Effect of changes in tidal ventilation on physiologic shunting

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HEDLEY-WHYTE, J., M. B. LAVER, AND H. H. BENJIXEN. Effect of changes in tidal ventilation on physiologic shunting. Am. J. Physiol. 206(4) : 891-897. 1964.—The rate and magnitude of the effects of the pressure-volume history of the lungs on the degree of physiologic shunting (pulmonary venous admixture) were investigated in 20 dogs, anesthetized and curarized. Atelectasis was promoted by decreasing end-expiratory transpulmonary pressure. Ventilation was with 100% oxygen using a constant-volume pump at a frequency of 20 breaths/min. The rates of increase or decrease in the physiologic shunt and of the gradients between derived alveolar oxygen tension and directly measured arterial oxygen tension (A-aD) showed a variation controlled by the pressure-volume history of the lungs. The physiologic shunts produced varied between 0.5% and 80% of the cardiac output. The interrelationships of the components of the shunt equation were studied and their relative value in predicting atelectasis was discussed. The data obtained were related to other observations made in anesthetized man.

atelectasis alveolar capillary shunt pulmonary ventilation pulmonary circulation lung inflation and A-aD dynamic compliance constant volume ventilation venous admixture pneumothorax anatomical shunt ventilatory requirements

IN THE NORMAL PULMONARY CIRCULATION during ventilation with 100% oxygen there are two forms of physiologic shunt that reduce the oxygenation of the arterial blood. The first is the anatomical shunt of venous blood draining into the left heart from the bronchial, pleural, or Thébesian veins, or from those pulmonary vessels which have no contact with alveoli. The second is the effective shunt caused by unoxygenated blood coming from nonventilated alveoli. The two sources of an increase in the A-aD are known, respectively, as the anatomical and the distribution component of the physiologic shunt. The aim of this present study was to determine the extent of the influence of the pressure-volume history of the lungs on shunting during constant-volume ventilation. The effect was observed also of changes in the pressure-volume history on the two variables that decide the magnitude of shunting, i.e., the A-aD and the arterial-mixed venous oxygen gradient (CaO₂ - CVO₂).

The hypothesis tested in this study was that different constant-volume ventilation histories could lead to large differences in the total physiologic shunt. Differentiation between the two components of the total physiologic shunt was not attempted, but if it be presumed that the anatomic component remains relatively small and constant, then large variations in the total physiologic shunt will reflect alveolar-capillary shunting due (most probably) to atelectasis (7).

Sackur in 1897 (13) first measured the amount of blood shunted through a collapsed lung. He described the formula which is still in use

\[ \frac{Q_s}{Q_t} = \frac{CaO_2 - CVO_2}{CaO_2 - CVO_2} \]

where \( Q_s \) is the venous admixture, \( Q_t \) the total blood flow, \( CaO_2 \) the \( O_2 \) content of blood leaving the alveolar capillary bed, \( CVO_2 \) the \( O_2 \) content of the arterial blood, and \( CVO_2 \) the \( O_2 \) content of mixed venous blood.

Following the classic work of Riley and Cournand (12) and Farhi and Rahn (6) on the A-aD, the occurrence of an increased A-aD during controlled ventilation anesthesia has been described (3, 15). No attempt was made by these authors to correlate the degree of increase of the A-aD with ventilation; however, they postulated that an increased shunt occurred during controlled ventilation. Finley et al. (7) in a study on venous admixture in the pulmonary circulation of anesthetized dogs found a mean physiologic shunt of 4.3% when using constant-volume ventilation with an end-expiratory resistance sufficient to produce a mean intratracheal
the rate of change of the A-aD. ventilation, with an intact chest, showed that those collapse. The occurrence of an increased A-aD sug-
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changes being due presumably to progressive alveolar
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methods and procedure
A total of 20 mongrel dogs, weighing 8-21 kg (avg.
pressure of 3 mm Hg. With an end-expiratory resistance producing a mean intratracheal pressure of 15 mm Hg they found a mean physiologic shunt of 1.0 %. They suggested that such changes were due to a decrease in the amount of atelectasis. Mead and Collier (9) showed that with constant-volume ventilation a gradual reduction in compliance took place and that this fall was reversible with a sustained passive inflation. Thus previous work seemed to point to a fall in compliance and a rise in A-aD, with controlled ventilation in the absence of a deep breath or end-expiratory resistance, these changes being due presumably to progressive alveolar collapse. The occurrence of an increased A-aD suggested that capillary blood flow persisted through collapsed (and unventilated) areas of the lung.

