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Quantitation of Factors Affecting the Alveolar-Arterial P_{O_2} Difference in Thoracotomy

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This study was conducted to quantitate the contributions of several factors to the alveolar–arterial P_{O_2} difference, A-aD_{O_2}, observed in thoracotomy. Thirteen dogs were ventilated with 100 per cent oxygen using either intermittent positive-pressure ventilation (IPPV) or continuous positive-pressure ventilation (CPPV) with an end-expiratory pressure of 3 cm H_2O. Control values of A-aD_{O_2}, oxygen consumption, cardiac output, absolute shunt (anatomic shunt), and physiologic deadspace were determined with the chest closed. Thoracotomy was then performed, and the same determinations repeated. Results confirmed the hypothesis that changes in cardiac output and shunt are the major determinants of the alterations of A-aD_{O_2} in thoracotomy. Decreased cardiac output observed during thoracotomy was responsible for average increases in A-aD_{O_2} of 19.3 per cent in dogs ventilated with IPPV and 25.2 per cent in dogs ventilated with CPPV. Increased absolute shunt flow observed in animals ventilated with IPPV was responsible for an increase in A-aD_{O_2} equal to 88.5 per cent of the control value. In animals ventilated with CPPV, absolute shunt flow was seen to decrease when the chest was opened. This decrease was responsible for a decrease in A-aD_{O_2} of 26.8 per cent of the control value. (Key words: Thoracotomy; Alveolar–arterial P_{O_2}; Intermittent positive-pressure ventilation; Continuous positive-pressure ventilation.)

RESULTS OF EXPERIMENTS in this and other laboratories[1–3] have demonstrated that an increase in the alveolar–arterial P_{O_2} difference, A-aD_{O_2}, occurs when the thoracic cavity is opened to the atmosphere. Pulmonary factors which could be responsible for this change include increased alveolar deadspace, decreased pulmonary diffusing capacity, and increased shunt flow. In addition, alterations in cardiac output and oxygen consumption could significantly affect mixed venous oxygenation and hence, the degree to which Pa_{O_2} is affected by intrapulmonary shunt flow. Niden and associates[4] studied pulmonary diffusion in the dog lung and observed no significant change in pulmonary diffusing capacity upon opening the chest. Therefore, alterations in diffusing capacity as a factor contributing to the observed A-aD_{O_2} change can be eliminated. Although a number of papers dealing with cardiopulmonary dynamics before and after thoracotomy appear in the literature,[1, 5–7] no attempt to quantitate the contribution of each of the remaining factors to the alterations in A-aD_{O_2} has been made.

The present study was undertaken to quantitate the contributions of deadspace, absolute shunt, cardiac output, and oxygen consumption to the increase in A-aD_{O_2} that accompanies thoracotomy. Since several of these factors are affected by transpulmonary pressure, it was desirable to consider A-aD_{O_2} with both intermittent positive-pressure ventilation (IPPV) and continuous positive-pressure ventilation (CPPV).

Experimental Methods

Two groups of experiments, differing only in the type of ventilation used, were performed on mongrel dogs averaging 12.6 kg in weight. Each of 13 dogs was anesthetized with approximately 30 mg/kg sodium pentobarbital. The dog was positioned in dorsal recumbency, 0.25 mg atropine was administered intramuscularly, a tracheotomy was performed, and the carotid artery was cannulated. In addition, a catheter was passed down the jugular vein and into the pulmonary artery as determined by pressure recordings from the catheter. Upon completion of the surgical procedure, the animal was heparinized with 10 mg/kg heparin. Mechanical ventilation was then begun, using a modified Model 607

