Anesthesiology
75:210–216, 1991

The Relationship Between the Arterial to End-tidal P_{CO_2} Difference and Hemoglobin Saturation in Patients with Congenital Heart Disease

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In right-to-left (RL) intracardiac shunting, the venous blood that is added to the oxygenated blood in the left heart is both poor in oxygen and rich in carbon dioxide. Thus, any given degree of arterial desaturation is associated with an obligatory arterial to end-tidal carbon dioxide tension difference ($Pa_{CO_2} - PET_{CO_2}$). This paper presents a theoretical analysis of the relationship between $Pa_{CO_2} - PET_{CO_2}$ and arterial hemoglobin saturation (Sa_{O_2}) in cyanotic heart disease. Using the shunt equation as a starting point, a curvilinear, negative correlation between $Pa_{CO_2} - PET_{CO_2}$ and Sa_{O_2} can be demonstrated. The slope of the regression of $Pa_{CO_2} - PET_{CO_2}$ against Sa_{O_2} is shown to be positively correlated to Hb concentration, Pa_{CO_2}, and the respiratory quotient R. The slope of the regression is also slightly increased at relatively high Sa_{O_2}s and at high inspired oxygen fractions, although these latter factors are of lesser significance. However, in addition to the above primary effects of RL shunting, secondary effects may occur if pulmonary perfusion is reduced sufficiently to cause "alveolar hypoperfusion," which also creates an alveolar dead space. Primary and secondary effects are additive. This theoretical analysis is illustrated with a study of 27 children with congenital heart disease. Their lungs were ventilated with a Servoventilator 900 C, and carbon dioxide single-breath tests were obtained on-line with the use of a computerized system based on the Siemens-Elema carbon dioxide analyzer 930. Blood was sampled for Pa_{CO_2} measurement and arterial Hb saturation was measured by pulse oximetry (Sp_{O_2}). The relationship between $Pa_{CO_2} - PET_{CO_2}$ and Sp_{O_2} was found to agree with that predicted by theory, confirming that in cyanotic heart disease, $Pa_{CO_2} - PET_{CO_2}$ increases by 0.2–0.4 kPa (2–3 mmHg) for every 10% reduction in Sp_{O_2}. Awareness of this relationship is necessary when attempting to estimate Pa_{CO_2} from PET_{CO_2} during anesthesia in cyanotic children. (Key words: Carbon dioxide: end-tidal carbon dioxide tension. Heart: cyanotic congenital diseases. Hemoglobin: oxygen saturation. Measurement techniques: pulse oximetry.)

IN RIGHT-TO-LEFT (RL) intracardiac shunting, the blood that is added to the oxygenated blood in the left heart is both poor in oxygen and rich in carbon dioxide. Thus, any degree of arterial desaturation is associated with an obligatory increase in the arterial (Pa_{CO_2}) to end-tidal carbon dioxide tension (PET_{CO_2}) difference ($Pa_{CO_2} - PET_{CO_2}$). This paper explores the theoretical relationship between $Pa_{CO_2} - PET_{CO_2}$ and Sa_{O_2}, which is illustrated by some observations obtained during anesthesia and surgery in children with cardiac disease.

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Received from the Department of Anesthesiology, University Hospital, Lund, Sweden. Accepted for publication April 18, 1991. Presented in part at Anaesthetic Research Society, Southampton, England, April, 1990.

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Theory

Figure 1 shows a carbon dioxide single-breath test ($SBT\text{-}CO_2$),[1] which is the plot of expired carbon dioxide against expired volume. It was obtained from a child with a RL shunt and with $Sp_{O_2} = 66\%$. There is a large alveolar dead space (the area on the right between the carbon dioxide curve and the line representing the carbon dioxide content of arterial blood), and consequently there is a large $Pa_{CO_2} - PET_{CO_2}$ difference. The following discussion will concentrate on the $Pa_{CO_2} - PET_{CO_2}$ difference, which may be regarded as the clinician's measure of the alveolar dead space fraction.

Derivation of the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} Relationship

The shunt equation can be written for both carbon dioxide and oxygen. For oxygen, it is:

$$\frac{\dot{Q}s}{\dot{Q}t} = \frac{(Cc'_{O_2} - Ca_{O_2})}{(Cc'_{O_2} - C\bar{v}_{O_2})} \quad (1)$$

where Ca, Cc′, and $C\bar{v}$ represent arterial, pulmonary end-capillary, and mixed venous blood oxygen contents, respectively.