Studies in this hospital (28) in 18 patients undergoing surgery, under general anesthesia and controlled ventilation, with an intact chest, showed that those patients having the largest fall in arterial carbon dioxide tension exhibited the least fall in arterial oxygen tension. These results suggest that a relationship exists between the pressure-volume history of the lungs and the rate of change of the A-aD.

METHODS AND PROCEDURE

A total of 20 mongrel dogs, weighing 8-21 kg (avg. 15 kg), were anesthetized with thiopental sodium (initial dose 10-25 mg/kg body wt.). Anesthesia was maintained with intravenous thiopental sodium in intermittent doses of 1-2 ml of a 2.5 % solution. A femoral artery was cannulated with a polyethylene catheter for arterial sampling and for measurement of arterial pressures. The tip of the catheter was placed in the abdominal aorta. Both femoral veins were cannulated to allow injections and infusions.

Atropine, 1 mg/kg, and hexamethonium bromide, 100 mg, were given intravenously. Dimethyl curare was given in doses of 4-8 mg for muscle paralysis. After giving 100 mg hexamethonium bromide these doses of dimethyl curare did not lead to a change in PaO2 or compliance. Six per cent dextran in normal saline was used to replace the blood drawn for sampling.

The dogs were supine throughout the experiment. A tracheostomy was performed and a tube (no. 38 French) was tied into the trachea. Great care was taken to secure a completely airtight fit. A no. 17 needle was inserted into the tracheostomy tube and connected to a Sanborn high-sensitivity pressure transducer (series no. 268B). Controlled constant-volume ventilation was started at a rate of 20/min with a tidal volume of approximately 40 ml/kg body wt. via a Harvard Apparatus Company respiratory pump. All the dogs were ventilated with 100 % oxygen throughout each experiment. The temperature of the dog was monitored with an esophageal electrode attached to a K-thermia blanket, model R.K. 101 (manufactured by Gorman-Rupp Industries, Inc., Belville, Ohio). The temperature of the dog was kept between 37 and 39 C.

A left thoracotomy was performed in all dogs and in 11 of the 20 dogs a polyethylene catheter was placed with the minimum of lung retraction into the branch of the pulmonary artery to the left upper lobe and secured so that the tip lay in the main left pulmonary artery. The chest was closed leaving a 9 in. long no. 32 French red rubber endotracheal tube placed so that the proximal inch of the tube lay within the common intrapleural space of the dog. Continuous measurements were made of the pressure within the intrathoracic portion of the tube with a no. 17 needle passed into the lumen of the tube, the needle being connected to a second Sanborn high-sensitivity (268B) pressure transducer. Since this chest tube was open to the atmosphere this continuous pressure recording gave values which varied in all the dogs according to the volume setting of the respirator between +0.6 mm Hg and -0.6 mm Hg. The absence of this continuous fluctuation around atmospheric pressure pointed to the development of a closed, or tension pneumothorax and if this happened the experiment was abandoned. Compared with an intact chest, the use of this chest tube thus served to decrease transpulmonary pressure at end expiration.

Since the constant-volume ventilation was dependent on there being no gas leak anywhere between the oxygen inlet to the Harvard constant-volume pump and the dog's lung, the constancy of ventilation was continually checked with a Wright ventilation meter placed on the expiratory exhaust of the pump. The accuracy of this ventilation meter was found to be of the same order as the Wright ventilation meters tested by Hall and
VOLUME AND PHYSIOLOGIC SHUNTING

FIG. 2. A: regression coefficient of A-aD in mm Hg on time in hours \( \frac{b}{t} \) versus ventilation. Data obtained in 18 dogs undergoing constant-volume ventilation with 100% O₂ for 4 hr. B: regression coefficient of total physiologic shunt in percent of cardiac output on time in hours \( \frac{Q_s \times 100}{Q_t} \). Data obtained in 9 dogs undergoing constant-volume ventilation with 100% O₂ for 4 hr.

Reeser (8). At any given tidal volume between 200 and 700 ml when delivering oxygen, the reading on the ventilation meter was required to agree within 5% with the setting for the stroke volume of the pump. If the reading varied outside this range the experiment was terminated.

