Anesthesiology
67:240–246, 1987

Separate Lung Blood Flow in Anesthetized Dogs: A Comparative Study Between Electromagnetometry and SF_6 and CO_2 Elimination

Åse Jolin Carlsson, M.D., Göran Hedenstierna, M.D.,† Hans Blomqvist, M.D.,‡ Åke Strandberg, M.D.§*

Anesthetized, prone dogs were intubated with a double-lumen endobronchial tube, and the lungs were ventilated independently. Three methods of recording differential blood flow were compared during unilateral lung hypoxia: 1) electromagnetic flow measurement, flow probes being fitted onto each main pulmonary artery after thoracotomy (QPr); 2) SF_6 elimination from each lung, the inert gas being continuously infused into a central vein (QSF_6); and 3) CO_2 elimination (QCO_2). During control conditions (100% O_2 to both lungs), the test lung QPr was 54% of cardiac output, and corresponding QSF_6 and QCO_2 were 56% and 52%, respectively. Hypoxic challenge with 8% O_2 to the test lung reduced QPR, QSF_6, and QCO_2 by 25%, 27%, and 7%, respectively. Ventilation of the test lung with pure nitrogen reduced its blood flow further, QPr, QSF_6, and QCO_2 being reduced by 39%, 42%, and 23%, respectively, from initial control. A strong correlation between test lung QPr and QSF_6 was seen with a slope of 0.90 (r:0.89, $P < 0.001$). Only 60% of the reduction in test lung blood flow was detected by CO_2 elimination, as compared to electromagnetic flow measurement or SF_6 elimination. The poor results obtained with CO_2 elimination can be explained by its dependence on the ventilation-perfusion ratio and the effect of oxygen tension on the CO_2 binding capacity of blood (Haldane effect). The findings emphasize the necessity of using an inert, poorly soluble gas for the measurement of separate lung blood flow. (Key words: Carbon dioxide. Hypoxia: Pulmonary vasoconstriction. Lung: blood flow; hypoxic pulmonary vasoconstriction. Measurement techniques: inert gas; lung blood flow. Sulphur hexafluoride.)

MUCH INTEREST HAS BEEN focused upon hypoxic pulmonary vasoconstriction (HPV) and its ability to counteract hypoxemia. Initially, HPV was detected by the increase in pulmonary artery pressure upon exposure to hypoxic gases,[1] a technique also used in later studies. However, a more detailed analysis of HPV requires that the effect of regional hypoxia on blood flow distribution can be measured. To this end, recording with electromagnetic flow probes around the main or lobar pulmonary arteries is a sensitive method, but it requires thoracotomy and, therefore, cannot be used in most human studies.[2] Injection of radioactive labelled microspheres and external counting of the activity, or excision of the lungs before counting in order to increase accuracy, are also methods with practical limitations.[3] Continuous infusion of the poorly soluble radioactive gas ^{133}Xe (blood gas partition coefficient, λ:0.18), and recording of the elimination from each lung by means of a double-lumen endobronchial catheter were used by Sykes *et al.*[4] However, the handling of radioactive material may limit the practical application of the technique. In theory, the even less soluble gas sulphurhexafluoride (SF_6) (λ:0.006[5]) could replace ^{133}Xe, but its detection requires rather laborious gas chromatography.

The practical difficulties inherent in the described techniques have called for simpler methods, especially for studies in humans. Carbon dioxide (CO_2) is produced in the body, and its elimination is easily detected breath-by-breath with an infrared meter or a mass spectrometer. The elimination of CO_2 from each lung has, therefore, been suggested as a measure of individual lung blood flow, either by recording the net CO_2 output (mixed expired CO_2 times lung ventilation),[6,7] or by the measurement of end-tidal CO_2.¶ However, this method is limited by its dependence of CO_2 elimination on ventilation/perfusion matching and the CO_2 dissociation curve. Limitations caused by the dissociation curve have recently been analyzed by Chen *et al.*,[8] but they did not consider the possible influence of variations in ventilation/perfusion ratios. We have made comparative measurements of individual lung blood flow by means of CO_2 elimination and electromagnetometry, taking into account both sources of errors. We have also made comparisons between SF_6-elimination and electromagnetometry. The study was undertaken in dogs subjected to graded unilateral hypoxia during intravenous anesthesia and mechanical ventilation.

* Research Fellow of Anesthesia, Department of Anesthesia, Karolinska Hospital.