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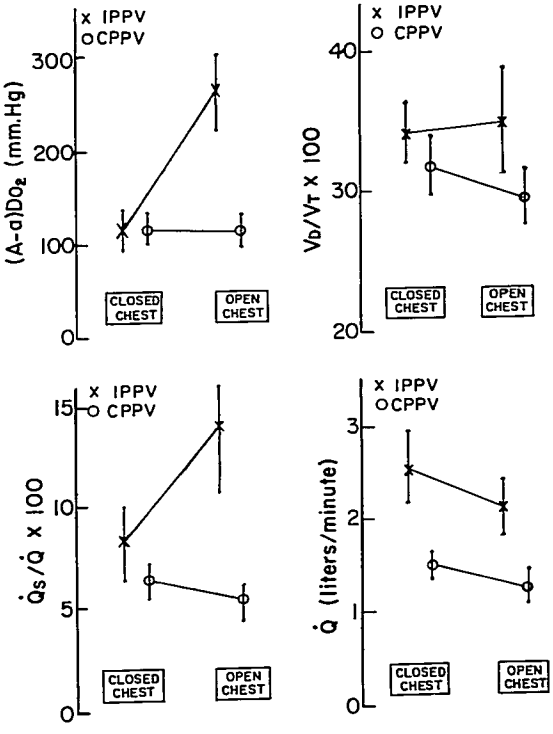

FIG. 1. Average A-aD_{O_2}, deadspace (V_D/V_T), shunt ($\dot{Q}_S/\dot{Q}$), and cardiac output ($\dot{Q}$) changes observed upon opening the chests in six experiments with IPPV and seven experiments with CPPV. Standard errors of the mean are indicated.

Harvard respirator. Gas, supplied to the ventilator from a Sanborn Model E-I-S spirometer, was delivered to the animal in the usual manner. The standard Harvard expiratory valve was replaced by one of two valves. A low-resistance solenoid valve which allowed free expiration to an end-expiratory pressure of 0 cm H_2O was used for intermittent positive-pressure ventilation, and a high-resistance pressure-operated valve allowing free expiration to an end-expiratory pressure of 3 cm H_2O was used for continuous positive-pressure ventilation. A sampling needle situated near the tracheotomy tube allowed sampling of the end-tidal gas. This was accomplished by means of a sampler triggered mechanically by the ventilator piston arm just prior to the beginning of each inspiration. The expiratory line was connected to the inlet of the spirometer by a large-bore, three-way stopcock. The stopcock enabled operation with an open circuit for collection of mixed expired gas or a closed circuit for monitoring of oxygen consumption with the spirometer. For six of the 13 dogs, IPPV was used, and for the remaining seven, CPPV was used. All dogs were ventilated with 100 per cent oxygen at a tidal volume of 24 ml/kg body weight and a minute volume of approximately 220 ml/kg body weight. Following a period of 30 minutes to

allow for nitrogen washout, oxygen consumption was determined, end-tidal and mixed expired gases were sampled, and mixed venous and arterial blood samples were obtained. The oxygen and carbon dioxide tensions of the gas samples and arterial blood samples were measured with an Instrumentation Laboratories Model 113 blood–gas analyzer. Oxygen contents of the arterial and mixed venous blood samples were determined with a Natelson microgasometer using a modified Van Slyke procedure,[8] and hemoglobin concentration was determined with the cyanmethemoglobin technique. Cardiac output ($\dot{Q}$) and physiologic deadspace (V_D/V_T) were calculated using the Fick equation and the modified Bohr equation, respectively. Since only the changes in deadspace were of interest, correction for apparatus deadspace was not made in the deadspace calculation. Absolute shunt was calculated using the modified shunt equation.[9] Two subsequent determinations were made at 30-minute intervals. Thoracotomy was then performed by creating bilateral openings measuring approximately 10 cm by 7 cm in the fourth intercostal space. The above determinations were repeated 15, 45, and 75 minutes after opening the chest.