Arterial pH was measured with a Beckman glass electrode with a Sanborn pH meter. Arterial carbon dioxide (PaCO₂) was measured with the Severinghaus electrode (14) and the arterial oxygen tension (PaO₂) was recorded with a modified Clark electrode (4) using a Sanborn polarization cell (model 350-1). Great care was taken to perform the polarographic measurements with the blood at 38°C at 3 min from sampling. The accuracy of the Severinghaus and Clark electrodes were repeatedly checked against blood equilibrated with known percentages of oxygen and carbon dioxide. The reproducibility of any particular sample was found to be within 2%. When two samples were withdrawn simultaneously they always agreed to better than 5% (i.e., at 500 mm Hg arterial O₂ tension the two samples will agree to within 25 mm Hg). Blood samples were drawn over a period of at least three respiratory cycles into syringes whose dead space was filled with heparin.

The oxygen contents of the pulmonary artery and arterial blood were obtained by the method of Van Slyke and Neill (16). All measurements were required to check to within ±0.2 ml/100 ml for any particular sample. Following the surgical preparation of the dog when, as described above, the dog was ventilated with a constant tidal volume of 40 ml/kg body wt., samples were drawn to determine the A-aD and physiologic shunt that had occurred. Immediately after this initial sampling the tidal volume was changed to a predetermined larger or smaller tidal volume and the time scale of the experiment was measured from this change in tidal volume (i.e., this change in tidal volume was taken as zero time). With the sole exception of the dog shown in Figs. 4 and 5, this new tidal volume was thereafter kept constant. During the remainder of each experiment blood samples were taken as described above.

The average rates of change of the A-aD and physiologic shunt were calculated in each of the dogs by determining the linear coefficients of regression of 1) A-aD (in mm Hg) and 2) physiologic shunt (in % of cardiac output) on time (in hr). Values obtained for the A-aD and physiologic shunt during the first 40 min after zero time were found to be influenced not only by the degree to which the tidal volume had been changed at zero time, but also by the speed and ease of anesthesia induction and surgical preparation. Thus values for the A-aD and physiologic shunt obtained during the first 40 min after zero time were regrettably excluded from the calculations of the average rate of change of the A-aD and physiologic shunt.

Since 100% O₂ was used the alveolar oxygen tension was calculated from the following equation

\[ \text{PaO}_2 = \text{Pb} - 47 - \text{PaCO}_2 \]  

(2)

The per cent physiologic shunt \( \frac{Q_s}{Q_t} \times 100 \) was calculated from the following equation

\[ \frac{Q_s}{Q_t} = \frac{C_aO_2 - C_vO_2}{C_aO_2 - C_vCO_2} \]  

(3)

\[ \text{PaO}_2 = \text{Pb} - 47 - \text{PaCO}_2 \]

\[ \frac{Q_s}{Q_t} = \frac{C_aO_2 - C_vO_2}{C_aO_2 - C_vCO_2} \]
where the alveolar oxygen tension (\(PAO_2\)) is derived as has been described above, the arterial oxygen tension (\(PaO_2\)) is measured polarographically, and the oxygen contents of arterial (\(CaO_2\)) and pulmonary arterial blood (\(CVO_2\)) are measured by the method of Van Slyke and Neill (16).

This form of the shunt equation is needed because pulmonary capillary blood cannot be sampled. Its use requires that oxygen is breathed and that the following assumptions are made:

1) \(Qt\) (total cardiac output). The equation assumes that all venous admixture stems from the pulmonary artery. Available evidence (1) suggests that a proportion of the anatomic shunt equal to approximately 0.8% of the pulmonary artery blood flow arises from the greater circulation. Thus the error from this source is approximately 0.8% and can probably be ignored.

2) \(CVO_2\) (mixed venous oxygen content). The equation assumes that the oxygen content of all venous admixture is the same as that found in the pulmonary artery. The error from this assumption is negligible if we consider that part of the anatomic shunt which arises from other than the pulmonary artery to be relatively constant and small, i.e., 0.8%.

3) \(PaO_2\) (alveolar oxygen tension). This is calculated from the alveolar air equation and assumes \(PaCO_2 = PaCO_2\).