† Associate Professor of Clinical Physiology, Department of Clinical Physiology, Huddinge Hospital.

‡ Resident in Anesthesiology, Department of Anesthesia, Danderyd Hospital.

§ Resident in Surgery, Department of Surgery, Huddinge Hospital.

Received from the Department of Anesthesia, Karolinska Hospital, Stockholm, Sweden; the Departments of Clinical Physiology and Surgery, Huddinge Hospital, Stockholm, Sweden; and the Department of Anesthesia, Danderyd Hospital, Stockholm, Sweden. Accepted for publication March 20, 1987. Supported by grants from the Swedish Medical Research Council No. 4X-5315, the Swedish Medical Association, and the Karolinska Institute.

Address reprint requests to Dr. Hedenstierna: Department of Clinical Physiology, Huddinge University Hospital, S-141 86 Huddinge, Sweden.

¶ Kim YD, Michalik R, Jones M, Lees DE, Jan G, Macnamara TE: A new method for continuous monitoring of the partition of pulmonary blood flow between two lungs (abstract). ANESTHESIOLOGY 55:A140, 1980

Materials and Methods

Preparation

Seven mongrel dogs (mean weight 21.4 kg, range 18–28 kg) were anesthetized with pentobarbital, 20–40 mg/kg, and paralyzed with pancuronium bromide, 0.1 mg/kg. Fentanyl 0.005–0.015 mg/kg was given during the thoracotomy described later. Additional doses of these drugs were given whenever necessary during the experiment which lasted approximately 8–9 h. Endobronchial intubation and lung isolation were achieved with a Kottmeier canine endobronchial tube (Rüsch). Lung isolation was identified by ventilating the lungs through one lumen while the other lumen was attached to a tube submerged 2–3 cm in water. Airway pressures up to 30 cm H_2O were used. Absence of bubbles was taken as an indication of isolation. In addition, lung isolation could be confirmed intraoperatively, as well as after the dog had been killed, by inspecting lung inflation while the chest was open. Each lung was ventilated separately but in phase with two synchronized ventilators (Erica®, Gambro Engström). Tidal volume was approximately 10–15 ml/kg to each lung. This resulted in an end-tidal CO_2 concentration of approximately 4%, which was monitored breath by breath by two infrared meters (Datex®, Gambro Engström). Mixed expired CO_2 concentration was intermittently recorded by connecting the CO_2 analyzers to the outlets of the expiratory mixing chambers built into the ventilators. The CO_2 analyzers were calibrated intermittently during the experiment with air and a test gas of 4.8% CO_2 in oxygen. The minute ventilation of each lung was measured by connecting the expiratory port of the ventilator to a 9-l water-sealed spirometer (Godart) for 2-min periods. Gas compressed in the ventilator tubings during inspiration was thus included in the recording of the minute ventilation, but this gas will also dilute the concentration of the expired CO_2 and SF_6, the calculation of CO_2 and SF_6 outputs from each lung being unaffected. Respiratory frequency was set at 12 breaths per minute.

The animals received continuous iv infusion of dextrose, 5%, with sodium chloride, 80 mmol/l. During the thoracic surgery (see below), the infusion rate was kept at 200–400 ml/h, but, postoperatively, the rate was lowered to approximately 100 ml/h.

Bilateral thoracotomy was performed through the fifth intercostal space. Each pulmonary artery was identified, and an electromagnetic flow probe was fitted onto each (blood flow meter: Nycotron model 376). To obtain a zero flow for calibration purposes, a thread was positioned around each artery proximal to the flow probe to permit intermittent occlusions of the artery. During surgery, the lungs were prevented from collapsing by means of a positive end-expiratory pressure (PEEP) of 5–7 cm H_2O. At the end of surgery, tubing was introduced into the pleural space on the right and left side, and a continuous negative pressure of approximately (15–20 cm H_2O was applied. The chest was closed by sutures. The surgical procedure took 2–3 h.

Catheterization

A thermodilution pulmonary artery catheter (Swan-Ganz 7F®, Edward's Lab) was floated to the wedge position from the femoral vein. Cardiac output was measured by thermodilution, injecting a 10 ml bolus of ice-cold glucose, 5%, in the right atrium. A cardiac output computer was used for the calculations (model 9520A, Edward's Lab). Four consecutive determinations were made at each condition of the study, and the mean value was calculated. Heart rate was monitored by a three-lead ECG. An arterial (femoral) and a venous (forepaw) catheter were inserted. Arterial and pulmonary artery pressure were measured by strain gauge transducers (no. 75 Statham), and were calibrated against a water column. All signals were recorded on an ink jet recorder (Mingograf 4®, Siemens Elema).

