$\dot{Q}tCaO_2 = (\dot{Q}t - \dot{Q}s) \cdot Cc'O_2 + \dot{Q}sC\bar{v}O_2. \quad (10)$$

Removing the parentheses,

$$\dot{Q}tCaO_2 = \dot{Q}tCc'O_2 - \dot{Q}sCc'O_2 + \dot{Q}sC\bar{v}O_2. \quad (11)$$

Transposing terms,

$$\dot{Q}sCc'O_2 - \dot{Q}sC\bar{v}O_2 = \dot{Q}tCc'O_2 - \dot{Q}tCaO_2. \quad (12)$$

Factoring out $\dot{Q}s$ and $\dot{Q}t$,

$$\dot{Q}s(Cc'O_2 - C\bar{v}O_2) = \dot{Q}t(Cc'O_2 - CaO_2). \quad (13)$$

Solving for the shunt fraction,

$$\dot{Q}s/\dot{Q}t = (Cc'O_2 - CaO_2)/(Cc'O_2 - C\bar{v}O_2). \quad (14)$$

Another Way of Writing the Shunt Equation

COMBINATION OF THE FICK AND SHUNT EQUATIONS. Solving CaO_2 from equation 7,

$$CaO_2 = (\dot{V}O_2 + \dot{Q}tC\bar{v}O_2)/\dot{Q}t. \quad (15)$$

Simplifying,

$$CaO_2 = \dot{V}O_2/\dot{Q}t + C\bar{v}O_2. \quad (16)$$

(This relationship could also be derived from equation 4.)

Solving CaO_2 from equation 14,

$$CaO_2 = Cc'O_2 - [\dot{Q}s/\dot{Q}t] \cdot (Cc'O_2 - C\bar{v}O_2). \quad (17)$$

Equating equations 16 and 17,

$$\dot{V}O_2/\dot{Q}t + C\bar{v}O_2 = Cc'O_2 - [\dot{Q}s/\dot{Q}t] \cdot (Cc'O_2 - C\bar{v}O_2). \quad (18)$$

Removing the parentheses,

$$\dot{V}O_2/\dot{Q}t + C\bar{v}O_2 = Cc'O_2 - [\dot{Q}s/\dot{Q}t] \cdot Cc'O_2 + [\dot{Q}s/\dot{Q}t] \cdot C\bar{v}O_2. \quad (19)$$

Transposing terms and factoring,

$$\dot{V}O_2/\dot{Q}t = Cc'O_2(1 - [\dot{Q}s/\dot{Q}t]) - C\bar{v}O_2\,(1 - [\dot{Q}s/\dot{Q}t]). \quad (20)$$

Factoring out $(1 - [\dot{Q}s/\dot{Q}t])$,

$$\dot{V}O_2/\dot{Q}t = (1 - [\dot{Q}s/\dot{Q}t]) \cdot (Cc'O_2 - C\bar{v}O_2). \quad (21)$$

Solving for $\dot{Q}s/\dot{Q}t$, we have the modified shunt equation,

$$\dot{Q}s/\dot{Q}t = 1 - [(\dot{V}O_2/\dot{Q}t)/(Cc'O_2 - C\bar{v}O_2)], \quad (22)$$

which is the same as equation 5.

REARRANGEMENT OF THE STANDARD SHUNT EQUATION. Another way of arriving at equation 22 is by rearranging equation 14, which may be solved for CaO_2.

$$CaO_2 = Cc'O_2 - [\dot{Q}s/\dot{Q}t] \cdot Cc'O_2 + [\dot{Q}s/\dot{Q}t] \cdot C\bar{v}O_2. \quad (23)$$

(Notice that this equation is similar to equation 17.)

Subtracting $C\bar{v}O_2$ from both terms and factoring,

$$CaO_2 - C\bar{v}O_2 = Cc'O_2(1 - [\dot{Q}s/\dot{Q}t]) - C\bar{v}O_2(1 - [\dot{Q}s/\dot{Q}t]). \quad (24)$$

Solving for $\dot{Q}s/\dot{Q}t$,

$$\dot{Q}s/\dot{Q}t = 1 - [(CaO_2 - C\bar{v}O_2)/(Cc'O_2 - C\bar{v}O_2)]. \quad (25)$$

From equation 16,

$$CaO_2 - C\bar{v}O_2 = \dot{V}O_2/\dot{Q}t. \quad (26)$$

Substituting equation 26 in equation 25 we have

$$\dot{Q}s/\dot{Q}t = 1 - [(\dot{V}O_2/\dot{Q}t)/(Cc'O_2 - C\bar{v}O_2)],$$

which is the same as equation 22.