The term $(Cc'_{O_2} - \bar{C}v_{O_2})$ can also be expressed as:

$$(Cc'_{O_2} - Ca_{O_2}) + (Ca_{O_2} - C\bar{v}_{O_2})$$

Therefore:

$$\frac{\dot{Q}s}{\dot{Q}t} = \frac{(Cc'_{O_2} - Ca_{O_2})}{(Cc'_{O_2} - Ca_{O_2}) + (Ca_{O_2} - C\bar{v}_{O_2})}$$

from which can be obtained:

$$\frac{\dot{Q}s}{\dot{Q}t} \cdot (Ca_{O_2} - C\bar{v}_{O_2}) = (Cc'_{O_2} - Ca_{O_2}) - \frac{\dot{Q}s}{\dot{Q}t} \cdot (Cc'_{O_2} - Ca_{O_2})$$

Therefore:

$$\frac{\dot{Q}s}{\dot{Q}t} \cdot (Ca_{O_2} - C\bar{v}_{O_2}) = (Cc'_{O_2} - Ca_{O_2})\left(1 - \frac{\dot{Q}s}{\dot{Q}t}\right) \quad (2)$$

and similarly, using Ca_{CO_2} and so on for blood carbon dioxide contents:

$$\frac{\dot{Q}s}{\dot{Q}t} \cdot (C\bar{v}_{CO_2} - Ca_{CO_2}) = (Ca_{CO_2} - Cc'_{CO_2})\left(1 - \frac{\dot{Q}s}{\dot{Q}t}\right) \quad (3)$$

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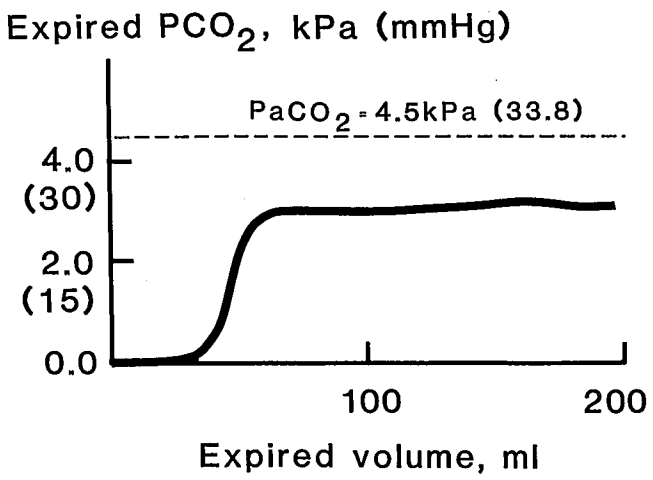

FIG. 1. CO_2 single-breath test from a child with a large RL shunt. There is a large alveolar deadspace (the area between the CO_2 curve and the line representing arterial CO_2), and consequently a large difference between Pa_{CO_2} and PET_{CO_2}. Sp_{O_2} was 66%.

Dividing equation 3 by equation 2:

$$\frac{C\bar{v}_{CO_2} - Ca_{CO_2}}{Ca_{O_2} - C\bar{v}_{O_2}} = \frac{Ca_{CO_2} - Cc'_{CO_2}}{Cc'_{O_2} - Ca_{O_2}}$$

Now, the ratio of the arterial − venous content differences for carbon dioxide and oxygen is by definition the respiratory quotient R.

Therefore:

$$R = \frac{Ca_{CO_2} - Cc'_{CO_2}}{Cc'_{O_2} - Ca_{O_2}} \quad (4)$$

Let us convert to clinically useful units, and assume that:

1) pulmonary end-capillary P_{CO_2} is equal to PET_{CO_2},

2) pulmonary end-capillary blood is fully saturated with oxygen.

Blood carbon dioxide content is roughly proportional to carbon dioxide tension (P_{CO_2}); the relationship is described by the carbon dioxide dissociation curve (see below). Blood oxygen content is in the form of oxyhemoglobin plus a small quantity in physical solution. The former is proportional to hemoglobin (Hb) concentration and saturation, and the latter is proportional to tension. Equation 4 can therefore be rewritten:

$$R = \frac{k \cdot (Pa_{CO_2} - PET_{CO_2})}{Hb \times 1.31 \cdot (100 - Sa_{O_2})/100 + \text{dissolved oxygen difference}} \quad (5)$$

The term k converts blood P_{CO_2} to content and is obtained from the carbon dioxide dissociation curve (see below). The constant 1.31 is the combining factor for Hb, in milliliters oxygen per gram Hb. It is the same for adult and fetal blood.[2] The "dissolved oxygen difference" is that between pulmonary end capillary blood and arterial blood.

Rearranging, we find that $Pa_{CO_2} - PET_{CO_2}$ is equal to:

$$(R \times Hb \times 1.31 \times (100 - Sa_{O_2})/100 + \text{dissolved oxygen difference})/k \quad (6)$$

Now the effect of dissolved oxygen is small (as discussed in appendix 1), and if it is ignored, we obtain:

$$Pa_{CO_2} - PET_{CO_2} = R \times Hb \times 0.0131 \times (100 - Sa_{O_2})/k \quad (7)$$

The relationship between $Pa_{CO_2} - PET_{CO_2}$ and Sa_{O_2} thus depends largely on the value of the term $R \times Hb \times 0.0131/k$.