SF_6 Elimination and Shunt

A mixture of three poorly soluble gases (SF_6, ethane, and cyclopropane) in saline was infused at a slow rate (3 ml/min) by a constant infusion pump. Mixed expired gas was collected from each lung under steady state conditions as described above for CO_2 collection. The concentration of the gases was measured in a gas chromatograph (Sigma 3®, Perkin Elmer). A 1-ml gas sample was injected into a 1.8 m-long stainless steel column filled with Porapac Q 70/80 mesh, the column flow being 20 ml/min and the oven temperature 110°C. A splitter divided the column flow so that 10% was distributed to an electron capture detector for SF_6 analysis, and 90% went to a flame ionization detector for analysis of ethane and cyclopropane. The coefficient of variation for duplicate samples was no larger than 3–4% for each gas.

The magnitude of the shunt, that is, the amount of mixed venous blood that bypasses the lungs without coming into contact with ventilated lung tissue, was calculated by measuring the retention of all three infused gases. Using an extrapolation method,[9] the shunt was calculated as perfusion of lung regions with a ventilation-perfusion ratio of less than 0.005.

Separate Lung Blood Flow

Blood flow of each lung was recorded or calculated in three different ways, as follows.

Electromagnetometry. The two flow probes, one on each main pulmonary artery, recorded blood flow in absolute units after a preceding zeroing procedure when blood flow was stopped for a few seconds by pulling the thread around the vessel. A new zeroing was done after the measurement to check whether a drift of the flow signal had occurred. No such drift was observed in any of the experiments. The flow in the test lung is presented as a percentage of the sum of the two probe flows ($\dot{Q}TL(Pr)$).

SF_6 Elimination. The SF_6 concentration of mixed expired gas from one lung, times the minute ventilation of that lung, yields the lung's SF_6 elimination. SF_6 elimination of the test lung, expressed as a percentage of the sum of the SF_6 elimination of both lungs, yields the percentage SF_6 test lung blood flow ($\dot{Q}TL(SF_6)$).

CO_2 Output. The calculations were the same as for SF_6 elimination, with mixed expired CO_2 concentration replacing SF_6. The resulting flow is called "CO_2 test-lung blood flow" ($\dot{Q}TL(CO_2)$).

Blood Gases

Arterial (a) and mixed venous ($\bar{v}$) blood gas samples, all iced and capped, were analyzed for oxygen (P_{O_2}) and carbon dioxide (P_{CO_2}) tensions, and were corrected according to the temperature of the animal (measured with a rectal thermistor probe). The blood gas analyzer (ABL-2®, Radiometer) was calibrated intermittently with known standards. Arterial and mixed venous blood were also drawn for spectrophotometric determination of hemoglobin concentration (OSM 2®, Radiometer).

Statistics

Data in the text, tables, and figures are presented as mean ± SE. Linear regression analyses were used for comparisons between separate lung blood flows measured by electromagnetometry on one hand and SF_6 elimination, or CO_2 output, on the other hand. Two-way analysis of variance with Scheffe's contrast was used for testing the significance of a difference in a circulatory or gas exchange variable between the control and the hypoxic conditions.

Procedure

The dog was in the prone position throughout the study. After the preparation was completed, the dog was ventilated for approximately 30 min with pure oxygen to both lungs (control situation). The end-tidal CO_2 concentration was monitored breath by breath, and, when the concentration was stable during a 4-min period, the measurements were commenced. Recordings were made of central vascular pressures, cardiac output by thermodilution, and blood samples were drawn for blood gas and hemoglobin analysis, and for gas chromatography. Mixed expired gas was simultaneously collected for on-line recording of CO_2 concentration and for gas chromatographic analysis of SF_6 concentration. Minute ventilation was measured by the water-sealed spirometer, and separate lung blood flows were recorded with the electromagnetic flow probes. The right lung was then ventilated with 8% O_2 in nitrogen, while the left lung continued to be ventilated with 100% O_2. After 20–25 min and a stable end-tidal CO_2 concentration for at least 4 min, the recordings were again repeated. The procedure was repeated after another 20 min with the right lung being ventilated with pure nitrogen, and, finally, after a new control period when both lungs were ventilated with oxygen.