4) \(CcO_2 = CaO_2 = (PAO_2 - PaO_2) \times 0.0031\) (0.0031 is the solubility coefficient of oxygen in blood). This assumes the hemoglobin is fully saturated in both the end-capillary and mixed arterial bloods. Since it is impossible to sample capillary blood, the assumption must be made that its oxygen tension is equal to that of the mixed alveolar air. This expectation is fulfilled provided that the diffusion and distribution effects are negligible. When the alveolar oxygen tension is higher than 200 mm Hg the diffusion barrier does indeed become negligible. Bartels and Rodewald (2) gave practical support to this assumption when they showed that the A-a difference in man remains constant when the alveolar oxygen tension is raised from 200-400 mm Hg. It might be expected that the occurrence of areas in the lung having different ventilation-perfusion ratios would lead to an oxygen difference between the alveolar air and the mixed capillary blood. Farhi and Rahn, however, have shown that when the fraction of nitrogen in the inspired air is reduced such a difference becomes negligible (6).

The use of 100% oxygen at normal atmospheric pressure thus has three distinct advantages: 1) The possible existence of a diffusion barrier does not cause an alveolar arterial oxygen difference. 2) The existence of an uneven distribution of ventilation to perfusion in the lungs results only in a minimal A-aD. 3) The complete saturation of hemoglobin allows the difference in content between end-capillary blood and arterial blood to be expressed in terms of the product of oxygen solubility times the A-aD.

We thus believe that when oxygen is breathed it is justified to equate \(PCO_2\) and \(PAO_2\).

The linear regression coefficients (\(b\)) were obtained by using the formula

\[
b = \frac{\sum xy - (\sum x)(\sum y)/N}{\sum x^2 - (\sum x)^2/N}
\]

![FIG. 3](data from 11 dogs undergoing constant-volume-controlled ventilation with 100% O₂ for 4 hr. Open circles are from two dogs who died during the 4-hr period.)

**TABLE 1.** Dog (11.2 kg) ventilated by a constant-volume pump with a tidal volume of 700 ml 100% O₂ (62.5 ml/kg body wt.) at a rate of 20/min

<table>
<thead>
<tr>
<th>Time, min</th>
<th>(PAO_2), mm Hg</th>
<th>(PaO_2), mm Hg</th>
<th>A-aD, mm Hg</th>
<th>(PaCO_2), mm Hg</th>
<th>(CcO_2 - CaO_2), ml/100 ml</th>
<th>(Q/Qt) X 100, %</th>
<th>H.P., mm Hg</th>
<th>U.O., ml/100 ml</th>
<th>U.O., ml/mm Hg</th>
<th>Dynamic Lung Compliance, ml/mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>663</td>
<td>154</td>
<td>509</td>
<td>39</td>
<td>1.6</td>
<td>9.5</td>
<td>16.6</td>
<td>132/104</td>
<td>20.1</td>
<td>12.2</td>
</tr>
<tr>
<td>½</td>
<td>683</td>
<td>541</td>
<td>142</td>
<td>19</td>
<td>0.4</td>
<td>9.0</td>
<td>4.4</td>
<td>120/86</td>
<td>21.2</td>
<td>11.7</td>
</tr>
<tr>
<td>1</td>
<td>687</td>
<td>556</td>
<td>139</td>
<td>15</td>
<td>0.4</td>
<td>11.0</td>
<td>3.6</td>
<td>110/90</td>
<td>20.4</td>
<td>11.0</td>
</tr>
<tr>
<td>2</td>
<td>689</td>
<td>590</td>
<td>99</td>
<td>13</td>
<td>0.3</td>
<td>12.6</td>
<td>2.4</td>
<td>108/84</td>
<td>22.7</td>
<td>10.4</td>
</tr>
<tr>
<td>180</td>
<td>689</td>
<td>634</td>
<td>55</td>
<td>13</td>
<td>0.2</td>
<td>14.9</td>
<td>1.1</td>
<td>96/76</td>
<td>24.3</td>
<td>9.5</td>
</tr>
<tr>
<td>210</td>
<td>689</td>
<td>633</td>
<td>46</td>
<td>13</td>
<td>0.1</td>
<td>15.3</td>
<td>0.7</td>
<td>96/76</td>
<td>24.7</td>
<td>9.5</td>
</tr>
</tbody>
</table>
where the x axis represents the independent variable, the time of constant-volume ventilation in hours, and the y axis represents the dependent variables, either 1) the A-aD (in mm Hg), or 2) the per cent physiologic shunt ($Q_S/Q_T \times 100$). Linear regression coefficients were used as they seemed the best method of expressing the rate of change of the dependent variables, the A-aD, and the total physiologic shunt.