Experimental Results

Figure 1 shows average data, along with the standard errors of the mean, from six dogs ventilated with IPPV and seven dogs ventilated with CPPV. With IPPV, the average closed-chest A-aD_{O_2} was 115.1 mm Hg. Average values of cardiac output, shunt, and physiologic deadspace were 2.53 l/min, 8.18 per cent, and 34.2 per cent, respectively. When the chest was opened, A-aD_{O_2} increased by an average of 124 per cent. This was accompanied by a decrease in cardiac output (16.7 per cent) and increases in shunt (69 per cent) and deadspace (1.6 per cent). Average closed-chest values of A-aD_{O_2}, cardiac output, shunt, and deadspace in the CPPV-ventilated dogs were 114.5 mm Hg, 1.51 l/min, 6.28 per cent, and 31.79 per cent, respectively. A-aD_{O_2} decreased by an average of 1.6 per cent when the chest was opened. A decrease in cardiac output (16.2 per cent) was observed, along with decreases in shunt (16.4 per cent) and deadspace (7.2 per cent). It should be noted that the closed-chest A-aD_{O_2} values are similar despite differences between $\dot{Q}$'s and $\dot{V}_{O_2}$'s in the two groups.

Data obtained from individual experiments are presented in tables 1 and 2. A paired variance analysis of the physiologic deadspace values obtained in these experiments indicated that the changes in deadspace observed during thoracotomy were not statistically significant. In addition, no change in oxygen consumption was observed when the chest was opened. Therefore, only cardiac output and shunt flow must be considered.

Data Analysis

The relationship of cardiac output ($\dot{Q}$), shunt ($\dot{Q}_s$) and A-aD_{O_2} during hyperoxia can be described by the shunt equation:

$$\frac{\dot{Q}_s}{\dot{Q}} = \frac{0.0031\text{A-a}D_{O_2}}{Ca_{O_2} - C\bar{v}_{O_2} + 0.0031\text{A-a}D_{O_2}} \quad (1)$$

Since ($Ca_{O_2} - C\bar{v}_{O_2}$) in this equation is equal to oxygen consumption rate ($\dot{V}_{O_2}$) divided by cardiac output, equation (1) can be rearranged as follows:

$$\text{A-a}D_{O_2} = 0.0031\frac{\dot{V}_{O_2}}{\dot{Q}[1/(\dot{Q}_s/\dot{Q}) - 1]} \quad (2)$$

Hence, for constant $\dot{V}_{O_2}$ the effects of alteration of $\dot{Q}$, $\dot{Q}_s$, or both on A-aD_{O_2} can be determined.

When the experimental data of tables 1 and 2 for $\dot{Q}$ and $\dot{Q}_s$ are inserted into equation 2, predicted values for A-aD_{O_2} are obtained. Comparison of these values with the experimentally determined values of A-aD_{O_2} allows evaluation of the accuracy of the experimental data. As can be seen from figure 2, agreement was very good.

Data obtained from equation 2, relating changes in cardiac output and absolute shunt to A-aD_{O_2}, are depicted by the solid lines in figure 3. It is evident from this figure that decreasing cardiac output while maintaining per cent shunt constant causes A-aD_{O_2} to increase. Furthermore, increasing shunt flow at a given cardiac output also increased A-aD_{O_2}. Figure 3 also shows graphically the

TABLE 1. Data from IPPV-ventilated Dogs (End-expiratory Pressure = 0 cm H_2O)