Results

Central Hemodynamics

Cardiac output, determined by thermodilution, was low, and averaged 1.7 l/min with a heart rate averaging 137 beats/min. Pulmonary artery and systemic artery pressures were normal. The lung shunt, measured by the inert gas retentions, was 6.6%. Results are shown in table 1.

Hypoxic challenge with 8% O_2 caused an increase in pulmonary artery mean pressure and a decrease in systemic arterial mean pressure. Cardiac output and heart rate were not significantly altered. The inert gas lung shunt remained unaltered, the inert gases being eliminated by nitrogen-ventilated areas as well as by oxygen-ventilated ones.

Augmentation of the hypoxic challenge by ventilating the test lung with pure nitrogen caused a significant increase in cardiac output compared to the initial control condition. The vascular pressures were not further altered, and the inert gas shunt remained unaffected.

On return to the control situation, all values returned towards the point of origin.

Test Lung Blood Flow

During the control period, test lung blood flow (in general, the right lung) averaged 54%, as measured by the electromagnetic flow probes (table 1). Fractional test lung blood flow measured by SF_6 elimination and CO_2 output were not significantly different from the electromagnetic flow values, the respective fractional blood flows of these being 56% and 52% of total blood flow. With the 8% O_2 hypoxic challenge, significant decreases in test lung blood flow were measured by electromagnetometry and SF_6 elimination, the decreases

TABLE 1. Central Hemodynamics during Control and Hypoxia

		Test Lung Blood Flow, % $\dot{Q}_T$				Heart Rate (beats/min)	Mean Arterial Pressure		Inert Gas Shunt (% Q_T)
		l/min	Pr	SF_6	CO_2		Pulmonary (mmHg)	Systemic (mmHg)	
Control	$\bar{x}$	1.70	53.5	55.9	51.5	137	20.5	118	6.6
100% O_2	SE	0.35	4.8	4.3	1.5	16	2.4	9	0.9
Hypoxia	$\bar{x}$	1.73	40.2*	40.6*	47.3	162	28.2†	100*	8.7
8% O_2	SE	0.38	3.5	4.4	1.3	8	3.8	5	2.1
Hypoxia	$\bar{x}$	1.85*	32.8†	32.3†	41.3†‡	147	27.4†	108*	6.8
0% O_2	SE	0.16	3.3	1.7	2.1	12	4.2	10	3.2
Control‡	$\bar{x}$	1.68	54.6	57.5	52.5	146	23.4	121	6.8
100% O_2	SE	0.22	3.9	2.3	2.0	23	3.1	11	2.1

Q_T = cardiac output (thermodilution); Pr, SF_6, CO_2 = percentage blood flow by electromagnetometry, SF_6 elimination, and CO_2 output, respectively.

* Significantly different from control, $P < 0.05$.
† Significantly different from control, $P < 0.01$.
‡ n = 6.

corresponding to 25% and 27% of the fractional blood flow, respectively. Test lung blood flow was not significantly altered when calculated by CO_2 output, although a mean fractional decrease corresponding to 8% was noted. Augmentation of the hypoxic challenge (0% O_2 to the test lung) caused a further mean decrease in test lung blood as measured with all three techniques. The difference compared to control was significant for all methods. However, the decrease as measured by electromagnetometry and SF_6 elimination (39% and 42%, respectively) was larger than measured by CO_2 output (23%). The mean decrease in $\dot{Q}TL(CO_2)$ was, thus, only approximately 60% of that measured by electromagnetometry or SF_6 elimination. (One dog died at the end of the measurements, before the completion of the CO_2-recordings.)

Upon return to the control situation, test lung blood flow increased towards initial control values with all three methods. Results are shown in table 1.

Linear regression analyses between fractional test lung blood flow by electromagnetometry on one hand, and by SF_6 elimination and CO_2 output on the other, are shown in figure 1. There was a high correlation between $\dot{Q}TL(SF_6)$ and $\dot{Q}TL(Pr)$, with a slope not far from that of the identity line (slope coefficient: 0.90) (also, the intercept was small and not significantly different from zero). The correlation between $\dot{Q}TL(CO_2)$ and $\dot{Q}TL(Pr)$ was not as favorable, and the slope of the regression line differed significantly from that of the identity line. Thus, the slope coefficient was no higher than 0.40, mainly because of the small changes on hypoxic challenge with 8% O_2. The slope coefficient increased to 0.62 when data from 8% O_2 challenge were excluded. Calculations were also made on end-tidal CO_2 concentration and separate lung ventilation (table 2), but a comparison with electromagnetometry was no better than for CO_2 output (slope coefficient: 0.40, r:0.64, $P < 0.01$).