The Carbon Dioxide Dissociation Curve

The term k is the slope of the carbon dioxide dissociation curve for whole blood, as illustrated in figure 2, prepared from Nunn.[3] It shows both bicarbonate and carbamino carbon dioxide carriage related to P_{CO_2} and to saturation. Bicarbonate, the main form of carriage, does not increase linearly with P_{CO_2}, and hence Pa_{CO_2} is a major determinant of k, which decreases as P_{CO_2} increases. (A small amount of carbon dioxide is carried in solution as

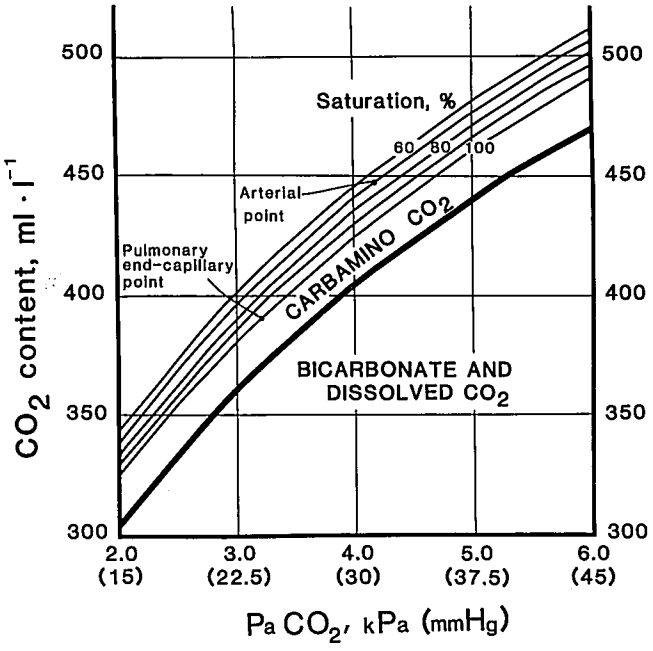

FIG. 2. CO_2 dissociation curve for whole blood, *i.e.*, CO_2 content *versus* P_{CO_2}, prepared from Nunn.[3] Most of the CO_2 is present as bicarbonate (thick line) but a small portion is carried in the carbamino form, *i.e.*, combined with amino acids, chiefly those in hemoglobin. Carbamino carrage is proportional to both Hb concentration (150 g · l^{-1} in this figure) and to saturation, and hence the different Sa_{O_2} lines.

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carbonic acid; in the current discussion, this is included as bicarbonate.)

Carbamino carbon dioxide carriage is little affected by P_{CO_2} but is proportional to Hb concentration and saturation. As saturation decreases, carbamino carbon dioxide carriage at constant P_{CO_2} increases; this is the Haldane effect. This further elevates the systemic arterial point, in effect increasing the slope of the dissociation curve between it and the end-capillary point. Sa_{O_2} is thus a determinant of k. In figure 2, the pulmonary end-capillary point is P_{CO_2} = 3.3 kPa (25 mmHg), with saturation = 100%. The arterial point is Sa_{O_2} = 70% and P_{CO_2} = 4.2 kPa (31.5 mmHg). The slope of the line between these two points, k, is about 60 ml carbon dioxide $\cdot l^{-1} \cdot kPa^{-1}$.

The Term R × Hb × 0.0131/k

In cyanotic children, Hb ranges from about 100 g $\cdot l^{-1}$ to 210 g $\cdot l^{-1}$. In the Pa_{CO_2} range of 4–5 kPa (30–40 mmHg), k varies between about 50 at Hb 100 g $\cdot l^{-1}$ to carbon dioxide of about 70 ml $\cdot l^{-1} \cdot kPa^{-1}$ in severely polycythemic children. (Hb concentration affects k indirectly *via* an effect on saturation. For any given shunt fraction, arterial saturation depends on mixed venous saturation, which in turn is dependent on Hb. The Haldane effect thus applies to a greater extent, and k, the slope of the dissociation curve, is in effect increased). Thus, at an R value of 0.8, the term R × Hb × 0.0131/k should be about 0.02–0.04 kPa carbon dioxide (0.1–0.3 mmHg) per percent desaturation in cyanotic children. Observe that the greatest Hb concentrations usually are seen in the most severely desaturated infants, and therefore Hb and k should change in the same direction. The effect of the spread of Hb values encountered by the anesthesiologist thus may be reduced.

In the simplified equation 7, the term R × Hb × 0.0131/k is the slope of the regression of $Pa_{CO_2} - PET_{CO_2}$ on Sa_{O_2}; the intercept is 100 times this value. Thus, in cyanotic, polycythemic children, $Pa_{CO_2} - PET_{CO_2}$ should increase by about 0.2–0.4 kPa (1–3 mmHg) for every 10% reduction in saturation at a respiratory quotient of 0.8.

$Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} Regression

Some predicted values for $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} are illustrated in figure 3. The method of their calculation, which includes the effect of dissolved oxygen, is detailed in appendix 2. The nonlinearity of the lines for the different Hb concentrations is due to the effect of dissolved oxygen and the effect of saturation on k. R is assumed to be 0.8.

Finally, it should be remembered that apart from the primary, obligatory effect of RL shunting as discussed above, secondary effects also may occur. These are due to failure of perfusion of lung parenchyma and occur if cardiac output cannot be increased sufficiently to compensate for the RL shunt. Secondary effects thus are most likely to occur at low saturations, at which the slope of the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} relationship will be increased.

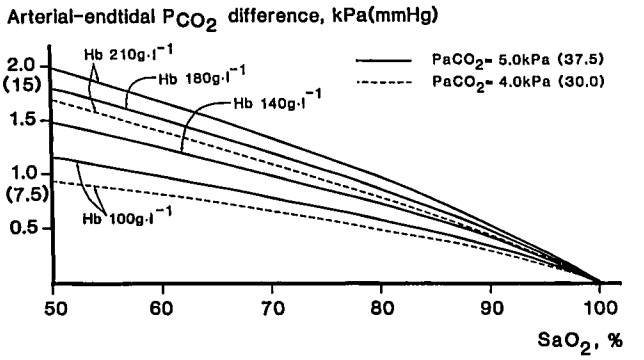

FIG. 3. Predicted values for $Pa_{CO_2} - PET_{CO_2}$ related to Sa_{O_2}. Thick lines show results for different Hb concentrations at a Pa_{CO_2} of 5 kPa (38 mmHg): dotted lines are for a Pa_{CO_2} of 4 kPa (30 mmHg). The derivation of these values is described in appendix 2.

Materials and Methods

Permission for the study was obtained from the local ethics committee. The bulk of the results were obtained from 15 children who had not previously presented and who had known RL (or mixed RL/left-to-right [LR]) shunts. Table 1 gives their ages at operation, their diagnoses, and their Sp_{O_2} and $Pa_{CO_2} - PET_{CO_2}$ values at the first measurement (patients 13–27). In order to provide more data at normal saturations, 12 children (patients 1–12), 10 of whose values were previously reported,[4] were included. At the time of their $Pa_{CO_2} - PET_{CO_2}$ differences were studied, pulse oximetry was not available. However, all had arterial oxygen tension (Pa_{O_2}) values in excess of 24 kPa (180 mmHg) and their mean Pa_{O_2} was 30 kPa (225 mmHg), and therefore these patients have been assumed to have had an Sp_{O_2} of 100%.

All children were undergoing closed or open cardiac surgery during fentanyl–nitrous oxide anesthesia with intermittent positive pressure ventilation. Some children also received 0.5% halothane. Measurements were obtained with the patients in the supine position, except with one, in whom palliative surgery was performed *via* thoracotomy. No patient was in overt cardiac failure preoperatively. Fractional inspired oxygen content (FI_{O_2}) was 0.5 in all cases. The ventilator, a Servo 900C, was set to give constant-flow, volume-controlled ventilation at a frequency of 25–35 breaths per min, depending on body weight, and an inspiratory time of 25% with an end-inspiratory pause of 10%. Minute volume was adjusted to give a Pa_{CO_2} of about 4 kPa (30 mmHg).

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TABLE 1. Diagnoses, Age, and Gas Exchange Data at the First Measurement

Patient Number	Diagnosis	Age	Sp_{O_2} (%)	Pulse Oximeter	$Pa_{CO_2} - PET_{CO_2}$, kPa (mmHg)	Hb Concentration ($g \cdot l^{-1}$)
1	PS	1.9 yr	100	—	−0.02 (−0.15)	137
2	AS	4.7 yr	100	—	0.25 (1.9)	141
3	PS	5.7 yr	100	—	−0.00 (−0.0)	130
4	PS	5.4 yr	100	—	0.22 (1.7)	145
5	AS	9 m	100	—	−0.01 (−0.1)	130
6	AS	7 yr	100	—	−0.21 (−1.6)	128
7	PDA	8.7 yr	100	—	0.14 (1.1)	139
8	PDA	6.7 yr	100	—	−0.18 (−1.4)	139
9	PDA	5.7 yr	100	—	0.06 (0.5)	139
10	PDA	6.4 yr	100	—	0.08 (0.6)	137
11	Coarctation	4.4 yr	100	—	−0.07 (−0.5)	128
12	Coarctation	5 yr	100	—	−0.21 (−1.6)	110
13	Single ventricle	2 m	95	NC	0.26 (2.0)	112
14	AVC	8 m	90.5	RAD	0.63 (4.7)	146
15	Fallot	9 m	88	NC	0.38 (2.9)	160
16	TGA	6 d	36	NC	4.69 (35.2)	174
17	AVC, PS	5 m	86	NC	0.80 (6.0)	164
18	Fallot	3 m	83.5	NC	0.59 (4.4)	194
19	TGA, PA	2.5 m	67	RAD	0.84 (6.3)	135
20	TGA TAPV	20 d	89	NC	0.88 (6.6)	193
21	DORV	5.4 yr	81	RAD	1.22 (9.1)	173
22	Fallot	2.2 yr	84	NC	0.60 (4.5)	155
23	TGA	1.5 yr	75	NC	0.72 (5.4)	201
24	TGA	2 m	71.5	NC	1.76 (13.2)	112
25	TGA, PS*	3 m	74	NC	0.99 (7.4)	180
26	Fallot	9 m	76	NC	1.28 (9.6)	192
27	AVC	2.3 yr	97	NC	0.09 (0.7)	138