	Weight (kg)	Closed Chest						Open Chest					
		$A\text{-}aD_{O_2}$ (mm Hg)	$\dot{V}_{O_2}$ (ml/min)	Hb (g/100 ml)	$\dot{Q}$ (l/min)	$\frac{\dot{Q}_s}{\dot{Q}} \times 100$	$\frac{V_D}{V_T} \times 100$	$A\text{-}aD_{O_2}$ (mm Hg)	$\dot{V}_{O_2}$ (ml/min)	Hb (g/100 ml)	$\dot{Q}$ (l/min)	$\frac{\dot{Q}_s}{\dot{Q}} \times 100$	$\frac{V_D}{V_T} \times 100$
Dog 1	11.8	135.2	82.7	12.3	1.05	7.49	38.20	225.5	96.3	11.8	1.07	11.07	41.80
Dog 2	11.8	102.4	112.0	10.1	3.78	16.07	40.50	416.0	127.0	12.0	2.68	21.52	47.29
Dog 3	13.6	30.6	129.0	12.2	3.04	2.80	30.02	204.5	119.0	12.3	3.23	14.76	36.03
Dog 4	12.3	89.7	80.0	15.5	2.24	7.28	28.19	114.3	83.0	16.0	1.39	5.60	22.85
Dog 5	13.6	104.3	86.7	12.8	1.61	5.66	31.51	280.0	91.7	13.8	1.49	12.24	25.10
Dog 6	15.0	138.5	81.7	13.8	1.96	9.08	36.22	305.4	84.0	14.7	1.87	16.03	35.45
Mean	13.0	115.1	95.4	12.8	2.53	8.18	34.20	257.8	100.2	11.2	2.11	13.84	34.75
SE	0.4	22.2	8.3	0.7	0.43	1.90	1.97	41.9	7.6	1.2	0.29	2.19	3.85

TABLE 2. Data from CPPV-ventilated Dogs (End-expiratory Pressure = 3 cm H_2O)

	Weight (kg)	Closed Chest						Open Chest					
		$A\text{-}aD_{O_2}$ (mm Hg)	$\dot{V}_{O_2}$ (ml/min)	Hb (g/100 ml)	$\dot{Q}$ (l/min)	$\frac{\dot{Q}_s}{\dot{Q}} \times 100$	$\frac{V_D}{V_T} \times 100$	$A\text{-}aD_{O_2}$ (mm Hg)	$\dot{V}_{O_2}$ (ml/min)	Hb (g/100 ml)	$\dot{Q}$ (l/min)	$\frac{\dot{Q}_s}{\dot{Q}} \times 100$	$\frac{V_D}{V_T} \times 100$
Dog 7	11.8	55.0	75.0	13.8	1.82	3.84	38.00	98.5	72.5	13.5	1.40	5.50	34.80
Dog 8	12.7	147.5	80.0	10.8	1.21	6.21	25.00	147.5	82.5	12.0	0.94	3.78	30.05
Dog 9	10.9	148.0	84.8	9.7	1.59	7.05	38.20	87.5	83.0	11.3	1.50	4.88	23.29
Dog 10	12.7	180.5	85.3	10.6	1.72	10.19	30.30	190.5	81.5	12.3	1.10	7.27	31.45
Dog 11	10.0	79.4	55.3	13.7	1.19	5.25	32.34	85.8	56.7	15.4	0.96	4.32	30.09
Dog 12	11.8	65.3	59.3	13.6	1.03	3.40	—	64.0	59.3	14.7	0.75	2.41	—
Dog 13	15.0	126.1	102.3	10.0	1.99	7.09	26.87	144.9	102.5	12.0	2.20	8.40	23.73
Mean	12.1	114.5	77.4	11.7	1.51	6.28	31.79	112.7	76.9	13.0	1.26	5.24	29.49
SE	0.6	18.2	6.1	0.7	0.14	0.90	2.25	16.2	5.9	0.6	0.19	0.70	2.06

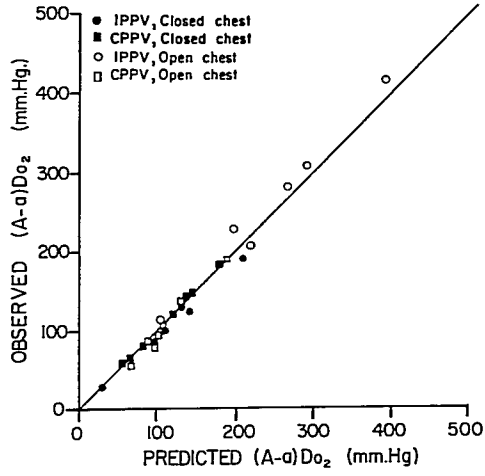

FIG. 2. Comparison of observed $A\text{-}aD_{O_2}$ values and $A\text{-}aD_{O_2}$ values predicted by equation 2.