VENTILATION AND GAS EXCHANGE

Total minute ventilation was kept approximately constant throughout the experiment, and was adjusted to result in normocapnia during the initial control

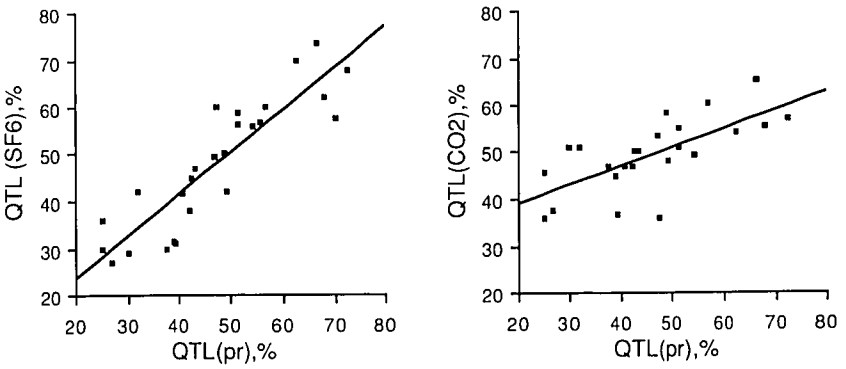

FIG. 1. Linear regression analyses between fractional test lung blood flows by electromagnetometry QTL(Pr) (x-axis) and SF_6 elimination, $QTL(SF_6)$, or CO_2 output, $QTL(CO_2)$ (Y = axis; left, and right panels, respectively). Following equations were obtained: $QTLSF_6 = 0.90 \times QTLPr + 5.7$ (r:0.89, $P < 0.001$, n:26); $QTLCO_2 = 0.40 \times QTLPr + 31.3$ (r:0.69, $P < 0.01$, n:25).

TABLE 2. Ventilation, Expired CO_2 Concentrations, and CO_2 Output during Control and Hypoxia

		Ventilation, l/min			CO_2 Concentration, %				CO_2 Output, ml/min	
					Mixed Expired		End-tidal			
		Total	Test Lung	Control Lung	Test Lung	Control Lung	Test Lung	Control Lung	Test Lung	Control Lung
Control 100% O_2	$\bar{x}$	5.48	2.75	2.73	1.12	1.08	4.00	3.97	30.7	29.6
	SE	0.42	0.20	0.23	0.16	0.14	0.56	0.53	2.1	3.1
Hypoxia 8% O_2	$\bar{x}$	5.48	2.78	2.72	1.03	1.17*	3.75	4.20	28.6	31.7
	SE	0.58	0.32	0.28	0.17	0.16	0.50	0.48	3.2	3.3
Hypoxia 0% O_2	$\bar{x}$	5.82	2.82	2.99	1.00*†	1.33†‡	3.53†‡	4.52†‡	28.2*†	39.9†‡
	SE	0.62	0.31	0.34	0.13	0.14	0.56	0.57	3.9	2.9
Control† 100% O_2	$\bar{x}$	5.98	2.95	3.01	1.10	0.98	3.40	3.18	32.5	29.7
	SE	0.72	0.35	0.37	0.13	0.16	0.34	0.47	4.1	4.2

* Significantly different from control, $P < 0.05$.
† n = 6.
‡ Significantly different from control, $P < 0.01$.

recordings. Ventilation of each lung was of approximately the same size (table 2). Peak airway pressure, measured in the Y-piece of the ventilator tubings, was high (test lung: 33 ± 1 cm H_2O (x ± SE), control lung: 41 ± 3 cm H_2O), mainly because of high resistance in the endobronchial tube. Mean airway pressure was 7 ± 1 cm H_2O and 8 ± 1 cm H_2O, respectively. Mixed expired and end-tidal CO_2 concentrations, used for the calculations of separate lung blood flows, are shown in table 2. It can be seen that the mixed expired CO_2 concentration was low with a mean of 1.1%. Inserting this figure in a modified Bohr equation (alveolar P_{CO_2} being replaced by Pa_{CO_2}**) resulted in a dead space fraction (VD/VT) as large as 0.84. A major part of it was made up by the apparatus dead space, 250 ml as measured by water displacement (from the Y-connection of each ventilator to the distal end of the endobronchial tube, sum of both airways).