Acyan = acyanotic; AS, PS = aortic, pulmonary stenosis; AVC = common atrioventricular canal; DORV = double outlet right ventricle; PDA = patent ductus arteriosus; TAPV = total anomalous pulmonary venous drainage; TGA = transposition of great vessels; VSD = ventricular septal defect; yr = year; m = month; d = day; NC = Nellcor; RAD = Radiometer.

* Operation *via* thoracotomy.

Arterial Hb oxygen saturation (Sp_{O_2}) was measured using pulse oximetry. One of two pulse oximeters was used; a Nellcor 100 or a Radiometer Oxi, with probes attached to the foot or hand. An on-line system was used for monitoring expired carbon dioxide.[5] A computer received signals for airway flow and pressure from the ventilator, and signals for expired P_{CO_2} from a Siemens-Elema carbon dioxide Analyzer 930.[6] These signals were calibrated daily. The carbon dioxide test gas was checked against the blood gas apparatus (ABL 2, Radiometer, Copenhagen) by tonometry.

Each measurement was made at steady state, as judged by stable PET_{CO_2} and Sp_{O_2} values. While the computer sampled three consecutive breaths, arterial blood was drawn for immediate blood gas analysis, and Sp_{O_2} and esophageal temperature were noted.

The computer[5] provided SBT-CO_2 (fig. 1) and calculated the temperature-corrected $Pa_{CO_2} - PET_{CO_2}$ difference from a supplied value for Pa_{CO_2}. PET_{CO_2} was corrected for nonlinearity in the analyzer[7] and also for tidal volume-dependent error if the actual tidal volume differed greatly from the one used when calibrating the carbon dioxide analyzer[4] (see Discussion). Sixty-one measurements were taken; 27 of these were taken during anesthesia prior to surgery and 11 during stable hemodynamic conditions after sternotomy. The remainder (n = 20) were made after completed surgery, *i.e.*, after cardiopulmonary bypass. No measurements were taken after closure of LR intracardiac shunts, since this is known to give a transient large increase in alveolar dead space without influencing oxygenation.[8] In the child in whom thoracotomy was performed, three measurements were taken: two were taken before surgery and one during thoracotomy, with the lung fully expanded.

Results

Figure 4 shows the relationship between $Pa_{CO_2} - PET_{CO_2}$ and Sp_{O_2} in the patients. The regression equation is $y = 4.61 - 0.0460x$ kPa ($y = 34.6 - 0.345x$ mmHg), $r = -0.87$, $P < 0.0001$. If the single observation with an Sp_{O_2} of 36% is omitted, the regression equation becomes $y = 3.80 - 0.0369 \times$ ($y = 28.5 - 0.277x$), $r = -0.87$. Both regression lines are illustrated in figure 4. If we omit the 12 children in whom a saturation of 100% was assumed, the regression equation becomes $y = 4.60 - 0.0458x$, $r = -0.84$ ($y = 34.5 - 0.344x$).

Before surgery, the term $(Pa_{CO_2} - PET_{CO_2})/(100$

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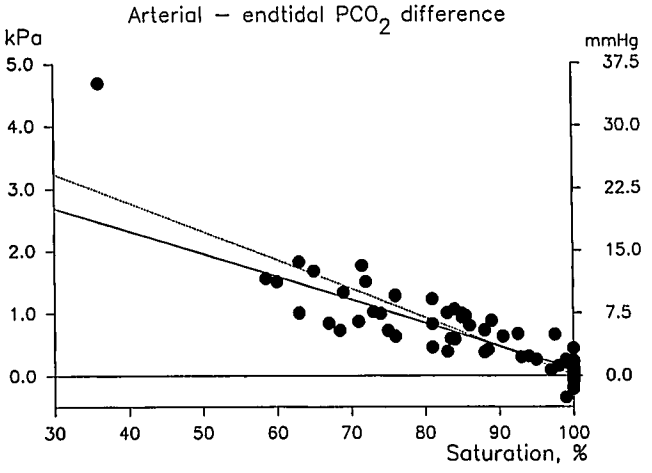

FIG. 4. The relationship between the $Pa_{CO_2} - PET_{CO_2}$ difference and Sp_{O_2} (percent) in the patients. The regression lines are (*top*) for the entire material and (*bottom*) with the single observation at Sp_{O_2} 36% omitted.