Dynamic lung compliance was obtained by relating the transpulmonary pressure change, as measured from the intratracheal and intrapleural pressure tracings, to the tidal volume corrected to BTPS. The assumption was made that zero flow occurred at the points of maximum and minimum transpulmonary pressure difference.

**RESULTS**

The mean duration of the study period of unchanged ventilation after zero time was 4.77 hr (sd ± 0.2 hr). The mean A-aD, immediately before the change in tidal volume made at zero time, was 254 mm Hg (sd ± 144 mm Hg). The mean physiologic shunt was 11.9% (sd ± 4.5%). These values with their large standard deviations reflect the influence of the varying ease of surgical preparation and the previous pressure-volume history of the lungs. From these initial values, the A-aD and physiologic shunt always increased when ventilation was with low tidal volumes, while both the A-aD and physiologic shunt always decreased when high tidal volumes were used. Figure 1 shows the effect of constant-volume ventilation in two dogs. The first dog (interrupted lines) was an 18.5-kg dog ventilated with a tidal volume of 200 ml and the second dog (continuous lines) was a 13.5-kg dog ventilated with a tidal volume of 700 ml. The time course of the changes in A-aD can be seen.

Figure 2A shows the relationship between the tidal volume (in ml/kg body wt.) and the rate of change of the A-aD (expressed as regression coefficients for A-aD, in mm Hg, on time, in hr). Figure 2A is derived from the 18 dogs who survived the experiment (two dogs who died before the end of the experiment are excluded). As has already been described, the changes in A-aD and physiologic shunt occurring in the first 40 min after zero time at the new tidal volume were excluded from the calculations of the average rate of change of the A-aD and physiologic shunt. It should be noted, however, that in all dogs in which the A-aD and physiologic shunt increased during the first 40 min some increase in gradient or shunt invariably continued after 40 min, while in those dogs in which there was a decrease in A-aD or physiologic shunt in the first 40 min some decrease always continued. Both before and after 40 min from zero time, dogs ventilated with a tidal volume in excess of 25 ml/kg body wt. showed a decrease in A-aD, while dogs ventilated with a tidal volume of less than 25 ml/kg body wt. invariably showed an increase in A-aD and physiologic shunt. A tidal volume of 25 ml/kg body wt. led to a PaCO₂ that became constant at 21 mm Hg after 1 hr. A stable PaCO₂ of 40 mm Hg required ventilation of 18 ml/kg body wt. As may be seen from Fig. 2A, this corresponds to a regression coefficient of approximately +30, i.e., the A-aD will increase an average of 30 mm Hg/hr during the study period. In Fig. 2B is shown the relationship between tidal volume and the regression coefficient of per cent physiologic shunt on time of constant unchanged ventilation, in hours. For all dogs ventilated with a tidal volume in excess of 25 ml/kg body wt., the mean value for the physiologic shunt was 7.2% after 40 min. Thus, in the

**FIG. 4.** Dynamic lung compliance versus A-aD: 8.0-kg dog ventilated initially (top of loop) with a constant tidal volume of 700 ml 100% O₂. Then ventilation changed to a constant tidal volume of 200 ml 100% O₂ (bottom of loop). Rate of ventilation 20/min throughout. Numbers beside each point refer to the time in minutes from the start of ventilation with a tidal volume of 700 ml.

**FIG. 5.** Dynamic lung compliance versus physiologic shunt; 8.0-kg dog ventilated initially (top of loop) with a constant tidal volume of 700 ml 100% O₂. Then ventilation changed to a constant tidal volume of 200 ml 100% O₂ (bottom of loop). Numbers beside each point refer to the time in minutes from the start of ventilation with a tidal volume of 700 ml.
4-hr study period with hyperventilation, the maximum possible average decrease in physiologic shunt is 7.2 %/4 per hr. This corresponds to a regression coefficient of $-1.8$. Clearly, therefore, Fig. 2B cannot express the effects of hyperventilation.