type of analysis carried out for each experiment. Two examples are given. The first, illustrating an experiment utilizing IPPV, shows the situation in which both cardiac output and shunt changes contribute to increased $A\text{-}aD_{O_2}$. The second, illustrating an experiment utilizing CCPV, shows a situation in which the effects of the two variables oppose each other, resulting in little alteration in $A\text{-}aD_{O_2}$. The X's in figure 3 represent calculations from the experiment on Dog 6 (see table 1). The observed closed-chest values of cardiac output and per cent shunt were 1.96 l/min and 9.08 per cent, respectively. When the chest was opened cardiac output decreased to 1.87 l/min, and shunt increased to 16.93 per cent. When the closed-chest data were inserted into equation 2, an $A\text{-}aD_{O_2}$ of 136.7 mm Hg (point A) was obtained. Decreasing the cardiac output to 1.87 l/min while maintaining shunt equal to the closed-chest value (9.08 per cent) caused an increase in the $A\text{-}aD_{O_2}$ equal to 4.5 per cent of the control value (point B). Increasing shunt from 9.08 per cent to 16.93 per cent at the open-chest cardiac-output value (1.87 l/min) caused a further increase in $A\text{-}aD_{O_2}$ equal to 108.8 per cent of the control value (point C). Thus, in this example, the combined effect of the two factors was an increase in $A\text{-}aD_{O_2}$ equal to 113.3 per cent of the control value. The second example presented in figure 3 corresponds to the data obtained from the experiment on Dog 10 (see table 2). It can be seen from the experimental data that in this animal cardiac output decreased from 1.72 l/min to 1.10 l/min and shunt decreased from 10.19 per cent to 7.27 per cent when the chest was opened. Under closed-chest conditions of this experiment, calculations predicted an $A\text{-}aD_{O_2}$ of 177.7 mm Hg (point A'). Decreasing the cardiac output to 1.10 l/min while maintaining the closed-chest shunt value (10.19 per cent) caused an increase in $A\text{-}aD_{O_2}$ equal to 56.6 per cent of the control value (point B'). Decreasing shunt to 7.27 per cent while maintaining cardiac output at the open-chest value (1.10 l/min) caused a decrease in $A\text{-}aD_{O_2}$ equal to 48.4 per cent of the control value. Hence, the predicted combined effect of the decreased cardiac output and the decreased shunt observed in this experiment during thoracotomy was an increase in $A\text{-}aD_{O_2}$ equal to 8.2 per cent of the control value, or 14.6

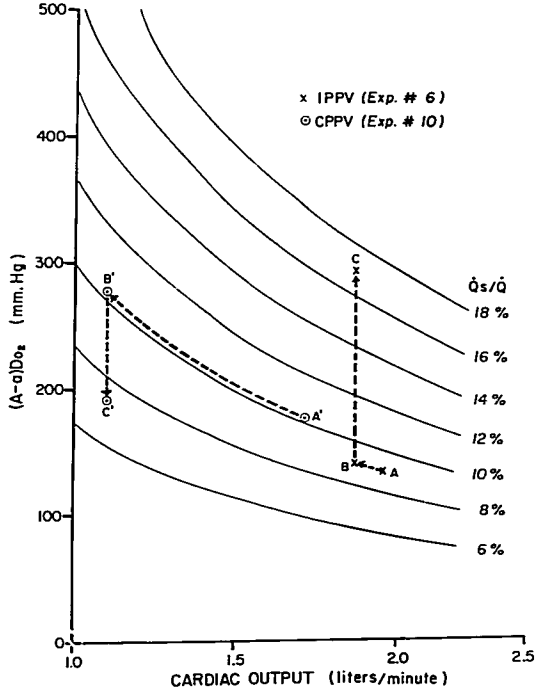

FIG. 3. Calculated A-aD_{O_2} as functions of cardiac output and shunt flow. Inspired gas was 100 per cent oxygen. Dashed lines represent two experiments (see text).