In all dogs, there was good oxygenation during the control period, *i.e.*, ventilation with pure oxygen. Pa_{CO_2} was at the upper range of normal. Pa_{O_2} was markedly reduced on hypoxic challenge with 8% O_2, and a further significant reduction was noted when the hypoxic challenge was augmented by ventilating the test lung with pure nitrogen. Pa_{CO_2} did not change to any significant extent during the hypoxic challenge. Upon return to control, Pa_{O_2} increased and was no longer different from the initial control value (table 3).

Discussion

The major finding in the present study is that there exists a close correlation between fractional lung blood flows measured by electromagnetometry and SF_6 elimination, and a poorer correlation between fractional blood flows measured by electromagnetometry and CO_2 elimination technique. Why the ability of the two gases (SF_6 and CO_2) to detect changes in fractional lung blood flow differed to such an extent will be discussed below.

Solubility and $\dot{V}A/\dot{Q}$ Ratios

The elimination of a gas from the blood during its passage through the lungs depends on the solubility of that gas and the ventilation/perfusion ratio ($\dot{V}A/\dot{Q}$) of the lung. These relationships are given in the following equation, deduced by Farhi:[10]

$$E = 1 - \frac{\lambda}{\lambda + \dot{V}A/\dot{Q}}, \quad (1)$$

where E = elimination; λ = blood: gas partition coefficient which equals solubility × (PB − P_{H_2O})/100, solubility expressed in ml/100 ml/mmHg; PB = barometric pressure, mmHg; and P_{H_2O} = water vapor pressure, mmHg.

Using the present data, we calculated the $\dot{V}A/\dot{Q}$ ratio of each lung during the hypoxic challenge with 0% O_2. This was accomplished by multiplying minute ventilation of each lung by (1 − VD/VT) (= 0.16; see Results: Ventilation and Gas Exchange) to yield alveolar ventilation ($\dot{V}A$; 0.45 and 0.48 l/min, respectively), and then to divide by individual lung blood flow as measured with electromagnetometry (0.61 and 1.24 l/min, respectively). A $\dot{V}A/\dot{Q}$ ratio of 0.73 was obtained for the test lung, and of 0.38 for the control lung. λ of SF_6 is 0.006 (5), and, when inserted into equation 1, it can be seen that the elimination of SF_6 from the test lung (shunt disregarded) can be calculated to be 99.2%. The corresponding figure for the control lung is 98.5%.

** Enghoff H: Volumen inefficax: Bemärkungen zur frage des schädlichen Raumes. Upsala Läk Fören Förh 44:191–218, 1938

Thus, the different $\dot{V}A/\dot{Q}$ ratios of the two lungs result in negligible differences in the elimination of the test gas. The calculations of fractional lung blood flow will accordingly be independent of the differences in $\dot{V}A/\dot{Q}$. However, it should be underscored that the inert gas shunt is not taken into account in the partitioning of lung blood flow. The influence of the shunt will be minimal if it is of equal size in both lungs, which can be expected under the control conditions. Since the overall shunt remained unaltered during hypoxia (table 1), it is reasonable to assume a maintained, and probably even, distribution of the inert gas shunt also under this situation.

Calculation of the CO_2 elimination is more difficult, because that gas has no single value for its solubility. Using a standard dissociation curve of CO_2[11] and the presently measured blood gas tensions, *p*H, temperature, and hematocrit, a hypothetical, effective λ of 3.92 is obtained in the P_{CO_2} range of 39–59 mmHg. Using the same calculations as for SF_6 it can be seen that the elimination of CO_2 from the test lung amounts to 15% of the gas in blood, whereas the elimination from the control lung is only half that size, *i.e.*, 8%. Thus, the higher $\dot{V}A/\dot{Q}$ ratio of the test lung results in an elimination of CO_2 that is more efficient than in the control lung. It can also be shown that the ratios between test lung and control lung CO_2 outputs ($\dot{V}CO_2$) and true lung blood flows ($\dot{Q}$) relate to each other according to

$$\frac{\dot{Q}TL}{\dot{Q}CL} = \frac{\dot{V}CO_2TL}{\dot{V}CO_2CL} \times \frac{1 + \frac{\lambda}{\dot{V}A/\dot{Q}TL}}{1 + \frac{\lambda}{\dot{V}A/\dot{Q}CL}}, \qquad (2)$$