$- Sp_{O_2}$) was not correlated to preoperative Hb concentration, nor was it affected by the absolute level of Pa_{CO_2}. When observations made prebypass were compared to those made postbypass, no significant difference in the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sp_{O_2} relationship was seen.

Discussion

This study consists of a theoretical analysis of the relationship between the $Pa_{CO_2} - PET_{CO_2}$ difference and Sa_{O_2} in cyanotic children, together with some clinical observations using Sp_{O_2}, intended to illustrate this relationship. In theory, the slope of the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} regression depends mainly on Hb and Pa_{CO_2}. However, neither of these effects could be demonstrated in the patients.

RL shunts have an obligatory (primary) effect on both oxygen uptake and carbon dioxide elimination, and thus an appreciable alveolar dead space always is present in cyanotic heart disease. This dead space may be described as "apparent" or "virtual" since it does not represent ventilation of any unperfused lung region, *i.e.*, an infinite ventilation/perfusion ($\dot{V}_A/\dot{Q}$) ratio. On the contrary, a RL shunt represents zero $\dot{V}_A/\dot{Q}$; nevertheless, the effect on the efficiency of carbon dioxide elimination, which is marked, can be quantified using the dead space concept.

In children, especially those with pure RL shunts, phase III of SBT-CO_2 is almost horizontal[4]; typically, PET_{CO_2} exceeds mean phase-III P_{CO_2} by 0–0.2 kPa (0–1.5 mmHg).† PE_{CO_2} therefore can reasonably be used as a measure of mean alveolar expired P_{CO_2}. Thus assumption[1] of the theory section is admissible, at least in a clinical setting. Only in children in overt heart failure is the phase-III slope be steep enough to invalidate this assumption, and usually in children with large RL shunts it is not.

In the Theory section above, it was pointed out that any secondary effects of RL shunting occurring because of failure of alveolar perfusion would produce an alveolar dead space additional to that created by the primary effect. Secondary effects at lower saturations therefore should displace the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sp_{O_2} curve upward. In the range 60–100% Sp_{O_2}, the current observations provide no firm evidence of this. The single observation at an Sp_{O_2} of 36% is, however, compatible with such an effect, although pulse oximeter nonlinearity also may be responsible for this deviation from the expected position. A previous study[9] did not demonstrate any certain secondary effects during RL shunting. This is true even if a correction for nonlinearity of carbon dioxide analysis (originally omitted) is applied to the older data. However, neither study rules out the possibility of secondary effects. To demonstrate their existence unequivocally, it would be necessary to sample, simultaneously, PET_{CO_2} and left atrial blood P_{CO_2} in children with RL shunts not at the atrial level; any discrepancy between the two P_{CO_2} values would be proof of secondary effects.

Causes of Experimental Error

Pulse Oximeter Error

The absorption characteristics of fetal and adult Hb are similar, [10] and therefore the presence of fetal Hb in the smallest children should not influence pulse oximetry. However, Nellcor pulse oximeters have been shown to be inaccurate in cyanotic children below about 70% saturation,[11] and both Nellcor and Radiometer devices show errors during desaturation episodes in volunteers.[12]

Tidal Volume-dependent Error in Expired Carbon Dioxide Analysis

The Siemens-Elema carbon dioxide analyzer 930 performs a new zero calibration during each inspiratory phase, when the the fractional inspired carbon dioxide content (FI_{CO_2}) of the gas in the cuvette is assumed to be zero. In fact, at very small tidal volumes, some carbon dioxide remains. Because the new zero is taken before linearization of the signal, this carbon dioxide has a disproportionate effect on the subsequent carbon dioxide measurement.[5] The carbon dioxide signal therefore was calibrated at tidal volumes similar to those expected to be used for the measurements; when there was a discrepancy between the two, PET_{CO_2} was corrected according to a correction curve.[4] The breath-to-breath variation in PET_{CO_2} was less than 0.1 kPa in children with RL shunts.

† Unpublished observations.