mm Hg. It should be noted in figure 3 that an equivalent change in cardiac output at a low value causes a change in A-aD_{O_2} greater than that which would occur at a higher value. Also, an equivalent change in per cent shunt at a low value, in general, causes a change in A-aD_{O_2} greater than that which would occur at a higher value.

Table 3 allows comparison of the effects of the two types of ventilation on thoracotomy; however, the results must be considered in light of the significantly lower control values of $\dot{Q}$ and $\dot{V}_{O_2}$ in dogs receiving CPPV. This table allows examination of the "cardiac-output" and "shunt" effects on the control values of A-aD_{O_2}, as well as the results of the interaction of the two effects. In addition, the table allows comparison of the two types of ventilation. As can be seen, the control values of A-aD_{O_2} for the two types of ventilation are of comparable magnitude despite the differences between $\dot{V}_{O_2}$'s and $\dot{Q}$'s in the two groups. Opening the chest in the experimental studies resulted in a 16–17 per cent decrease in cardiac output regardless of the type of ventilation used. Insertion of this information into equation 2 indicates that with IPPV, the decrease in cardiac output caused A-aD_{O_2} to increase by approximately 19 per cent. Analysis of the data from CPPV-ventilated animals predicts an increase in A-aD_{O_2} of approximately 25 per cent resulting from the decreased cardiac output. This "cardiac-output" effect was altered significantly, how-

TABLE 3. Average Calculated Data

	Control	$\Delta\dot{Q}$ Effect		$\Delta\dot{Q}_s/\dot{Q}$ Effect		Combined Effect	
	$A\text{-}aD_{O_2}$ (mm Hg)	$\Delta\dot{Q}$ (% Control)	$\Delta A\text{-}aD_{O_2}$ (% Control)	$\Delta\dot{Q}_s/\dot{Q}$ (% Control)	$\Delta A\text{-}aD_{O_2}$ (% Control)	$\Delta A\text{-}aD_{O_2}$ (% Control)	Final $A\text{-}aD_{O_2}$ (mm Hg)
IPPV	118.6	−16.7	19.3	69.2	88.5	107.8	246.6
CPPV	113.5	−16.2	25.2	−16.4	−26.8	−1.6	111.6

ever, by the "shunt" effect. The magnitude and direction of this modification were dependent upon the type of ventilation. With IPPV, shunt increased in the experimental studies by approximately 69 per cent of the control value. Calculations predict that this shunt change causes $A\text{-}aD_{O_2}$ to increase by approximately 88 per cent of the control value. Hence, the combined "cardiac-output" and "shunt" effects in IPPV-ventilated dogs resulted in an increase in $A\text{-}aD_{O_2}$ equal to approximately 108 per cent of the control value. In dogs ventilated with CPPV, the average "shunt" effect opposed the "cardiac-output" effect. An average decrease in absolute shunt flow equal to approximately 16 per cent of the control value was observed in the experimental studies. Analysis of the data indicated that this alteration in shunt flow was responsible for a decrease in $A\text{-}aD_{O_2}$ equal to approximately 30 per cent of the control value. Hence, the combined "cardiac-output" and "shunt" effects in dogs ventilated with CPPV resulted in little change in the observed $A\text{-}aD_{O_2}$'s.