The effects of large tidal volumes are shown best in Fig. 2A, where it may be seen that they produce correspondingly large rates of fall in the A-aD. As may be seen from Fig. 3, the resulting small A-aDs correspond to small total physiologic shunts. This Fig. 3, obtained from 11 dogs, shows the relationship between the A-aD and physiologic shunt. It would appear that, with constant-volume ventilation, until an alveolar-arterial oxygen difference of over 400 mm Hg is reached, the A-aD may be used to reflect the amount of physiologic shunting. The open circle points shown in the bottom right-hand corner of Fig. 3 are taken from two dogs who died in the course of the experiment. The results obtained from these two dogs have been excluded from the other figures.

The effects of extreme hyperventilation are shown in Table 1. The greatest decrease in A-aD and physiologic shunt occurred in the first 40 min. As has already been pointed out, the actual magnitude of this initial change depends, in part, on the A-aD and physiologic shunt present at the start of the study. The tidal volumes used to hyperventilate this dog (62.7 ml/kg body wt.) caused such a reduction in A-aD in the first 40 min that (as shown in Fig. 2A) the regression coefficient for A-aD on time was smaller than for a lesser tidal volume. Apart from this problem with presenting the results of hyperventilation, the use of linear regression coefficients in Fig. 2 may also be criticized on the grounds that they do not allow Fig. 2 to reflect the way these changes in A-aD and physiologic shunt come to equilibrium after a certain amount of time. However, in the vast majority of dogs equilibrium was not approached in 4.77 hr and Fig. 2 is satisfactory in that it does show the average change per hour between 0.67 and 4.77 hr and the per cent physiologic shunt which resulted from prolonged constant ventilation at different tidal volumes. Table 2 shows the effects of hyperventilation.

Figure 4 shows the relationship obtained in one dog between dynamic lung compliance and A-aD. This dog, while it was being prepared, was ventilated with a constant tidal volume of 200 ml. The reading marked as zero was obtained at the same time that the tidal volume was changed to 700 ml. Then, starting at the right-hand side of the graph, the values on the top of the loop were obtained with this tidal volume of 87.5 ml/kg body wt. over a period of 6 min. The tidal volume was then changed without interruption of ventilation to 25 ml/kg body wt. and the bottom of the loop was obtained over the next 4 hr. Figure 5 is the identical experiment with per cent physiologic shunt plotted as the abscissa.

**DISCUSSION**

This study shows that the rate of change of the A-aD and the total physiologic shunt are controllable by the pressure-volume history of the lungs.

The magnitude of the variations in total physiologic shunt produced on ventilation with 100 % oxygen are explicable only on the basis of changes in the alveolar capillary shunt. These changes are of such magnitude that, taken in conjunction with the changes in lung compliance, they point to a variation in the amount of atelectasis present. This conclusion assumes of course that the anatomic shunt is both small and relatively constant. Aviado et al. (1), in a study on the contribution of the bronchial circulation to the venous admixture in pulmonary venous blood, found an anatomic shunt of 0.8 % due to the bronchial circulation. These authors reviewed the values found in the dog by four other groups of authors and found the average value obtained was also 0.8 %. Since the pleural and Thbesian vessels probably carry an inconsequential amount of blood, the estimate of the anatomic shunt as 2 % of the cardiac output would appear correct. Aviado et al. (1) found no change in the amount of shunt when the pressure was varied in the isolated segment of the thoracic aorta, which in the dog gives rise to the majority of the bronchial arteries. This points to the correctness of the assumption that the anatomic shunt is relatively constant in the dog at 2 % of the cardiac output.

Previously the PaCO$_2$ has been used as an index of the adequacy of controlled ventilation (11). This present study and parallel work in humans shows that the maintenance of a normal or slightly decreased PaCO$_2$ may lead to decreased oxygenation. However, it should be remembered that this present study was undertaken with

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**TABLE 2. Dog (15 kg) ventilated by a constant-volume pump with a tidal volume of 250 ml 100 % O$_2$ (16.7 ml/kg body wt.) at a rate of 20/min**

<table>
<thead>
<tr>
<th>Time, min</th>
<th>PaO$_2$, mm Hg</th>
<th>PaCO$_2$, mm Hg</th>
<th>A-aD, mm Hg</th>
<th>PaCO$_2$-PaCO$_2$, ml/mm Hg</th>
<th>Dynamic Lung Compliance, ml/mm Hg</th>
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<td>86</td>
<td>569</td>
<td>46</td>
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</table>