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Error in Measurement of $Pa_{CO_2} - PET_{CO_2}$

PET_{CO_2} was measured by a carbon dioxide analyzer calibrated against a test gas containing 4.6% carbon dioxide in equal parts oxygen and nitrous oxide; the carbon dioxide content of this test gas was obtained by tonometry against the blood gas analyzer. Thus, the P_{CO_2} values both of gas and of blood phases were calibrated to the same standard; in addition, the possibility of error due to nitrous oxide was eliminated, since all measurements were taken during nitrous oxide anesthesia at an FI_{O_2} of 0.5. However, blood gas analyzers are susceptible to drift; the effects of this were minimized by making measurements only when the blood gas apparatus gave control P_{CO_2} values within 0.1 kPa of its own standard.

The above headings represent what probably were the major sources of error in the obtained $Pa_{CO_2} - PET_{CO_2}$ *versus* Sp_{O_2} relationship. Of these, probably pulse oximetry was the greatest source of error[11,12]; considerable effort was applied to avoiding error in P_{CO_2} measurement.

Other Causes of Spread in the Measurements

Nonachievement of ventilatory steady state should not alter oxygen uptake significantly but will change the Pa_{CO_2} – venous carbon dioxide tension difference and therefore the Pa_{CO_2} – pulmonary end-capillary carbon dioxide tension difference. This produces an apparent change in R and thus a change in the slope of $Pa_{CO_2} - PET_{CO_2}$ *versus* Sp_{O_2}. However, no measurements were taken when carbon dioxide elimination was changing.

Changes in Hb concentration also can be expected to change the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} relationship. In particular, hemodilution of polycythemic children after cardiac bypass reduces it. This could not be demonstrated in the patients in the current study. (After bypass, full saturation usually is obtained, and the question thus becomes an academic one.)

The presence of mixed shunts, *i.e.*, both RL and LR, should not affect the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} relationship; the underlying theory (equation 3) still applies. Large LR shunts may increase the slope of phase III of SBT-CO_2 and thereby slightly increase the difference between mean alveolar P_{CO_2} and PET_{CO_2}, but this should have little effect on the results.

Prediction of Pa_{CO_2} from PET_{CO_2} in Clinical Practice

In the current data, obtained during routine clinical practice, there is considerable spread in the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sp_{O_2} relationship, and it would be difficult to claim that figure 4 could be used as the basis for an accurate noninvasive method for calculating Pa_{CO_2} from PET_{CO_2} in cyanotic children. Nevertheless, the pediatric anesthesiologist should be aware of the theoretical obligatory increase in $Pa_{CO_2} - PET_{CO_2}$ of 0.3–0.5 kPa (2–4 mmHg) per 10% reduction in Sp_{O_2}, a finding that is confirmed by the clinical observations.

Secondary effects of RL shunting may appear at lower saturations. This additional (true) alveolar dead space will cause a greater $Pa_{CO_2} - PET_{CO_2}$ difference than is predicted by figure 3, as is demonstrated by the lone observation at Sp_{O_2} 36%. It also should be noted that dead spaces other than that due to RL shunting—*e.g.*, occurring after closure of a septal defect[10] or because of obstructive airway disease or pulmonary embolism—invalidate the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} relationship described here. Obstructive airway disease and the $\dot{V}/\dot{Q}$ spread associated with pulmonary edema are recognizable by the sloping SBT-CO_2; they were not seen in this investigation. Pulmonary embolism, an unlikely diagnosis in this group of patients, is recognizable by the presence of vigorous cardiogenic oscillations, which are not a feature of cyanotic heart disease.

The relationship described for children with cyanotic heart disease assumes full oxygen saturation of pulmonary end-capillary blood. This relationship cannot be applied to adults, in whom there is no correlation between Pa_{O_2} and alveolar dead space during anesthesia.[9] In neonates, in whom the measurement of PET_{CO_2} is difficult, an apparent deviation from the relationship illustrated in figure 3 might be seen.

Appendices

Appendix 1: The Effect of Dissolved Oxygen on the $Pa_{CO_2} - PET_{CO_2}$ vs Sa_{O_2} Relationship

The effect of dissolved oxygen (equations 5 and 6) is to increase the slope of the theoretical $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} relationship compared to that obtained from the simplified equation (equation 7). The difference in dissolved oxygen content between pulmonary end-capillary and systemic arterial blood is proportional to the tension difference. At an FI_{O_2} of 0.5, Pc'_{O_2} is about 44 kPa (330 mmHg). At a Pa_{O_2} of, for instance, 5 kPa, the difference in dissolved oxygen content therefore is about 44 – 5 = 39 times the solubility coefficient, which is 0.225 ml · l^{-1} · kPa^{-1} at 37° C. The oxygen difference in this example is thus 39 times 0.225, which is 8.8 ml oxygen · l^{-1}. A likely range in cyanotic children would be 7–20 ml oxygen · l^{-1}. The difference is least at low values of FI_{O_2}. FI_{O_2} thus is a minor determinant of the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} relationship.