the equation being a derivation of equation 1. By inserting the calculated λ and $\dot{V}A/\dot{Q}$ ratios in equation 2, it will be found that $\dot{V}CO_2TL/\dot{V}CO_2CL$ is almost twice as high as $\dot{Q}TL/\dot{Q}CL$. This means that only half the decrease in $\dot{Q}TL$ after hypoxic challenge would be detected by the CO_2 elimination technique. However, in this study, the CO_2 technique detected somewhat more of the real change, approximately 60%, and Kim *et al.*¶ using the same technique, detected 70% of the "true" change in blood flow. This sensitivity, which was better than predicted, may be explained by the Haldane effect which will act in the opposite direction to that of a change in the $\dot{V}A/\dot{Q}$ ratio.

Haldane Effect

Hypoxia will move the CO_2 dissociation curve to the left, increasing the CO_2 capacity of the blood for a given P_{CO_2}. This is called the Haldane effect. It means that less CO_2 will be eliminated *via* the hypoxic lung for a given change in P_{CO_2} than in a normoxic or hyperoxic lung.

TABLE 3. Arterial and Mixed Venous Blood Gases during Control and Hypoxia

		Pa_{O_2}	Pa_{CO_2}	P_vO_2	P_vCO_2
Control 100% O_2	$\bar{x}$	488	44.8	59.1	50.8
	SE	31	6.2	3.4	7.0
Hypoxia 8% O_2	$\bar{x}$	120*	44.8	46.0*	50.5
	SE	20	7.7	2.9	7.3
Hypoxia 0% O_2	$\bar{x}$	53.8*	48.9	31.4*	55.3
	SE	5.5	7.3	3.3	7.1
Control† 100% O_2	$\bar{x}$	485	40.1	55.1	46.1
	SE	28	4.6	4.1	7.0

* Significantly different from control, $P < 0.01$.
† n = 6.

The influence of the Haldane effect on the CO_2 elimination was tested by means of the computer programs of Kelman,[12,13] which enable a conversion of P_{CO_2} to CO_2 content of the blood, taking into consideration the effects of P_{O_2}, hemoglobin concentration, hematocrit, temperature, and the buffering capacity of the blood. A hypothetical situation was assumed where all variables but Pa_{O_2} were kept constant.†† At an end-capillary test-lung P_{CO_2} of 45 mmHg (to approximately fit with the arterial P_{CO_2}), the corresponding CO_2-content increased from 52.5 to 55.0 ml/100 ml blood when P_{O_2} of that blood fell from 485 mmHg (as in arterial blood during control situation) to 31.4 mmHg (as in mixed venous blood during hypoxic challenge, a tension assumed to exist also in the hypoxic lung). Subtraction from a mixed venous CO_2 content of 60.7 ml/100 ml (present data during hypoxia) results in a calculated elimination of 8.2 and 5.7 ml CO_2/100 ml blood from the hyperoxic and hypoxic blood, respectively. Thus, CO_2 elimination was approximately 40% less efficient from the hypoxic blood, causing a similarly 40% exaggeration of the calculated change in lung blood flow distribution during a hypoxic challenge. However, this error is smaller than that caused by the different $\dot{V}A/\dot{Q}$ ratios in the two lungs during the hypoxic challenge.

Net Effect on CO_2 Elimination

The combined effect of different $\dot{V}A/\dot{Q}$ ratios and oxygen tensions in the two lungs on the CO_2 elimination can also be tested in theoretical experiments using the Kelman computer programs, provided that a P_{O_2} and P_{CO_2} value can be ascribed to each lung. The test situation with a hypoxic challenge of 0% O_2 was stud-

†† The measured hemoglobin concentration (13.0 g/100 ml), hematocrit (33.8), and temperature (38.1° C) have been used together with a standard buffer line (apH: 7.25, aP_{CO_2}: 72 mmHg, bpH: 7.50, bP_{CO_2}: 26 mmHg) and a standard dissociation curve.