Note: The values on the top of the loop are obtained with this tidal volume of 87.5 ml/kg body wt. over a period of 6 min. The tidal volume was then changed without interruption of ventilation to 25 ml/kg body wt. and the bottom of the loop was obtained over the next 4 hr.
a chest catheter open to the atmosphere leading into the dogs’ common intrapleural space and that the parallel studies in human employed pressure-regulated respirators, set at a frequency of 20-25 breaths/min. In other studies in humans, at a rate of 10-12 breaths/min at a tidal volume which leads to a normal PaCO_2 (6-8 ml/kg body wt.) a Harvard constant-volume piston pump ventilating with 100% oxygen gives a pattern of ventilation which is compatible with a PaO_2 of over 600 mm Hg (unpublished observations). Ventilating twice as fast with pressure-regulated respirators which have a less favorable wave pattern than the Harvard constant-volume piston pump, the resulting patterns of ventilation led to a normal PaCO_2, but a continually falling PaO_2 (9a). Thus, with the increased use of long-term, controlled ventilation, the importance of the past and present pattern of ventilation and the limited value of PaCO_2 measurements must be recognized. Even when they are combined with O_2 saturation measurements, PaCO_2 measurements cannot predict the onset of hypoxemia and marked atelectasis. Whether a certain constant-pressure-volume history will in time lead to hypoxemia and atelectasis can only be foretold by knowing the rate of change of the total physiologic shunt. Such measurements, requiring as they do an analysis of the mixed venous blood, are not readily obtainable in the human. However, the close correlation found between the total physiologic shunt and A-aD suggest that, when breathing oxygen, knowledge of the rates of change of the A-aD will suffice in predicting if long-term constant-volume ventilation will lead to atelectasis and hypoxemia.

Lung compliance has previously been thought to give an indication of the occurrence of atelectasis (5). The wide difference found in physiologic shunt and A-aD (Figs. 4, 5) for given values of lung compliance suggest that no simple relationship exists between lung compliance and the degree of venoarterial shunting. This problem bears further investigation.

Hyperventilation may also exert an effect on the anatomic shunt. Since we have assumed an anatomic shunt of 2% of the cardiac output, the findings of total physiologic shunts of less than 2% would suggest that no shunt, caused by atelectasis, is present, and that the anatomic shunt has been reduced. This may be due to the high intrapulmonary pressure stretching the bronchial arteries and capillaries more than the other vessels of the lung. Thus their resistance to flow becomes proportionately greater.

The results of a parallel study showed that, in patients ventilated at a rate of 20-25 breaths/min with an intact chest, the largest fall in PaCO_2 was associated with the least fall in PaO_2. Down to a PaCO_2 of 24 mm Hg no PaO_2 rose during periods of measurement (2a). In this present study dogs ventilated with a constant tidal volume of less than 25 ml/kg body wt. did not show a rising PaO_2 (Fig. 2A). A tidal volume of 25 ml/kg body wt. led to a PaCO_2 which stabilized at 21 mm Hg. This would suggest that the use in this present study of a preparation with a tube open to the atmosphere leading into the common intrapleural space did not prevent the rate of change of the A-aD being roughly comparable to the rates of change of A-aD which occurred in those 18 patients who were ventilated, as has been described, at 20-25 breaths/min. The intrapleural pressure of man undergoing controlled ventilation depends on the pressure-volume history of the lungs and the total chest compliance. With a tidal volume of 800 ml and a total chest compliance of 0.051/cm HgO, the intrapleural pressure varies from +3 to -5 cm H_2O (10). As tidal volume increases the intrapleural pressure will become closer to atmospheric pressure. Thus we do not feel that the cathereter placed in the dog's common intrapleural space, in this study, affects the applicability of the concept that the rate of change of the A-aD and total physiologic shunt is controllable by the pressure-volume history of the lungs. It is only by appreciating that the rate of change of the total physiologic shunt, up to a very large fraction of the cardiac output, is controllable by the pressure-volume history of the lungs that we can hope to give long-term, controlled ventilation with a large enough tidal volume delivered at the best rate and pattern for insuring full oxygenation and preventing atelectasis.

REFERENCES