However, in the current context, the importance of the dissolved oxygen difference is not its absolute magnitude, which is fairly constant at any given FI_{O_2}, but rather its magnitude in relation to the total pulmonary end-capillary to arterial oxygen content difference. With a small RL shunt, producing an Sa_{O_2} of 90%, the total pulmonary end-capillary to arterial oxygen content difference may be only 30 ml · l^{-1}, and the dissolved oxygen difference may be one fourth to one third of this differ-

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ence. With a shunt producing an Sa_{O_2} of 50%, dissolved oxygen represents only 6–7% of the total difference. Thus, R × Hb × 0.0131/k gives a better estimate of the slope of the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} regression at low saturations than at high.

Appendix 2: Derivation of Figure 3

The respiratory quotient R is defined as the ratio of the arterial – venous gas content differences for carbon dioxide and oxygen. In the Theory section above, it was shown that R also is equal to the ratio of the arterial – pulmonary end-capillary content differences for these gases:

$$R = (Ca_{CO_2} - Cc'_{CO_2})/(Cc'_{O_2} - Ca_{O_2}) \quad (4)$$

Let us assume some values: Pa_{CO_2} = 4.2 kPa (32 mmHg), R = 0.8, Sa_{O_2} = 70%, and Hb = 150 g·l^{-1}.

Appendix 3: The Pulmonary End-capillary to Arterial Oxygen Difference ($Cc'_{O_2} - Ca_{O_2}$)

Oxygen carriage as oxyhemoglobin: We assume the pulmonary end-capillary blood to be fully saturated, and therefore the volume of oxygen in the form of oxyhemoglobin is 1.31 times the Hb concentration. At a Hb of 150 g·l^{-1}, this is 197 ml oxygen·l^{-1}.

Oxygen transported in physical solution: From the alveolar gas equation, it can be estimated that at an FI_{O_2} of 0.5 and at the PET_{CO_2} values obtained, alveolar oxygen tension (P_{O_2}) and therefore pulmonary end-capillary P_{O_2} is about 44 kPa (330 mmHg). Only a small error is introduced by using this as a standard value for FI_{O_2} = 0.5. The solubility coefficient of oxygen at 37° C is 0.225 ml·l^{-1}·kPa^{-1}. The volume of dissolved oxygen in end-capillary blood is therefore 44 × 0.225 ml. Arterial dissolved oxygen can be estimated at the chosen saturation as 0.225 × Pa_{O_2}; Pa_{O_2} can be estimated using a Hb dissociation curve nomogram.[3] At an Sa_{O_2} of 70%, Pa_{O_2} is about 5 kPa (38 mmHg).

Thus the pulmonary end-capillary – arterial oxygen content difference is given by:

$$(Hb \times 1.31 + 44 \times 0.225) - (Hb \times 1.31 \times Sa_{O_2}/100 + 0.225 \times Pa_{O_2})$$

Substituting our assumed values for Hb and Sa_{O_2}, this yields an oxygen difference of 67.7 ml·l^{-1}, and therefore, multiplying by R, the carbon dioxide difference must be 54 ml.

The Arterial to Pulmonary End-capillary Carbon Dioxide Difference ($Ca_{CO_2} - Cc'_{CO_2}$)

Arterial blood: At our arterial value of 4.2 kPa (32 mmHg) in figure 2 we can read the total carbon dioxide content, which is 448 ml·l^{-1} at Sa_{O_2} 70%. Of this, 34 ml carbon dioxide·l^{-1} is in the carbamino form.

Pulmonary end-capillary blood, being fully saturated, contains less carbamino carbon dioxide than does arterial blood, and only a small error is introduced if a standardized, P_{CO_2}-independent value of 20 ml carbon dioxide·l^{-1} is chosen at a Hb of 150 g·l^{-1}. (The error is proportionately greater at higher Hb concentrations). The bicarbonate content of pulmonary end-capillary blood is now the only component of the term $Ca_{CO_2} - Cc'_{CO_2}$) that is not known. From the above, we know that this expression is equal to 54 ml·l^{-1}. Pulmonary end-capillary bicarbonate is therefore 448 – 54 – 20 = 374 ml carbon dioxide·l^{-1}. This value can be entered into figure 2 to obtain the P_{CO_2} of pulmonary end-capillary blood, 3.3 kPa (25 mmHg). Thus, in this example, a child with a Hb of 150 g·l^{-1}, an Sa_{O_2} of 70%, and a Pa_{CO_2} of 4.2 kPa (32 mmHg) has a $Pa_{CO_2} - PET_{CO_2}$ difference of 0.9 kPa (7 mmHg).

In this way we can obtain the arterial-to-pulmonary end-capillary (= $Pa_{CO_2} - PET_{CO_2}$) carbon dioxide difference for different values of the variables Sa_{O_2}, R, Pa_{CO_2}, and Hb, in order to obtain a range of values for the $Pa_{CO_2} - PET_{CO_2}$ *versus* Sa_{O_2} relationship, on which figure 3 is based.

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