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GLOSSARY

α Oxygen solubility coefficient. At 37°C, α = 0.0031 ml of oxygen per mm Hg of partial pressure of oxygen.

$AaDo_2$ Alveolar–arterial oxygen partial pressure difference. The difference in mean alveolar oxygen partial pressure (P_{AO_2}) and arterial oxygen partial pressure (Pao_2).

Cao_2 Total arterial oxygen content. Composed of oxygen dissolved in plasma and chemically bound to hemoglobin. Dissolved oxygen is proportional to the partial pressure and thus can increase without limit. Oxygen attached to hemoglobin has a limit, depending on the amount of hemoglobin present in the blood.

$Cc'O_2$ Total pulmonary end-capillary oxygen content. $Cc'O_2$ is not measured but is calculated from mean alveolar partial pressure for oxygen (P_{AO_2}). See below.

Co_2 Total blood oxygen content (oxyhemoglobin and oxygen dissolved in plasma).

$C\bar{v}O_2$ Total mixed venous oxygen content. Blood is sampled from the pulmonary artery.

D Diffusion or transfer factor that measures the amount of oxygen diffusing between the alveolar-capillary membrane and pulmonary capillary blood. It also involves diffusion through the plasma, the red cell membrane, and the chemical reaction of oxygen with hemoglobin, expressed in milliliters of oxygen in standard conditions per minute per mm Hg pressure difference.

F_{IO_2} Inspired oxygen fraction. Room air has an F_{IO_2} of 0.2093, and pure oxygen has an F_{IO_2} of 1.0.

Hb Hemoglobin concentration in blood. Expressed in milligrams per deciliter.

$PaCO_2$ Carbon dioxide partial pressure in arterial blood. Measured with a Severinghaus carbon dioxide electrode.

P_ACO_2 Carbon dioxide partial pressure in alveolar gas. In normal lungs $P_ACO_2 = PaCO_2$.

Pao_2 Oxygen partial pressure in arterial blood. Measured with a Clark oxygen electrode.

P_{AO_2} Oxygen partial pressure in alveolar gas. Because the lung has multiple compartments with different alveolar partial pressures, mean P_{AO_2} is calculated with the alveolar gas equation.

P_B Barometric pressure expressed in mm Hg.

$Pc'O_2$ Oxygen partial pressure in the pulmonary end-capillary blood after the oxygen uptake has taken place. In clinical practice and pulmonary physiology, $Pc'O_2$ is assumed to be equal to mean P_{AO_2}.

Pco_2 Partial pressure of carbon dioxide.

pH Negative logarithm of the hydrogen ion concentration ($[H^+]$). Measured with a pH electrode.

P_{IO_2} Partial pressure of oxygen in inspired gas. It is calculated as follows: $P_{IO_2} = (P_B - 47) \times F_{IO_2}$ (47 = partial pressure of water vapor at 37°C).

Po_2 Partial pressure of oxygen.

$\dot{Q}s$ Amount of blood that is shunted (bypasses the ventilated alveoli), expressed in liters per minute. In clinical practice $\dot{Q}s$ is calculated as a fraction of total cardiac output ($\dot{Q}t$).

$\dot{Q}t$ Amount of blood that passes through the heart per unit time, expressed in liters per minute.

$\dot{Q}s/\dot{Q}t$ Shunt fraction ratio of shunted blood to total cardiac output.

R Respiratory exchange ratio. Ratio of carbon dioxide elimination ($\dot{V}co_2$) and oxygen uptake ($\dot{V}o_2$) by the lungs. Respiratory quotient is restricted to metabolic carbon dioxide output and oxygen uptake by the tissues.

Sao_2 Hemoglobin oxygen saturation in arterial blood, expressed as a percentage of the oxygen capacity of hemoglobin.

$Sc'O_2$ Hemoglobin oxygen saturation in pulmonary end-capillary blood, expressed as a percentage of the oxygen capacity of hemoglobin.

SO_2 Hemoglobin oxygen saturation.

$S\bar{v}O_2$ Hemoglobin oxygen saturation in mixed venous blood, expressed as a percentage of the oxygen capacity of hemoglobin.

$\dot{V}A/\dot{Q}c$ Ratio of the alveolar ventilation to the blood perfusion volume flow through the pulmonary parenchyma. This ratio is a fundamental determinant of the oxygen and carbon dioxide pressure of the alveolar gas and of the end-capillary blood.

$\dot{V}CO_2$ Carbon dioxide elimination by the lungs. Under steady-state conditions, $\dot{V}CO_2$ is equal to metabolic carbon dioxide production.

$\dot{V}O_2$ Oxygen uptake by the lungs. Under steady-state conditions, $\dot{V}O_2$ is equal to metabolic oxygen consumption.