ied. It was assumed that the P_{O_2} of the test lung equalled mixed venous P_{O_2}, and that P_{O_2} of the control lung (ventilated with 100% O_2) equalled arterial P_{O_2} during control conditions (when both lungs were ventilated with 100% O_2). The end-tidal CO_2 concentrations in table 2 were used for calculating P_{CO_2} of each lung. However, it is also necessary to take alveolar, or parallel, dead space into account because it has a diluting effect on the end-tidal CO_2 concentrations. Total dead space was large, as mentioned above, and part of it must have been non-perfused but ventilated alveoli. It was assumed that the parallel dead space was equally distributed between the two lungs (which may not be completely true). End-capillary/end-tidal CO_2 tension differences of 5, 10, 15, and 20 mmHg were tested, these differences fitting in with small to very large parallel dead spaces. The measured values of Hb, hematocrit, temperature, and an assumed standard buffer line with zero base excess were used for the calculations. The resulting elimination of CO_2 from the test lung equalled 5.5–5.7 ml/100 ml blood, and that of the control lung 4.2–4.4 ml/100 ml, depending on the end-capillary/end-tidal CO_2 tension difference. Thus, the test lung had a 25–35% more efficient elimination of CO_2 than the control lung. According to equation 2, this results in an underestimation of test lung blood flow of approximately 65–75%. This is in fair agreement with our observation of an underestimation of 60%, and similar to that observed by Kim *et al.*¶ It should be underscored that the calculations are based on several assumptions, and they do, therefore, give only an indication of the size of the different errors involved in measuring individual lung blood flow by CO_2 elimination technique. However, the fair agreement between theoretical calculations and practical measurements lends support to the following conclusions: 1) The assessment of individual fractional lung blood flow by the elimination of an inert, poorly soluble gas is an accurate method under most conditions; a comparison between SF_6 elimination and electromagnetometry resulted in a close agreement; and 2) the assessment of the individual fractional lung blood flow by CO_2 elimination technique, or measurement of end-tidal CO_2, is an inaccurate technique, being influenced by the degree of blood flow redistribution (change in VA/Q ratio) and the magnitude of the hypoxic challenge (Haldane effect). These sources of errors cannot easily be corrected for, since there are individual variations in the distribution of $\dot{V}A/\dot{Q}$ ratios and in the CO_2 binding capacity of blood.

References

1. von Euler US, Liljestrand G: Observations on the pulmonary arterial blood pressure in the cat. Acta Physiol Scand 12:301–320, 1946
2. Schenk WG Jr, Dedichen H: Electronic measurement of blood flow. Am J Surg 114:111, 1967
3. Wagner HN Jr, Rhodes BA, Sasaki Y, Ryan JP: Studies of the circulation with radioactive microspheres. Invest Radiol 4:374–386, 1969
4. Sykes MK, Mill AEG, Loh L, Tait AR: Evaluation of a new method for the continuous measurement of the distribution of the blood flow between the two lungs. Br J Anaesth 49:285–292, 1977
5. Wagner PD, Naumann PF, Laravuso RB: Simultaneous measurement of eight foreign gases in blood by gas chromatography. J Appl Physiol 36:600–605, 1974
6. Williams JJ, Chen L, Aukburg SJ, Alexander CM, Domino KB, Marshall BE: Computerized measure of CO_2 production to determine differential pulmonary blood flow (abstract). ANESTHESIOLOGY 59:A496, 1983
7. Chen L, Miller FL, Williams JJ, Alexander CM, Domino KB, Marshall BE: Hypoxic pulmonary vasoconstriction is not potentiated by repeated intermittent hypoxia in closed chest dogs. ANESTHESIOLOGY 63:608–610, 1985
8. Chen L, Miller FL, Aukburg SJ, Sedrak W, Marshall BE: Influence of the haldane effect on measurement of intermittent hypoxic pulmonary vasoconstriction (abstract). ANESTHESIOLOGY 61:A3, 1984
9. Wagner PD, Saltzman HA, West JB: Measurement of continuous distributions of ventilation perfusion ratios: Theory. J Appl Physiol 36:588–599, 1974b
10. Farhi LE: Elimination of inert gas by the lung. Respir Physiol 3:1–11, 1967
11. van Slyke DD, Sendroy J Jr: Studies of gas electrolyte equilibria in blood. XV. Line charts for graphic calculation by the Henderson-Hasselbach equation, and for calculating plasma carbon dioxide content from whole blood content. J Biol Chem 79:781–798, 1928
12. Kelman GR: Digital computer subroutine for the conversion of oxygen tension into saturation. J Appl Physiol 21:1375–1376, 1966
13. Kelman GR: Digital computer procedure for the conversion of P_{CO_2} into blood content. Respir Physiol 3:111–115, 1967