Discussion

A discussion of alterations of $A\text{-}aD_{O_2}$ under a given set of conditions is not complete unless all factors, both pulmonary and systemic, that may affect alveolar or arterial P_{O_2} are considered. Pulmonary factors affecting alveolar or arterial P_{O_2} include diffusing capacity of the pulmonary membrane, alterations of deadspace, and alterations in shunt flow. As mentioned previously, Niden and associates[4] have reported that no significant alteration in diffusing capacity occurs when the chest is opened. In addition, the experimental data obtained from this study reveal that no significant change in physiologic deadspace occurs when the chest is opened.

Systemic factors which could contribute to alterations of $A\text{-}aD_{O_2}$ include changes in oxygen consumption and cardiac output. Alterations in oxygen consumption by the tissues would significantly affect mixed venous oxygen content and thereby affect the degree to which Pa_{O_2} is affected by venous admixture. The experimental results reported here, along with those recently reported by Aoyagi and Pipper,[1] indicate that opening the chest does not cause alterations in tissue oxygen consumption. Hence, this factor is not significant in the alterations of $A\text{-}aD_{O_2}$ accompanying thoracotomy. Thus, shunt flow and cardiac output are left as possible contributing factors.

Results of this study indicate that alterations in absolute shunt flow are indeed significant in determining the open-chest $A\text{-}aD_{O_2}$ value. Furthermore, the degree to which absolute shunt is affected by opening the chest is dependent upon the type of ventilation used. Quantitation of this effect reveals that the altered absolute shunt flow can cause $A\text{-}aD_{O_2}$ to increase significantly, as was seen with IPPV (88.5 per cent of the control value), or to decrease, as was seen with CPPV (26.8 per cent of the control value).

In considering mechanism by which the type of mechanical ventilation affects shunt flow, it is necessary to examine the effects of IPPV and CPPV on the distribution of ventilation. Since end-inspiratory pressures were of similar magnitude, it may be assumed that the end-inspiratory lung volumes (end-expiratory volume) differed as a result of different end-expiratory pressures. Although lung volumes were not measured, it may be assumed that the resting volume with IPPV was lower

than that with CPPV since lung volume is dependent upon transpulmonary pressure. The lower resting volume with IPPV could promote greater shunt flow, as follows. As a consequence of the lower resting volume, progressive atelectasis could occur more rapidly than with the larger resting lung volumes which accompany CPPV, thereby producing poorer ventilation distribution and resulting in greater absolute shunt flow.

Cardiac output has repeatedly been shown to decrease when the chest is opened.[5–6, 10–12] Fermoso and associates[11] have attributed this decrease to a shift in the cardiopulmonary function curve resulting from increased extracardiac pressure. Such a decrease at constant oxygen consumption would cause a decrease in mixed venous oxygen content, and through shunted blood, significantly affect Pa_{O_2}. The experimental data obtained in this study indicate that cardiac output decreases by approximately 16 per cent when the chest is opened, regardless of the type of ventilation used. Analysis of the data reveals that this decrease causes $A\text{-}aD_{O_2}$ to increase by approximately 19 per cent with IPPV and 25 per cent with CPPV. It should be emphasized that the "cardiac-output" effect significantly alters $A\text{-}aD_{O_2}$ and that the cardiac output decreases when the chest is opened, regardless of the type of ventilation used. The "absolute-shunt" effect, on the other hand, may be modified by use of CPPV.

We have shown in this study that alterations in $A\text{-}aD_{O_2}$ observed during thoracotomy during breathing of 100 per cent oxygen are due solely to alterations in cardiac output and absolute shunt. Furthermore, we have quantitated the effects of the changes in cardiac output and changes in absolute shunt flow on $A\text{-}aD_{O_2}$. All that remains to complete the quantitation of factors contributing to the $A\text{-}aD_{O_2}$ in thoracotomy is to quantitate the effects of changes in relative shunt (shunt due to excess blood flow in regard to ventilation). Since all other contributing factors have been quantitated, the effects of changes in relative shunt may be determined by simple calculation of total shunt from animals ventilated with room air (relative shunt = total shunt − absolute shunt). This determination is left for a future study.

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